Supplementary Material

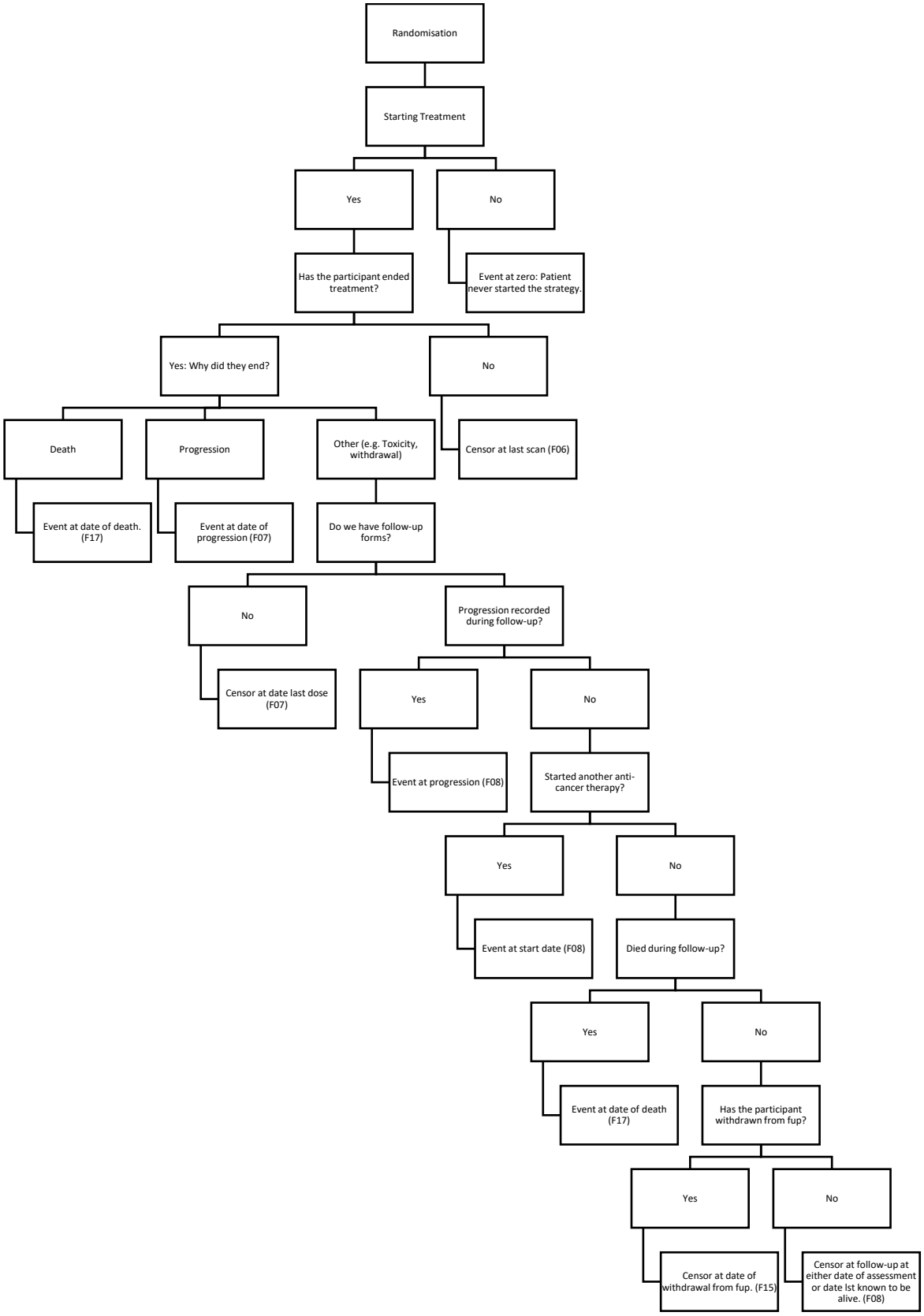
Contents

List of Tables

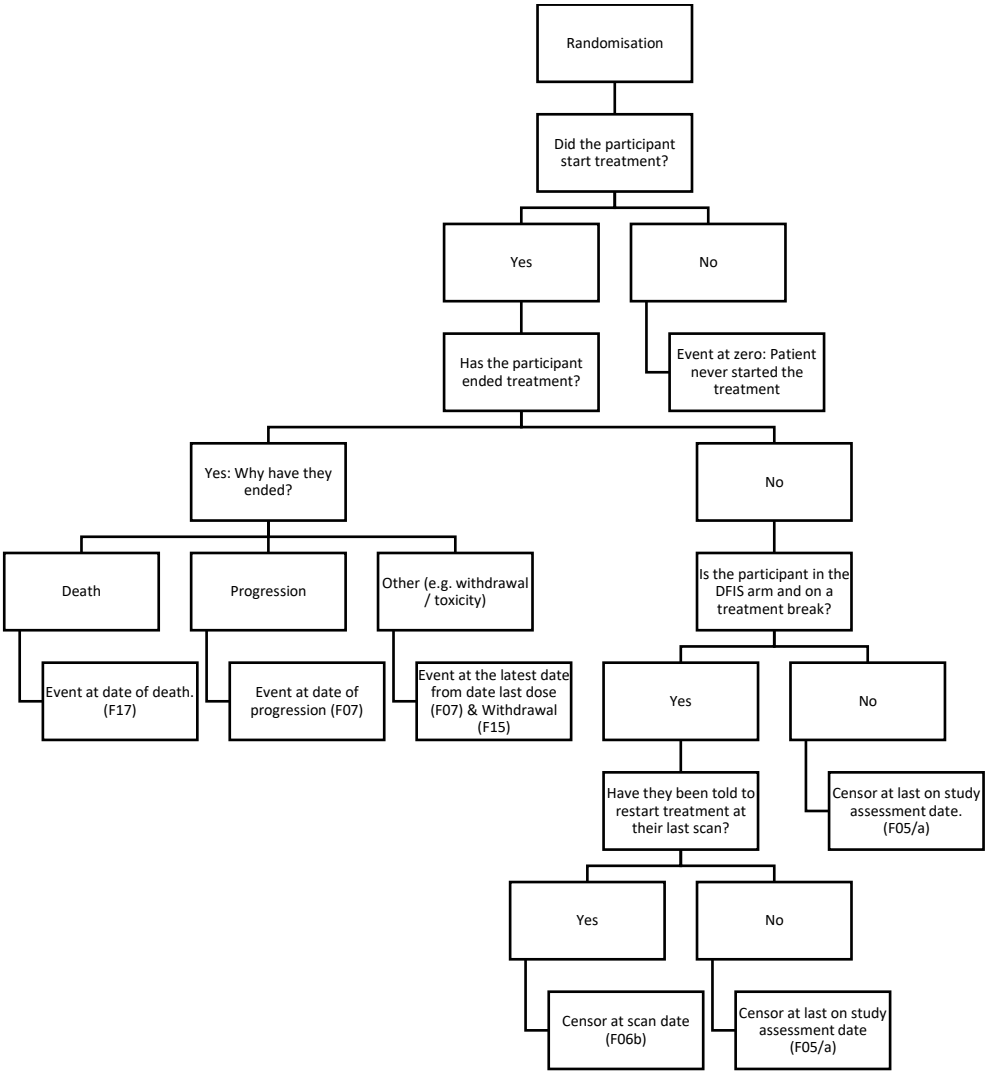
List of Figures

1 Additional Clarification on the Derivation of Secondary Endpoints

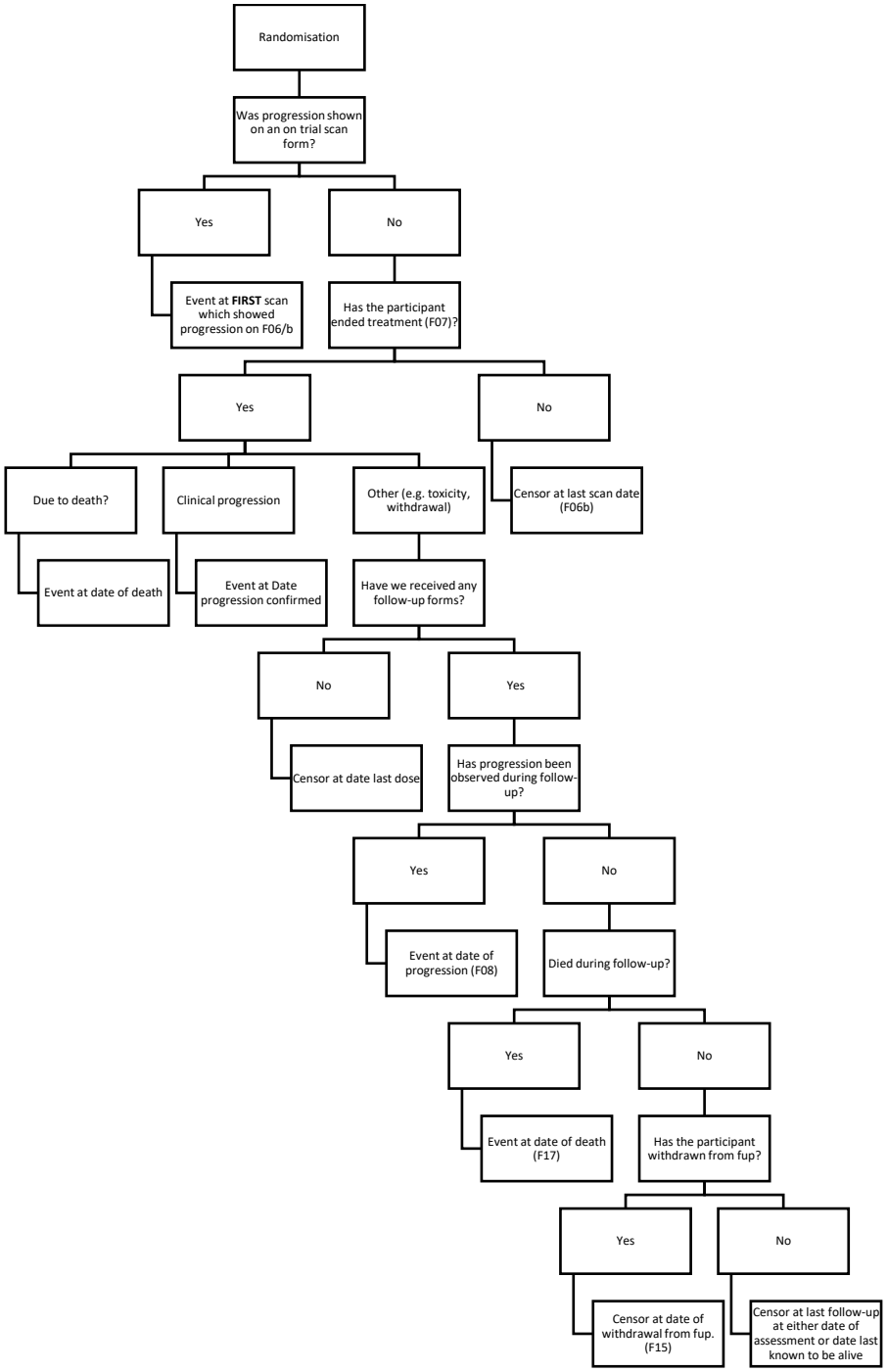
Supplementary Figure 1: Flowchart of the derivation of Time to Strategy Failure



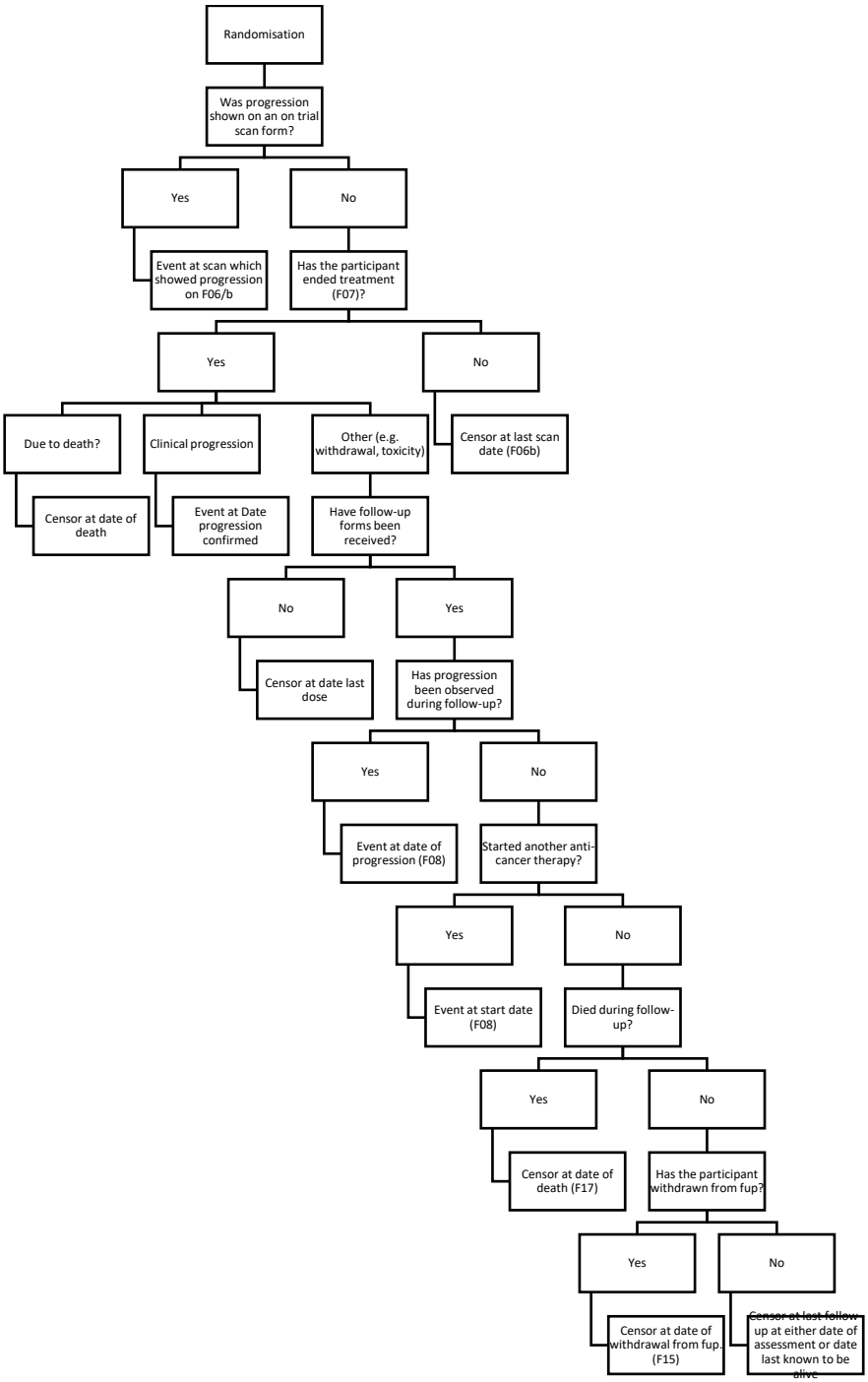
Supplementary Figure 2: Flowchart of the derivation of Time to Treatment Failure



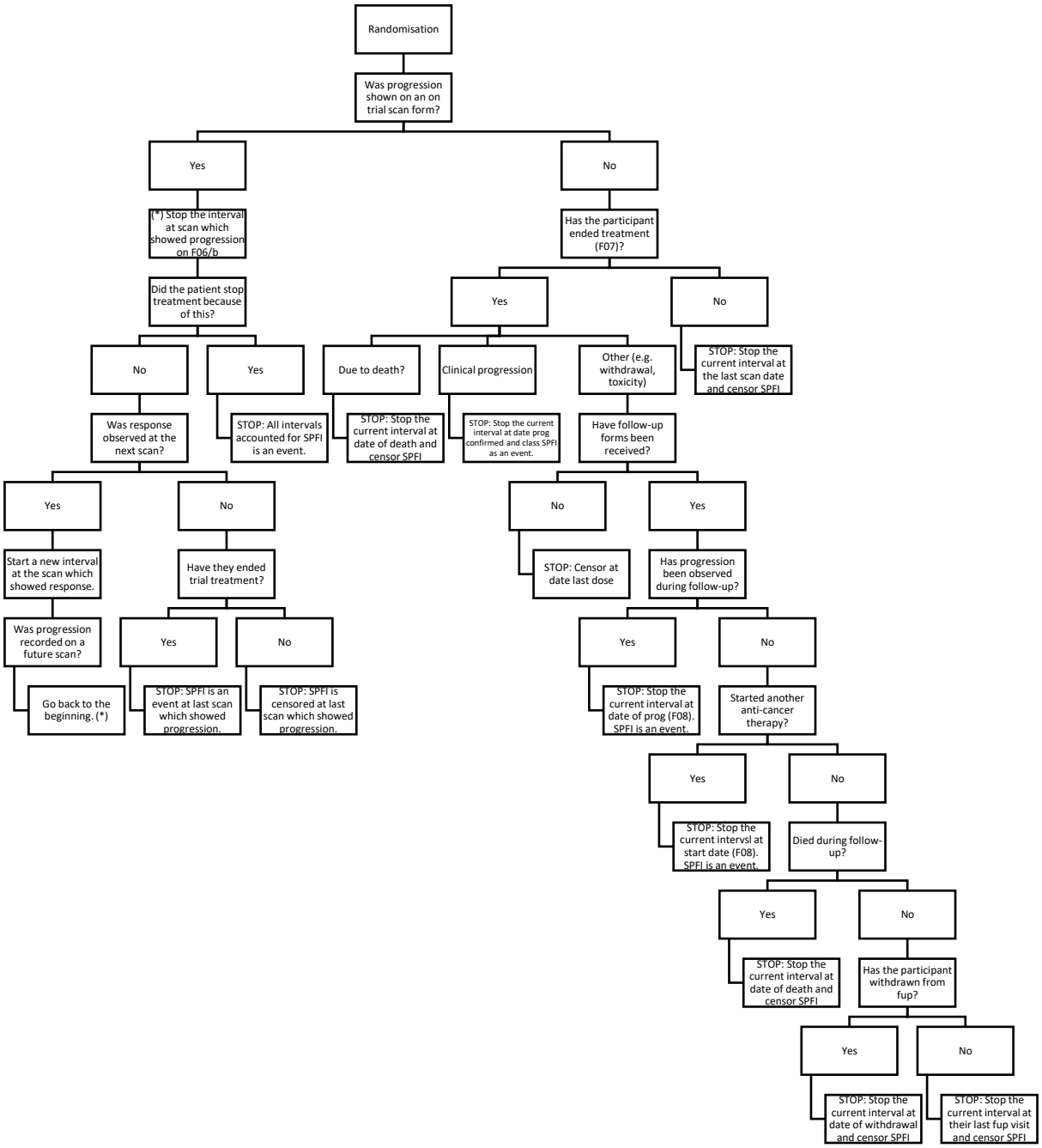
Supplementary Figure 3: Flowchart of the derivation of Progression-Free Survival



Supplementary Figure 4: Flowchart of the derivation of Summative Progression-Free Interval in the CCS Arm



Supplementary Figure 5: Flow-chart of the derivation of Summative Progression-Free Interval in the DFIS Arm



2 Additional Tables and Figures from the Main Trial Analysis

2.1 Participant Flow

Supplementary Table 1: Non-Mutually Exclusive Reasons for Participants Discontinuing Trial Treatment, by Randomisation Allocation (G5_ParticipantFlow)

	Conventional Continuation Strategy (CCS)	Drug-Free Interval Strategy (DFIS)	Total
Reason(s) for treatment discontinuation			
Clinician-led withdrawal from study	14 (2.7%)	34 (6.5%)	48 (4.6%)
Death	12 (2.3%)	31 (6.0%)	43 (4.1%)
Disease progression (Clinical (non radiological))	24 (4.6%)	49 (9.4%)	73 (7.0%)
Disease progression (Radiological)	253 (48.4%)	203 (39.0%)	456 (43.7%)
Medical Reasons (non-toxicity related)	36 (6.9%)	20 (3.8%)	56 (5.4%)
Other	18 (3.4%)	18 (3.5%)	36 (3.5%)
Radiotherapy	5 (1.0%)	5 (1.0%)	10 (1.0%)
Surgery	9 (1.7%)	2 (0.4%)	11 (1.1%)
Toxicity	140 (26.8%)	135 (26.0%)	275 (26.4%)
Withdrawal from study	12 (2.3%)	23 (4.4%)	35 (3.4%)
Total	523 (100%)	520 (100%)	1043 (100%)
Reason(s) for treatment discontinuation: Prior to Week 24			
Clinician-led withdrawal from study	5 (2.0%)	9 (3.7%)	14 (2.8%)
Death	10 (4.0%)	9 (3.7%)	19 (3.8%)
Disease progression (Clinical (non radiological))	11 (4.3%)	16 (6.5%)	27 (5.4%)
Disease progression (Radiological)	89 (35.2%)	91 (37.1%)	180 (36.1%)

	Conventional Continuation Strategy (CCS)	Drug-Free Interval Strategy (DFIS)	Total
Medical Reasons (non-toxicity related)	16 (6.3%)	9 (3.7%)	25 (5.0%)
Other	7 (2.8%)	4 (1.6%)	11 (2.2%)
Radiotherapy	3 (1.2%)	2 (0.8%)	5 (1.0%)
Surgery	6 (2.4%)	0 (0.0%)	6 (1.2%)
Toxicity	100 (39.5%)	97 (39.6%)	197 (39.6%)
Withdrawal from study	6 (2.4%)	8 (3.3%)	14 (2.8%)
Total	253 (100%)	245 (100%)	498 (100%)
Reason(s) for treatment discontinuation: Post Week 24			
Clinician-led withdrawal from study	9 (3.3%)	25 (9.1%)	34 (6.2%)
Death	2 (0.7%)	22 (8.0%)	24 (4.4%)
Disease progression (Clinical (non radiological))	13 (4.8%)	33 (12.0%)	46 (8.4%)
Disease progression (Radiological)	164 (60.7%)	112 (40.7%)	276 (50.6%)
Medical Reasons (non-toxicity related)	20 (7.4%)	11 (4.0%)	31 (5.7%)
Other	11 (4.1%)	14 (5.1%)	25 (4.6%)
Radiotherapy	2 (0.7%)	3 (1.1%)	5 (0.9%)
Surgery	3 (1.1%)	2 (0.7%)	5 (0.9%)
Toxicity	40 (14.8%)	38 (13.8%)	78 (14.3%)
Withdrawal from study	6 (2.2%)	15 (5.5%)	21 (3.9%)
Total	270 (100%)	275 (100%)	545 (100%)

Note, the number in the total row refers to the number of reasons

Supplementary Table 2: Other Reasons for Participants Discontinuing Trial Treatment, by Randomisation Allocation (G5_ParticipantFlow)

Conventional Continuation Strategy (CCS)	**Prior to Week 24?**	**Drug-Free Interval Strategy (DFIS)**	**Prior to Week 24?**
Assessment by colorectal surgeon as to the appropriateness of conservative over surgical mangement	No	Acute Pancreatitis complicated by acute Ischemic colitis	Yes
Brain metastasis	Yes	Change of treatment	No
Clinician and Patient choice - regime changed to 2 wks on 1 wk off. Star emailed.	Yes	Clinician did not feel it was appropriate to restart trial despite the pp having disease progression	No
Delay due to teeth extraction	No	Decrease in performance status. No longer fit for trial treatment.	Yes
General Frailty	No	Due to large number of CT scans pt had. In light of excellent response and continued good health	No
Initially considered DP due to original SLD total which changed following a corrected measurement	No	Due treatment break but now not clinically appropriate for any further breaks	No
MDT decision due to unequivocal progression in liver	Yes	Extended time off drug due to pt choice	No
Mets from 2nd primary - biopsy proven	No	Increase NT lesions	No
Patient finding travel too much. Patient decision	No	Lost to follow-up	Yes
Patient moved country	No	NOT suitable to continue on trial pathway	No
Patient needed dose escalation and also wanted home delivery	Yes	Patient choice	No

Conventional Continuation Strategy (CCS)	Prior to Week 24?	Drug-Free Interval Strategy (DFIS)	Prior to Week 24?
Patient wanted to stop Pazopanib for trip abroad without side effects	Yes	Patient had TIA so to remain off Sunitinib at the moment ? Change to different treatment at next apt	No
Protocol violation	Yes	Patient moving country	No
Pthas been off sun too long. To continue off study. Due to SAE relating to left thigh haematoma	No	Patient preference	No
Toxicity due to poor wound healing on TKI	No	Patients condition deteriorated following randomisation and therefore treatment was not commenced.	Yes
Transferring to 2 weeks on 1 week off regime	No	Treatment break continued after progression for > 28 days	No
patient compliance	Yes	mixed response and bothersome toxitcities	No
time elapsed off treatment greater than 28 days	No	treatment delay > 28 days (3 months)	No

Supplementary Table 3: The Number of Expected Questionnaire Booklets (Number Returned, Percent Returned) at each Timepoint by Randomisation Allocation (G5_ParticipantFlow)

	Conventional Continuation Strategy (CCS)	Drug-Free Interval Strategy (DFIS)
Baseline	461 (444, 96.3%)	459 (451, 98.3%)
Week 6	453 (393, 86.8%)	453 (395, 87.2%)
Week 12	388 (327, 84.3%)	398 (332, 83.4%)
Week 18	320 (280, 87.5%)	325 (279, 85.8%)

	Conventional Continuation Strategy (CCS)	**Drug-Free Interval Strategy (DFIS)**
Week 24 (C)	283 (243, 85.9%)	285 (234, 82.1%)
Week 30 (C)	244 (211, 86.5%)	249 (201, 80.7%)
Week 36 (C)	215 (188, 87.4%)	236 (197, 83.5%)
Week 42 (C)	178 (152, 85.4%)	220 (189, 85.9%)
Week 24	283 (169, 59.7%)	285 (177, 62.1%)
Week 26	244 (165, 67.6%)	249 (180, 72.3%)
Week 28	244 (165, 67.6%)	249 (176, 70.7%)
Week 30	244 (162, 66.4%)	249 (176, 70.7%)
Week 32	215 (152, 70.7%)	237 (174, 73.4%)
Week 34	215 (153, 71.2%)	237 (169, 71.3%)
Week 36	215 (143, 66.5%)	236 (167, 70.8%)
Week 38	178 (127, 71.3%)	221 (158, 71.5%)
Week 40	178 (126, 70.8%)	221 (157, 71.0%)
Week 42	178 (125, 70.2%)	220 (151, 68.6%)
Week 44	159 (115, 72.3%)	206 (145, 70.4%)
Week 46	159 (111, 69.8%)	206 (143, 69.4%)
Week 48	159 (142, 89.3%)	205 (183, 89.3%)
Week 54	137 (125, 91.2%)	194 (170, 87.6%)
Week 60	129 (119, 92.2%)	182 (158, 86.8%)
Week 66	112 (105, 93.8%)	158 (142, 89.9%)

	Conventional Continuation Strategy (CCS)	Drug-Free Interval Strategy (DFIS)
Week 72	105 (98, 93.3%)	152 (133, 87.5%)
Week 78	90 (82, 91.1%)	140 (124, 88.6%)
Week 84	84 (78, 92.9%)	132 (118, 89.4%)
Week 90	74 (67, 90.5%)	127 (112, 88.2%)
Week 96	71 (64, 90.1%)	116 (104, 89.7%)
Week 102	61 (54, 88.5%)	109 (100, 91.7%)
Week 108	56 (50, 89.3%)	107 (100, 93.5%)
Week 114	50 (42, 84.0%)	102 (94, 92.2%)
Week 120	42 (41, 97.6%)	99 (93, 93.9%)
Week 126	37 (35, 94.6%)	93 (80, 86.0%)
Week 132	33 (33, 100.0%)	91 (83, 91.2%)
Week 138	29 (27, 93.1%)	87 (76, 87.4%)
Week 144	25 (24, 96.0%)	84 (74, 88.1%)
Week 150	21 (21, 100.0%)	77 (70, 90.9%)
Week 156	21 (19, 90.5%)	75 (66, 88.0%)
Week 162	17 (15, 88.2%)	74 (66, 89.2%)
Week 168	15 (14, 93.3%)	73 (59, 80.8%)
Week 174	14 (13, 92.9%)	69 (54, 78.3%)
Week 180	14 (13, 92.9%)	63 (50, 79.4%)
Week 186	10 (8, 80.0%)	58 (45, 77.6%)
Week 192	10 (9, 90.0%)	54 (39, 72.2%)
Week 198	10 (9, 90.0%)	47 (39, 83.0%)
Week 204	10 (8, 80.0%)	42 (31, 73.8%)

	Conventional Continuation Strategy (CCS)	Drug-Free Interval Strategy (DFIS)
Week 210	10 (9, 90.0%)	37 (29, 78.4%)
Week 216	10 (10, 100.0%)	35 (30, 85.7%)
Week 222	9 (7, 77.8%)	35 (26, 74.3%)
Week 228	8 (8, 100.0%)	30 (25, 83.3%)
Week 234	7 (5, 71.4%)	30 (24, 80.0%)
Week 240	5 (5, 100.0%)	26 (21, 80.8%)
Week 246	5 (5, 100.0%)	24 (21, 87.5%)
Week 252	5 (4, 80.0%)	21 (17, 81.0%)
Week 258	5 (3, 60.0%)	20 (17, 85.0%)
Week 264	4 (2, 50.0%)	20 (17, 85.0%)
Week 270	4 (3, 75.0%)	19 (15, 78.9%)
Week 276	4 (2, 50.0%)	17 (13, 76.5%)
Week 282	4 (3, 75.0%)	13 (11, 84.6%)
Week 288	3 (3, 100.0%)	11 (7, 63.6%)
Week 294	2 (1, 50.0%)	9 (7, 77.8%)
Week 300	1 (1, 100.0%)	9 (7, 77.8%)
Week 306	1 (0, 0.0%)	7 (6, 85.7%)
Week 312	1 (1, 100.0%)	6 (4, 66.7%)
Week 318	0 (0, .%)	6 (6, 100.0%)
Week 324	0 (0, .%)	6 (5, 83.3%)
Week 330	0 (0, .%)	5 (5, 100.0%)
Week 336	0 (0, .%)	5 (5, 100.0%)
Week 342	0 (0, .%)	5 (5, 100.0%)

	Conventional Continuation Strategy (CCS)	Drug-Free Interval Strategy (DFIS)
Week 348	0 (0, .%)	3 (3, 100.0%)
Week 354	0 (0, .%)	3 (3, 100.0%)
Week 360	0 (0, .%)	3 (3, 100.0%)
Week 366	0 (0, .%)	3 (3, 100.0%)
Week 372	0 (0, .%)	3 (2, 66.7%)
Week 378	0 (0, .%)	3 (2, 66.7%)
Week 384	0 (0, .%)	3 (3, 100.0%)
Week 390	0 (0, .%)	3 (2, 66.7%)
Week 396	0 (0, .%)	3 (3, 100.0%)
Week 402	0 (0, .%)	3 (3, 100.0%)
Week 408	0 (0, .%)	3 (3, 100.0%)
Week 414	0 (0, .%)	3 (1, 33.3%)
Week 420	0 (0, .%)	2 (1, 50.0%)
Week 426	0 (0, .%)	1 (1, 100.0%)
Week 432	0 (0, .%)	1 (1, 100.0%)
6 months fup	330 (186, 56.4%)	274 (141, 51.5%)
18 months fup	211 (108, 51.2%)	162 (86, 53.1%)
30 months fup	131 (70, 53.4%)	104 (52, 50.0%)
42 months fup	84 (41, 48.8%)	56 (19, 33.9%)

	Conventional Continuation Strategy (CCS)	Drug-Free Interval Strategy (DFIS)
54 months fup	38 (12, 31.6%)	27 (8, 29.6%)
66 months fup	20 (7, 35.0%)	13 (5, 38.5%)
78 months fup	9 (2, 22.2%)	4 (1, 25.0%)
Total	7401 (5764, 77.9%)	9327 (7383, 79.2%)

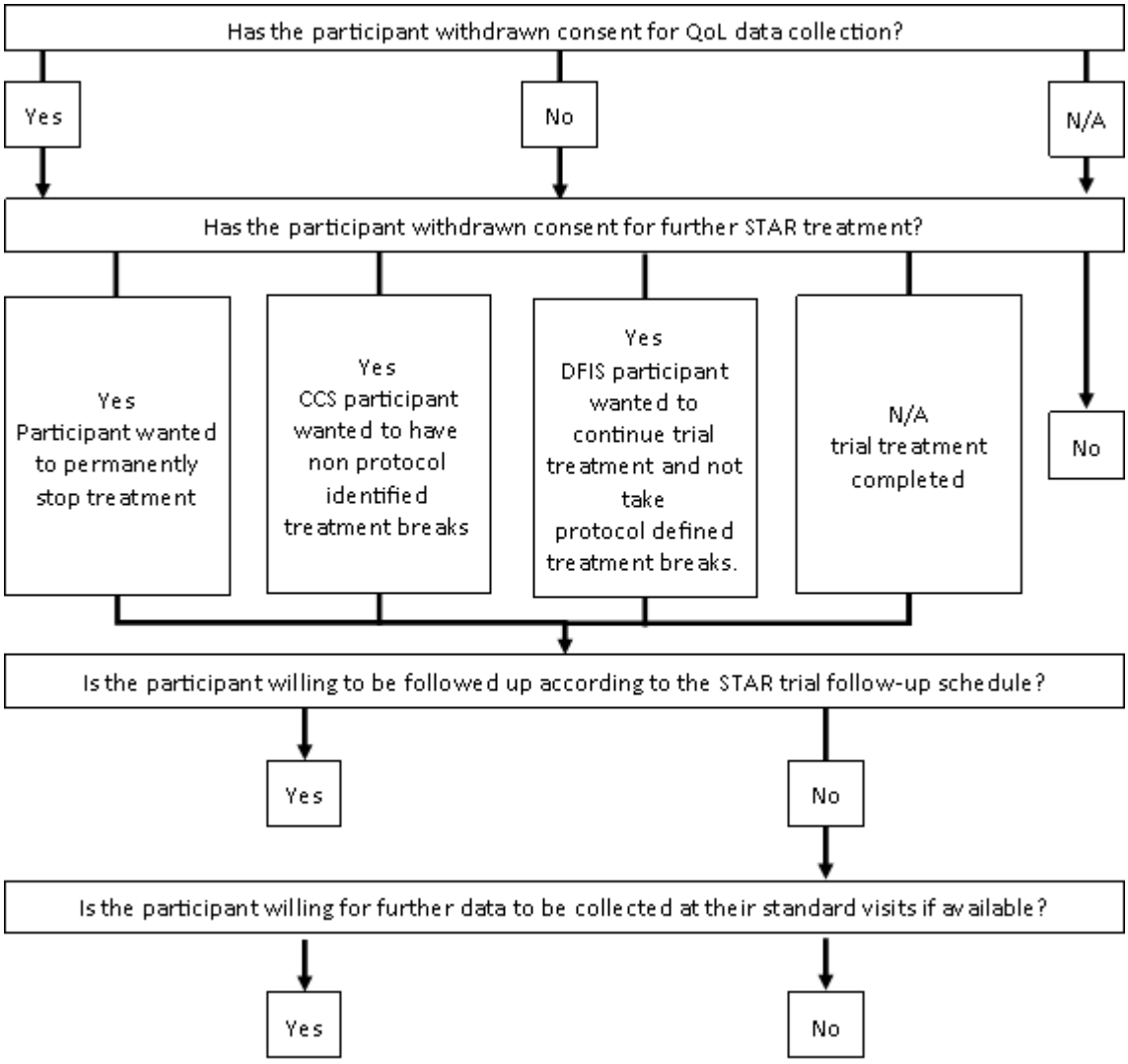
Supplementary Table 4: Withdrawal Information, by Randomisation Allocation (G5_ParticipantFlow)

	Conventional Continuation Strategy (CCS) (n=32)	Drug-Free Interval Strategy (DFIS) (n=31)	Total (n=63)
Withdrawal from quality of life			
Yes	27 (84.4%)	19 (59.4%)	46 (71.9%)
No	5 (15.6%)	12 (37.5%)	17 (26.6%)
N/A	0 (0.0%)	1 (3.1%)	1 (1.6%)
Withdrawal of treatment			
Yes - Participant wanted to permanently stop treatment	12 (37.5%)	13 (40.6%)	25 (39.1%)
Yes - CCS participant wanted to have non protocol identified treatment breaks	4 (12.5%)	0 (0.0%)	4 (6.3%)

	Conventional Continuation Strategy (CCS) (n=32)	Drug-Free Interval Strategy (DFIS) (n=31)	Total (n=63)
Yes - DFIS participant wanted to continue trial treatment and not take protocol defined treatment breaks	0 (0.0%)	12 (37.5%)	12 (18.8%)
N/A - trial treatment completed	10 (31.3%)	4 (12.5%)	14 (21.9%)
No	6 (18.8%)	3 (9.4%)	9 (14.1%)
Continue FUP			
Yes	12 (37.5%)	15 (46.9%)	27 (42.2%)
No	14 (43.8%)	14 (43.8%)	28 (43.8%)
N/A	6 (18.8%)	3 (9.4%)	9 (14.1%)
Continue to collect data at standard visits			
Yes	3 (9.4%)	4 (12.5%)	7 (10.9%)
No	11 (34.4%)	10 (31.3%)	21 (32.8%)
N/A	18 (56.3%)	18 (56.3%)	36 (56.3%)
Withdrawal reason given			
Yes	24 (75.0%)	29 (90.6%)	53 (82.8%)
No	8 (25.0%)	3 (9.4%)	11 (17.2%)
Total	32 (100%)	32 (100%)	64 (100%)

Note one patient withdrew from treatment and quality of life and then withdrew from follow-up at a later time point, the numbers in the heading refer to the number of patients considered whereas the number in the total row relates to the number of reasons. Note, these are presented as N (%) for each category, where % is calculated out of the total number of occurrences.

Supplementary Figure 6: Withdrawal Data Collection on STAR



Supplementary Table 5: Reasons for Participant Withdrawal, by Randomisation Allocation (G5_ParticipantFlow)

Conventional Continuation Strategy (CCS)	**Drug-Free Interval Strategy (DFIS)**
After 20 cycles of treatment, participant wants to take a break.	Both the patient and the consultant wanted to continue on treatment and not follow the treatment break schedule.
Does not want to complete any further QoLs happy for data to be collected for follow up	Did not want DFIS - as metastases were responding, wanted to continue treatment without break
Finds them a burden, no longer wishes to complete them	Didnt want to take allocated treatment break. Finds questionnaires upsetting
Following toxicities decided would rather have treatment/follow up at a hospital more local to her. did not wish to complete Qols.	Disease progression, severe pain. Too unwell
Grade 3 toxicities unbearable. Wanted to come off treatment completely and have a period of active surveillance.	Does not want to attend 6 weekly clinic visits as he finds them stressful
He said he couldn't see the point of completing the QOL now he is off the study and doesn't want to be followed up anymore	Doesnt want to restart treatment at present due to toxicity of drug. Slow progression of disease. Would prefer surveillance at the moment
In pain and would rather not complete any more forms but happy to have data collected by research nurse for follow-up	Feels she is deteriorating
Moved site	Moving to Holland, no local site carrying out STAR trial
Patient did not feel relevant now he is off trial treatment	Participant preference
Patient expressed a desire to stop receiving QoLs due to the loss of his significant other	Participant wanted to continue on Sutent but did not wish to have protocol defined breaks.
Patient has moved to Spain Dec 2019	Patient found them irrelevant

Conventional Continuation Strategy (CCS)	Drug-Free Interval Strategy (DFIS)
Patient now too ill to attend clinic appointments	Patient has been informed of disease progression. Not for TKI's but just palliative radiotherapy. General health insidiously deteriorating. Patient does not wish to continute with QoL, blood tests or observations.
Patient states that she finds the questionnaires too long and difficult to answer	Patient prefers to take the trial medication differently than the trial protocol stipulates I one week on, week off over 6 weeks as he feels it is better tolerated
Patient wanted to have non protocol identified breaks. Consultant Prof Powles agreed with this.	Patient stated that he has nothing to offer the trial as he has stopped taking trial treatment. He is under the care of another hospital.
Patient was taken off treatment due to a reaction. The patient then decided to withdraw consent for follow up due to the implications of coming in for additional visits.	Patient upset with 12 weeks CT scans and regular follow up visits once patient has been on treatment break since 2015
Patient wished for treatment breaks which were not in protocol	Patient was frightened if not on treatment disease could progress. So was not keen to go on a treatment break
Pt has a painful right knee. Wants to stop Pazopanib so that she is fit enough for any potential treatment	Performance status 2, disease has progressed.
Questionnaires are too long and difficult to read/answer (Patient is elderly)	Quality of Life forms repetitive and time consuming. Does not want to take a treatment break.
They do not want to complete anymore QoL	Side effects from Pazopanib
Toxcities	Stopped taking Sunitinib due to toxicity, patient declined re-instating at a lower dose.
Toxicities causing problems with life balance	Symptomatic toxicities

Conventional Continuation Strategy (CCS)	Drug-Free Interval Strategy (DFIS)
Toxicity	The patient is no longer having treatment at Broomfield. They are under care of The Royal Marsden
Wants home delivery	Toxicities too much
patient 524 does not speak English as his first language. When he joined the study, he was happy to complete the questionnaires with the help of relatives and friends but as he went through the study he was less able to get help with the questionnairesand was unable to complete them on his own. At cycle 6, he declined to do any further QoL's	Toxicities were un-manageable for patient.
	Toxicity of Sunitinib
	Wants to continue on Pazopanib without treatment breaks to ensure stabilisation of disease
	Wants to start new treatment
	pazopanib did not suit him
	wanted to receive standard treatment at a more local hospital as travelling becoming an issue

Supplementary Table 6:: Protocol Violations / Deviations, by Randomisation Allocation (G5_ParticipantFlow)

	Conventional Continuation Strategy (CCS) (n=38)	**Drug-Free Interval Strategy (DFIS) (n=33)**	**Total (n=71)**
Eligibility Breach			
Yes	26 (63.4%)	24 (68.6%)	50 (65.8%)
No	15 (36.6%)	11 (31.4%)	26 (34.2%)
Participant has been overdosed			
Yes	5 (12.2%)	3 (8.6%)	8 (10.5%)
No	35 (85.4%)	32 (91.4%)	67 (88.2%)
Missing	1 (2.4%)	0 (0.0%)	1 (1.3%)
Participant has been underdosed			
Yes	10 (24.4%)	7 (20.0%)	17 (22.4%)
No	30 (73.2%)	28 (80.0%)	58 (76.3%)
Missing	1 (2.4%)	0 (0.0%)	1 (1.3%)
Total	41 (100%)	35 (100%)	76 (100%)

Note, the numbers in the heading refer to the number of participants considered, the number in the total row refers to the number of reasons. Note, these are presented as N (%) for each category, where % is calculated out of the total number of occurrences.

Supplementary Table 7: Eligibility Criteria Breached, by Randomisation Allocation (G5_ParticipantFlow)

	Conventional Continuation Strategy (CCS) (n=25)	**Drug-Free Interval Strategy (DFIS) (n=24)**	**Total (n=49)**
Does the patient have histological confirmation of a component of clear cell renal cell cancer?	0 (0.0%)	1 (3.8%)	1 (1.9%)
Does the patient have uni-dimensionally measurable disease?	1 (3.7%)	1 (3.8%)	2 (3.8%)
Does the patient have adequate renal biochemistry?	1 (3.7%)	1 (3.8%)	2 (3.8%)
Is the patient able and willing to comply with the terms of the protocol?	23 (85.2%)	22 (84.6%)	45 (84.9%)
Does the patient have poorly controlled hypertension despite maximal medical therapy?	2 (7.4%)	1 (3.8%)	3 (5.7%)
Total	27 (100%)	26 (100%)	53 (100%)

Note, the numbers in the heading refer to the number of participants considered, the number in the total row refers to the number of breaches. Note, these are presented as N (%) for each category, where % is calculated out of the total number of occurrences. Note that one participant violated the same eligibility criteria twice across two separate protocol violations which explains the 50 total in Supplementary Table 6 *equating to 49 participants in*

Supplementary Table 7.

2.2 Baseline Characteristics

Supplementary Table 8: Key Demographic and Disease Related Characteristics, by Randomisation Allocation Received, in the Safety population (G6_BaselineCharacteristics)

	Conventional Continuation Strategy (CCS) (n=485)	**Drug-Free Interval Strategy (DFIS) (n=431)**	**Total (n=916)**
Ethnic origin			
White	470 (96.9%)	413 (95.8%)	883 (96.4%)
Mixed - White and Black Caribbean	1 (0.2%)	0 (0.0%)	1 (0.1%)
Other mixed background	2 (0.4%)	0 (0.0%)	2 (0.2%)
Asian - Indian	3 (0.6%)	2 (0.5%)	5 (0.5%)
Asian - Pakistani	2 (0.4%)	2 (0.5%)	4 (0.4%)
Other Asian background	0 (0.0%)	1 (0.2%)	1 (0.1%)
Black - Caribbean	2 (0.4%)	1 (0.2%)	3 (0.3%)
Black - African	0 (0.0%)	1 (0.2%)	1 (0.1%)
Other Black background	1 (0.2%)	0 (0.0%)	1 (0.1%)
Other ethnic group	2 (0.4%)	2 (0.5%)	4 (0.4%)
Not stated	2 (0.4%)	9 (2.1%)	11 (1.2%)
Age (Years)			
Median (range)	65.00 (38.00, 90.00)	67.00 (22.00, 88.00)	66.00 (22.00, 90.00)
IQR	59.00, 72.00	59.00, 72.00	59.00, 72.00
Missing	0	0	0
F04 Stratification Factor: Sex			
Male	351 (72.4%)	315 (73.1%)	666 (72.7%)
Female	134 (27.6%)	116 (26.9%)	250 (27.3%)
ECOG Performance Status			

	Conventional Continuation Strategy (CCS) (n=485)	Drug-Free Interval Strategy (DFIS) (n=431)	Total (n=916)
0	258 (53.2%)	245 (56.8%)	503 (54.9%)
1	227 (46.8%)	182 (42.2%)	409 (44.7%)
Missing	0 (0.0%)	4 (0.9%)	4 (0.4%)
Disease present in bones			
Yes	119 (24.5%)	83 (19.3%)	202 (22.1%)
No	365 (75.3%)	348 (80.7%)	713 (77.8%)
Missing	1 (0.2%)	0 (0.0%)	1 (0.1%)
Time since initial diagnosis (Years)			
Mean (s.d.)	2.64 (4.20)	2.79 (4.54)	2.71 (4.36)
Missing	1	1	2
Haemoglobin (g/dL)			
Mean (s.d.)	13.32 (4.16)	13.04 (1.92)	13.19 (3.30)
Missing	0	0	0
ANC ($x10^9$/L)			
Mean (s.d.)	5.44 (2.34)	5.40 (2.23)	5.42 (2.29)
Missing	0	0	0
Platelets ($x10^9$/L)			
Mean (s.d.)	293.32 (107.43)	298.53 (117.56)	295.77 (112.28)
Missing	0	0	0
Corrected serum calcium (mmol/L)			
Mean (s.d.)	2.41 (0.16)	2.39 (0.15)	2.40 (0.16)
Missing	56	54	110

	Conventional Continuation Strategy (CCS) (n=485)	Drug-Free Interval Strategy (DFIS) (n=431)	Total (n=916)
Lactate dehyrogenase (IU/L)			
Mean (s.d.)	332.09 (215.89)	313.46 (184.92)	323.33 (202.03)
Missing	5	5	10
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group			
Favourable risk (0 factors)	215 (44.3%)	191 (44.3%)	406 (44.3%)
Intermediate risk (1-2 factors)	235 (48.5%)	208 (48.3%)	443 (48.4%)
Poor risk (> = 3 factors)	35 (7.2%)	32 (7.4%)	67 (7.3%)
Randomised Under Stratification Factor: Age Group			
<60	131 (27.0%)	112 (26.0%)	243 (26.5%)
>=60	354 (73.0%)	319 (74.0%)	673 (73.5%)
Randomised Under Stratification Factor: Disease Status			
Metastatic	475 (97.9%)	421 (97.7%)	896 (97.8%)
Locally advanced	10 (2.1%)	10 (2.3%)	20 (2.2%)
Randomised Under Stratification Factor: Previous Nephrectomy			
Yes	366 (75.5%)	324 (75.2%)	690 (75.3%)
No	119 (24.5%)	107 (24.8%)	226 (24.7%)
Randomised Under Stratification Factor: TKI Received			

	Conventional Continuation Strategy (CCS) (n=485)	Drug-Free Interval Strategy (DFIS) (n=431)	Total (n=916)
Sunitinib	203 (41.9%)	184 (42.7%)	387 (42.2%)
Pazopanib	282 (58.1%)	247 (57.3%)	529 (57.8%)
Randomised Under Stratification Factor: Sex			
Male	351 (72.4%)	315 (73.1%)	666 (72.7%)
Female	134 (27.6%)	116 (26.9%)	250 (27.3%)

Note, these are presented as N (%) for each categorical variable, where % is calculated out of the total population given in the table header.

Supplementary Table 9: Key Demographic and Disease Related Characteristics, by Randomisation Allocation, in the EQ5D QoL population (G6_BaselineCharacteristics)

	Conventional Continuation Strategy (CCS) (n=438)	Drug-Free Interval Strategy (DFIS) (n=431)	Total (n=869)
Ethnic origin			
White	423 (96.6%)	414 (96.1%)	837 (96.3%)
Mixed - White and Black Caribbean	1 (0.2%)	0 (0.0%)	1 (0.1%)
Other mixed background	2 (0.5%)	0 (0.0%)	2 (0.2%)
Asian - Indian	3 (0.7%)	2 (0.5%)	5 (0.6%)
Asian - Pakistani	2 (0.5%)	2 (0.5%)	4 (0.5%)
Other Asian background	0 (0.0%)	1 (0.2%)	1 (0.1%)
Black - Caribbean	2 (0.5%)	1 (0.2%)	3 (0.3%)
Black - African	0 (0.0%)	1 (0.2%)	1 (0.1%)

	Conventional Continuation Strategy (CCS) (n=438)	Drug-Free Interval Strategy (DFIS) (n=431)	Total (n=869)
Other Black background	1 (0.2%)	0 (0.0%)	1 (0.1%)
Other ethnic group	2 (0.5%)	2 (0.5%)	4 (0.5%)
Not stated	2 (0.5%)	8 (1.9%)	10 (1.2%)
Age (Years)			
Median (range)	65.00 (38.00, 87.00)	67.00 (22.00, 90.00)	66.00 (22.00, 90.00)
IQR	59.00, 72.00	59.00, 72.00	59.00, 72.00
Missing	0	0	0
F04 Stratification Factor: Sex			
Male	320 (73.1%)	314 (72.9%)	634 (73.0%)
Female	118 (26.9%)	117 (27.1%)	235 (27.0%)
ECOG Performance Status			
0	238 (54.3%)	242 (56.1%)	480 (55.2%)
1	200 (45.7%)	185 (42.9%)	385 (44.3%)
Missing	0 (0.0%)	4 (0.9%)	4 (0.5%)
Disease present in bones			
Yes	103 (23.5%)	94 (21.8%)	197 (22.7%)
No	334 (76.3%)	337 (78.2%)	671 (77.2%)
Missing	1 (0.2%)	0 (0.0%)	1 (0.1%)
Time since initial diagnosis (Years)			
Mean (s.d.)	2.62 (4.20)	2.78 (4.50)	2.70 (4.35)
Missing	1	1	2
Haemoglobin (g/dL)			

	Conventional Continuation Strategy (CCS) (n=438)	Drug-Free Interval Strategy (DFIS) (n=431)	Total (n=869)
Mean (s.d.)	13.38 (4.34)	13.04 (1.91)	13.21 (3.36)
Missing	0	0	0
ANC (x10⁹/L)			
Mean (s.d.)	5.43 (2.38)	5.43 (2.24)	5.43 (2.31)
Missing	0	0	0
Platelets (x10⁹/L)			
Mean (s.d.)	293.48 (108.31)	298.00 (116.56)	295.72 (112.43)
Missing	0	0	0
Corrected serum calcium (mmol/L)			
Mean (s.d.)	2.41 (0.17)	2.38 (0.14)	2.40 (0.15)
Missing	50	54	104
Lactate dehyrogenase (IU/L)			
Mean (s.d.)	326.18 (207.24)	320.24 (201.08)	323.24 (204.11)
Missing	4	5	9
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group			
Favourable risk (0 factors)	192 (43.8%)	189 (43.9%)	381 (43.8%)
Intermediate risk (1-2 factors)	213 (48.6%)	211 (49.0%)	424 (48.8%)
Poor risk (> = 3 factors)	33 (7.5%)	31 (7.2%)	64 (7.4%)
Randomised Under Stratification Factor: Age Group			
<60	117 (26.7%)	115 (26.7%)	232 (26.7%)

	Conventional Continuation Strategy (CCS) (n=438)	Drug-Free Interval Strategy (DFIS) (n=431)	Total (n=869)
>=60	321 (73.3%)	316 (73.3%)	637 (73.3%)
Randomised Under Stratification Factor: Disease Status			
Metastatic	429 (97.9%)	423 (98.1%)	852 (98.0%)
Locally advanced	9 (2.1%)	8 (1.9%)	17 (2.0%)
Randomised Under Stratification Factor: Previous Nephrectomy			
Yes	328 (74.9%)	324 (75.2%)	652 (75.0%)
No	110 (25.1%)	107 (24.8%)	217 (25.0%)
Randomised Under Stratification Factor: TKI Received			
Sunitinib	186 (42.5%)	187 (43.4%)	373 (42.9%)
Pazopanib	252 (57.5%)	244 (56.6%)	496 (57.1%)
Randomised Under Stratification Factor: Sex			
Male	320 (73.1%)	314 (72.9%)	634 (73.0%)
Female	118 (26.9%)	117 (27.1%)	235 (27.0%)

Note, these are presented as N (%) for each categorical variable, where % is calculated out of the total population given in the table header.

Supplementary Table 10: Key Demographic and Disease Related Characteristics, by Randomisation Allocation, in the FKSI QoL population (G6_BaselineCharacteristics)

	Conventional Continuation Strategy (CCS) (n=436)	**Drug-Free Interval Strategy (DFIS) (n=446)**	**Total (n=882)**
Ethnic origin			
White	421 (96.6%)	428 (96.0%)	849 (96.3%)
Mixed - White and Black Caribbean	1 (0.2%)	0 (0.0%)	1 (0.1%)
Other mixed background	2 (0.5%)	0 (0.0%)	2 (0.2%)
Asian - Indian	3 (0.7%)	2 (0.4%)	5 (0.6%)
Asian - Pakistani	2 (0.5%)	2 (0.4%)	4 (0.5%)
Other Asian background	0 (0.0%)	1 (0.2%)	1 (0.1%)
Black - Caribbean	2 (0.5%)	1 (0.2%)	3 (0.3%)
Black - African	0 (0.0%)	1 (0.2%)	1 (0.1%)
Other Black background	1 (0.2%)	0 (0.0%)	1 (0.1%)
Other ethnic group	2 (0.5%)	2 (0.4%)	4 (0.5%)
Not stated	2 (0.5%)	9 (2.0%)	11 (1.2%)
Age (Years)			
Median (range)	65.00 (38.00, 87.00)	67.00 (22.00, 90.00)	66.00 (22.00, 90.00)
IQR	59.00, 71.00	59.00, 72.00	59.00, 72.00
Missing	0	0	0
F04 Stratification Factor: Sex			
Male	318 (72.9%)	322 (72.2%)	640 (72.6%)
Female	118 (27.1%)	124 (27.8%)	242 (27.4%)
ECOG Performance Status			
0	237 (54.4%)	250 (56.1%)	487 (55.2%)

	Conventional Continuation Strategy (CCS) (n=436)	Drug-Free Interval Strategy (DFIS) (n=446)	Total (n=882)
1	199 (45.6%)	192 (43.0%)	391 (44.3%)
Missing	0 (0.0%)	4 (0.9%)	4 (0.5%)
Disease present in bones			
Yes	102 (23.4%)	94 (21.1%)	196 (22.2%)
No	333 (76.4%)	352 (78.9%)	685 (77.7%)
Missing	1 (0.2%)	0 (0.0%)	1 (0.1%)
Time since initial diagnosis (Years)			
Mean (s.d.)	2.62 (4.22)	2.71 (4.42)	2.67 (4.32)
Missing	1	1	2
Haemoglobin (g/dL)			
Mean (s.d.)	13.38 (4.35)	12.99 (1.92)	13.18 (3.35)
Missing	0	0	0
ANC ($x10^9$/L)			
Mean (s.d.)	5.41 (2.33)	5.42 (2.22)	5.42 (2.27)
Missing	0	0	0
Platelets ($x10^9$/L)			
Mean (s.d.)	293.60 (108.56)	299.18 (117.68)	296.42 (113.24)
Missing	0	0	0
Corrected serum calcium (mmol/L)			
Mean (s.d.)	2.41 (0.17)	2.39 (0.14)	2.40 (0.15)
Missing	50	54	104
Lactate dehyrogenase (IU/L)			

	Conventional Continuation Strategy (CCS) (n=436)	Drug-Free Interval Strategy (DFIS) (n=446)	Total (n=882)
Mean (s.d.)	326.84 (206.36)	321.67 (200.54)	324.23 (203.34)
Missing	4	5	9
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group			
Favourable risk (0 factors)	191 (43.8%)	195 (43.7%)	386 (43.8%)
Intermediate risk (1-2 factors)	212 (48.6%)	219 (49.1%)	431 (48.9%)
Poor risk (> = 3 factors)	33 (7.6%)	32 (7.2%)	65 (7.4%)
Randomised Under Stratification Factor: Age Group			
<60	117 (26.8%)	120 (26.9%)	237 (26.9%)
>=60	319 (73.2%)	326 (73.1%)	645 (73.1%)
Randomised Under Stratification Factor: Disease Status			
Metastatic	427 (97.9%)	436 (97.8%)	863 (97.8%)
Locally advanced	9 (2.1%)	10 (2.2%)	19 (2.2%)
Randomised Under Stratification Factor: Previous Nephrectomy			
Yes	326 (74.8%)	336 (75.3%)	662 (75.1%)
No	110 (25.2%)	110 (24.7%)	220 (24.9%)
Randomised Under Stratification Factor: TKI Received			
Sunitinib	184 (42.2%)	190 (42.6%)	374 (42.4%)

	Conventional Continuation Strategy (CCS) (n=436)	Drug-Free Interval Strategy (DFIS) (n=446)	Total (n=882)
Pazopanib	252 (57.8%)	256 (57.4%)	508 (57.6%)
Randomised Under Stratification Factor: Sex			
Male	318 (72.9%)	322 (72.2%)	640 (72.6%)
Female	118 (27.1%)	124 (27.8%)	242 (27.4%)

Note, these are presented as N (%) for each categorical variable, where % is calculated out of the total population given in the table header.

Supplementary Table 11: Key Demographic and Disease Related Characteristics, by Randomisation Allocation, in the FACT-G QoL population (G6_BaselineCharacteristics)

	Conventional Continuation Strategy (CCS) (n=425)	Drug-Free Interval Strategy (DFIS) (n=431)	Total (n=856)
Ethnic origin			
White	410 (96.5%)	413 (95.8%)	823 (96.1%)
Mixed - White and Black Caribbean	1 (0.2%)	0 (0.0%)	1 (0.1%)
Other mixed background	2 (0.5%)	0 (0.0%)	2 (0.2%)
Asian - Indian	3 (0.7%)	2 (0.5%)	5 (0.6%)
Asian - Pakistani	2 (0.5%)	2 (0.5%)	4 (0.5%)
Other Asian background	0 (0.0%)	1 (0.2%)	1 (0.1%)
Black - Caribbean	2 (0.5%)	1 (0.2%)	3 (0.4%)
Black - African	0 (0.0%)	1 (0.2%)	1 (0.1%)
Other Black background	1 (0.2%)	0 (0.0%)	1 (0.1%)
Other ethnic group	2 (0.5%)	2 (0.5%)	4 (0.5%)

	Conventional Continuation Strategy (CCS) (n=425)	Drug-Free Interval Strategy (DFIS) (n=431)	Total (n=856)
Not stated	2 (0.5%)	9 (2.1%)	11 (1.3%)
Age (Years)			
Median (range)	65.00 (38.00, 87.00)	67.00 (22.00, 90.00)	66.00 (22.00, 90.00)
IQR	59.00, 71.00	59.00, 72.00	59.00, 72.00
Missing	0	0	0
F04 Stratification Factor: Sex			
Male	313 (73.6%)	308 (71.5%)	621 (72.5%)
Female	112 (26.4%)	123 (28.5%)	235 (27.5%)
ECOG Performance Status			
0	229 (53.9%)	242 (56.1%)	471 (55.0%)
1	196 (46.1%)	185 (42.9%)	381 (44.5%)
Missing	0 (0.0%)	4 (0.9%)	4 (0.5%)
Disease present in bones			
Yes	97 (22.8%)	89 (20.6%)	186 (21.7%)
No	327 (76.9%)	342 (79.4%)	669 (78.2%)
Missing	1 (0.2%)	0 (0.0%)	1 (0.1%)
Time since initial diagnosis (Years)			
Mean (s.d.)	2.58 (4.19)	2.76 (4.54)	2.67 (4.37)
Missing	1	1	2
Haemoglobin (g/dL)			
Mean (s.d.)	13.38 (4.39)	12.98 (1.92)	13.18 (3.38)
Missing	0	0	0

	Conventional Continuation Strategy (CCS) (n=425)	Drug-Free Interval Strategy (DFIS) (n=431)	Total (n=856)
ANC (x10⁹/L)			
Mean (s.d.)	5.40 (2.31)	5.43 (2.21)	5.41 (2.25)
Missing	0	0	0
Platelets (x10⁹/L)			
Mean (s.d.)	294.31 (108.98)	299.58 (116.49)	296.96 (112.79)
Missing	0	0	0
Corrected serum calcium (mmol/L)			
Mean (s.d.)	2.41 (0.17)	2.39 (0.14)	2.40 (0.16)
Missing	47	51	98
Lactate dehyrogenase (IU/L)			
Mean (s.d.)	327.73 (207.92)	322.81 (202.78)	325.26 (205.24)
Missing	4	5	9
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group			
Favourable risk (0 factors)	186 (43.8%)	190 (44.1%)	376 (43.9%)
Intermediate risk (1-2 factors)	206 (48.5%)	210 (48.7%)	416 (48.6%)
Poor risk (> = 3 factors)	33 (7.8%)	31 (7.2%)	64 (7.5%)
Randomised Under Stratification Factor: Age Group			
<60	116 (27.3%)	117 (27.1%)	233 (27.2%)
>=60	309 (72.7%)	314 (72.9%)	623 (72.8%)

	Conventional Continuation Strategy (CCS) (n=425)	Drug-Free Interval Strategy (DFIS) (n=431)	Total (n=856)
Randomised Under Stratification Factor: Disease Status			
Metastatic	417 (98.1%)	421 (97.7%)	838 (97.9%)
Locally advanced	8 (1.9%)	10 (2.3%)	18 (2.1%)
Randomised Under Stratification Factor: Previous Nephrectomy			
Yes	319 (75.1%)	325 (75.4%)	644 (75.2%)
No	106 (24.9%)	106 (24.6%)	212 (24.8%)
Randomised Under Stratification Factor: TKI Received			
Sunitinib	179 (42.1%)	181 (42.0%)	360 (42.1%)
Pazopanib	246 (57.9%)	250 (58.0%)	496 (57.9%)
Randomised Under Stratification Factor: Sex			
Male	313 (73.6%)	308 (71.5%)	621 (72.5%)
Female	112 (26.4%)	123 (28.5%)	235 (27.5%)

Note, these are presented as N (%) for each categorical variable, where % is calculated out of the total population given in the table header.

Supplementary Table 12: Key Demographic and Disease Related Characteristics, by (Randomised Under) TKI Received, in the ITT population (G6_BaselineCharacteristics)

	Sunitinib (n=388)	**Pazopanib (n=531)**	**Total (n=919)**
Ethnic origin			
White	374 (96.4%)	511 (96.2%)	885 (96.3%)
Mixed - White and Black Caribbean	0 (0.0%)	1 (0.2%)	1 (0.1%)
Other mixed background	1 (0.3%)	1 (0.2%)	2 (0.2%)
Asian - Indian	2 (0.5%)	3 (0.6%)	5 (0.5%)
Asian - Pakistani	2 (0.5%)	2 (0.4%)	4 (0.4%)
Other Asian background	0 (0.0%)	1 (0.2%)	1 (0.1%)
Black - Caribbean	1 (0.3%)	2 (0.4%)	3 (0.3%)
Black - African	1 (0.3%)	1 (0.2%)	2 (0.2%)
Other Black background	0 (0.0%)	1 (0.2%)	1 (0.1%)
Other ethnic group	2 (0.5%)	2 (0.4%)	4 (0.4%)
Not stated	5 (1.3%)	6 (1.1%)	11 (1.2%)
Age (Years)			
Median (range)	65.00 (37.00, 88.00)	67.00 (22.00, 90.00)	66.00 (22.00, 90.00)
IQR	58.00, 70.00	60.00, 73.00	59.00, 72.00
Missing	0	0	0
F04 Stratification Factor: Sex			
Male	296 (76.3%)	372 (70.1%)	668 (72.7%)
Female	92 (23.7%)	159 (29.9%)	251 (27.3%)
ECOG Performance Status			
0	223 (57.5%)	281 (52.9%)	504 (54.8%)

	Sunitinib (n=388)	Pazopanib (n=531)	Total (n=919)
1	163 (42.0%)	248 (46.7%)	411 (44.7%)
Missing	2 (0.5%)	2 (0.4%)	4 (0.4%)
Disease present in bones			
Yes	83 (21.4%)	119 (22.4%)	202 (22.0%)
No	305 (78.6%)	411 (77.4%)	716 (77.9%)
Missing	0 (0.0%)	1 (0.2%)	1 (0.1%)
Time since initial diagnosis (Years)			
Mean (s.d.)	2.43 (3.98)	2.91 (4.61)	2.71 (4.36)
Missing	1	1	2
Haemoglobin (g/dL)			
Mean (s.d.)	13.24 (1.89)	13.13 (4.04)	13.18 (3.31)
Missing	0	0	0
ANC (x10⁹/L)			
Mean (s.d.)	5.36 (2.26)	5.47 (2.31)	5.42 (2.29)
Missing	0	0	0
Platelets (x10⁹/L)			
Mean (s.d.)	292.15 (110.74)	298.44 (113.10)	295.78 (112.09)
Missing	0	0	0
Corrected serum calcium (mmol/L)			
Mean (s.d.)	2.41 (0.16)	2.40 (0.15)	2.40 (0.16)
Missing	106	3	109
Lactate dehyrogenase (IU/L)			
Mean (s.d.)	314.45 (178.11)	330.26 (217.50)	323.63 (201.96)
Missing	7	4	11

	Sunitinib (n=388)	Pazopanib (n=531)	Total (n=919)
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group			
Favourable risk (0 factors)	174 (44.8%)	231 (43.5%)	405 (44.1%)
Intermediate risk (1-2 factors)	187 (48.2%)	260 (49.0%)	447 (48.6%)
Poor risk (> = 3 factors)	27 (7.0%)	40 (7.5%)	67 (7.3%)
Randomised Under Stratification Factor: Age Group			
<60	118 (30.4%)	126 (23.7%)	244 (26.6%)
>=60	270 (69.6%)	405 (76.3%)	675 (73.4%)
Randomised Under Stratification Factor: Disease Status			
Metastatic	380 (97.9%)	519 (97.7%)	899 (97.8%)
Locally advanced	8 (2.1%)	12 (2.3%)	20 (2.2%)
Randomised Under Stratification Factor: Previous Nephrectomy			
Yes	295 (76.0%)	397 (74.8%)	692 (75.3%)
No	93 (24.0%)	134 (25.2%)	227 (24.7%)
Randomised Under Stratification Factor: Sex			
Male	296 (76.3%)	372 (70.1%)	668 (72.7%)
Female	92 (23.7%)	159 (29.9%)	251 (27.3%)

Note, these are presented as N (%) for each categorical variable, where % is calculated out of the total population given in the table header.

Supplementary Table 13: Key Demographic and Disease Related Characteristics, by (Randomised Under) TKI Received, in the PP population (G6_BaselineCharacteristics)

	Sunitinib (n=368)	**Pazopanib (n=503)**	**Total (n=871)**
Ethnic origin			
White	356 (96.7%)	484 (96.2%)	840 (96.4%)
Mixed - White and Black Caribbean	0 (0.0%)	1 (0.2%)	1 (0.1%)
Other mixed background	1 (0.3%)	1 (0.2%)	2 (0.2%)
Asian - Indian	2 (0.5%)	3 (0.6%)	5 (0.6%)
Asian - Pakistani	2 (0.5%)	2 (0.4%)	4 (0.5%)
Other Asian background	0 (0.0%)	1 (0.2%)	1 (0.1%)
Black - Caribbean	1 (0.3%)	2 (0.4%)	3 (0.3%)
Black - African	0 (0.0%)	1 (0.2%)	1 (0.1%)
Other Black background	0 (0.0%)	1 (0.2%)	1 (0.1%)
Other ethnic group	2 (0.5%)	2 (0.4%)	4 (0.5%)
Not stated	4 (1.1%)	5 (1.0%)	9 (1.0%)
Age (Years)			
Median (range)	65.50 (37.00, 88.00)	67.00 (22.00, 86.00)	66.00 (22.00, 88.00)
IQR	58.00, 71.00	60.00, 73.00	59.00, 72.00
Missing	0	0	0
F04 Stratification Factor: Sex			
Male	282 (76.6%)	352 (70.0%)	634 (72.8%)
Female	86 (23.4%)	151 (30.0%)	237 (27.2%)
ECOG Performance Status			
0	214 (58.2%)	267 (53.1%)	481 (55.2%)
1	152 (41.3%)	234 (46.5%)	386 (44.3%)

	Sunitinib (n=368)	Pazopanib (n=503)	Total (n=871)
Missing	2 (0.5%)	2 (0.4%)	4 (0.5%)
Disease present in bones			
Yes	79 (21.5%)	111 (22.1%)	190 (21.8%)
No	289 (78.5%)	391 (77.7%)	680 (78.1%)
Missing	0 (0.0%)	1 (0.2%)	1 (0.1%)
Time since initial diagnosis (Years)			
Mean (s.d.)	2.48 (4.06)	2.93 (4.67)	2.74 (4.42)
Missing	1	1	2
Haemoglobin (g/dL)			
Mean (s.d.)	13.28 (1.87)	13.16 (4.13)	13.21 (3.37)
Missing	0	0	0
ANC (x10⁹/L)			
Mean (s.d.)	5.39 (2.28)	5.46 (2.34)	5.43 (2.32)
Missing	0	0	0
Platelets (x10⁹/L)			
Mean (s.d.)	289.35 (110.89)	300.10 (113.75)	295.55 (112.61)
Missing	0	0	0
Corrected serum calcium (mmol/L)			
Mean (s.d.)	2.42 (0.16)	2.40 (0.15)	2.40 (0.15)
Missing	102	3	105
Lactate dehyrogenase (IU/L)			
Mean (s.d.)	315.01 (181.16)	324.61 (208.23)	320.57 (197.25)
Missing	6	4	10

	Sunitinib (n=368)	Pazopanib (n=503)	Total (n=871)
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group			
Favourable risk (0 factors)	164 (44.6%)	220 (43.7%)	384 (44.1%)
Intermediate risk (1-2 factors)	177 (48.1%)	244 (48.5%)	421 (48.3%)
Poor risk (> = 3 factors)	27 (7.3%)	39 (7.8%)	66 (7.6%)
Randomised Under Stratification Factor: Age Group			
<60	110 (29.9%)	119 (23.7%)	229 (26.3%)
>=60	258 (70.1%)	384 (76.3%)	642 (73.7%)
Randomised Under Stratification Factor: Disease Status			
Metastatic	360 (97.8%)	491 (97.6%)	851 (97.7%)
Locally advanced	8 (2.2%)	12 (2.4%)	20 (2.3%)
Randomised Under Stratification Factor: Previous Nephrectomy			
Yes	279 (75.8%)	376 (74.8%)	655 (75.2%)
No	89 (24.2%)	127 (25.2%)	216 (24.8%)
Randomised Under Stratification Factor: Sex			
Male	282 (76.6%)	352 (70.0%)	634 (72.8%)
Female	86 (23.4%)	151 (30.0%)	237 (27.2%)

Note, these are presented as N (%) for each categorical variable, where % is calculated out of the total population given in the table header.

2.3 Treatment Received

Supplementary Table 14: Post-Trial Treatment, by TKI received, in the ITT population (G8_TreatmentReceived)

	Sunitinib (n=385)	**Pazopanib (n=534)**	**Total (n=919)**
Is the participant recorded as having any systemic anti-cancer treatment during follow-up			
Yes	252 (65.5%)	314 (58.8%)	566 (61.6%)
No	81 (21.0%)	122 (22.8%)	203 (22.1%)
N/A	52 (13.5%)	98 (18.4%)	150 (16.3%)
Is the participant recorded as having any radiotherapy treatment during follow-up			
Yes	114 (29.6%)	125 (23.4%)	239 (26.0%)
No	219 (56.9%)	311 (58.2%)	530 (57.7%)
N/A	52 (13.5%)	98 (18.4%)	150 (16.3%)
Is the participant recorded as having any anti-cancer surgery during follow-up			
Yes	23 (6.0%)	44 (8.2%)	67 (7.3%)
No	310 (80.5%)	392 (73.4%)	702 (76.4%)
N/A	52 (13.5%)	98 (18.4%)	150 (16.3%)
Is the participant recorded as having palliative care during follow-up?			
Yes	139 (36.1%)	186 (34.8%)	325 (35.4%)
No	194 (50.4%)	250 (46.8%)	444 (48.3%)
N/A	52 (13.5%)	98 (18.4%)	150 (16.3%)

Note, these are presented as N (%), where % is calculated out of the total number given in the table header.

Supplementary Table 15: Anti-Cancer therapy received in follow-up, by Randomisation Allocation, in the ITT population - non mutually exclusive (G8_TreatmentReceived)

	Conventional Continuation Strategy (CCS)	**Drug-Free Interval Strategy (DFIS)**	**Total**
Name of anti-cancer treatment recorded as being received during follow-up			
Nivolumab	114 (21.5%)	106 (25.4%)	220 (23.2%)
Axitinib	125 (23.6%)	92 (22.1%)	217 (22.9%)
Sunitinib	79 (14.9%)	66 (15.8%)	145 (15.3%)
Cabozantinib	69 (13.0%)	54 (12.9%)	123 (13.0%)
Pazopanib	70 (13.2%)	37 (8.9%)	107 (11.3%)
Everolimus	37 (7.0%)	31 (7.4%)	68 (7.2%)
Other	17 (3.2%)	5 (1.2%)	22 (2.3%)
Denosumab	6 (1.1%)	5 (1.2%)	11 (1.2%)
Lenvatinib	4 (0.8%)	5 (1.2%)	9 (1.0%)
Everolimus and Lenvatinib	5 (0.9%)	4 (1.0%)	9 (1.0%)
Prednisolone	1 (0.2%)	2 (0.5%)	3 (0.3%)
Savolitinib	1 (0.2%)	2 (0.5%)	3 (0.3%)
Tivozanib	0 (0.0%)	3 (0.7%)	3 (0.3%)
Zoledronate	1 (0.2%)	2 (0.5%)	3 (0.3%)
Sorafenib	1 (0.2%)	1 (0.2%)	2 (0.2%)
Tasquinimod	0 (0.0%)	1 (0.2%)	1 (0.1%)
Missing	0 (0.0%)	1 (0.2%)	1 (0.1%)
Total	530 (100%)	417 (100%)	947 (100%)

Note, this is not distinct for participants but distinct in the sense of the repeat recording of the same treatment

Supplementary Table 16: Other anti-Cancer therapy received in follow-up, by randomisation allocation, in the ITT population - Not mutually exclusive (G8_TreatmentReceived)

Other treatment recorded as being received during follow-up - CCS	**Other treatment recorded as being received during follow-up - DFIS**
AZD2014	AVELUMAB
AZD2014	HIGH DOSE IL-2
BICALUTAMIDE	IPILIMUMAB
BYL719	MENZ 9136
CAPECITABINE	NIVOLUMAB AND IPILIMUMAB
CARBOZANTINIB AND DENOSUMAB	
CB-839/PLACEBO	
CHOP AND RITUXIMAB	
DEXAMETHASONE	
DEXAMETHASONE	
DURVALUMAB	
DURVALUMAB	
DURVALUMAB / TREMELIMUMAB	
EVEROLIMUS/DENOSUMAB	
OXALIPLATIN	
SAVOLITINIB + DURVALUMAB	
SAVOLITINIB 600MG + MED14736	

Note, this is not distinct for participants but distinct in the sense of the repeat recording of the same treatment

Supplementary Table 17: Number of Distinct Anti-Cancer Treatment Types, by Randomisation Allocation, in the ITT population (G8_TreatmentReceived)

	Conventional Continuation Strategy (CCS) (n=461)	**Drug-Free Interval Strategy (DFIS) (n=458)**	**Total (n=919)**
Number of distinct treatment types recorded in follow-up			
0	146 (31.7%)	209 (45.6%)	355 (38.6%)
1	185 (40.1%)	139 (30.3%)	324 (35.3%)
2	92 (20.0%)	85 (18.6%)	177 (19.3%)
3	34 (7.4%)	21 (4.6%)	55 (6.0%)
4	4 (0.9%)	4 (0.9%)	8 (0.9%)

2.4 Overall Survival

Supplementary Table 18: Other Causes of Death Reported, by Randomisation Allocation, in the PP Population (P1b_OSPrimaryAnalysis)

Conventional Continuation Strategy (CCS)	Drug-Free Interval Strategy (DFIS)
(a) Bronchopneumonia (b) Metastatic clear cell renal cell carcinoma	Adenocarcinoma and transverse colon cancer
1. Spontaneous right peritoneal haemorrhage. 2. Low molecular weight, Heparin treatment for pulmonar	Aspiration
1a - Probable Pulmonary Embolism, 1b - Immobility secondary to insertion of intramedullary nail,	Aspiration pneumonia
Acute renal failure	Brain tumour
Baseline renal impairment	Bronchopneumonia, carcinomatosis renal cell carcinoma
Bilateral atypical pneumonia	COPD
Bone	Caraniomatosis
Bowel perforation	Carcinomatosis
Carcinomatosis	Carcinomatosis, Osteomyelitis, hypertension, cerebrovascular disease
Community acquired Pneumonia	Clinician-led withdrawal from study. Pt died 17/05/16 due to illness-cancer
Community acquired pneumonia	Dementia
Community acquired pneumonia	Depression
Community acquired pneumonia	Hepatic Encephalopathy
Community aquired infection	Hospital acquired pneumonia
Emergency laparotomy procedure for a transverse colon perforation	Intracerebral haemmorrhage, intracerebral metastases

Conventional Continuation Strategy (CCS)	Drug-Free Interval Strategy (DFIS)
Frontal lobe bleed	Ischaemic stroke/transient ischaemic attacks
General frailty	Klebsiella Pneumonia
Haemorrhagic Stroke	Large bowel ischaemia
He had had a cerebellar haemorrhage on 09-11-2019 causing dysphagia	Left Intra cerebral bleed
Heart failure	Left sided pleural effusion
Hepatorenal failure	Metastatic hypernephroma
Hospital acquired pneumonia	Mid lower zone pneumonia
Hypercalcaemia	Pneumonia
Hypertension	Pneumonia
Intra pleural metastatic disease	Pneumonia, COPD
Intracerebral Haemorrhage	Pneumonia, Hypertension
Ischaemic disease	Pneumonia, renal failure
Lobar pneumonia	Pulmonary Embolism
Lower respiratory tract infection	Pulmonary embolism
Metastases to lung, lymph nodes and adrenal	Pulmonay embolism
Multiple strokes	Renal Failure
Neuro-endocrine Stromal Tumour	Sepsis
Periphic Abcess	Sepsis cellulitis. Ischaemic Heart disease
Pneumonia	Sepsis, intra-abdominal infection, perforated peptic ulcer
Pneumonia	Sepsis, pneumonia, type II diadetes
Pneumonia	Severe Sepsis
Small bowl perforation	Spinal cord compression

Conventional Continuation Strategy (CCS)	Drug-Free Interval Strategy (DFIS)
Spontaneous intra-cranial bleed. Cerebral metastases	Sudden death syndrome; 1) Ischaemic heart disease 2) Renal cancer
Type 2 Diabetes	Type 2 diabetes, Hypertension, Congestive cardiac failure, Hypothyroidism
Urinary sepsis	kidney failure second to agressive bony metastasis
Urosepsis	pneumonia
acute on chronic renal failure - left ventricular heart failure	
co-existing colorectal cancer	
haemoptysis, pulmonary embolism	
intracranial haemorrhage	

Supplementary Table 19: Mutually Exclusive Causes of Death, by TKI, in the PP Population (P1b_OSPrimaryAnalysis)

	Sunitinib (n=280)	Pazopanib (n=368)	Total (n=648)
Renal Cancer	234 (83.6%)	292 (79.3%)	526 (81.2%)
Renal Cancer, Other	24 (8.6%)	37 (10.1%)	61 (9.4%)
Unknown	8 (2.9%)	8 (2.2%)	16 (2.5%)
Other	4 (1.4%)	11 (3.0%)	15 (2.3%)
Renal Cancer, Cardiovascular Related	2 (0.7%)	7 (1.9%)	9 (1.4%)
Renal Cancer, Cardiovascular Related, Other	2 (0.7%)	3 (0.8%)	5 (0.8%)
Cardiovascular Related	3 (1.1%)	0 (0.0%)	3 (0.5%)
Trial Toxicity	0 (0.0%)	3 (0.8%)	3 (0.5%)
Renal Cancer, Trial Toxicity	0 (0.0%)	2 (0.5%)	2 (0.3%)

	Sunitinib (n=280)	Pazopanib (n=368)	Total (n=648)
Renal Cancer, Trial Toxicity, Cardiovascular Related, Other	1 (0.4%)	1 (0.3%)	2 (0.3%)
Trial Toxicity, Cardiovascular Related	1 (0.4%)	1 (0.3%)	2 (0.3%)
Trial Toxicity, Other	0 (0.0%)	2 (0.5%)	2 (0.3%)
Renal Cancer, Trial Toxicity, Other	1 (0.4%)	0 (0.0%)	1 (0.2%)
Renal Cancer, Unknown	0 (0.0%)	1 (0.3%)	1 (0.2%)

Note, these are presented as N (%), where % is calculated out of the total number given in the table header.

Supplementary Table 20: Other Causes of Death Reported, by TKI, in the PP Population (P1b_OSPrimaryAnalysis)

Randomised under Sunitinib	Randomised under Pazopanib
Acute renal failure	(a) Bronchopneumonia (b) Metastatic clear cell renal cell carcinoma
Baseline renal impairment	1. Spontaneous right peritoneal haemorrhage. 2. Low molecular weight, Heparin treatment for pulmonar
Bronchopneumonia, carcinomatosis renal cell carcinoma	1a - Probable Pulmonary Embolism, 1b - Immobility secondary to insertion of intramedullary nail,
Carcinomatosis	Adenocarcinoma and transverse colon cancer
Carcinomatosis	Aspiration
Community acquired pneumonia	Aspiration pneumonia
Community acquired pneumonia	Bilateral atypical pneumonia
Community aquired infection	Bone
He had had a cerebellar haemorrhage on 09-11-2019 causing dysphagia	Bowel perforation

Randomised under Sunitinib	Randomised under Pazopanib
Hepatorenal failure	Brain tumour
Hospital acquired pneumonia	COPD
Hypertension	Caraniomatosis
Intracerebral Haemorrhage	Carcinomatosis, Osteomyelitis, hypertension, cerebrovascular disease
Left sided pleural effusion	Clinician-led withdrawal from study. Pt died 17/05/16 due to illness-cancer
Lobar pneumonia	Community acquired Pneumonia
Lower respiratory tract infection	Community acquired pneumonia
Metastatic hypernephroma	Dementia
Multiple strokes	Depression
Pneumonia	Emergency laparotomy procedure for a transverse colon perforation
Pneumonia	Frontal lobe bleed
Pneumonia	General frailty
Pneumonia, renal failure	Haemorrhagic Stroke
Pulmonary embolism	Heart failure
Sepsis	Hepatic Encephalopathy
Sepsis, intra-abdominal infection, perforated peptic ulcer	Hospital acquired pneumonia
Spinal cord compression	Hypercalcaemia
Spontaneous intra-cranial bleed. Cerebral metastases	Intra pleural metastatic disease
Urinary sepsis	Intracerebral haemmorrhage, intracerebral metastases

Randomised under Sunitinib	Randomised under Pazopanib
acute on chronic renal failure - left ventricular heart failure	Ischaemic disease
haemoptysis, pulmonary embolism	Ischaemic stroke/transient ischaemic attacks
intracranial haemorrhage	Klebsiella Pneumonia
pneumonia	Large bowel ischaemia
	Left Intra cerebral bleed
	Metastases to lung, lymph nodes and adrenal
	Mid lower zone pneumonia
	Neuro-endocrine Stromal Tumour
	Periphic Abcess
	Pneumonia
	Pneumonia
	Pneumonia, COPD
	Pneumonia, Hypertension
	Pulmonary Embolism
	Pulmonay embolism
	Renal Failure
	Sepsis cellulitis. Ischaemic Heart disease
	Sepsis, pneumonia, type II diadetes
	Severe Sepsis
	Small bowl perforation
	Sudden death syndrome; 1) Ischaemic heart disease 2) Renal cancer
	Type 2 Diabetes

Randomised under Sunitinib	Randomised under Pazopanib
	Type 2 diabetes, Hypertension, Congestive cardiac failure, Hypothyroidism
	Urosepsis
	co-existing colorectal cancer
	kidney failure second to agressive bony metastasis

Supplementary Table 21: Other Causes of Death Reported, by Randomisation Allocation, in the ITT Population (P1c_OSSensitivityAnalysis_ITT)

Conventional Continuation Strategy (CCS)	Drug-Free Interval Strategy (DFIS)
(a) Bronchopneumonia (b) Metastatic clear cell renal cell carcinoma	1a Pneumonia 1b Metastatic RCC 1c Type 2 Diabetes Mellitus
1. Spontaneous right peritoneal haemorrhage. 2. Low molecular weight, Heparin treatment for pulmonar	Adenocarcinoma and transverse colon cancer
1a - Probable Pulmonary Embolism, 1b - Immobility secondary to insertion of intramedullary nail,	Aspiration
Acute renal failure	Aspiration pneumonia
Baseline renal impairment	Brain tumour
Bilateral atypical pneumonia	Bronchopneumonia, carcinomatosis renal cell carcinoma
Bone	COPD
Bowel perforation	Caraniomatosis
Carcinomatosis	Carcinomatosis
Community acquired Pneumonia	Carcinomatosis, Osteomyelitis, hypertension, cerebrovascular disease

Conventional Continuation Strategy (CCS)	Drug-Free Interval Strategy (DFIS)
Community acquired pneumonia	Clinician-led withdrawal from study. Pt died 17/05/16 due to illness-cancer
Community acquired pneumonia	Dementia
Community acquired pneumonia	Depression
Community aquired infection	Hepatic Encephalopathy
Emergency laparotomy procedure for a transverse colon perforation	Hospital acquired pneumonia
Frontal lobe bleed	Intracerebral haemmorrhage, intracerebral metastases
General frailty	Ischaemic stroke/transient ischaemic attacks
Haemorrhagic Stroke	Klebsiella Pneumonia
He had had a cerebellar haemorrhage on 09-11-2019 causing dysphagia	Large bowel ischaemia
Heart failure	Left Intra cerebral bleed
Hepatorenal failure	Left sided pleural effusion
Hospital acquired pneumonia	Metastatic hypernephroma
Hypercalcaemia	Mid lower zone pneumonia
Hypertension	Pneumonia
Intra pleural metastatic disease	Pneumonia
Intracerebral Haemorrhage	Pneumonia, COPD
Ischaemic disease	Pneumonia, Hypertension
Lobar pneumonia	Pneumonia, renal failure
Lower respiratory tract infection	Pulmonary Embolism
Metastases to lung, lymph nodes and adrenal	Pulmonary embolism

Conventional Continuation Strategy (CCS)	**Drug-Free Interval Strategy (DFIS)**
Multiple strokes	Pulmonay embolism
Neuro-endocrine Stromal Tumour	Renal Failure
Periphic Abcess	Sepsis
Pneumonia	Sepsis cellulitis. Ischaemic Heart disease
Pneumonia	Sepsis, Bowel perforation (not operated)
Pneumonia	Sepsis, intra-abdominal infection, perforated peptic ulcer
Possible PE/MI. Patient found at home. No post mortem complete to our knowledge.	Sepsis, pneumonia, type II diadetes
Small bowl perforation	Severe Sepsis
Spontaneous intra-cranial bleed. Cerebral metastases	Spinal cord compression
Traumatic injury leading to subdural and extradural brain haematoma	Sudden death syndrome; 1) Ischaemic heart disease 2) Renal cancer
Type 2 Diabetes	Type 2 diabetes, Hypertension, Congestive cardiac failure, Hypothyroidism
Urinary sepsis	kidney failure second to agressive bony metastasis
Urosepsis	pneumonia
acute on chronic renal failure - left ventricular heart failure	
chest infection	
co-existing colorectal cancer	
haemoptysis, pulmonary embolism	
intracranial haemorrhage	

Supplementary Table 22: Mutually Exclusive Causes of Death, by TKI, in the ITT Population (P1c_OSSensitivityAnalysis_ITT)

	Sunitinib (n=293)	**Pazopanib (n=385)**	**Total (n=678)**
Renal Cancer	245 (83.6%)	305 (79.2%)	550 (81.1%)
Renal Cancer, Other	24 (8.2%)	40 (10.4%)	64 (9.4%)
Other	5 (1.7%)	12 (3.1%)	17 (2.5%)
Unknown	8 (2.7%)	8 (2.1%)	16 (2.4%)
Renal Cancer, Cardiovascular Related	2 (0.7%)	7 (1.8%)	9 (1.3%)
Renal Cancer, Cardiovascular Related, Other	2 (0.7%)	3 (0.8%)	5 (0.7%)
Cardiovascular Related	4 (1.4%)	0 (0.0%)	4 (0.6%)
Trial Toxicity	0 (0.0%)	3 (0.8%)	3 (0.4%)
Renal Cancer, Trial Toxicity	0 (0.0%)	2 (0.5%)	2 (0.3%)
Renal Cancer, Trial Toxicity, Cardiovascular Related, Other	1 (0.3%)	1 (0.3%)	2 (0.3%)
Trial Toxicity, Cardiovascular Related	1 (0.3%)	1 (0.3%)	2 (0.3%)
Trial Toxicity, Other	0 (0.0%)	2 (0.5%)	2 (0.3%)
Renal Cancer, Trial Toxicity, Other	1 (0.3%)	0 (0.0%)	1 (0.1%)
Renal Cancer, Unknown	0 (0.0%)	1 (0.3%)	1 (0.1%)

Note, this table is presented a N (%) where % is calculated out of the total given in the table header.

Supplementary Table 23: Other Causes of Death Reported, by TKI, in the ITT Population (P1c_OSSensitivityAnalysis_ITT)

Randomised under Sunitinib	**Randomised under Pazopanib**
Acute renal failure	(a) Bronchopneumonia (b) Metastatic clear cell renal cell carcinoma

Randomised under Sunitinib	Randomised under Pazopanib
Baseline renal impairment	1. Spontaneous right peritoneal haemorrhage. 2. Low molecular weight, Heparin treatment for pulmonar
Bronchopneumonia, carcinomatosis renal cell carcinoma	1a - Probable Pulmonary Embolism, 1b - Immobility secondary to insertion of intramedullary nail,
Carcinomatosis	1a Pneumonia 1b Metastatic RCC 1c Type 2 Diabetes Mellitus
Carcinomatosis	Adenocarcinoma and transverse colon cancer
Community acquired pneumonia	Aspiration
Community acquired pneumonia	Aspiration pneumonia
Community aquired infection	Bilateral atypical pneumonia
He had had a cerebellar haemorrhage on 09-11-2019 causing dysphagia	Bone
Hepatorenal failure	Bowel perforation
Hospital acquired pneumonia	Brain tumour
Hypertension	COPD
Intracerebral Haemorrhage	Caraniomatosis
Left sided pleural effusion	Carcinomatosis, Osteomyelitis, hypertension, cerebrovascular disease
Lobar pneumonia	Clinician-led withdrawal from study. Pt died 17/05/16 due to illness-cancer
Lower respiratory tract infection	Community acquired Pneumonia
Metastatic hypernephroma	Community acquired pneumonia
Multiple strokes	Dementia
Pneumonia	Depression

Randomised under Sunitinib	Randomised under Pazopanib
Pneumonia	Emergency laparotomy procedure for a transverse colon perforation
Pneumonia	Frontal lobe bleed
Pneumonia, renal failure	General frailty
Possible PE/MI. Patient found at home. No post mortem complete to our knowledge.	Haemorrhagic Stroke
Pulmonary embolism	Heart failure
Sepsis	Hepatic Encephalopathy
Sepsis, intra-abdominal infection, perforated peptic ulcer	Hospital acquired pneumonia
Spinal cord compression	Hypercalcaemia
Spontaneous intra-cranial bleed. Cerebral metastases	Intra pleural metastatic disease
Urinary sepsis	Intracerebral haemmorrhage, intracerebral metastases
acute on chronic renal failure - left ventricular heart failure	Ischaemic disease
haemoptysis, pulmonary embolism	Ischaemic stroke/transient ischaemic attacks
intracranial haemorrhage	Klebsiella Pneumonia
pneumonia	Large bowel ischaemia
	Left Intra cerebral bleed
	Metastases to lung, lymph nodes and adrenal
	Mid lower zone pneumonia
	Neuro-endocrine Stromal Tumour
	Periphic Abcess
	Pneumonia

Randomised under Sunitinib	Randomised under Pazopanib
	Pneumonia
	Pneumonia, COPD
	Pneumonia, Hypertension
	Pulmonary Embolism
	Pulmonay embolism
	Renal Failure
	Sepsis cellulitis. Ischaemic Heart disease
	Sepsis, Bowel perforation (not operated)
	Sepsis, pneumonia, type II diadetes
	Severe Sepsis
	Small bowl perforation
	Sudden death syndrome; 1) Ischaemic heart disease 2) Renal cancer
	Traumatic injury leading to subdural and extradural brain haematoma
	Type 2 Diabetes
	Type 2 diabetes, Hypertension, Congestive cardiac failure, Hypothyroidism
	Urosepsis
	chest infection
	co-existing colorectal cancer
	kidney failure second to agressive bony metastasis

2.5 QALYs

Supplementary Table 24: Key baseline characteristics, by baseline questionnaire missing status, in the ITT population (P2b_EQ5D_PrimaryImputation)

	Yes (n=51)	No (n=868)	Total (n=919)
Ethnic origin			
White	49 (96.1%)	836 (96.3%)	885 (96.3%)
Mixed - White and Black Caribbean	0 (0.0%)	1 (0.1%)	1 (0.1%)
Other mixed background	0 (0.0%)	2 (0.2%)	2 (0.2%)
Asian - Indian	0 (0.0%)	5 (0.6%)	5 (0.5%)
Asian - Pakistani	0 (0.0%)	4 (0.5%)	4 (0.4%)
Other Asian background	0 (0.0%)	1 (0.1%)	1 (0.1%)
Black - Caribbean	0 (0.0%)	3 (0.3%)	3 (0.3%)
Black - African	1 (2.0%)	1 (0.1%)	2 (0.2%)
Other Black background	0 (0.0%)	1 (0.1%)	1 (0.1%)
Other ethnic group	0 (0.0%)	4 (0.5%)	4 (0.4%)
Not stated	1 (2.0%)	10 (1.2%)	11 (1.2%)
F04 Stratification Factor: Age Group			
<60	12 (23.5%)	232 (26.7%)	244 (26.6%)
>=60	39 (76.5%)	636 (73.3%)	675 (73.4%)
F04 Stratification Factor: Sex			
Male	34 (66.7%)	634 (73.0%)	668 (72.7%)
Female	17 (33.3%)	234 (27.0%)	251 (27.3%)
ECOG Performance Status			
0	24 (47.1%)	480 (55.3%)	504 (54.8%)
1	27 (52.9%)	384 (44.2%)	411 (44.7%)
Missing	0 (0.0%)	4 (0.5%)	4 (0.4%)
Disease present in bones			
Yes	5 (9.8%)	197 (22.7%)	202 (22.0%)
No	46 (90.2%)	670 (77.2%)	716 (77.9%)
Missing	0 (0.0%)	1 (0.1%)	1 (0.1%)
Time since initial diagnosis (Years)			
Mean (s.d.)	2.87 (4.56)	2.70 (4.35)	2.71 (4.36)
Missing	0	2	2

	Yes (n=51)	No (n=868)	Total (n=919)
Haemoglobin (g/dL)			
Mean (s.d.)	12.62 (1.94)	13.21 (3.37)	13.18 (3.31)
Missing	0	0	0
ANC (x10⁹/L)			
Mean (s.d.)	5.18 (1.81)	5.44 (2.31)	5.42 (2.29)
Missing	0	0	0
Platelets (x10⁹/L)			
Mean (s.d.)	295.18 (106.77)	295.82 (112.46)	295.78 (112.09)
Missing	0	0	0
Corrected serum calcium (mmol/L)			
Mean (s.d.)	2.43 (0.18)	2.40 (0.15)	2.40 (0.16)
Missing	6	103	109
Lactate dehyrogenase (IU/L)			
Mean (s.d.)	329.88 (158.45)	323.27 (204.23)	323.63 (201.96)
Missing	2	9	11
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group			
Favourable risk (0 factors)	25 (49.0%)	380 (43.8%)	405 (44.1%)
Intermediate risk (1-2 factors)	23 (45.1%)	424 (48.8%)	447 (48.6%)
Poor risk (> = 3 factors)	3 (5.9%)	64 (7.4%)	67 (7.3%)
Randomised Under Stratification Factor: Age Group			
<60	12 (23.5%)	232 (26.7%)	244 (26.6%)
>=60	39 (76.5%)	636 (73.3%)	675 (73.4%)
Randomised Under Stratification Factor: Disease Status			
Metastatic	48 (94.1%)	851 (98.0%)	899 (97.8%)
Locally advanced	3 (5.9%)	17 (2.0%)	20 (2.2%)
Randomised Under Stratification Factor: Previous Nephrectomy			
Yes	41 (80.4%)	651 (75.0%)	692 (75.3%)
No	10 (19.6%)	217 (25.0%)	227 (24.7%)
Randomised Under Stratification Factor: TKI Received			

	Yes (n=51)	No (n=868)	Total (n=919)
Sunitinib	16 (31.4%)	372 (42.9%)	388 (42.2%)
Pazopanib	35 (68.6%)	496 (57.1%)	531 (57.8%)
Randomised Under Stratification Factor: Sex			
Male	34 (66.7%)	634 (73.0%)	668 (72.7%)
Female	17 (33.3%)	234 (27.0%)	251 (27.3%)

Note, the categorical variables are presented as N (%), where % is calculated out of the total number given in the table header.

Supplementary Table 25: Key baseline characteristics and variables considered for the imputation model, by 6 months follow-up questionnaire missing status, in the ITT population (P2b_EQ5D_PrimaryImputation)

	Yes (n=283)	No (n=323)	Total (n=606)
Ethnic origin			
White	268 (94.7%)	315 (97.5%)	583 (96.2%)
Mixed - White and Black Caribbean	1 (0.4%)	0 (0.0%)	1 (0.2%)
Other mixed background	1 (0.4%)	0 (0.0%)	1 (0.2%)
Asian - Indian	3 (1.1%)	0 (0.0%)	3 (0.5%)
Asian - Pakistani	3 (1.1%)	0 (0.0%)	3 (0.5%)
Other Asian background	1 (0.4%)	0 (0.0%)	1 (0.2%)
Black - Caribbean	2 (0.7%)	0 (0.0%)	2 (0.3%)
Black - African	1 (0.4%)	0 (0.0%)	1 (0.2%)
Other ethnic group	1 (0.4%)	2 (0.6%)	3 (0.5%)
Not stated	2 (0.7%)	6 (1.9%)	8 (1.3%)
F04 Stratification Factor: Age Group			
<60	73 (25.8%)	92 (28.5%)	165 (27.2%)
>=60	210 (74.2%)	231 (71.5%)	441 (72.8%)
F04 Stratification Factor: Sex			

	Yes (n=283)	No (n=323)	Total (n=606)
Male	205 (72.4%)	226 (70.0%)	431 (71.1%)
Female	78 (27.6%)	97 (30.0%)	175 (28.9%)
ECOG Performance Status			
0	134 (47.3%)	214 (66.3%)	348 (57.4%)
1	148 (52.3%)	108 (33.4%)	256 (42.2%)
Missing	1 (0.4%)	1 (0.3%)	2 (0.3%)
Disease present in bones			
Yes	56 (19.8%)	57 (17.6%)	113 (18.6%)
No	227 (80.2%)	265 (82.0%)	492 (81.2%)
Missing	0 (0.0%)	1 (0.3%)	1 (0.2%)
Time since initial diagnosis (Years)			
Mean (s.d.)	2.98 (4.61)	2.90 (4.27)	2.94 (4.43)
Missing	0	2	2
Haemoglobin (g/dL)			
Mean (s.d.)	13.23 (1.84)	13.68 (4.85)	13.47 (3.76)
Missing	0	0	0
ANC ($x10^9$/L)			
Mean (s.d.)	5.35 (2.11)	5.02 (1.85)	5.18 (1.98)
Missing	0	0	0
Platelets ($x10^9$/L)			
Mean (s.d.)	289.80 (100.09)	278.80 (97.20)	283.94 (98.63)
Missing	0	0	0
Corrected serum calcium (mmol/L)			
Mean (s.d.)	2.39 (0.14)	2.39 (0.14)	2.39 (0.14)

	Yes (n=283)	No (n=323)	Total (n=606)
Missing	45	30	75
Lactate dehyrogenase (IU/L)			
Mean (s.d.)	297.48 (147.20)	304.07 (147.01)	301.01 (147.01)
Missing	5	2	7
Randomisation treatment			
Conventional Continuation Strategy (CCS)	153 (54.1%)	184 (57.0%)	337 (55.6%)
Drug-Free Interval Strategy (DFIS)	130 (45.9%)	139 (43.0%)	269 (44.4%)
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group			
Favourable risk (0 factors)	129 (45.6%)	168 (52.0%)	297 (49.0%)
Intermediate risk (1-2 factors)	139 (49.1%)	145 (44.9%)	284 (46.9%)
Poor risk (> = 3 factors)	15 (5.3%)	10 (3.1%)	25 (4.1%)
Randomised Under Stratification Factor: Age Group			
<60	74 (26.1%)	91 (28.2%)	165 (27.2%)
>=60	209 (73.9%)	232 (71.8%)	441 (72.8%)
Randomised Under Stratification Factor: Disease Status			
Metastatic	275 (97.2%)	318 (98.5%)	593 (97.9%)
Locally advanced	8 (2.8%)	5 (1.5%)	13 (2.1%)
Randomised Under Stratification Factor: Previous Nephrectomy			
Yes	218 (77.0%)	264 (81.7%)	482 (79.5%)
No	65 (23.0%)	59 (18.3%)	124 (20.5%)

	Yes (n=283)	No (n=323)	Total (n=606)
Randomised Under Stratification Factor: TKI Received			
Sunitinib	119 (42.0%)	140 (43.3%)	259 (42.7%)
Pazopanib	164 (58.0%)	183 (56.7%)	347 (57.3%)
Randomised Under Stratification Factor: Sex			
Male	205 (72.4%)	227 (70.3%)	432 (71.3%)
Female	78 (27.6%)	96 (29.7%)	174 (28.7%)
Was the 6 months follow-up questionnaire due during the pandemic?			
Yes	5 (1.8%)	12 (3.7%)	17 (2.8%)
No	278 (98.2%)	311 (96.3%)	589 (97.2%)
Was the baseline questionnaire imputed?			
Yes	17 (6.0%)	14 (4.3%)	31 (5.1%)
No	266 (94.0%)	309 (95.7%)	575 (94.9%)
What is the last recorded on treatment EQ5D Utility Index			
Mean (s.d.)	0.70 (0.27)	0.75 (0.24)	0.73 (0.25)
Missing	0	0	0

Note, the categorical variables are presented as N (%), where % is calculated out of the total number given in the table header.

Supplementary Table 26: Key baseline characteristics and variables considered for the imputation model, by 18 months follow-up questionnaire missing status, in the ITT population (P2b_EQ5D_PrimaryImputation)

	Yes (n=176)	No (n=189)	Total (n=365)
Ethnic origin			

	Yes (n=176)	No (n=189)	Total (n=365)
White	167 (94.9%)	184 (97.4%)	351 (96.2%)
Other mixed background	1 (0.6%)	0 (0.0%)	1 (0.3%)
Asian - Indian	1 (0.6%)	0 (0.0%)	1 (0.3%)
Asian - Pakistani	1 (0.6%)	0 (0.0%)	1 (0.3%)
Black - Caribbean	2 (1.1%)	0 (0.0%)	2 (0.5%)
Other ethnic group	1 (0.6%)	2 (1.1%)	3 (0.8%)
Not stated	3 (1.7%)	3 (1.6%)	6 (1.6%)
F04 Stratification Factor: Age Group			
<60	56 (31.8%)	48 (25.4%)	104 (28.5%)
>=60	120 (68.2%)	141 (74.6%)	261 (71.5%)
F04 Stratification Factor: Sex			
Male	118 (67.0%)	136 (72.0%)	254 (69.6%)
Female	58 (33.0%)	53 (28.0%)	111 (30.4%)
ECOG Performance Status			
0	107 (60.8%)	122 (64.6%)	229 (62.7%)
1	67 (38.1%)	67 (35.4%)	134 (36.7%)
Missing	2 (1.1%)	0 (0.0%)	2 (0.5%)
Disease present in bones			
Yes	34 (19.3%)	28 (14.8%)	62 (17.0%)
No	142 (80.7%)	160 (84.7%)	302 (82.7%)
Missing	0 (0.0%)	1 (0.5%)	1 (0.3%)
Time since initial diagnosis (Years)			
Mean (s.d.)	3.29 (4.41)	2.97 (4.35)	3.13 (4.37)
Missing	0	1	1

	Yes (n=176)	No (n=189)	Total (n=365)
Haemoglobin (g/dL)			
Mean (s.d.)	13.63 (1.75)	13.42 (1.73)	13.52 (1.74)
Missing	0	0	0
ANC (x10⁹/L)			
Mean (s.d.)	5.08 (1.74)	4.91 (1.86)	4.99 (1.80)
Missing	0	0	0
Platelets (x10⁹/L)			
Mean (s.d.)	270.32 (90.99)	273.63 (93.28)	272.03 (92.07)
Missing	0	0	0
Corrected serum calcium (mmol/L)			
Mean (s.d.)	2.39 (0.13)	2.38 (0.12)	2.38 (0.12)
Missing	27	19	46
Lactate dehyrogenase (IU/L)			
Mean (s.d.)	296.82 (141.48)	287.81 (124.64)	292.15 (132.91)
Missing	3	3	6
Randomisation treatment			
Conventional Continuation Strategy (CCS)	101 (57.4%)	106 (56.1%)	207 (56.7%)
Drug-Free Interval Strategy (DFIS)	75 (42.6%)	83 (43.9%)	158 (43.3%)
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group			
Favourable risk (0 factors)	99 (56.3%)	95 (50.3%)	194 (53.2%)
Intermediate risk (1-2 factors)	72 (40.9%)	89 (47.1%)	161 (44.1%)
Poor risk (> = 3 factors)	5 (2.8%)	5 (2.6%)	10 (2.7%)

	Yes (n=176)	No (n=189)	Total (n=365)
Randomised Under Stratification Factor: Age Group			
<60	57 (32.4%)	47 (24.9%)	104 (28.5%)
>=60	119 (67.6%)	142 (75.1%)	261 (71.5%)
Randomised Under Stratification Factor: Disease Status			
Metastatic	172 (97.7%)	185 (97.9%)	357 (97.8%)
Locally advanced	4 (2.3%)	4 (2.1%)	8 (2.2%)
Randomised Under Stratification Factor: Previous Nephrectomy			
Yes	143 (81.3%)	158 (83.6%)	301 (82.5%)
No	33 (18.8%)	31 (16.4%)	64 (17.5%)
Randomised Under Stratification Factor: TKI Received			
Sunitinib	65 (36.9%)	85 (45.0%)	150 (41.1%)
Pazopanib	111 (63.1%)	104 (55.0%)	215 (58.9%)
Randomised Under Stratification Factor: Sex			
Male	118 (67.0%)	137 (72.5%)	255 (69.9%)
Female	58 (33.0%)	52 (27.5%)	110 (30.1%)
Was the 18 months follow-up questionnaire due during the pandemic?			
Yes	14 (8.0%)	10 (5.3%)	24 (6.6%)
No	162 (92.0%)	179 (94.7%)	341 (93.4%)
Was the baseline questionnaire imputed?			
Yes	10 (5.7%)	6 (3.2%)	16 (4.4%)

	Yes (n=176)	No (n=189)	Total (n=365)
No	166 (94.3%)	183 (96.8%)	349 (95.6%)
What is the last recorded on treatment EQ5D Utility Index			
Mean (s.d.)	0.73 (0.23)	0.78 (0.21)	0.76 (0.22)
Missing	0	0	0
EQ-5D Utility Score at 6 months fup			
Mean (s.d.)	0.69 (0.26)	0.74 (0.24)	0.73 (0.25)
Missing	100	34	134

Note, the categorical variables are presented as N (%), where % is calculated out of the total number given in the table header.

Supplementary Table 27: Key baseline characteristics and variables considered for the imputation model, by 30 months follow-up questionnaire missing status, in the ITT population (P2b_EQ5D_PrimaryImputation)

	Yes (n=106)	No (n=119)	Total (n=225)
Ethnic origin			
White	103 (97.2%)	116 (97.5%)	219 (97.3%)
Black - Caribbean	0 (0.0%)	1 (0.8%)	1 (0.4%)
Other ethnic group	2 (1.9%)	0 (0.0%)	2 (0.9%)
Not stated	1 (0.9%)	2 (1.7%)	3 (1.3%)
F04 Stratification Factor: Age Group			
<60	33 (31.1%)	25 (21.0%)	58 (25.8%)
>=60	73 (68.9%)	94 (79.0%)	167 (74.2%)
F04 Stratification Factor: Sex			
Male	73 (68.9%)	91 (76.5%)	164 (72.9%)

	Yes (n=106)	No (n=119)	Total (n=225)
Female	33 (31.1%)	28 (23.5%)	61 (27.1%)
ECOG Performance Status			
0	66 (62.3%)	90 (75.6%)	156 (69.3%)
1	39 (36.8%)	29 (24.4%)	68 (30.2%)
Missing	1 (0.9%)	0 (0.0%)	1 (0.4%)
Disease present in bones			
Yes	15 (14.2%)	17 (14.3%)	32 (14.2%)
No	91 (85.8%)	101 (84.9%)	192 (85.3%)
Missing	0 (0.0%)	1 (0.8%)	1 (0.4%)
Time since initial diagnosis (Years)			
Mean (s.d.)	3.83 (5.09)	3.73 (4.67)	3.78 (4.86)
Missing	0	1	1
Haemoglobin (g/dL)			
Mean (s.d.)	13.50 (1.89)	13.74 (1.63)	13.63 (1.75)
Missing	0	0	0
ANC ($x10^9$/L)			
Mean (s.d.)	5.02 (1.69)	4.75 (1.93)	4.88 (1.82)
Missing	0	0	0
Platelets ($x10^9$/L)			
Mean (s.d.)	269.38 (89.07)	258.81 (95.79)	263.79 (92.63)
Missing	0	0	0
Corrected serum calcium (mmol/L)			
Mean (s.d.)	2.37 (0.10)	2.38 (0.11)	2.38 (0.11)
Missing	13	11	24

	Yes (n=106)	No (n=119)	Total (n=225)
Lactate dehyrogenase (IU/L)			
Mean (s.d.)	296.09 (107.41)	289.58 (130.03)	292.62 (119.80)
Missing	3	1	4
Randomisation treatment			
Conventional Continuation Strategy (CCS)	64 (60.4%)	67 (56.3%)	131 (58.2%)
Drug-Free Interval Strategy (DFIS)	42 (39.6%)	52 (43.7%)	94 (41.8%)
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group			
Favourable risk (0 factors)	61 (57.5%)	65 (54.6%)	126 (56.0%)
Intermediate risk (1-2 factors)	43 (40.6%)	50 (42.0%)	93 (41.3%)
Poor risk (> = 3 factors)	2 (1.9%)	4 (3.4%)	6 (2.7%)
Randomised Under Stratification Factor: Age Group			
<60	33 (31.1%)	25 (21.0%)	58 (25.8%)
>=60	73 (68.9%)	94 (79.0%)	167 (74.2%)
Randomised Under Stratification Factor: Disease Status			
Metastatic	101 (95.3%)	118 (99.2%)	219 (97.3%)
Locally advanced	5 (4.7%)	1 (0.8%)	6 (2.7%)
Randomised Under Stratification Factor: Previous Nephrectomy			
Yes	90 (84.9%)	103 (86.6%)	193 (85.8%)
No	16 (15.1%)	16 (13.4%)	32 (14.2%)
Randomised Under Stratification Factor: TKI Received			

	Yes (n=106)	No (n=119)	Total (n=225)
Sunitinib	36 (34.0%)	54 (45.4%)	90 (40.0%)
Pazopanib	70 (66.0%)	65 (54.6%)	135 (60.0%)
Randomised Under Stratification Factor: Sex			
Male	74 (69.8%)	91 (76.5%)	165 (73.3%)
Female	32 (30.2%)	28 (23.5%)	60 (26.7%)
Was the 30 months follow-up questionnaire due during the pandemic?			
Yes	21 (19.8%)	14 (11.8%)	35 (15.6%)
No	85 (80.2%)	105 (88.2%)	190 (84.4%)
Was the baseline questionnaire imputed?			
Yes	1 (0.9%)	5 (4.2%)	6 (2.7%)
No	105 (99.1%)	114 (95.8%)	219 (97.3%)
What is the last recorded on treatment EQ5D Utility Index			
Mean (s.d.)	0.78 (0.17)	0.77 (0.22)	0.77 (0.20)
Missing	0	0	0
EQ-5D Utility Score at 6 months fup			
Mean (s.d.)	0.73 (0.25)	0.76 (0.25)	0.75 (0.25)
Missing	56	28	84
EQ-5D Utility Score at 18 months fup			
Mean (s.d.)	0.71 (0.21)	0.82 (0.17)	0.79 (0.19)
Missing	65	24	89

Note, the categorical variables are presented as N (%), where % is calculated out of the total number given in the table header.

Supplementary Table 28: Key baseline characteristics and variables considered for the imputation model, by 42 months follow-up questionnaire missing status, in the ITT population (P2b_EQ5D_PrimaryImputation)

	Yes (n=66)	No (n=60)	Total (n=126)
Ethnic origin			
White	65 (98.5%)	58 (96.7%)	123 (97.6%)
Black - Caribbean	0 (0.0%)	1 (1.7%)	1 (0.8%)
Not stated	1 (1.5%)	1 (1.7%)	2 (1.6%)
F04 Stratification Factor: Age Group			
<60	19 (28.8%)	12 (20.0%)	31 (24.6%)
>=60	47 (71.2%)	48 (80.0%)	95 (75.4%)
F04 Stratification Factor: Sex			
Male	43 (65.2%)	44 (73.3%)	87 (69.0%)
Female	23 (34.8%)	16 (26.7%)	39 (31.0%)
ECOG Performance Status			
0	39 (59.1%)	47 (78.3%)	86 (68.3%)
1	27 (40.9%)	13 (21.7%)	40 (31.7%)
Disease present in bones			
Yes	8 (12.1%)	7 (11.7%)	15 (11.9%)
No	57 (86.4%)	53 (88.3%)	110 (87.3%)
Missing	1 (1.5%)	0 (0.0%)	1 (0.8%)
Time since initial diagnosis (Years)			
Mean (s.d.)	4.84 (5.55)	3.49 (4.20)	4.19 (4.98)
Missing	1	0	1
Haemoglobin (g/dL)			
Mean (s.d.)	13.52 (1.76)	13.67 (1.38)	13.59 (1.59)

	Yes (n=66)	No (n=60)	Total (n=126)
Missing	0	0	0
ANC (x10⁹/L)			
Mean (s.d.)	5.28 (1.88)	4.46 (1.60)	4.89 (1.79)
Missing	0	0	0
Platelets (x10⁹/L)			
Mean (s.d.)	284.67 (117.22)	252.30 (77.37)	269.25 (101.16)
Missing	0	0	0
Corrected serum calcium (mmol/L)			
Mean (s.d.)	2.39 (0.10)	2.38 (0.12)	2.38 (0.11)
Missing	7	9	16
Lactate dehyrogenase (IU/L)			
Mean (s.d.)	280.78 (104.04)	323.15 (159.02)	300.94 (134.19)
Missing	1	1	2
Randomisation treatment			
Conventional Continuation Strategy (CCS)	39 (59.1%)	41 (68.3%)	80 (63.5%)
Drug-Free Interval Strategy (DFIS)	27 (40.9%)	19 (31.7%)	46 (36.5%)
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group			
Favourable risk (0 factors)	37 (56.1%)	32 (53.3%)	69 (54.8%)
Intermediate risk (1-2 factors)	28 (42.4%)	26 (43.3%)	54 (42.9%)
Poor risk (> = 3 factors)	1 (1.5%)	2 (3.3%)	3 (2.4%)
Randomised Under Stratification Factor: Age Group			
<60	19 (28.8%)	11 (18.3%)	30 (23.8%)

	Yes (n=66)	No (n=60)	Total (n=126)
>=60	47 (71.2%)	49 (81.7%)	96 (76.2%)
Randomised Under Stratification Factor: Disease Status			
Metastatic	64 (97.0%)	59 (98.3%)	123 (97.6%)
Locally advanced	2 (3.0%)	1 (1.7%)	3 (2.4%)
Randomised Under Stratification Factor: Previous Nephrectomy			
Yes	57 (86.4%)	53 (88.3%)	110 (87.3%)
No	9 (13.6%)	7 (11.7%)	16 (12.7%)
Randomised Under Stratification Factor: TKI Received			
Sunitinib	23 (34.8%)	29 (48.3%)	52 (41.3%)
Pazopanib	43 (65.2%)	31 (51.7%)	74 (58.7%)
Randomised Under Stratification Factor: Sex			
Male	43 (65.2%)	45 (75.0%)	88 (69.8%)
Female	23 (34.8%)	15 (25.0%)	38 (30.2%)
Was the 42 months follow-up questionnaire due during the pandemic?			
Yes	25 (37.9%)	20 (33.3%)	45 (35.7%)
No	41 (62.1%)	40 (66.7%)	81 (64.3%)
Was the baseline questionnaire imputed?			
Yes	1 (1.5%)	2 (3.3%)	3 (2.4%)
No	65 (98.5%)	58 (96.7%)	123 (97.6%)
What is the last recorded on treatment EQ5D Utility Index			

	Yes (n=66)	No (n=60)	Total (n=126)
Mean (s.d.)	0.77 (0.22)	0.80 (0.19)	0.78 (0.21)
Missing	0	0	0
EQ-5D Utility Score at 6 months fup			
Mean (s.d.)	0.70 (0.30)	0.81 (0.17)	0.77 (0.23)
Missing	36	11	47
EQ-5D Utility Score at 18 months fup			
Mean (s.d.)	0.81 (0.16)	0.82 (0.15)	0.81 (0.15)
Missing	38	11	49
EQ-5D Utility Score at 30 months fup			
Mean (s.d.)	0.69 (0.28)	0.83 (0.19)	0.78 (0.23)
Missing	38	10	48

Note, the categorical variables are presented as N (%), where % is calculated out of the total number given in the table header.

Supplementary Table 29: Key baseline characteristics and variables considered for the imputation model, by 54 months follow-up questionnaire missing status, in the ITT population (P2b_EQ5D_PrimaryImputation)

	Yes (n=33)	No (n=18)	Total (n=51)
Ethnic origin			
White	32 (97.0%)	17 (94.4%)	49 (96.1%)
Not stated	1 (3.0%)	1 (5.6%)	2 (3.9%)
F04 Stratification Factor: Age Group			
<60	5 (15.2%)	5 (27.8%)	10 (19.6%)
>=60	28 (84.8%)	13 (72.2%)	41 (80.4%)
F04 Stratification Factor: Sex			

	Yes (n=33)	No (n=18)	Total (n=51)
Male	22 (66.7%)	13 (72.2%)	35 (68.6%)
Female	11 (33.3%)	5 (27.8%)	16 (31.4%)
ECOG Performance Status			
0	21 (63.6%)	14 (77.8%)	35 (68.6%)
1	12 (36.4%)	4 (22.2%)	16 (31.4%)
Disease present in bones			
Yes	4 (12.1%)	0 (0.0%)	4 (7.8%)
No	29 (87.9%)	18 (100.0%)	47 (92.2%)
Time since initial diagnosis (Years)			
Mean (s.d.)	5.41 (5.75)	3.75 (4.20)	4.84 (5.29)
Missing	0	1	1
Haemoglobin (g/dL)			
Mean (s.d.)	13.73 (1.52)	13.62 (1.31)	13.69 (1.44)
Missing	0	0	0
ANC (x10⁹/L)			
Mean (s.d.)	5.29 (2.16)	4.64 (1.37)	5.06 (1.93)
Missing	0	0	0
Platelets (x10⁹/L)			
Mean (s.d.)	281.82 (141.36)	260.33 (51.15)	274.24 (117.42)
Missing	0	0	0
Corrected serum calcium (mmol/L)			
Mean (s.d.)	2.36 (0.12)	2.39 (0.08)	2.37 (0.11)
Missing	5	5	10
Lactate dehyrogenase (IU/L)			

	Yes (n=33)	No (n=18)	Total (n=51)
Mean (s.d.)	290.00 (185.71)	311.39 (114.97)	297.70 (162.83)
Missing	1	0	1
Randomisation treatment			
Conventional Continuation Strategy (CCS)	20 (60.6%)	11 (61.1%)	31 (60.8%)
Drug-Free Interval Strategy (DFIS)	13 (39.4%)	7 (38.9%)	20 (39.2%)
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group			
Favourable risk (0 factors)	19 (57.6%)	8 (44.4%)	27 (52.9%)
Intermediate risk (1-2 factors)	14 (42.4%)	10 (55.6%)	24 (47.1%)
Randomised Under Stratification Factor: Age Group			
<60	5 (15.2%)	5 (27.8%)	10 (19.6%)
>=60	28 (84.8%)	13 (72.2%)	41 (80.4%)
Randomised Under Stratification Factor: Disease Status			
Metastatic	31 (93.9%)	18 (100.0%)	49 (96.1%)
Locally advanced	2 (6.1%)	0 (0.0%)	2 (3.9%)
Randomised Under Stratification Factor: Previous Nephrectomy			
Yes	31 (93.9%)	16 (88.9%)	47 (92.2%)
No	2 (6.1%)	2 (11.1%)	4 (7.8%)
Randomised Under Stratification Factor: TKI Received			
Sunitinib	12 (36.4%)	10 (55.6%)	22 (43.1%)
Pazopanib	21 (63.6%)	8 (44.4%)	29 (56.9%)

	Yes (n=33)	No (n=18)	Total (n=51)
Randomised Under Stratification Factor: Sex			
Male	22 (66.7%)	13 (72.2%)	35 (68.6%)
Female	11 (33.3%)	5 (27.8%)	16 (31.4%)
Was the 54 months follow-up questionnaire due during the pandemic?			
Yes	16 (48.5%)	7 (38.9%)	23 (45.1%)
No	17 (51.5%)	11 (61.1%)	28 (54.9%)
Was the baseline questionnaire imputed?			
Yes	1 (3.0%)	0 (0.0%)	1 (2.0%)
No	32 (97.0%)	18 (100.0%)	50 (98.0%)
What is the last recorded on treatment EQ5D Utility Index			
Mean (s.d.)	0.78 (0.17)	0.85 (0.26)	0.80 (0.21)
Missing	0	0	0
EQ-5D Utility Score at 6 months fup			
Mean (s.d.)	0.78 (0.21)	0.75 (0.29)	0.77 (0.24)
Missing	12	3	15
EQ-5D Utility Score at 18 months fup			
Mean (s.d.)	0.80 (0.15)	0.88 (0.13)	0.84 (0.15)
Missing	16	4	20
EQ-5D Utility Score at 30 months fup			
Mean (s.d.)	0.80 (0.18)	0.81 (0.29)	0.81 (0.24)
Missing	15	2	17
EQ-5D Utility Score at 42 months fup			

	Yes (n=33)	No (n=18)	Total (n=51)
Mean (s.d.)	0.78 (0.18)	0.89 (0.11)	0.82 (0.16)
Missing	16	6	22

Note, the categorical variables are presented as N (%), where % is calculated out of the total number given in the table header.

Supplementary Table 30: Key baseline characteristics and variables considered for the imputation model, by 66 months follow-up questionnaire missing status, in the ITT population (P2b_EQ5D_PrimaryImputation)

	Yes (n=13)	No (n=12)	Total (n=25)
Ethnic origin			
White	13 (100.0%)	11 (91.7%)	24 (96.0%)
Not stated	0 (0.0%)	1 (8.3%)	1 (4.0%)
F04 Stratification Factor: Age Group			
<60	2 (15.4%)	3 (25.0%)	5 (20.0%)
>=60	11 (84.6%)	9 (75.0%)	20 (80.0%)
F04 Stratification Factor: Sex			
Male	10 (76.9%)	8 (66.7%)	18 (72.0%)
Female	3 (23.1%)	4 (33.3%)	7 (28.0%)
ECOG Performance Status			
0	11 (84.6%)	8 (66.7%)	19 (76.0%)
1	2 (15.4%)	4 (33.3%)	6 (24.0%)
Disease present in bones			
Yes	2 (15.4%)	1 (8.3%)	3 (12.0%)
No	11 (84.6%)	11 (91.7%)	22 (88.0%)
Time since initial diagnosis (Years)			

	Yes (n=13)	No (n=12)	Total (n=25)
Mean (s.d.)	3.83 (4.37)	5.74 (5.43)	4.75 (4.90)
Missing	0	0	0
Haemoglobin (g/dL)			
Mean (s.d.)	13.52 (1.78)	13.47 (1.25)	13.49 (1.52)
Missing	0	0	0
ANC (x10⁹/L)			
Mean (s.d.)	5.18 (1.95)	4.72 (1.21)	4.96 (1.62)
Missing	0	0	0
Platelets (x10⁹/L)			
Mean (s.d.)	310.08 (183.82)	256.17 (69.15)	284.20 (140.86)
Missing	0	0	0
Corrected serum calcium (mmol/L)			
Mean (s.d.)	2.38 (0.11)	2.41 (0.08)	2.39 (0.10)
Missing	4	3	7
Lactate dehyrogenase (IU/L)			
Mean (s.d.)	245.08 (99.13)	318.25 (115.63)	280.20 (111.51)
Missing	0	0	0
Randomisation treatment			
Conventional Continuation Strategy (CCS)	8 (61.5%)	7 (58.3%)	15 (60.0%)
Drug-Free Interval Strategy (DFIS)	5 (38.5%)	5 (41.7%)	10 (40.0%)
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group			
Favourable risk (0 factors)	9 (69.2%)	5 (41.7%)	14 (56.0%)
Intermediate risk (1-2 factors)	4 (30.8%)	7 (58.3%)	11 (44.0%)

	Yes (n=13)	No (n=12)	Total (n=25)
Randomised Under Stratification Factor: Age Group			
<60	2 (15.4%)	3 (25.0%)	5 (20.0%)
>=60	11 (84.6%)	9 (75.0%)	20 (80.0%)
Randomised Under Stratification Factor: Disease Status			
Metastatic	12 (92.3%)	12 (100.0%)	24 (96.0%)
Locally advanced	1 (7.7%)	0 (0.0%)	1 (4.0%)
Randomised Under Stratification Factor: Previous Nephrectomy			
Yes	13 (100.0%)	11 (91.7%)	24 (96.0%)
No	0 (0.0%)	1 (8.3%)	1 (4.0%)
Randomised Under Stratification Factor: TKI Received			
Sunitinib	9 (69.2%)	5 (41.7%)	14 (56.0%)
Pazopanib	4 (30.8%)	7 (58.3%)	11 (44.0%)
Randomised Under Stratification Factor: Sex			
Male	10 (76.9%)	8 (66.7%)	18 (72.0%)
Female	3 (23.1%)	4 (33.3%)	7 (28.0%)
Was the 66 months follow-up questionnaire due during the pandemic?			
Yes	7 (53.8%)	6 (50.0%)	13 (52.0%)
No	6 (46.2%)	6 (50.0%)	12 (48.0%)
Was the baseline questionnaire imputed?			
Yes	0 (0.0%)	1 (8.3%)	1 (4.0%)

	Yes (n=13)	No (n=12)	Total (n=25)
No	13 (100.0%)	11 (91.7%)	24 (96.0%)
What is the last recorded on treatment EQ5D Utility Index			
Mean (s.d.)	0.74 (0.31)	0.87 (0.15)	0.80 (0.25)
Missing	0	0	0
EQ-5D Utility Score at 6 months fup			
Mean (s.d.)	0.75 (0.33)	0.73 (0.22)	0.74 (0.27)
Missing	4	2	6
EQ-5D Utility Score at 18 months fup			
Mean (s.d.)	0.86 (0.17)	0.80 (0.15)	0.82 (0.16)
Missing	6	3	9
EQ-5D Utility Score at 30 months fup			
Mean (s.d.)	0.70 (0.31)	0.81 (0.20)	0.76 (0.26)
Missing	5	3	8
EQ-5D Utility Score at 42 months fup			
Mean (s.d.)	0.76 (0.16)	0.80 (0.19)	0.79 (0.17)
Missing	8	4	12
EQ-5D Utility Score at 54 months fup			
Mean (s.d.)	0.66 (0.39)	0.78 (0.37)	0.72 (0.36)
Missing	8	7	15

Note, the categorical variables are presented as N (%), where % is calculated out of the total number given in the table header.

Supplementary Table 31: Key baseline characteristics and variables considered for the imputation model, by 78 months follow-up questionnaire missing status, in the ITT population (P2b_EQ5D_PrimaryImputation)

	Yes (n=7)	No (n=3)	Total (n=10)
Ethnic origin			
White	7 (100.0%)	3 (100.0%)	10 (100.0%)
F04 Stratification Factor: Age Group			
<60	1 (14.3%)	1 (33.3%)	2 (20.0%)
>=60	6 (85.7%)	2 (66.7%)	8 (80.0%)
F04 Stratification Factor: Sex			
Male	5 (71.4%)	1 (33.3%)	6 (60.0%)
Female	2 (28.6%)	2 (66.7%)	4 (40.0%)
ECOG Performance Status			
0	5 (71.4%)	3 (100.0%)	8 (80.0%)
1	2 (28.6%)	0 (0.0%)	2 (20.0%)
Disease present in bones			
Yes	2 (28.6%)	0 (0.0%)	2 (20.0%)
No	5 (71.4%)	3 (100.0%)	8 (80.0%)
Time since initial diagnosis (Years)			
Mean (s.d.)	4.91 (5.59)	5.40 (2.59)	5.06 (4.73)
Missing	0	0	0
Haemoglobin (g/dL)			
Mean (s.d.)	13.36 (2.12)	13.30 (0.36)	13.34 (1.74)
Missing	0	0	0
ANC ($x10^9$/L)			
Mean (s.d.)	5.28 (1.57)	4.89 (1.40)	5.16 (1.45)
Missing	0	0	0
Platelets ($x10^9$/L)			

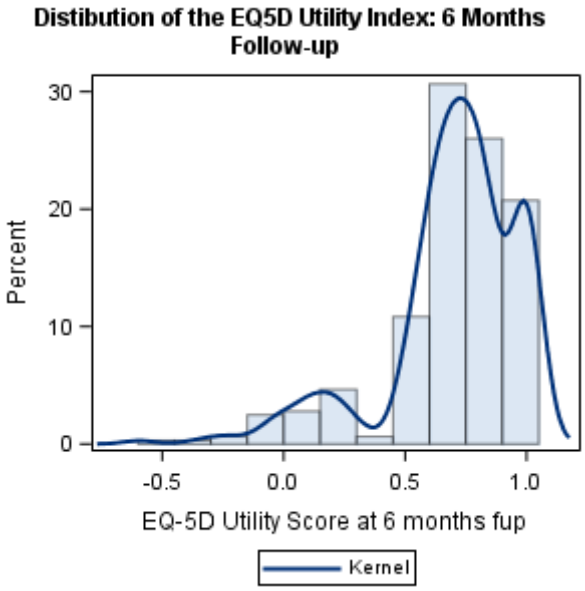
	Yes (n=7)	No (n=3)	Total (n=10)
Mean (s.d.)	352.86 (250.05)	258.33 (26.41)	324.50 (209.58)
Missing	0	0	0
Corrected serum calcium (mmol/L)			
Mean (s.d.)	2.40 (0.14)	2.40 (.)	2.40 (0.12)
Missing	3	2	5
Lactate dehyrogenase (IU/L)			
Mean (s.d.)	167.00 (40.48)	401.67 (17.90)	237.40 (118.38)
Missing	0	0	0
Randomisation treatment			
Conventional Continuation Strategy (CCS)	5 (71.4%)	2 (66.7%)	7 (70.0%)
Drug-Free Interval Strategy (DFIS)	2 (28.6%)	1 (33.3%)	3 (30.0%)
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group			
Favourable risk (0 factors)	5 (71.4%)	1 (33.3%)	6 (60.0%)
Intermediate risk (1-2 factors)	2 (28.6%)	2 (66.7%)	4 (40.0%)
Randomised Under Stratification Factor: Age Group			
<60	1 (14.3%)	1 (33.3%)	2 (20.0%)
>=60	6 (85.7%)	2 (66.7%)	8 (80.0%)
Randomised Under Stratification Factor: Disease Status			
Metastatic	7 (100.0%)	3 (100.0%)	10 (100.0%)
Randomised Under Stratification Factor: Previous Nephrectomy			
Yes	7 (100.0%)	3 (100.0%)	10 (100.0%)

	Yes (n=7)	No (n=3)	Total (n=10)
Randomised Under Stratification Factor: TKI Received			
Sunitinib	4 (57.1%)	2 (66.7%)	6 (60.0%)
Pazopanib	3 (42.9%)	1 (33.3%)	4 (40.0%)
Randomised Under Stratification Factor: Sex			
Male	5 (71.4%)	1 (33.3%)	6 (60.0%)
Female	2 (28.6%)	2 (66.7%)	4 (40.0%)
Was the 78 months follow-up questionnaire due during the pandemic?			
Yes	4 (57.1%)	3 (100.0%)	7 (70.0%)
No	3 (42.9%)	0 (0.0%)	3 (30.0%)
Was the baseline questionnaire imputed?			
No	7 (100.0%)	3 (100.0%)	10 (100.0%)
What is the last recorded on treatment EQ5D Utility Index			
Mean (s.d.)	0.83 (0.28)	0.91 (0.16)	0.86 (0.24)
Missing	0	0	0
EQ-5D Utility Score at 6 months fup			
Mean (s.d.)	0.91 (0.08)	0.79 (0.18)	0.85 (0.14)
Missing	4	0	4
EQ-5D Utility Score at 18 months fup			
Mean (s.d.)	0.89 (0.15)	0.86 (0.19)	0.88 (0.14)
Missing	3	1	4
EQ-5D Utility Score at 30 months fup			

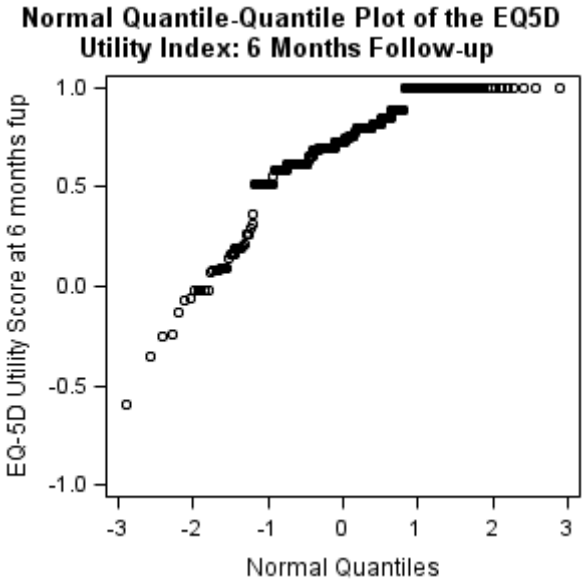
	Yes (n=7)	No (n=3)	Total (n=10)
Mean (s.d.)	0.86 (0.17)	1.00 (.)	0.88 (0.16)
Missing	2	2	4
EQ-5D Utility Score at 42 months fup			
Mean (s.d.)	0.85 (.)	0.84 (0.06)	0.84 (0.04)
Missing	6	1	7
EQ-5D Utility Score at 54 months fup			
Mean (s.d.)	0.91 (0.13)	0.58 (0.59)	0.74 (0.40)
Missing	5	1	6
EQ-5D Utility Score at 66 months fup			
Mean (s.d.)	0.91 (0.13)	0.80 (0.17)	0.84 (0.15)
Missing	5	0	5

Note, the categorical variables are presented as N (%), where % is calculated out of the total number given in the table header.

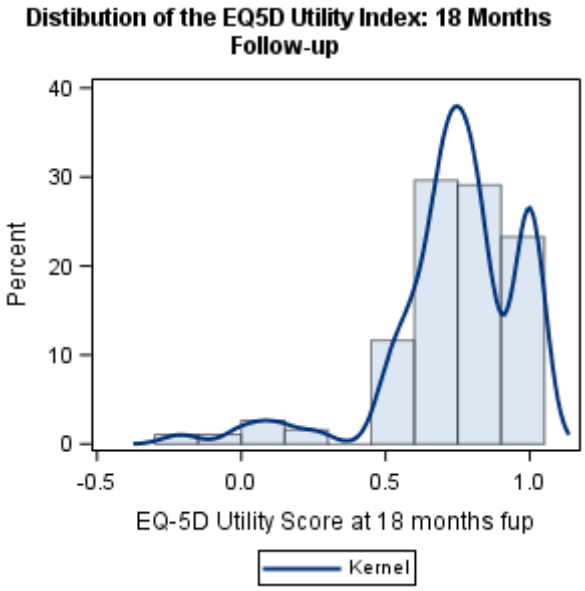
Supplementary Figure 7: Histogram of the EQ-5D Utility Index at 6-months follow (P2b_EQ5D_PrimaryImputation)



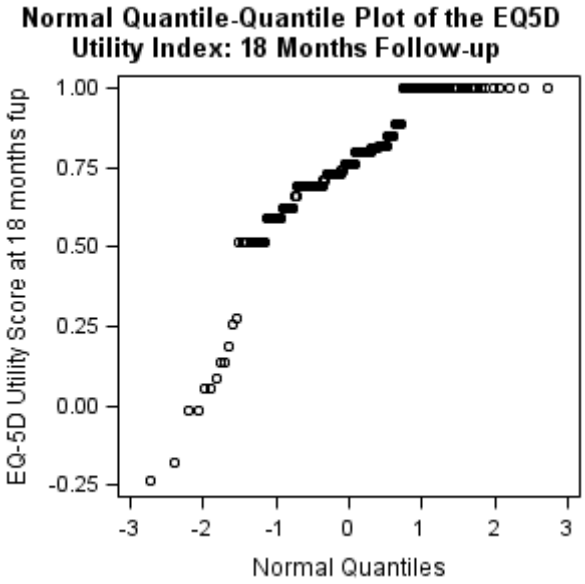
Supplementary Figure 8: QQ-Plot of the EQ-5D Utility Index at 6-months follow (P2b_EQ5D_PrimaryImputation)



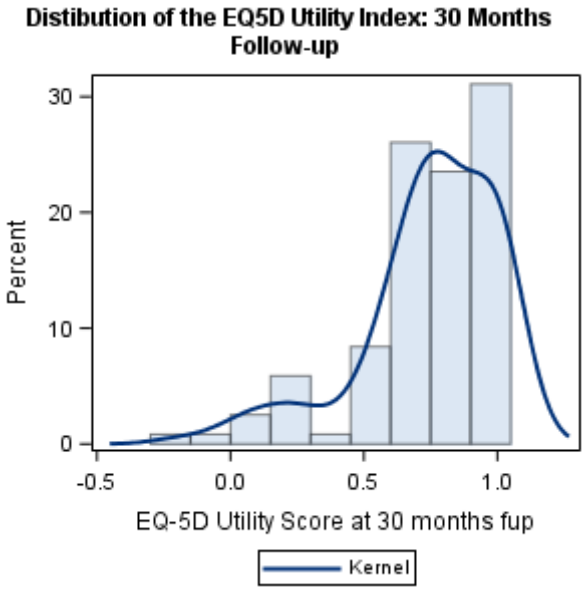
Supplementary Figure 9: Histogram of the EQ-5D Utility Index at 18-months follow (P2b_EQ5D_PrimaryImputation)



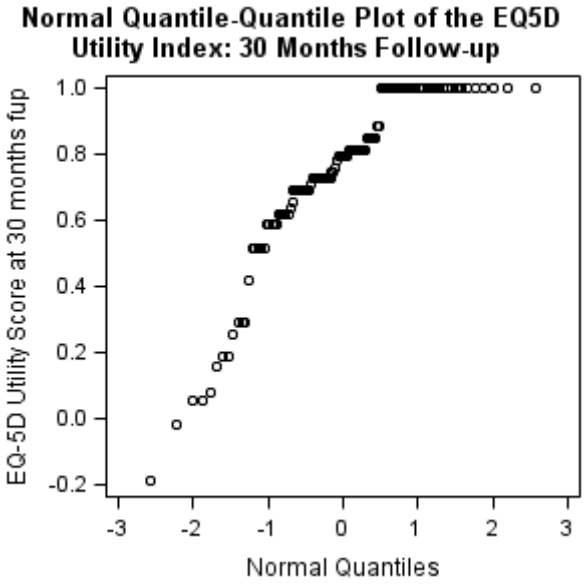
Supplementary Figure 10: QQ-Plot of the EQ-5D Utility Index at 18-months follow (P2b_EQ5D_PrimaryImputation)



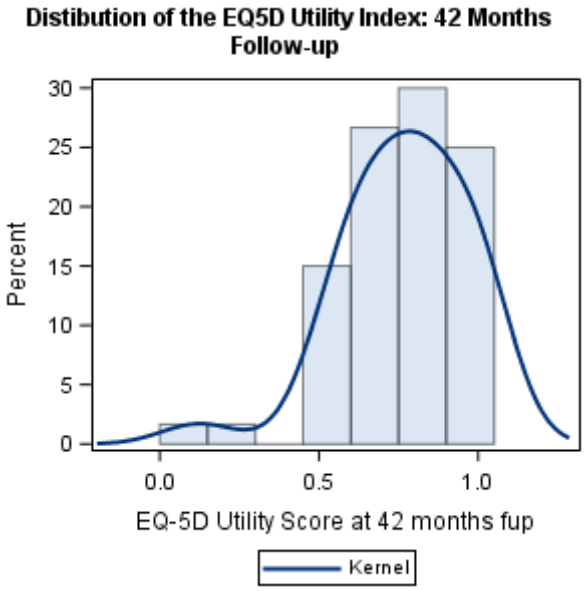
Supplementary Figure 11: Histogram of the EQ-5D Utility Index at 30-months follow (P2b_EQ5D_PrimaryImputation)



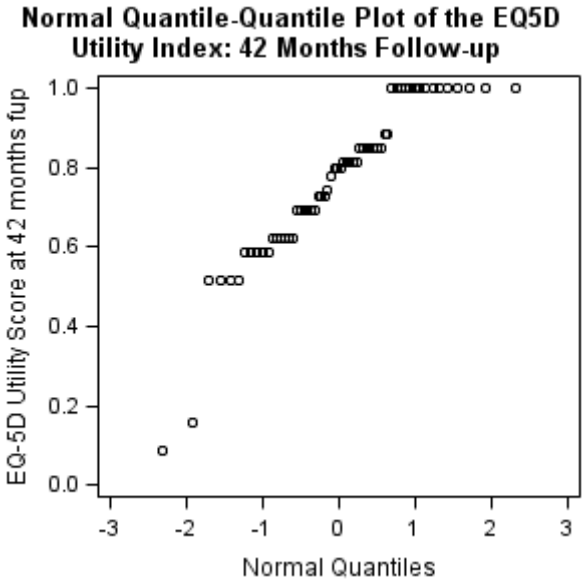
Supplementary Figure 12: QQ-Plot of the EQ-5D Utility Index at 30-months follow (P2b_EQ5D_PrimaryImputation)



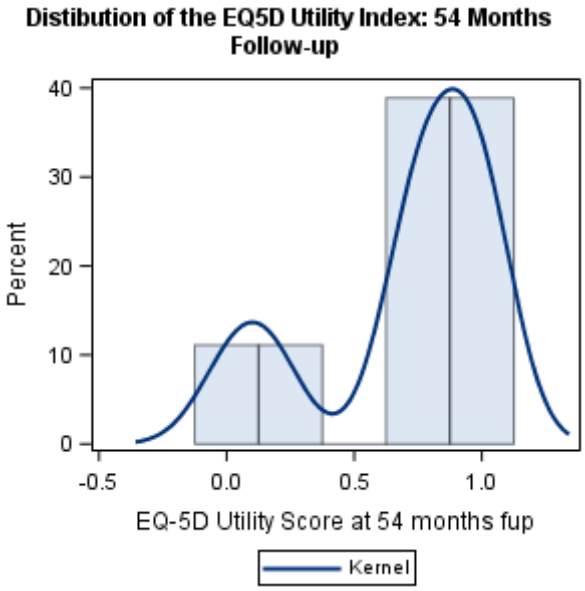
Supplementary Figure 13: Histogram of the EQ-5D Utility Index at 42-months follow (P2b_EQ5D_PrimaryImputation)



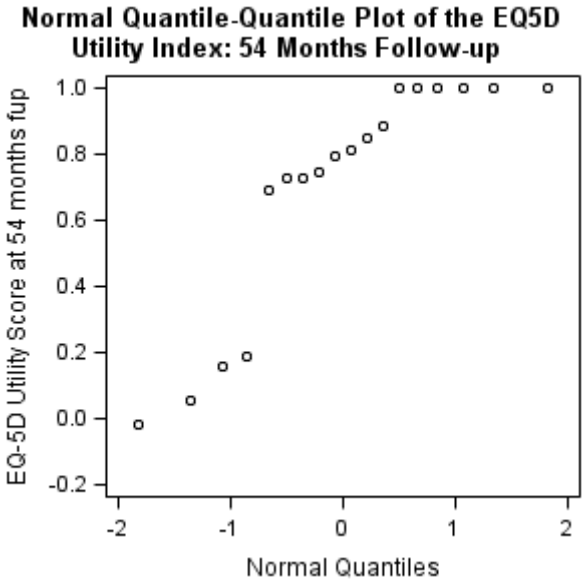
Supplementary Figure 14: QQ-Plot of the EQ-5D Utility Index at 42-months follow (P2b_EQ5D_PrimaryImputation)



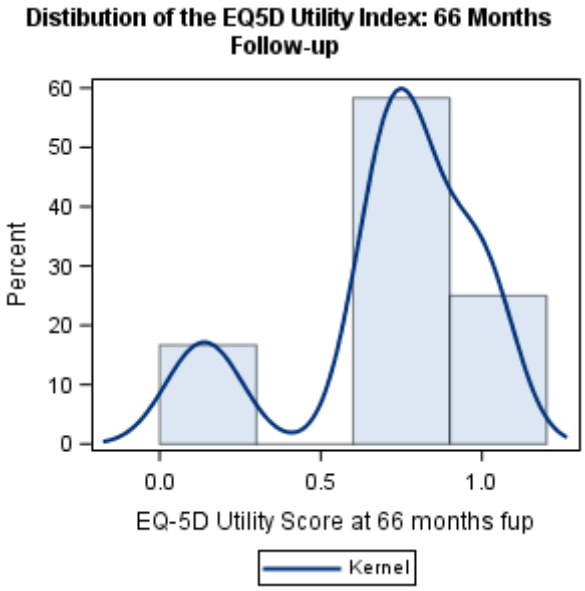
Supplementary Figure 15: Histogram of the EQ-5D Utility Index at 54-months follow (P2b_EQ5D_PrimaryImputation)



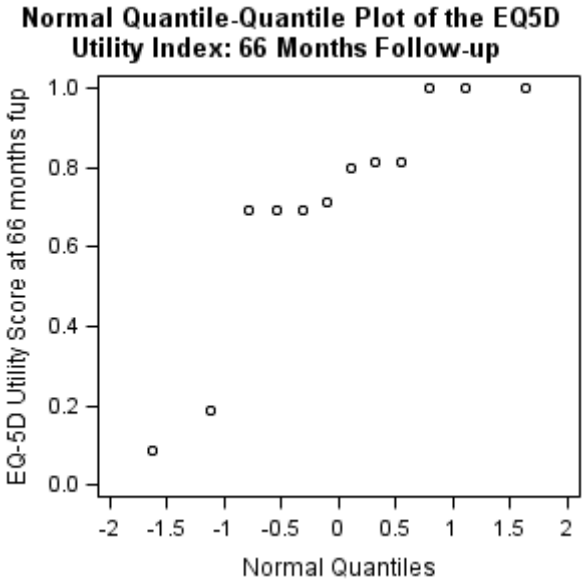
Supplementary Figure 16: QQ-Plot of the EQ-5D Utility Index at 54-months follow (P2b_EQ5D_PrimaryImputation)



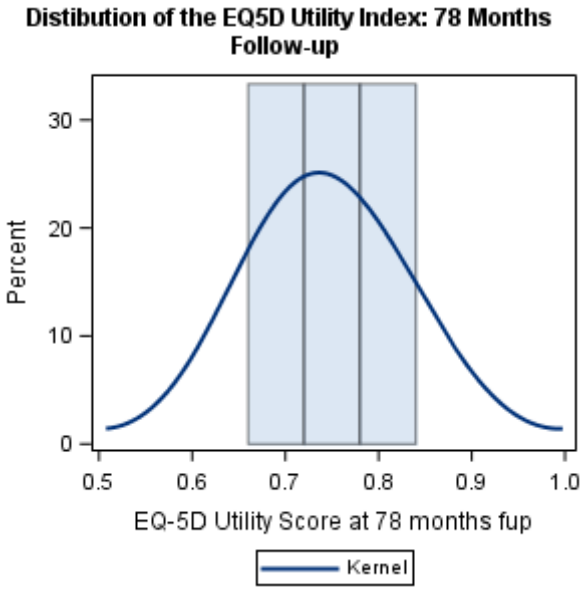
Supplementary Figure 17: Histogram of the EQ-5D Utility Index at 66-months follow (P2b_EQ5D_PrimaryImputation)



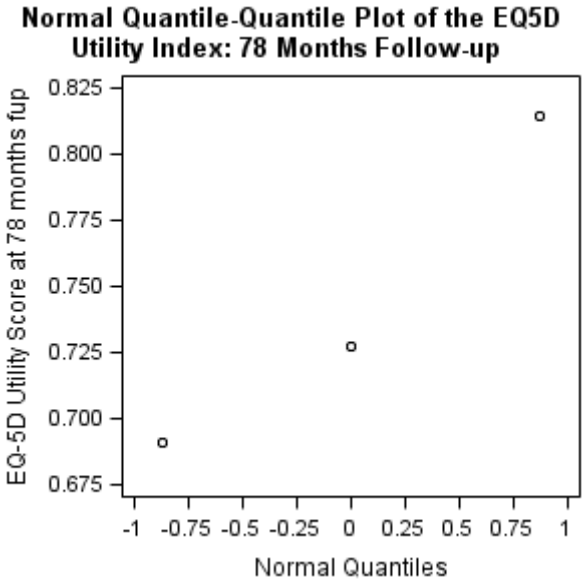
Supplementary Figure 18: QQ-Plot of the EQ-5D Utility Index at 66-months follow (P2b_EQ5D_PrimaryImputation)



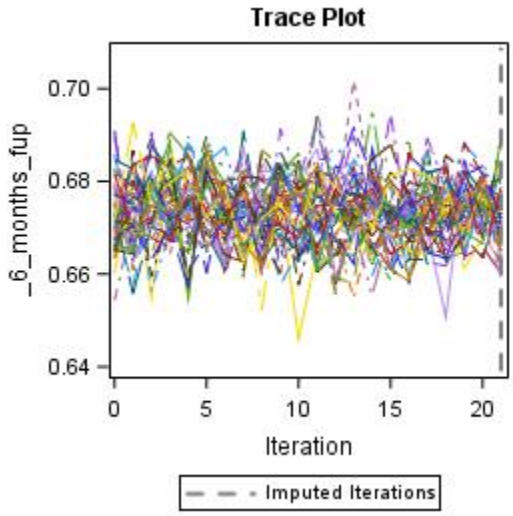
Supplementary Figure 19: Histogram of the EQ-5D Utility Index at 78-months follow (P2b_EQ5D_PrimaryImputation)



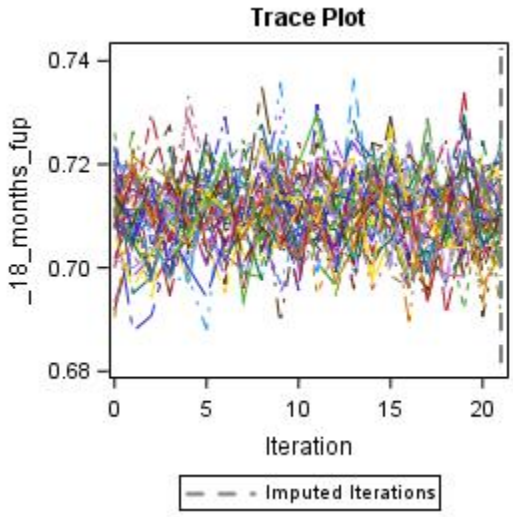
Supplementary Figure 20: QQ-Plot of the EQ-5D Utility Index at 78-months follow (P2b_EQ5D_PrimaryImputation)



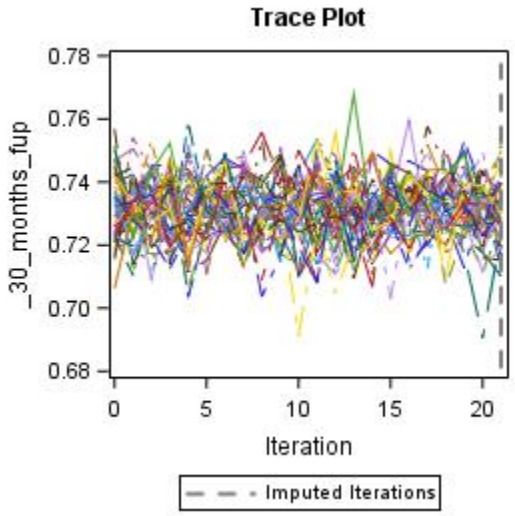
Supplementary Figure 21: Trace Plot for the imputation of EQ-5D utility score at 6 months follow-up across N Imputations (P2b_EQ5D_PrimaryImputation)



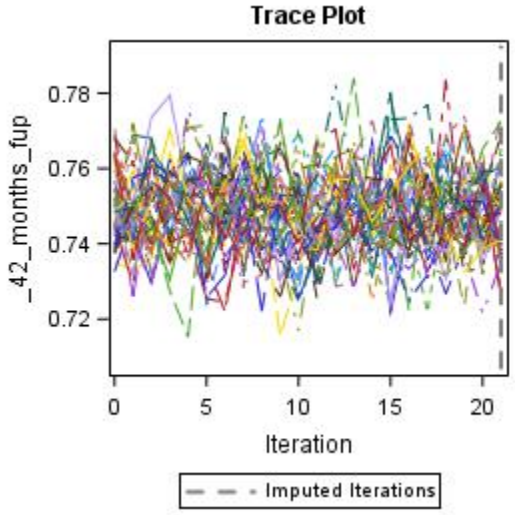
Supplementary Figure 22: Trace Plot for the imputation of EQ-5D utility score at 18 months follow-up across N Imputations (P2b_EQ5D_PrimaryImputation)



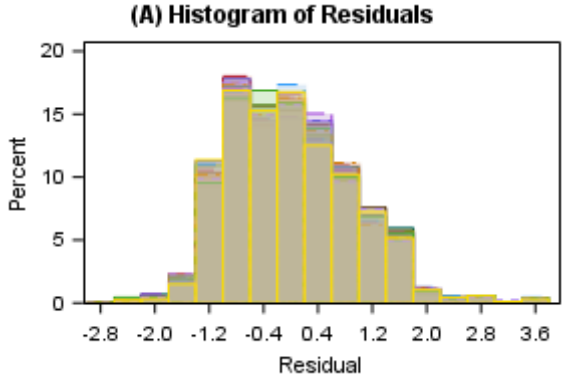
Supplementary Figure 23: Trace Plot for the imputation of EQ-5D utility score at 30 months follow-up across N Imputations (P2b_EQ5D_PrimaryImputation)



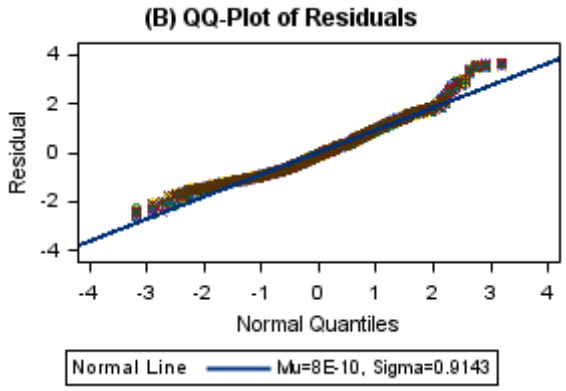
Supplementary Figure 24: Trace Plot for the imputation of EQ-5D utility score at 42 months follow-up across N Imputations (P2b_EQ5D_PrimaryImputation)



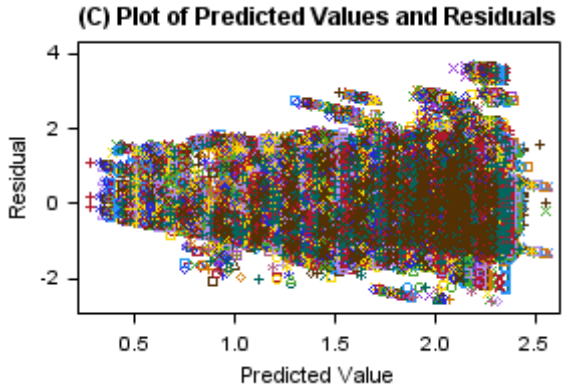
Supplementary Figure 25: Finite Mixture Model Diagnostics - QALYs Primary Analysis – (A) Histogram of Residuals (P2c_QALYs_PrimaryAnalysis)



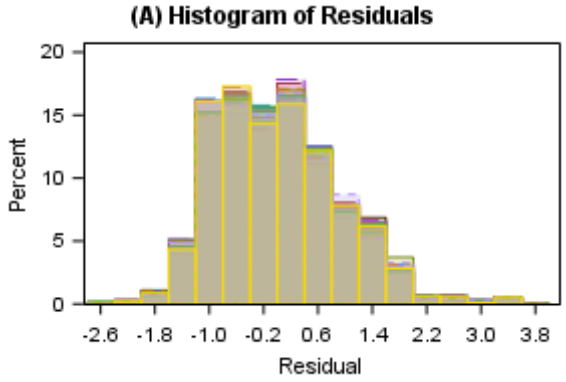
Supplementary Figure 26: Finite Mixture Model Diagnostics - QALYs Primary Analysis – (B) QQ-Plot of Residuals (P2c_QALYs_PrimaryAnalysis)



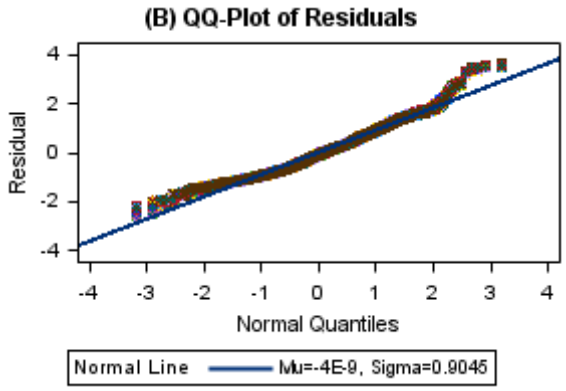
Supplementary Figure 27: Finite Mixture Model Diagnostics - QALYs Primary Analysis – (C) Plot of Predicted Values and Residuals (P2c_QALYs_PrimaryAnalysis)



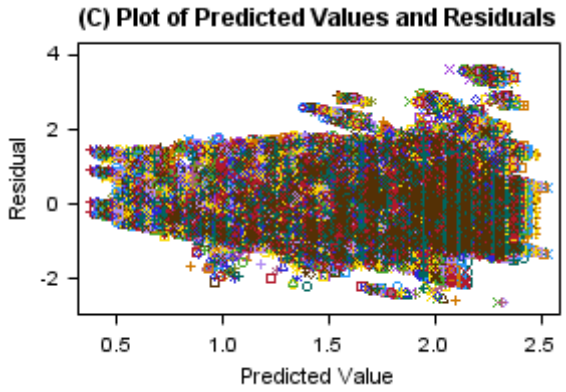
Supplementary Figure 28: Finite Mixture Model Diagnostics - QALY ITT Sensitivity Analysis – (A) Histogram of Residuals (P2d_QALYs_SensitivityAnalysis_ITT)



Supplementary Figure 29: Finite Mixture Model Diagnostics - QALY ITT Sensitivity Analysis – (B) QQ Plot of Residuals (P2d_QALYs_SensitivityAnalysis_ITT)



Supplementary Figure 30: Finite Mixture Model Diagnostics - QALY ITT Sensitivity Analysis – (C) Plot of Predicted Values and Residuals (P2d_QALYs_SensitivityAnalysis_ITT)



2.6 Secondary Time to Event Analysis

Supplementary Table 32: Piecewise Hazards Model Results for Time to Treatment Failure in the ITT population - 2 Intervals (S2a_TTF)

	Estimate	Standard Error	Hazard Ratio	95% Confidence Limit for Hazard Ratio	Test Statistic	P value
Intercept	-2.10	0.26	0.12	[0.07, 0.21]	.	.
Time Interval	.	.	.		68.59	<.001
Week 24 to end of follow-up vs. 0-24 weeks	-0.57	0.07	0.57	[0.49, 0.65]	.	.
Randomisation Allocation	.	.	.		24.35	<.001
Drug-Free Interval Strategy (DFIS) vs Conventional Continuation Strategy (CCS)	-0.34	0.07	0.71	[0.62, 0.82]	.	.
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	.		13.76	0.001
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	0.20	0.08	1.23	[1.05, 1.43]	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	0.56	0.16	1.75	[1.28, 2.39]	.	.
Randomised Under Stratification Factor: Sex	.	.	.		5.85	0.016

	Estimate	Standard Error	Hazard Ratio	95% Confidence Limit for Hazard Ratio	Test Statistic	P value
Female vs Male	0.18	0.08	1.20	[1.04, 1.40]	.	.
Randomised Under Stratification Factor: Age Group	.	.	.		1.17	0.279
>=60 vs <60	0.08	0.08	1.09	[0.93, 1.27]	.	.
Randomised Under Stratification Factor: Disease Status	.	.	.		0.79	0.374
Metastatic vs Locally advanced	-0.21	0.23	0.81	[0.51, 1.28]	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	.		0.73	0.393
Yes vs No	-0.08	0.10	0.92	[0.76, 1.11]	.	.
Randomised Under Stratification Factor: TKI Received	.	.	.		0.69	0.405
Pazopanib vs Sunitinib	0.06	0.07	1.06	[0.93, 1.21]	.	.

Supplementary Table 33: Piecewise Hazards Model Results for Time to Treatment Failure in the ITT population - 3 Intervals (S2a_TTF)

	Estimate	Standard Error	Hazard Ratio	95% Confidence Limit for Hazard Ratio	Test Statistic	P value
Intercept	-2.10	0.26	0.12	[0.07, 0.21]	.	.
End of Average Treatment Break Length to end of follow-up vs. 0-24 weeks	-0.62	0.08	0.54	[0.46, 0.62]	.	.
Time Interval	.	.	.		71.39	<.001
Week 24 to End of Average Treatment Break Length vs. 0-24 weeks	-0.42	0.10	0.65	[0.54, 0.80]	.	.
Randomisation Allocation	.	.	.		22.80	<.001
Drug-Free Interval Strategy (DFIS) vs Conventional Continuation Strategy (CCS)	-0.33	0.07	0.72	[0.63, 0.82]	.	.
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	.		13.58	0.001
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	0.20	0.08	1.22	[1.05, 1.42]	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	0.56	0.16	1.75	[1.28, 2.39]	.	.
Randomised Under Stratification Factor: Sex	.	.	.		5.81	0.016

	Estimate	Standard Error	Hazard Ratio	95% Confidence Limit for Hazard Ratio	Test Statistic	P value
Female vs Male	0.18	0.08	1.20	[1.03, 1.39]	.	.
Randomised Under Stratification Factor: Age Group	.	.	.		1.09	0.297
>=60 vs <60	0.08	0.08	1.08	[0.93, 1.26]	.	.
Randomised Under Stratification Factor: Disease Status	.	.	.		0.79	0.374
Metastatic vs Locally advanced	-0.21	0.23	0.81	[0.51, 1.28]	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	.		0.63	0.428
Yes vs No	-0.08	0.10	0.93	[0.77, 1.12]	.	.
Randomised Under Stratification Factor: TKI Received	.	.	.		0.74	0.389
Pazopanib vs Sunitinib	0.06	0.07	1.06	[0.93, 1.21]	.	.

Supplementary Table 34: Piecewise Hazards Model Results for Progression-Free Survival in the ITT population - 2 Intervals (S3_PFS)

	Estimate	Standard Error	Hazard Ratio	95% Confidence Limit for Hazard Ratio	Test Statistic	P value
Intercept	-2.25	0.26	0.11	[0.06, 0.18]	.	.
Time Interval	.	.	.		23.39	<.001
Week 24 to end of follow-up vs. 0-24 weeks	0.36	0.07	1.44	[1.24, 1.66]	.	.
Randomisation Allocation	.	.	.		23.62	<.001
Drug-Free Interval Strategy (DFIS) vs Conventional Continuation Strategy (CCS)	0.33	0.07	1.40	[1.22, 1.60]	.	.
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	.		10.46	0.005
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	0.18	0.08	1.19	[1.02, 1.40]	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	0.51	0.16	1.67	[1.21, 2.30]	.	.
Randomised Under Stratification Factor: Sex	.	.	.		4.37	0.036

	Estimate	Standard Error	Hazard Ratio	95% Confidence Limit for Hazard Ratio	Test Statistic	P value
Female vs Male	-0.16	0.08	0.85	[0.73, 0.99]	.	.
Randomised Under Stratification Factor: Age Group	.	.	.		0.59	0.441
>=60 vs <60	-0.06	0.08	0.94	[0.81, 1.10]	.	.
Randomised Under Stratification Factor: Disease Status	.	.	.		7.77	0.005
Metastatic vs Locally advanced	-0.63	0.23	0.53	[0.34, 0.83]	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	.		6.83	0.009
Yes vs No	-0.26	0.10	0.77	[0.64, 0.94]	.	.
Randomised Under Stratification Factor: TKI Received	.	.	.		0.05	0.829
Pazopanib vs Sunitinib	-0.01	0.07	0.99	[0.86, 1.13]	.	.

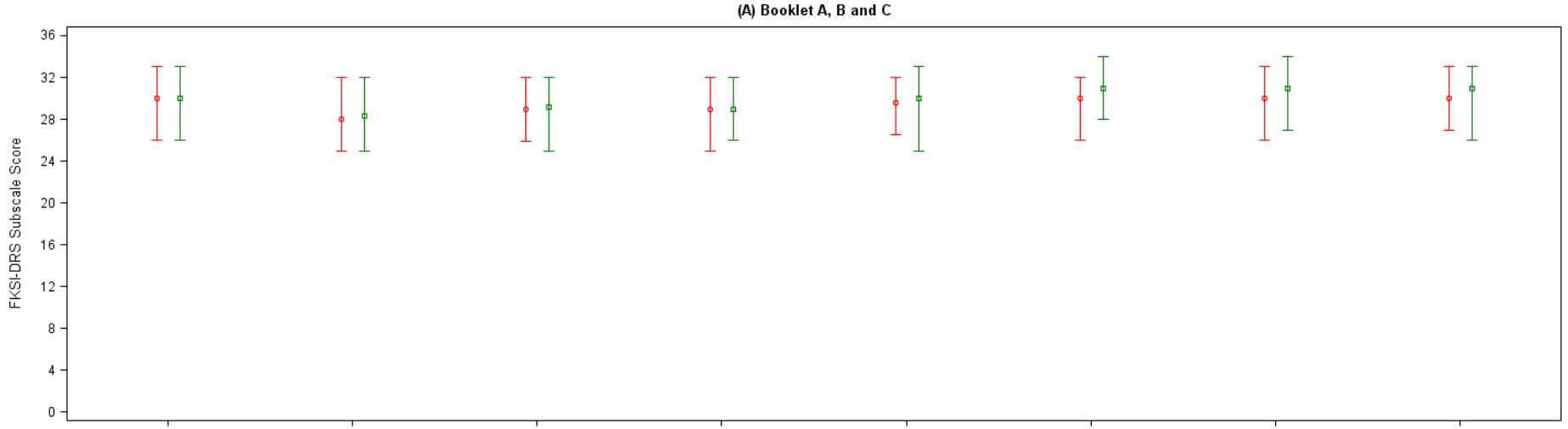
Supplementary Table 35: Piecewise Hazards Model Results for Progression-Free Survival in the ITT population - 3 Intervals (S3_PFS)

	Estimate	Standard Error	Hazard Ratio	95% Confidence Limit for Hazard Ratio	Test Statistic	P value
Intercept	-2.35	0.26	0.10	[0.06, 0.16]	.	.
End of Average Treatment Break Length to end of follow-up vs. 0-24 weeks	0.14	0.08	1.15	[0.97, 1.35]	.	.
Time Interval	.	.	.		80.44	<.001
Week 24 to End of Average Treatment Break Length vs. 0-24 weeks	0.73	0.09	2.08	[1.75, 2.46]	.	.
Randomisation Allocation	.	.	.		17.30	<.001
Drug-Free Interval Strategy (DFIS) vs Conventional Continuation Strategy (CCS)	0.29	0.07	1.33	[1.16, 1.52]	.	.
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	.		11.71	0.003
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	0.17	0.08	1.19	[1.02, 1.39]	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	0.55	0.16	1.73	[1.26, 2.39]	.	.
Randomised Under Stratification Factor: Sex	.	.	.		3.01	0.082
Female vs Male	-0.13	0.08	0.88	[0.75, 1.02]	.	.

	Estimate	Standard Error	Hazard Ratio	95% Confidence Limit for Hazard Ratio	Test Statistic	P value
Randomised Under Stratification Factor: Age Group	.	.	.		0.56	0.456
>=60 vs <60	-0.06	0.08	0.94	[0.81, 1.10]	.	.
Randomised Under Stratification Factor: Disease Status	.	.	.		5.65	0.017
Metastatic vs Locally advanced	-0.54	0.23	0.58	[0.37, 0.91]	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	.		4.64	0.031
Yes vs No	-0.21	0.10	0.81	[0.67, 0.98]	.	.
Randomised Under Stratification Factor: TKI Received	.	.	.		0.09	0.761
Pazopanib vs Sunitinib	-0.02	0.07	0.98	[0.86, 1.12]	.	.

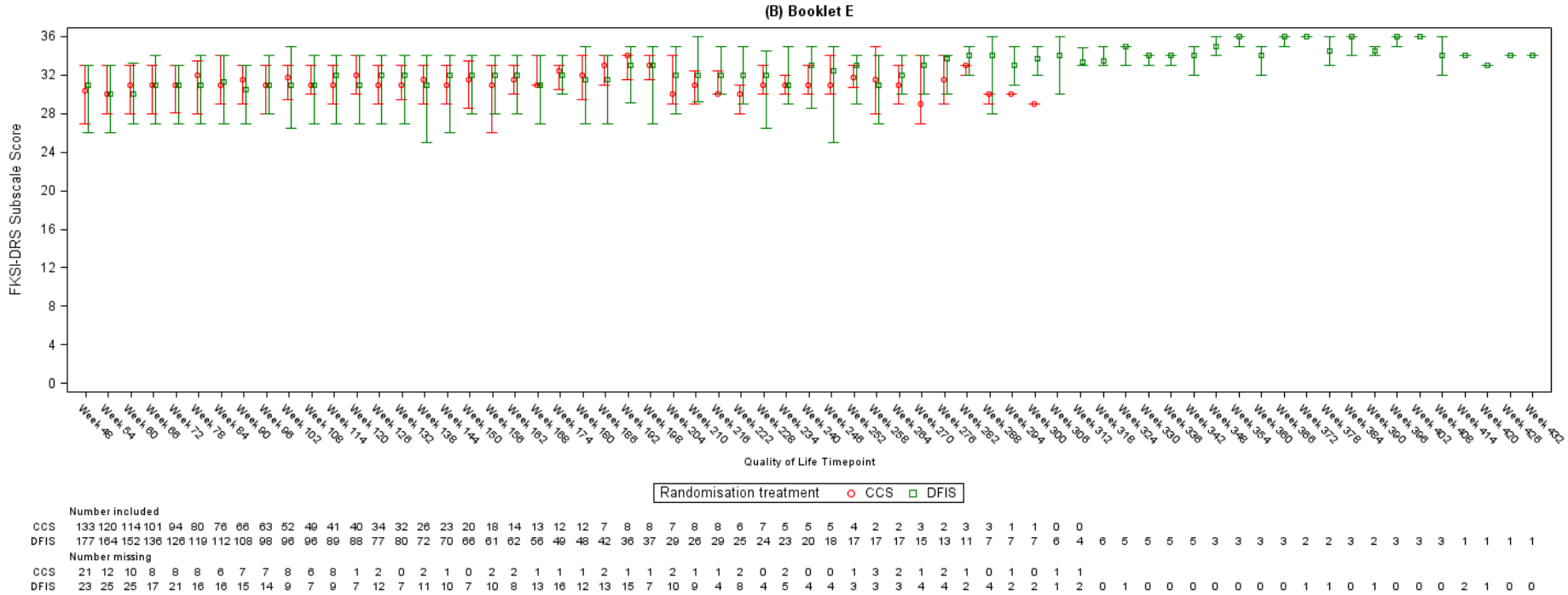
2.7 Additional Information on the Secondary QoL Analysis

Supplementary Figure 31: FSKI-DRS Subscale Score Summary Statistics, Median and Interquartile Range, by Randomisation Allocation – (A) Booklets A, B and C



Number included								
CCS	436	374	307	265	232	200	178	146
DFIS	446	379	322	270	230	190	191	182
Number missing								
CCS	0	55	62	39	39	34	30	26
DFIS	0	61	67	48	50	54	40	33

Supplementary Figure 32: FSKI-DRS Subscale Score Summary Statistics, Median and Interquartile Range, by Randomisation Allocation – (B) Booklet E

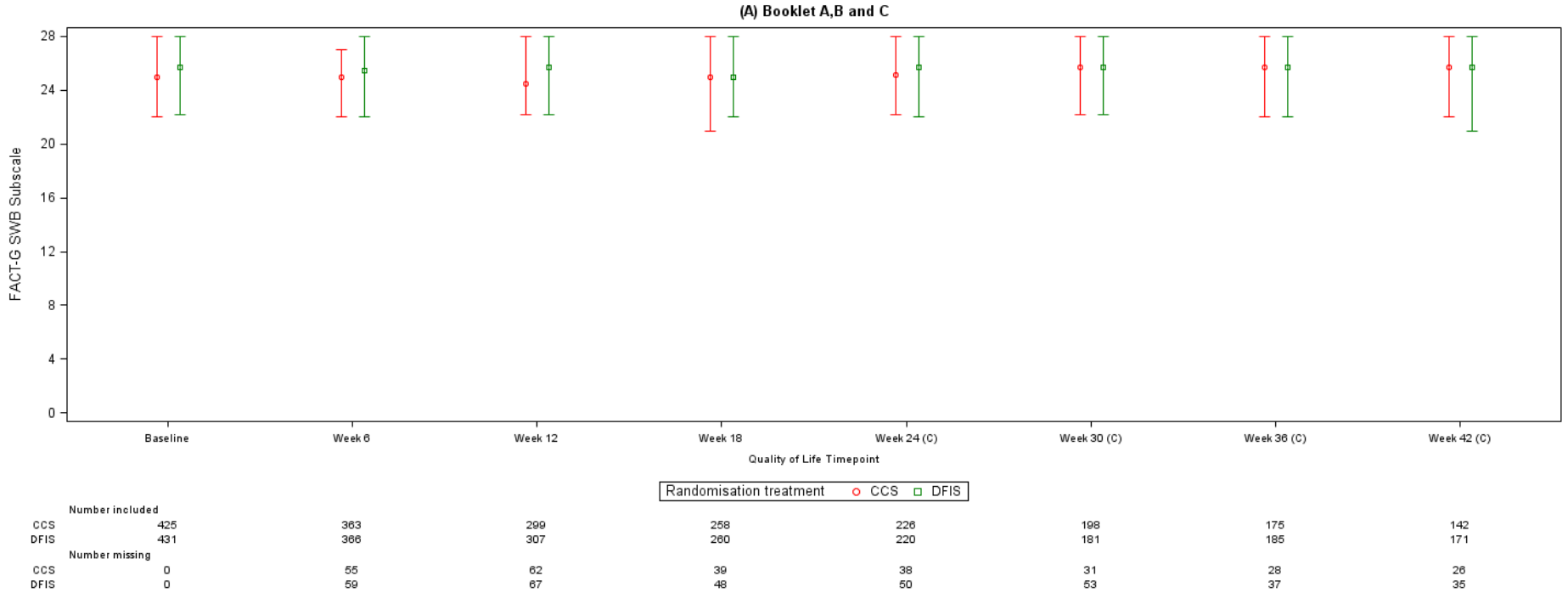


Supplementary Table 36: Results of mixed modelling for the FKIS-DRS score, only including timepoints where both strategies have results (Week 312) (S6_FKSI15)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 7426	.	.	.	.	.
Intercept	11.28	1.28	.	.	.
Quality of Life Timepoint	0.03	0.02	1, 645	0.24	0.622
FKSI-DRS Score at Baseline	0.56	0.03	1, 5996	460.40	<.001
Randomisation treatment	.	.	1, 5996	6.38	0.012
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.68	0.27	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.07	0.02	1, 5996	8.34	0.004
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 5996	0.54	0.585
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	0.10	0.30	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-0.48	0.63	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 5996	0.45	0.502

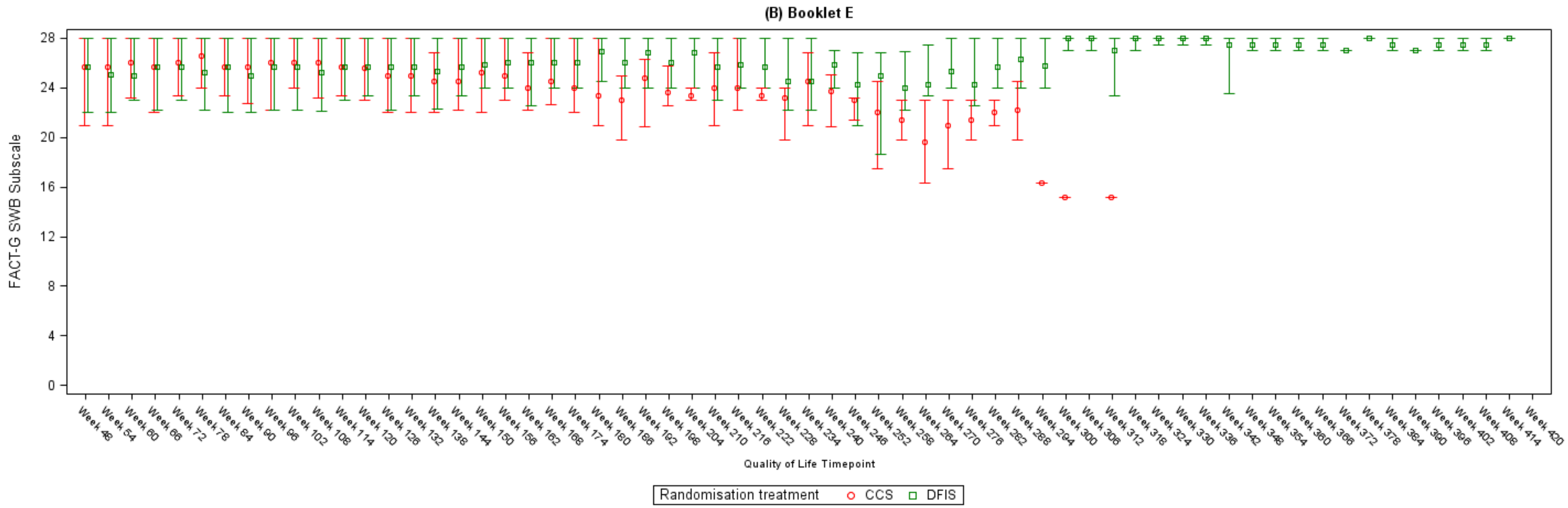
	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Female vs. Male	-0.20	0.30	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 5996	0.00	0.965
>=60vs. <60	-0.01	0.29	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 5996	0.59	0.442
Metastatic vs. Locally advanced	0.72	0.93	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 5996	0.42	0.519
Yes vs. No	-0.24	0.37	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 5996	5.99	0.014
Pazopanib vs. Sunitinib	-0.64	0.26	.	.	.

Supplementary Figure 33: FACT-G Social/Family Well-Being Subscale Summary Statistics, Median and Interquartile Range, by Randomisation Allocation - (A) Booklets A, B and C



Number included								
CCS	425	363	299	258	226	198	175	142
DFIS	431	366	307	260	220	181	185	171
Number missing								
CCS	0	55	62	39	38	31	28	26
DFIS	0	59	67	48	50	53	37	35

Supplementary Figure 34: FACT-G Social/Family Well-Being Subscale Summary Statistics, Median and Interquartile Range, by Randomisation Allocation - (B) Booklet E

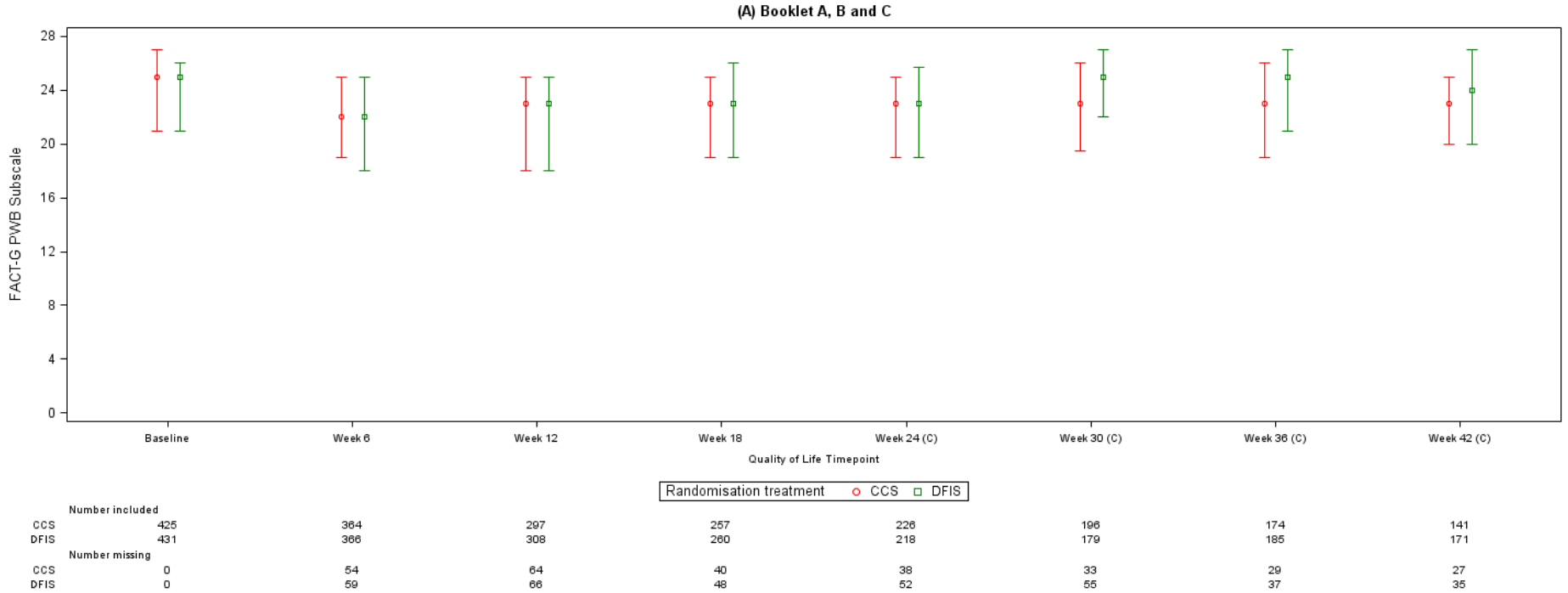


	Week 48	54	60	66	72	78	84	90	96	102	108	114	120	126	132	138	144	150	156	162	168
Number included																					
CCS	131	118	112	100	94	77	74	64	61	51	48	39	38	33	31	25	22	19	17	13	12
DFIS	169	158	144	130	121	113	107	101	94	89	92	85	86	73	78	68	67	64	58	60	54
Number missing																					
CCS	19	12	10	8	7	9	6	7	7	7	5	8	1	2	0	2	1	0	2	2	1
DFIS	22	22	26	16	19	16	15	16	13	12	7	9	5	13	6	12	10	7	11	8	13

	Week 174	180	186	192	198	204	210	216	222	228	234	240	246	252	258	264	270	276	282	288	294
Number included																					
CCS	11	11	7	8	8	6	7	7	5	6	4	4	4	3	2	2	3	2	2	2	1
DFIS	47	46	41	34	35	27	25	26	23	21	21	18	18	15	16	16	14	12	10	6	6
Number missing																					
CCS	1	1	1	0	0	2	1	1	2	0	2	0	0	1	2	1	0	1	1	0	0
DFIS	16	12	12	15	7	10	8	5	8	5	5	4	2	3	2	2	3	3	1	4	2

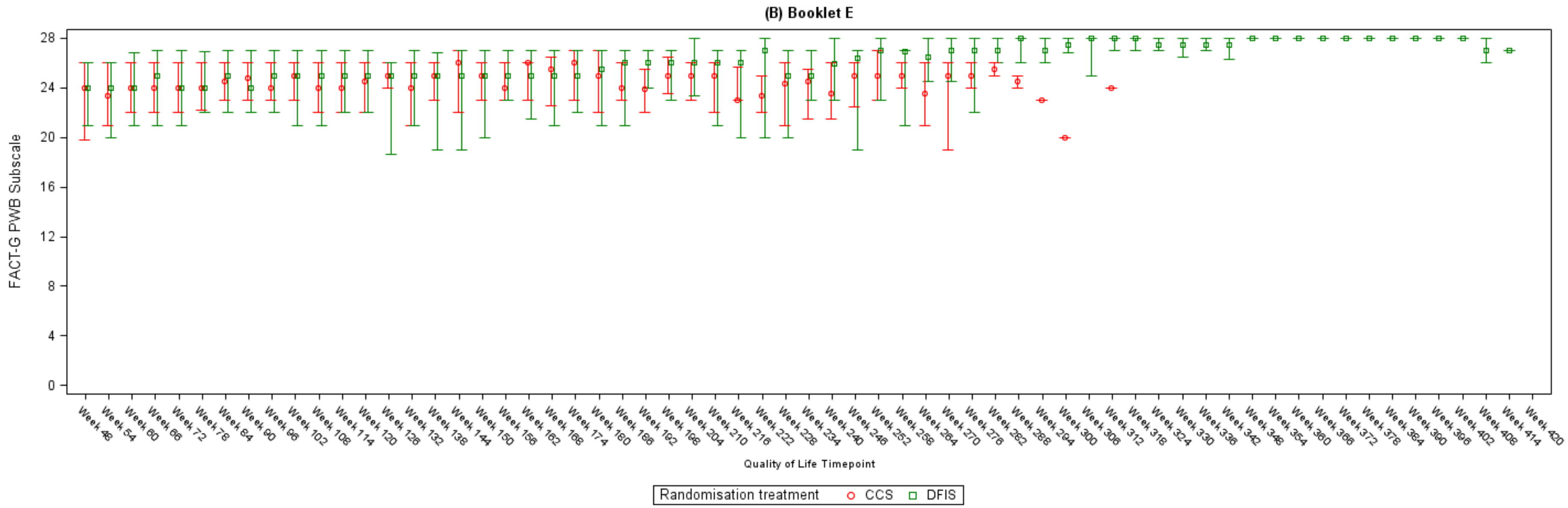
	Week 300	306	312	318	324	330	336	342	348	354	360	366	372	378	384	390	396	402	408	414	420
Number included																					
CCS	1	0	1																		
DFIS	6	5	3	5	4	4	4	4	2	2	2	2	1	1	2	1	2	2	2	1	0
Number missing																					
CCS	0	1	0																		
DFIS	2	1	2	0	1	0	0	0	0	0	0	0	1	1	0	1	0	0	0	1	1

Supplementary Figure 35: FACT-G Physical Well-Being Subscale Summary Statistics, Median and Interquartile Range, by Randomisation Allocation - (A) Booklets A, B and C



Number included								
CCS	425	364	297	257	226	196	174	141
DFIS	431	366	308	260	218	179	185	171
Number missing								
CCS	0	54	64	40	38	33	29	27
DFIS	0	59	66	48	52	55	37	35

Supplementary Figure 36: FACT-G Physical Well-Being Subscale Summary Statistics, Median and Interquartile Range, by Randomisation Allocation - (B) Booklet E

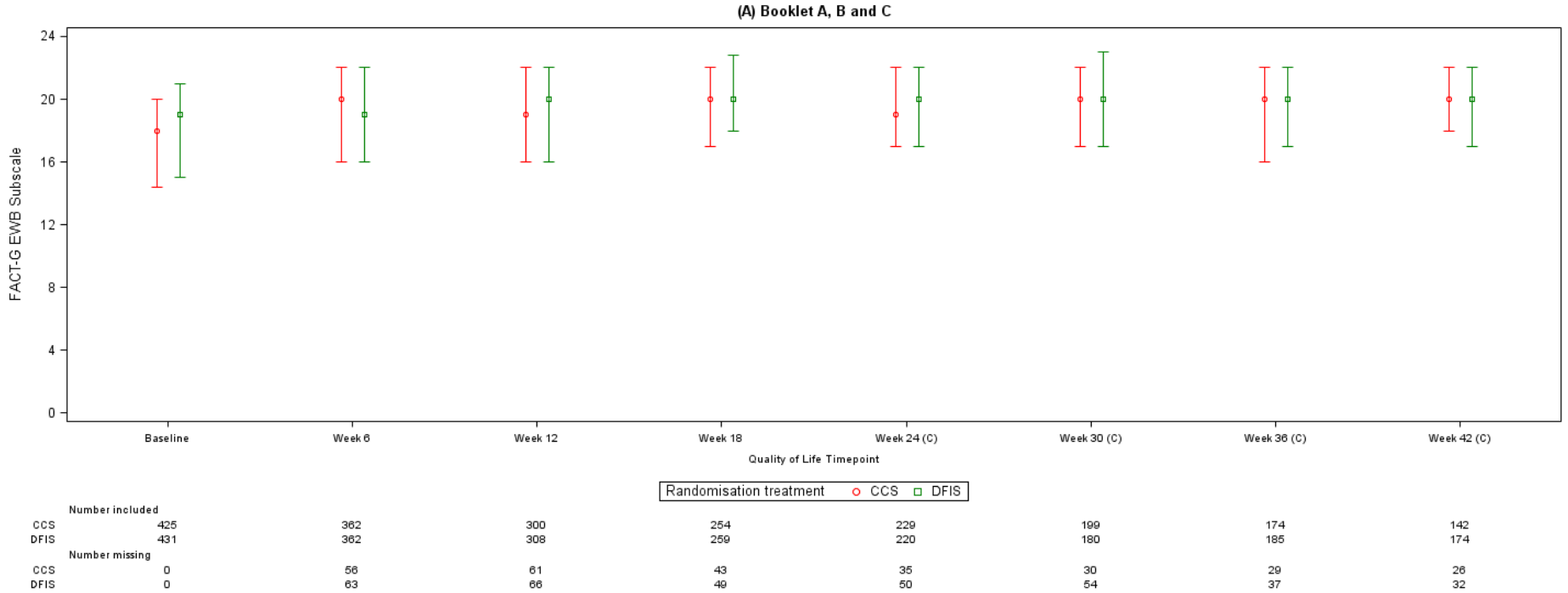


	Week 48	Week 54	Week 60	Week 66	Week 72	Week 78	Week 84	Week 90	Week 96	Week 102	Week 108	Week 114	Week 120	Week 126	Week 132	Week 138	Week 144	Week 150	Week 156	Week 162	Week 168
Number included																					
CCS	131	117	113	101	94	78	74	64	61	51	47	39	38	33	31	25	22	19	17	13	12
DFIS	168	157	144	130	121	112	106	100	94	88	92	85	86	73	77	69	67	64	59	60	54
Number missing																					
CCS	19	13	9	7	7	8	6	7	7	7	6	8	1	2	0	2	1	0	2	2	1
DFIS	23	23	26	16	19	17	16	17	13	13	7	9	5	13	7	11	10	7	10	8	13

	Week 174	Week 180	Week 186	Week 192	Week 198	Week 204	Week 210	Week 216	Week 222	Week 228	Week 234	Week 240	Week 246	Week 252	Week 258	Week 264	Week 270	Week 276	Week 282	Week 288	Week 294
Number included																					
CCS	11	11	7	8	8	6	7	7	5	6	4	4	4	3	2	2	3	2	2	2	1
DFIS	47	46	41	34	35	27	25	26	23	21	21	18	18	15	16	16	14	12	9	6	6
Number missing																					
CCS	1	1	1	0	0	2	1	1	2	0	2	0	0	1	2	1	0	1	1	0	0
DFIS	16	12	12	15	7	10	8	5	8	5	5	4	2	3	2	2	3	3	2	4	2

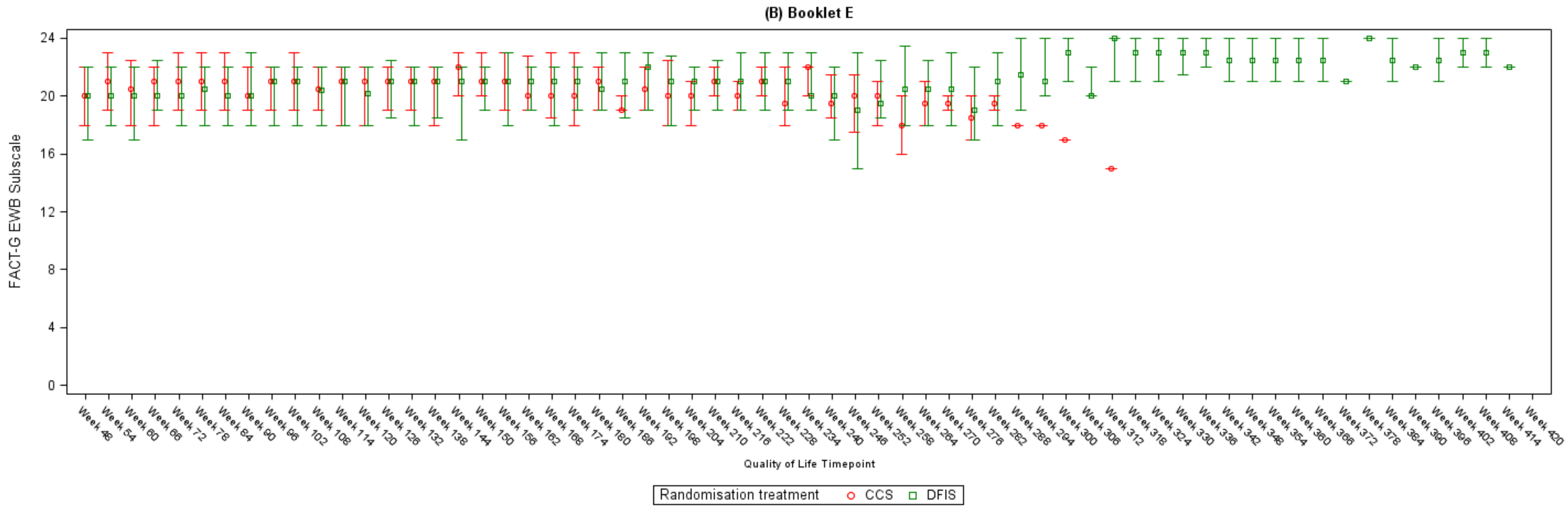
	Week 300	Week 306	Week 312	Week 318	Week 324	Week 330	Week 336	Week 342	Week 348	Week 354	Week 360	Week 366	Week 372	Week 378	Week 384	Week 390	Week 396	Week 402	Week 408	Week 414	Week 420
Number included																					
CCS	1	0	1																		
DFIS	6	5	3	5	4	4	4	4	2	2	2	2	1	1	2	1	2	2	2	1	0
Number missing																					
CCS	0	1	0																		
DFIS	2	1	2	0	1	0	0	0	0	0	0	0	1	1	0	1	0	0	0	1	1

Supplementary Figure 37: FACT-G Emotional Well-Being Subscale Summary Statistics, Median and Interquartile Range, by Randomisation Allocation - (A) Booklets A, B and C



Number included								
CCS	425	362	300	254	229	199	174	142
DFIS	431	362	308	259	220	180	185	174
Number missing								
CCS	0	56	61	43	35	30	29	26
DFIS	0	63	66	49	50	54	37	32

Supplementary Figure 38: FACT-G Emotional Well-Being Subscale Summary Statistics, Median and Interquartile Range, by Randomisation Allocation - (B) Booklet E

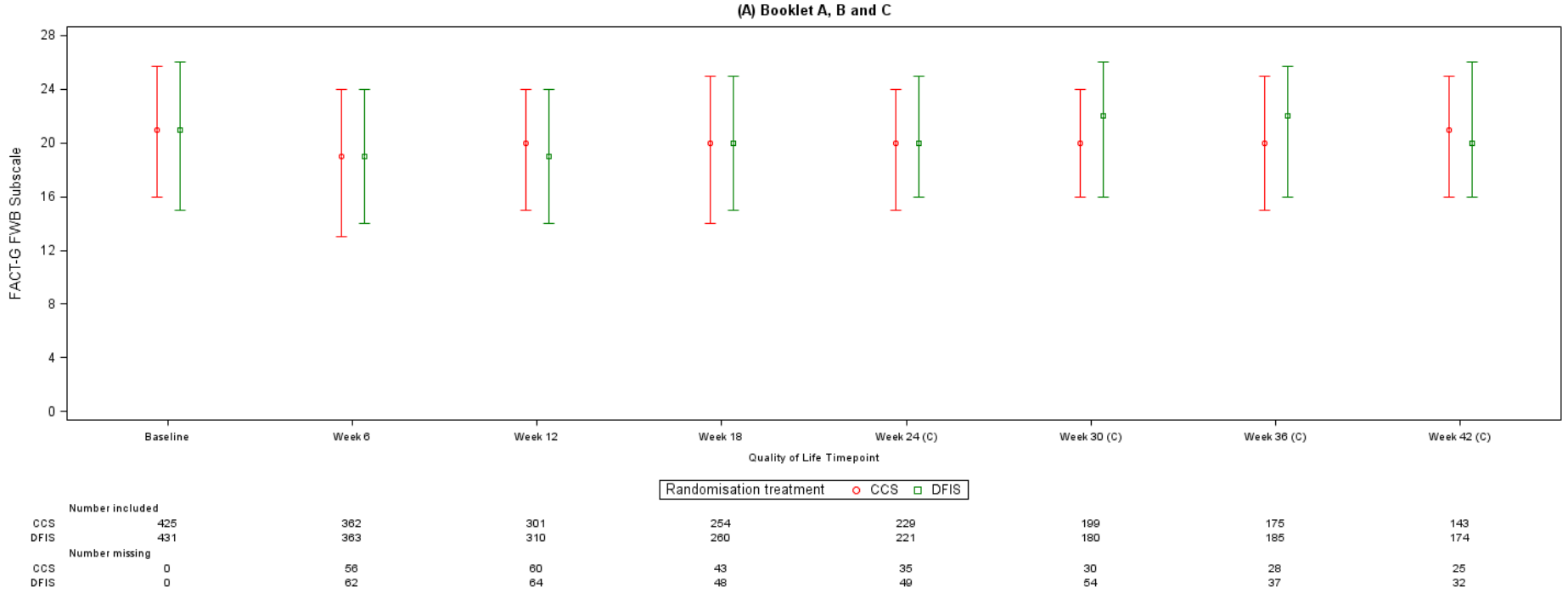


	Week 48	Week 54	Week 60	Week 66	Week 72	Week 78	Week 84	Week 90	Week 96	Week 102	Week 108	Week 114	Week 120	Week 126	Week 132	Week 138	Week 144	Week 150	Week 156	Week 162	Week 168
Number included																					
CCS	130	118	112	99	93	79	74	64	61	51	48	38	37	33	29	25	22	19	17	13	12
DFIS	170	154	143	128	119	114	106	100	94	91	91	85	84	72	76	68	66	64	58	58	53
Number missing																					
CCS	20	12	10	9	8	7	6	7	7	7	5	9	2	2	2	2	1	0	2	2	1
DFIS	21	26	27	18	21	15	16	17	13	10	8	9	7	14	8	12	11	7	11	10	14

	Week 174	Week 180	Week 186	Week 192	Week 198	Week 204	Week 210	Week 216	Week 222	Week 228	Week 234	Week 240	Week 246	Week 252	Week 258	Week 264	Week 270	Week 276	Week 282	Week 288	Week 294
Number included																					
CCS	11	11	7	8	8	6	7	7	5	6	4	4	4	3	2	2	2	2	2	2	1
DFIS	48	46	40	34	35	27	24	26	23	22	21	18	18	16	16	16	14	12	10	6	7
Number missing																					
CCS	1	1	1	0	0	2	1	1	2	0	2	0	0	1	2	1	1	1	1	0	0
DFIS	15	12	13	15	7	10	9	5	8	4	5	4	2	2	2	2	3	3	1	4	1

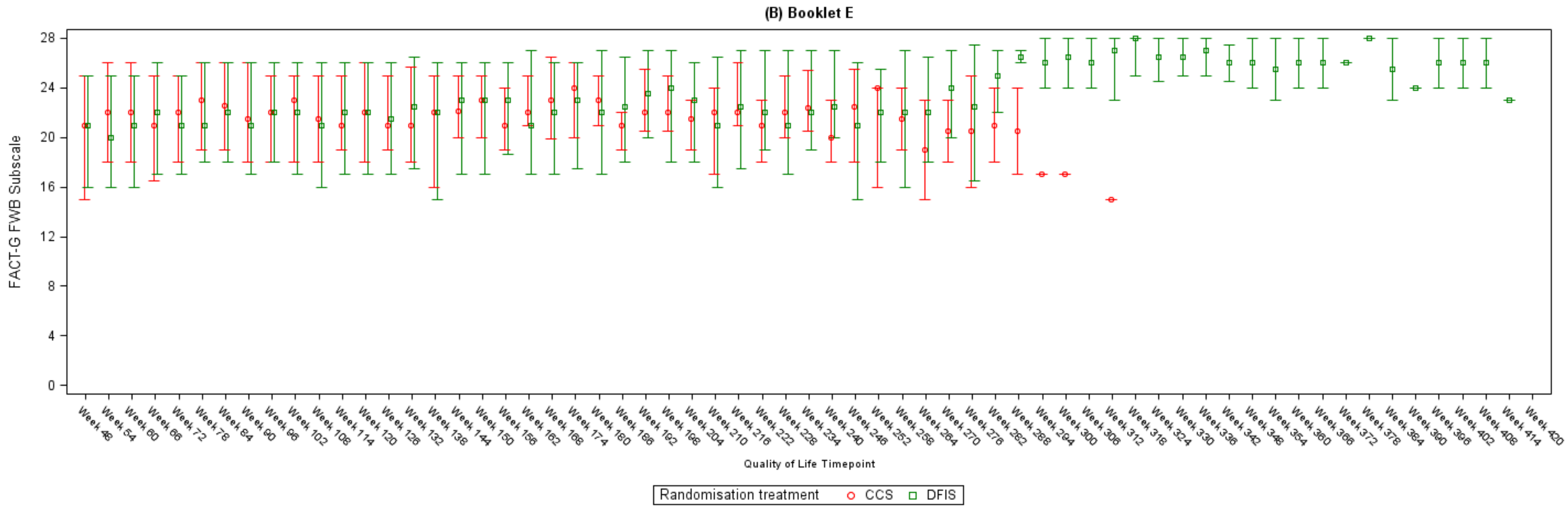
	Week 300	Week 306	Week 312	Week 318	Week 324	Week 330	Week 336	Week 342	Week 348	Week 354	Week 360	Week 366	Week 372	Week 378	Week 384	Week 390	Week 396	Week 402	Week 408	Week 414	Week 420
Number included																					
CCS	1	0	1																		
DFIS	6	5	3	5	4	4	4	4	2	2	2	2	1	1	2	1	2	2	2	1	0
Number missing																					
CCS	0	1	0																		
DFIS	2	1	2	0	1	0	0	0	0	0	0	0	1	1	0	1	0	0	0	1	1

Supplementary Figure 39: FACT-G Functional Well-being Subscale Summary Statistics, Median and Interquartile Range, by Randomisation Allocation - (A) Booklets A, B and C



Number included								
CCS	425	362	301	254	229	199	175	143
DFIS	431	363	310	260	221	180	185	174
Number missing								
CCS	0	56	60	43	35	30	28	25
DFIS	0	62	64	48	49	54	37	32

Supplementary Figure 40: FACT-G Functional Well-being Subscale Summary Statistics, Median and Interquartile Range, by Randomisation Allocation - (B) Booklet E



	48	54	60	66	72	78	84	90	96	102	108	114	120	126	132	138
Number included																
CCS	130	118	111	100	93	79	74	64	61	51	48	39	37	33	29	25
DFIS	169	156	144	130	121	114	106	100	95	91	92	85	85	72	76	67
Number missing																
CCS	20	12	11	8	8	7	6	7	7	7	5	8	2	2	2	2
DFIS	22	24	26	16	19	15	16	17	12	10	7	9	6	14	8	13

	144	150	156	162	168	174	180	186	192	198	204	210	216	222	228	234
Number included																
CCS	22	19	17	13	12	11	11	7	8	8	6	7	7	5	6	4
DFIS	66	64	58	59	53	48	46	40	34	35	27	24	26	23	22	21
Number missing																
CCS	1	0	2	2	1	1	1	1	0	0	2	1	1	2	0	2
DFIS	11	7	11	9	14	15	12	13	15	7	10	9	5	8	4	5

	240	246	252	258	264	270	276	282	288	294	300	306	312	318	324	330
Number included																
CCS	4	4	3	2	2	2	2	2	2	1	1	0	1			
DFIS	18	18	16	15	16	14	12	10	6	7	6	5	3	5	4	4
Number missing																
CCS	0	0	1	2	1	1	1	1	0	0	0	1	0			
DFIS	4	2	2	3	2	3	3	1	4	1	2	1	2	0	1	0

	336	342	348	354	360	366	372	378	384	390	396	402	408	414	420
Number included															
CCS															
DFIS	4	4	2	2	2	2	1	1	2	1	2	2	2	1	0
Number missing															
CCS															
DFIS	0	0	0	0	0	0	1	1	0	1	0	0	0	1	1

Supplementary Table 37: Results of mixed modelling for the FACT-G Physical Well-Being Subscale, only including timepoints were both strategies have results (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 7125	.	.	.	.	.
Intercept	6.94	1.32	.	.	.
Quality of Life Timepoint	0.04	0.02	1, 625	1.25	0.265
FACT-G Physical Well-Being Subscale at Baseline	0.57	0.03	1, 5739	334.21	<.001
Randomisation treatment	.	.	1, 5739	4.25	0.039
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.59	0.29	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.05	0.02	1, 5739	5.71	0.017
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 5739	1.59	0.203
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.31	0.32	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-1.18	0.67	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 5739	0.66	0.417

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Female vs. Male	-0.25	0.31	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 5739	2.94	0.087
>=60vs. <60	0.53	0.31	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 5739	1.67	0.196
Metastatic vs. Locally advanced	1.29	1.00	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 5739	1.51	0.219
Yes vs. No	-0.47	0.39	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 5739	4.18	0.041
Pazopanib vs. Sunitinib	-0.57	0.28	.	.	.

Supplementary Table 38: Results of mixed modelling for the FACT-G Social/Family Well-Being Subscale, only including timepoints were both strategies have results (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 7139	.	.	.	.	.
Intercept	9.92	0.99	.	.	.
Quality of Life Timepoint	0.01	0.01	1, 624	0.28	0.598
FACT-G Social/Family Well-Being Subscale at Baseline	0.56	0.02	1, 5755	562.84	<.001
Randomisation treatment	.	.	1, 5755	1.62	0.204
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.28	0.22	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.03	0.02	1, 5755	3.31	0.069
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 5755	0.24	0.789
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.16	0.25	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-0.00	0.51	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 5755	0.09	0.766

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Female vs. Male	0.07	0.24	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 5755	1.84	0.175
>=60vs. <60	0.33	0.24	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 5755	0.85	0.356
Metastatic vs. Locally advanced	0.73	0.79	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 5755	0.16	0.687
Yes vs. No	-0.12	0.30	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 5755	4.13	0.042
Pazopanib vs. Sunitinib	-0.44	0.22	.	.	.

Supplementary Table 39: Results of mixed modelling for the FACT-G Emotional Well-Being Subscale, only including timepoints were both strategies have results (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 7115	.	.	.	.	.
Intercept	8.77	0.89	.	.	.
Quality of Life Timepoint	0.05	0.01	1, 623	5.70	0.017
FACT-G Emotional Well-Being Subscale at Baseline	0.56	0.02	1, 5735	599.15	<.001
Randomisation treatment	.	.	1, 5735	0.34	0.562
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.12	0.20	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.06	0.02	1, 5735	13.21	<.001
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 5735	1.69	0.185
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.41	0.23	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-0.54	0.47	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 5735	2.69	0.101

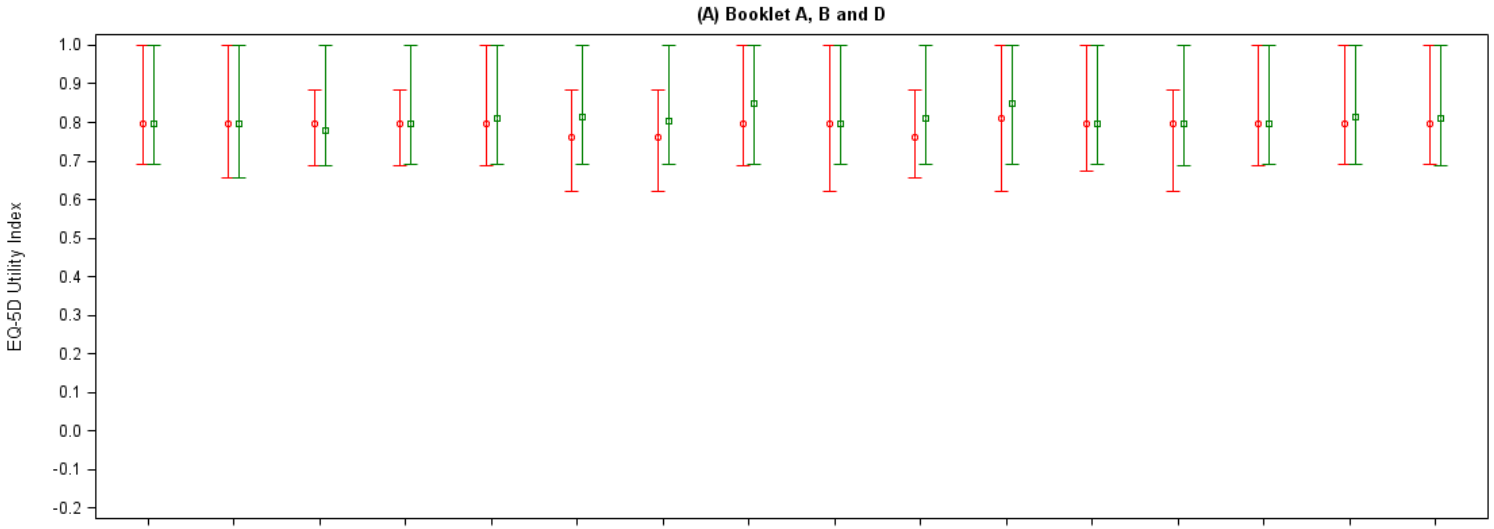
	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Female vs. Male	-0.37	0.23	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 5735	2.75	0.097
>=60vs. <60	0.38	0.23	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 5735	0.50	0.482
Metastatic vs. Locally advanced	0.51	0.72	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 5735	1.94	0.163
Yes vs. No	-0.39	0.28	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 5735	0.07	0.790
Pazopanib vs. Sunitinib	-0.05	0.20	.	.	.

Supplementary Table 40: Results of mixed modelling for the FACT-G Functional Well-Being Subscale, only including timepoints were both strategies have results (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 7132	.	.	.	.	.
Intercept	6.15	1.36	.	.	.
Quality of Life Timepoint	0.01	0.02	1, 625	2.62	0.106
FACT-G Functional Well-Being Subscale at Baseline	0.62	0.03	1, 5750	577.99	<.001
Randomisation treatment	.	.	1, 5750	2.75	0.098
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.54	0.32	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.06	0.03	1, 5750	5.66	0.017
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 5750	2.94	0.053
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.66	0.36	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-1.67	0.75	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 5750	0.33	0.569

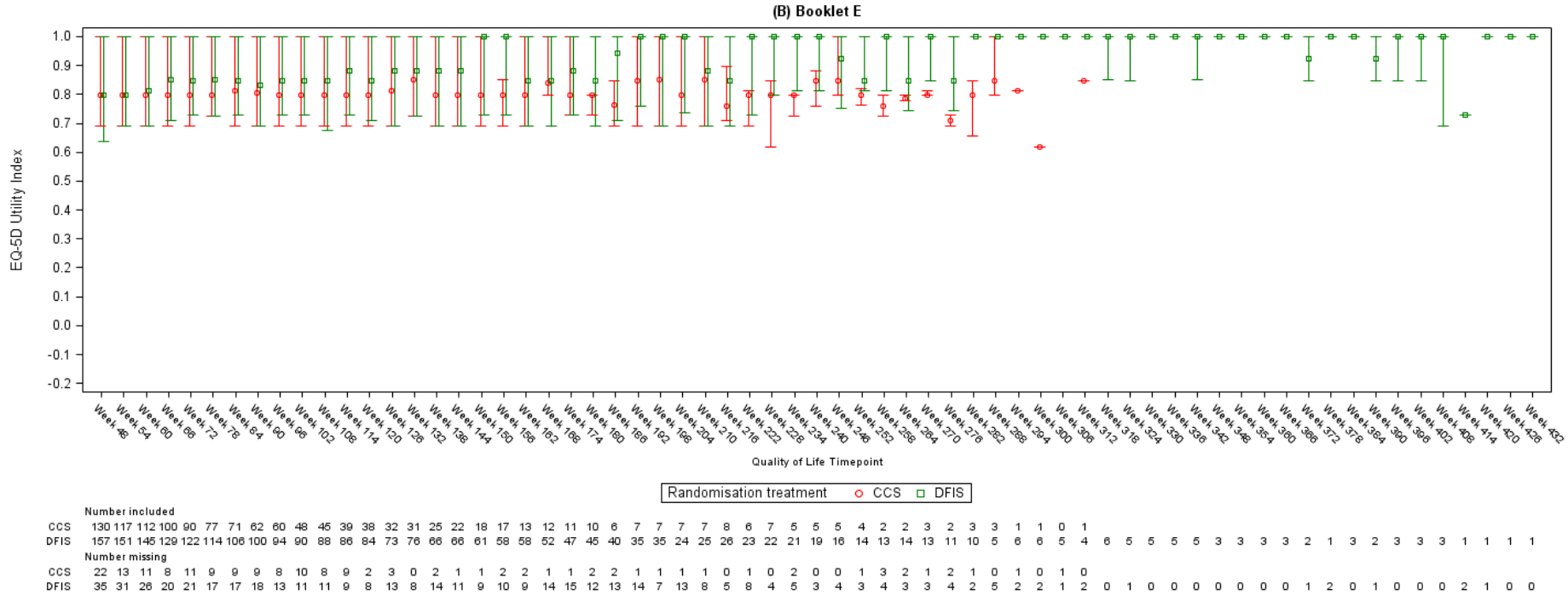
	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Female vs. Male	-0.20	0.36	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 5750	0.17	0.684
>=60vs. <60	0.14	0.36	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 5750	1.00	0.318
Metastatic vs. Locally advanced	1.14	1.14	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 5750	2.35	0.125
Yes vs. No	-0.68	0.44	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 5750	1.85	0.174
Pazopanib vs. Sunitinib	-0.43	0.32	.	.	.

Supplementary Figure 41: EQ-5D-3L Utility Index Summary Statistics, Median and Interquartile Range, by Randomisation Allocation – (A) Booklets A, B and D

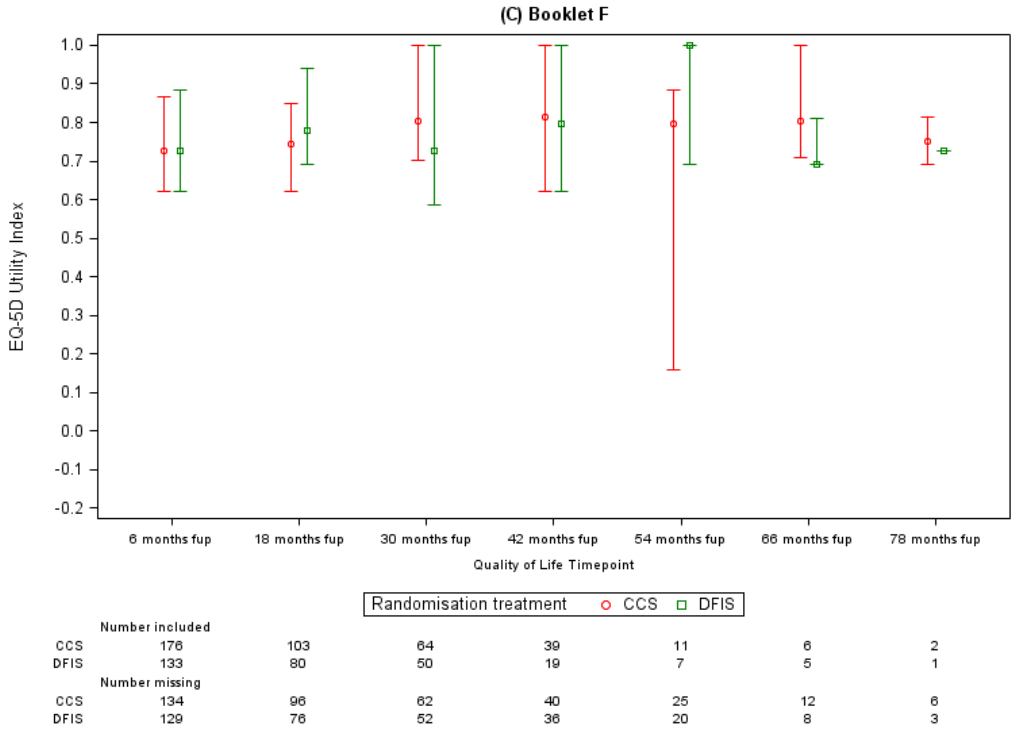


	Baseline	Week 6	Week 12	Week 18	Week 24	Week 26	Week 28	Week 30	Week 32	Week 34	Week 36	Week 38	Week 40	Week 42	Week 44	Week 46
Number included																
CCS	438	363	295	261	156	151	153	153	142	145	135	120	118	119	110	106
DFIS	431	361	309	256	163	165	166	163	161	158	154	147	146	135	131	130
Number missing																
CCS	0	68	74	43	114	82	80	80	64	61	71	50	52	51	42	46
DFIS	0	64	67	52	106	68	67	70	62	65	68	61	62	72	62	63

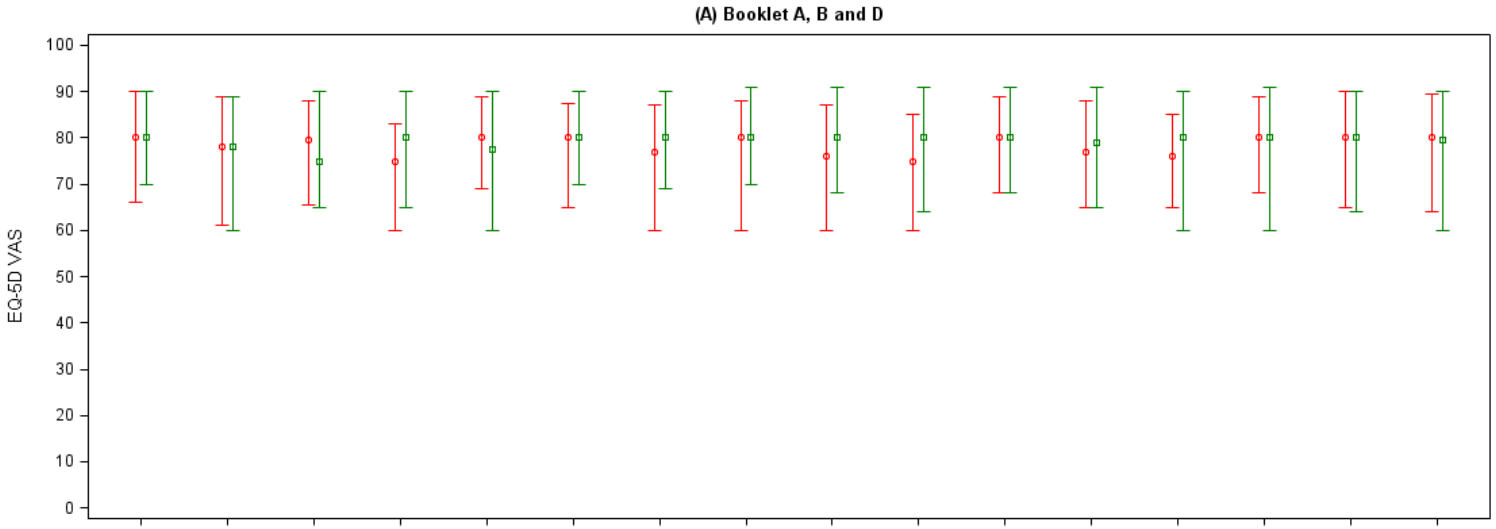
Supplementary Figure 42: EQ-5D-3L Utility Index Summary Statistics, Median and Interquartile Range, by Randomisation Allocation – (B) Booklet E



Supplementary Figure 43: EQ-5D-3L Utility Index Summary Statistics, Median and Interquartile Range, by Randomisation Allocation – (A) Booklet F

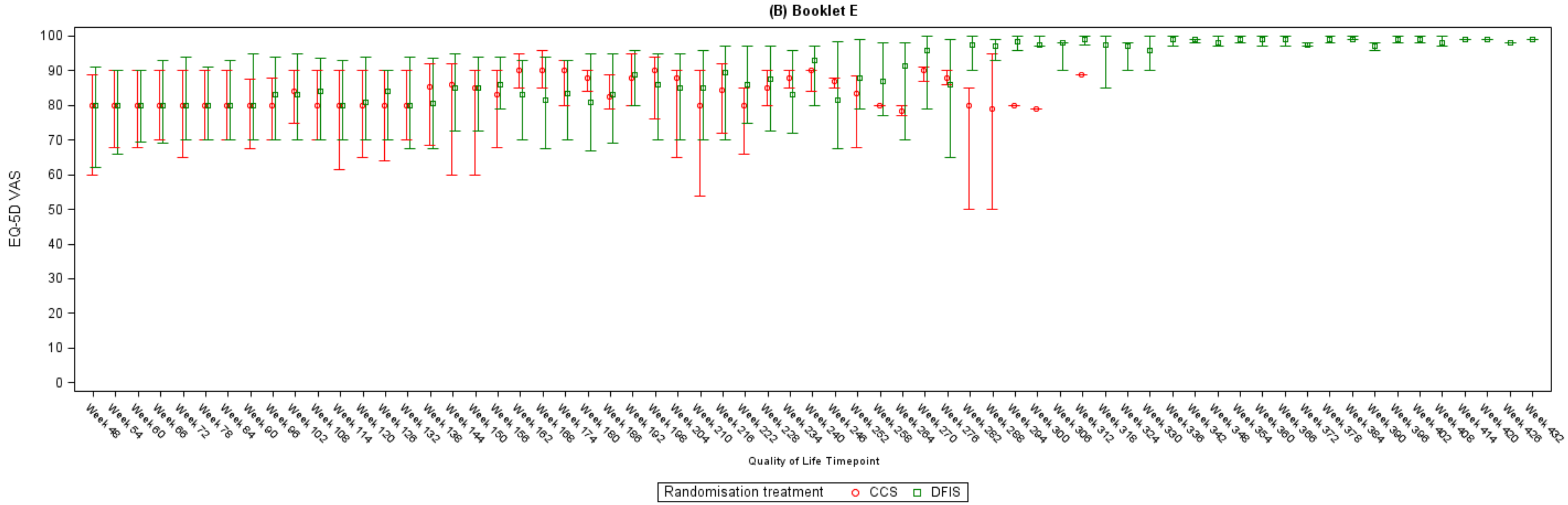


Supplementary Figure 44: EQ-5D-3L VAS Summary Statistics, Median and Interquartile Range, by Randomisation Allocation – (A) Booklets A, B and D



Number included																
CCS	405	351	292	247	153	152	151	149	141	143	131	119	118	118	109	104
DFIS	400	342	296	248	158	165	159	161	163	157	154	147	146	137	131	130
Number missing																
CCS	33	80	77	57	117	81	82	84	65	63	75	51	52	52	43	48
DFIS	31	83	80	60	111	68	74	72	60	66	68	61	62	70	62	63

Supplementary Figure 45: EQ-5D-3L VAS Summary Statistics, Median and Interquartile Range, by Randomisation Allocation – (B) Booklet E



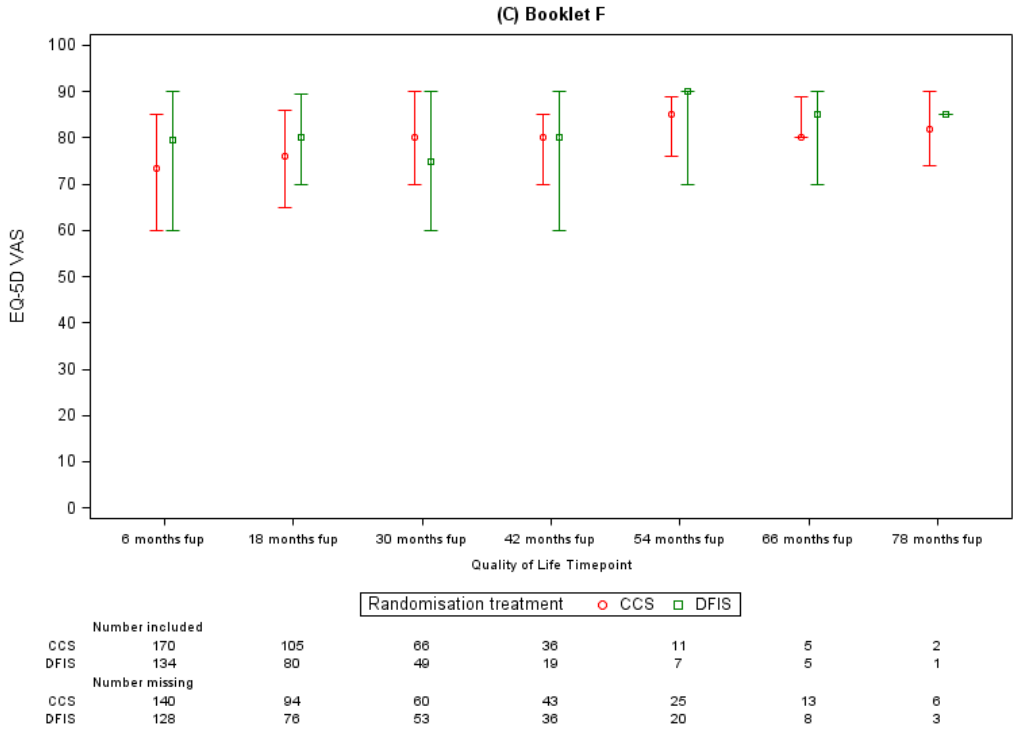
	Week 48	Week 54	Week 60	Week 66	Week 72	Week 78	Week 84	Week 90	Week 96	Week 102	Week 108	Week 114	Week 120	Week 126	Week 132	Week 138	Week 144
Number included																	
CCS	124	113	111	96	90	73	71	60	60	50	46	40	39	33	29	24	21
DFIS	155	148	144	131	122	116	108	102	93	89	88	85	80	69	76	68	64
Number missing																	
CCS	28	17	12	12	11	13	9	11	8	8	7	8	1	2	2	3	2
DFIS	37	34	27	18	21	15	15	16	14	12	11	10	12	17	8	12	13

	Week 150	Week 156	Week 162	Week 168	Week 174	Week 180	Week 186	Week 192	Week 198	Week 204	Week 210	Week 216	Week 222	Week 228	Week 234	Week 240	Week 246
Number included																	
CCS	19	17	13	11	11	11	6	7	7	7	7	8	6	7	5	5	5
DFIS	60	56	57	52	46	43	41	34	33	27	25	26	23	20	21	18	16
Number missing																	
CCS	0	2	2	2	1	1	2	1	1	1	1	0	1	0	2	0	0
DFIS	10	12	10	14	16	14	12	15	9	10	8	5	8	6	5	4	4

	Week 252	Week 258	Week 264	Week 270	Week 276	Week 282	Week 288	Week 294	Week 300	Week 306	Week 312	Week 318	Week 324	Week 330	Week 336	Week 342	Week 348
Number included																	
CCS	4	1	2	3	2	3	3	1	1	0	1						
DFIS	13	14	14	13	11	10	6	6	6	5	4	6	5	5	5	5	3
Number missing																	
CCS	1	4	2	1	2	1	0	1	0	1	0						
DFIS	4	3	3	3	4	2	4	2	2	1	2	0	1	0	0	0	0

	Week 354	Week 360	Week 366	Week 372	Week 378	Week 384	Week 390	Week 396	Week 402	Week 408	Week 414	Week 420	Week 426	Week 432
Number included														
CCS														
DFIS	3	3	3	2	2	3	2	3	3	3	1	1	1	1
Number missing														
CCS														
DFIS	0	0	0	1	1	0	1	0	0	0	2	1	0	0

Supplementary Figure 46: : EQ-5D-3L VAS Summary Statistics, Median and Interquartile Range, by Randomisation Allocation – (C) - Booklet F



2.8 Ancillary Analysis of Overall Survival

Supplementary Table 41: Piecewise Hazards Model Results for Overall Survival in the PP population (P1d_OS_SensitivityAnalysis_Piecewise)

	Estimate	Standard Error	Hazard Ratio	95% Confidence Limit for Hazard Ratio	Test Statistic	P value
Intercept	-3.96	0.32	0.02	[0.01, 0.04]	.	.
Time Interval	.	.	.		17.07	<.001
Week 24 to end of follow-up vs. 0-24 weeks	0.49	0.12	1.64	[1.30, 2.07]	.	.
Randomisation Allocation	.	.	.		0.69	0.407
Conventional Continuation Strategy (CCS) vs. Drug-Free Interval Strategy (DFIS)	-0.07	0.08	0.94	[0.80, 1.09]	.	.
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	.		30.34	<.001
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	0.32	0.09	1.38	[1.15, 1.66]	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	0.97	0.18	2.64	[1.86, 3.74]	.	.
Randomised Under Stratification Factor: Sex	.	.	.		0.11	0.743

	Estimate	Standard Error	Hazard Ratio	95% Confidence Limit for Hazard Ratio	Test Statistic	P value
Female vs Male	0.03	0.09	1.03	[0.86, 1.23]	.	.
Randomised Under Stratification Factor: Age Group	.	.	.		0.03	0.867
>=60 vs <60	0.02	0.09	1.02	[0.85, 1.21]	.	.
Randomised Under Stratification Factor: Disease Status	.	.	.		0.18	0.671
Metastatic vs Locally advanced	-0.12	0.27	0.89	[0.52, 1.52]	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	.		11.32	<.001
Yes vs No	-0.37	0.11	0.69	[0.56, 0.86]	.	.
Randomised Under Stratification Factor: TKI Received	.	.	.		0.36	0.550
Pazopanib vs Sunitinib	0.05	0.08	1.05	[0.90, 1.23]	.	.

Supplementary Table 42: Cox Regression Analysis Results for Overall Survival in the PP Population (P1f_OS_SensitivityAnalysis_CombMot)

	DF	Estimate	Standard Error	Hazard Ratio Estimate (HR)	95% CI for HR	Test Statistic	p-value
Randomisation treatment	1	.	.	.		0.45	0.503
Conventional Continuation Strategy (CCS) vs. Drug-Free Interval Strategy (DFIS)	1	-0.05	0.08	0.95	[0.81, 1.11]	.	.
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group Combined	1	.	.	.		12.73	<.001
Intermediate or Poor Risk (1 or more factors) vs. Favourable Risk (0 factors)	1	0.33	0.09	1.40	[1.16, 1.68]	.	.
Randomised Under Stratification Factor: Sex	1	.	.	.		0.04	0.840
Female vs. Male	1	0.02	0.09	1.02	[0.86, 1.21]	.	.
Randomised Under Stratification Factor: Age Group	1	.	.	.		0.24	0.628
>=60 vs. <60	1	0.04	0.09	1.04	[0.87, 1.25]	.	.
Randomised Under Stratification Factor: Disease Status	1	.	.	.		0.07	0.794

	DF	Estimate	Standard Error	Hazard Ratio Estimate (HR)	95% CI for HR	Test Statistic	p-value
Metastatic vs. Locally advanced	1	-0.07	0.27	0.93	[0.55, 1.59]	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	1	.	.	.		24.23	<.001
Yes vs. No	1	-0.50	0.10	0.61	[0.50, 0.74]	.	.
Randomised Under Stratification Factor: TKI Received	1	.	.	.		0.14	0.705
Pazopanib vs. Sunitinib	1	0.03	0.08	1.03	[0.88, 1.21]	.	.

Supplementary Table 43: Cox Regression Analysis Results for Overall Survival in the ITT Population (P1f_OS_SensitivityAnalysis_CombMot)

	DF	Estimate	Standard Error	Hazard Ratio Estimate (HR)	95% CI for HR	Test Statistic	p-value
Randomisation treatment	1	.	.	.		0.05	0.817
Conventional Continuation Strategy (CCS) vs. Drug-Free Interval Strategy (DFIS)	1	-0.02	0.08	0.98	[0.84, 1.14]	.	.

	DF	Estimate	Standard Error	Hazard Ratio Estimate (HR)	95% CI for HR	Test Statistic	p-value
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group Combined	1	.	.	.		15.25	<.001
Intermediate or Poor Risk (1 or more factors) vs. Favourable Risk (0 factors)	1	0.36	0.09	1.43	[1.19, 1.71]	.	.
Randomised Under Stratification Factor: Sex	1	.	.	.		0.04	0.834
Female vs. Male	1	0.02	0.09	1.02	[0.86, 1.21]	.	.
Randomised Under Stratification Factor: Age Group	1	.	.	.		0.33	0.565
>=60 vs. <60	1	0.05	0.09	1.05	[0.89, 1.25]	.	.
Randomised Under Stratification Factor: Disease Status	1	.	.	.		0.10	0.751
Metastatic vs. Locally advanced	1	-0.09	0.27	0.92	[0.54, 1.56]	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	1	.	.	.		22.39	<.001
Yes vs. No	1	-0.47	0.10	0.63	[0.52, 0.76]	.	.
Randomised Under Stratification Factor: TKI Received	1	.	.	.		0.05	0.815
Pazopanib vs. Sunitinib	1	0.02	0.08	1.02	[0.87, 1.19]	.	.

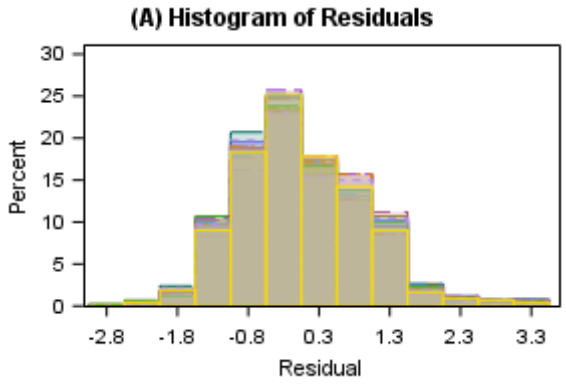
2.9 Ancillary Analysis of QALYs

Supplementary Table 44: Combined Marginal Effects of the Finite Mixture Model with Two Components for QALYs, from Week 24, in the PP population (P2e_QALYs_SensitivityAnalysis_24w)

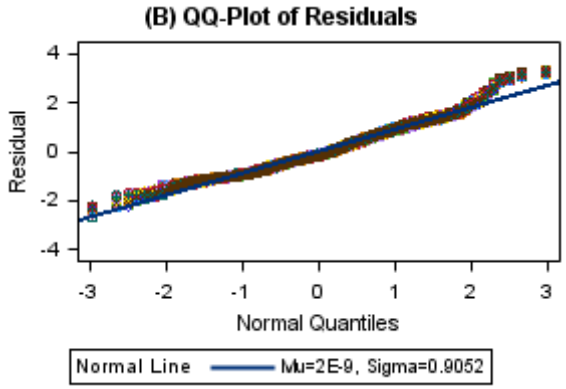
	Estimate	Standard Error	95% Confidence Interval
Intercept	2.34	0.56	(1.24, 3.44)
Randomisation Allocation	.	.	
DFIS vs CCS	0.27	0.13	(0.00, 0.53)
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	
Intermediate risk (1-2 factors) vs. Poor risk (> = 3 factors)	-0.36	0.55	(-1.43, 0.72)
Favourable risk (0 factors) vs Poor risk (> = 3 factors)	-0.29	0.57	(-1.40, 0.83)
Randomised Under Stratification Factor: Sex	.	.	
Female vs Male	-0.11	0.15	(-0.41, 0.20)
Randomised Under Stratification Factor: Age Group	.	.	
<60 vs >=60	0.04	0.15	(-0.26, 0.33)
Randomised Under Stratification Factor: Disease Status	.	.	
Locally advanced s Metastatic	-0.15	0.51	(-1.15, 0.84)
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	
No vs Yes	-0.19	0.20	(-0.59, 0.20)
Randomised Under Stratification Factor: TKI Received	.	.	

	Estimate	Standard Error	95% Confidence Interval
Pazopanib vs Sunitinib	-0.19	0.14	(-0.46, 0.07)

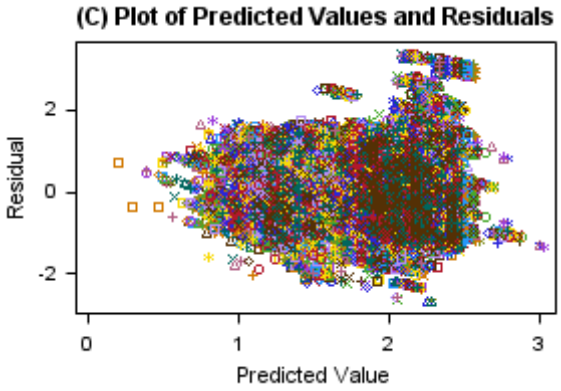
Supplementary Figure 47: Finite Mixture Model Diagnostics - QALYs, Measured from Week 24, Sensitivity Analysis – (A) Histogram of Residuals (P2e_QALYs_SensitivityAnalysis_24w)



Supplementary Figure 48:Finite Mixture Model Diagnostics - QALYs, Measured from Week 24, Sensitivity Analysis – (B) QQ Plot of Residuals (P2e_QALYs_SensitivityAnalysis_24w)



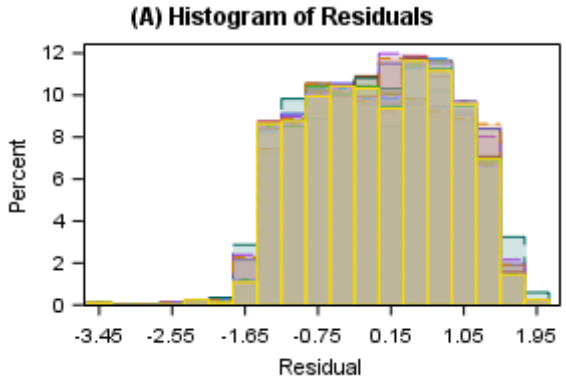
Supplementary Figure 49: Finite Mixture Model Diagnostics - QALYs, Measured from Week 24, Sensitivity Analysis (C) Plot of Predicted Values and Residuals (P2e_QALYs_SensitivityAnalysis_24w)



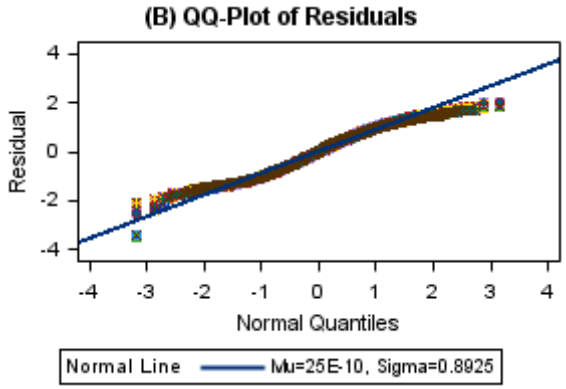
Supplementary Table 45: Combined Marginal Effects of the Finite Mixture Model with Two Components for QALYs, up to 12 months post-randomisation, in the PP population (P2g_QALYs_SensitivityAnalysis_12m)

	Estimate	Standard Error	95% Confidence Interval
Intercept	0.39	0.05	(0.29, 0.49)
Randomisation Allocation	.	.	
DFIS vs CCS	0.02	0.02	(-0.02, 0.05)
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	
Intermediate risk (1-2 factors) vs. Poor risk (> = 3 factors)	0.11	0.04	(0.03, 0.18)
Favourable risk (0 factors) vs Poor risk (> = 3 factors)	0.16	0.05	(0.07, 0.25)
Randomised Under Stratification Factor: Sex	.	.	
Female vs Male	-0.03	0.02	(-0.06, 0.01)
Randomised Under Stratification Factor: Age Group	.	.	
<60 vs >=60	-0.01	0.02	(-0.05, 0.02)
Randomised Under Stratification Factor: Disease Status	.	.	
Locally advanced s Metastatic	-0.07	0.09	(-0.24, 0.10)
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	
No vs Yes	-0.03	0.03	(-0.08, 0.03)
Randomised Under Stratification Factor: TKI Received	.	.	
Pazopanib vs Sunitinib	-0.03	0.02	(-0.06, 0.00)

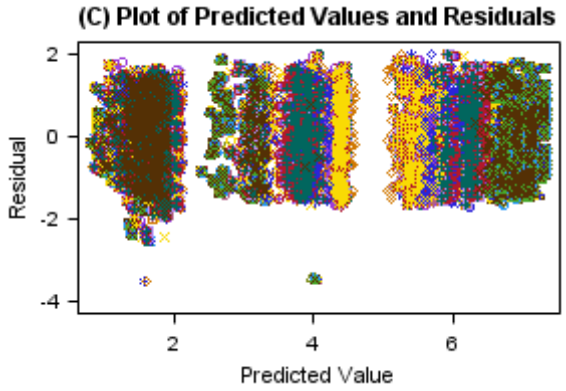
Supplementary Figure 50: Finite Mixture Model Diagnostics - QALYs, Calculated up to 12 Months Post-Randomisation, Sensitivity Analysis – (A) Histogram of Residuals (P2g_QALYs_SensitivityAnalysis_12m)



Supplementary Figure 51: Finite Mixture Model Diagnostics - QALYs, Calculated up to 12 Months Post-Randomisation, Sensitivity Analysis – (A) Histogram of Residuals (P2g_QALYs_SensitivityAnalysis_12m)



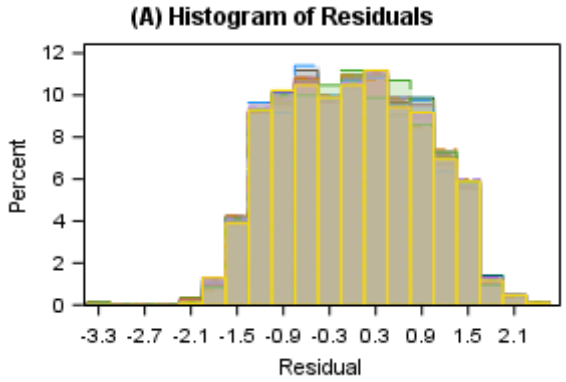
Supplementary Figure 52: Finite Mixture Model Diagnostics - QALYs, Calculated up to 12 Months Post-Randomisation, Sensitivity Analysis – (C) Plot of Predicted Values and Residuals (P2g_QALYs_SensitivityAnalysis_12m)



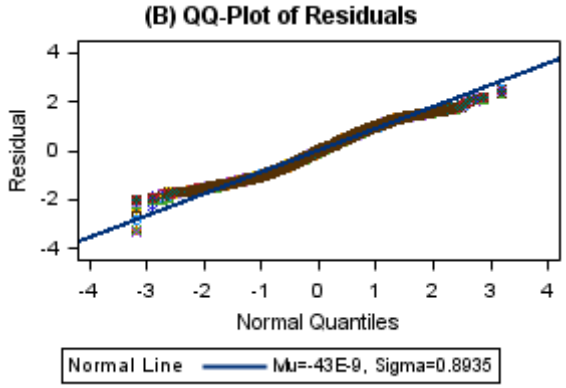
Supplementary Table 46: Combined Marginal Effects of the Finite Mixture Model with Two Components for QALYs, up to 24 months post-randomisation, in the PP population (P2h_QALYs_SensitivityAnalysis_24m)

	Estimate	Standard Error	95% Confidence Interval
Intercept	0.58	0.07	(0.43, 0.72)
Randomisation Allocation	.	.	
DFIS vs CCS	0.02	0.03	(-0.04, 0.09)
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	
Intermediate risk (1-2 factors) vs. Poor risk (> = 3 factors)	0.34	0.07	(0.21, 0.47)
Favourable risk (0 factors) vs Poor risk (> = 3 factors)	0.53	0.07	(0.39, 0.67)
Randomised Under Stratification Factor: Sex	.	.	
Female vs Male	-0.06	0.03	(-0.13, 0.00)
Randomised Under Stratification Factor: Age Group	.	.	
<60 vs >=60	-0.05	0.04	(-0.12, 0.02)
Randomised Under Stratification Factor: Disease Status	.	.	
Locally advanced s Metastatic	-0.09	0.11	(-0.30, 0.13)
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	
No vs Yes	-0.06	0.05	(-0.15, 0.03)
Randomised Under Stratification Factor: TKI Received	.	.	
Pazopanib vs Sunitinib	-0.09	0.03	(-0.15, -0.02)

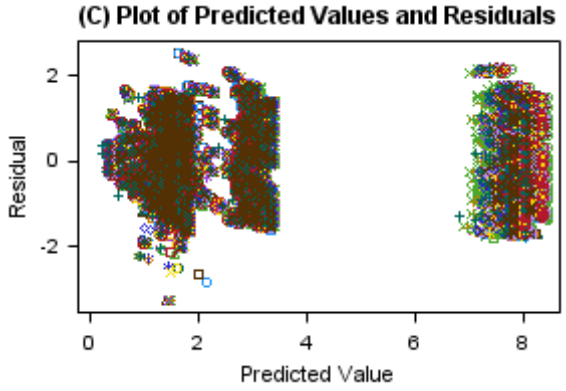
Supplementary Figure 53: Finite Mixture Model Diagnostics - QALYs, Calculated up to 24 Months Post-Randomisation, Sensitivity Analysis – (A) Histogram of Residuals (P2h_QALYs_SensitivityAnalysis_24m)



Supplementary Figure 54: Finite Mixture Model Diagnostics - QALYs, Calculated up to 24 Months Post-Randomisation, Sensitivity Analysis – (B) QQ-Plot of Residuals (P2h_QALYs_SensitivityAnalysis_24m)



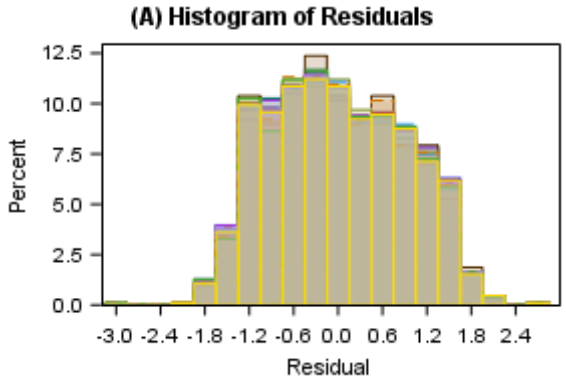
Supplementary Figure 55: Finite Mixture Model Diagnostics - QALYs, Calculated up to 24 Months Post-Randomisation, Sensitivity Analysis – (C) Plot of Predicted Values and Residuals (P2h_QALYs_SensitivityAnalysis_24m)



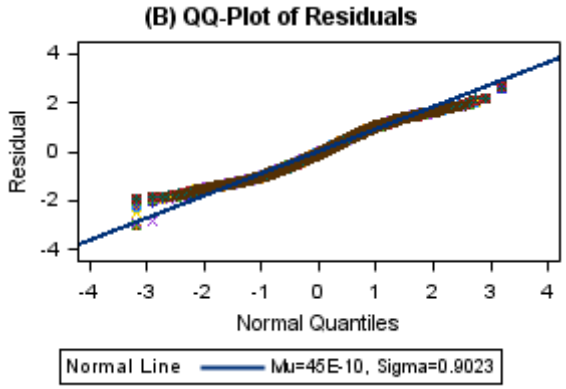
Supplementary Table 47: Combined Marginal Effects of the Finite Mixture Model with Two Components for QALYs, up to 36 months post-randomisation, in the PP population (P2f_QALYs_SensitivityAnalysis_36m)

	Estimate	Standard Error	95% Confidence Interval
Intercept	0.76	0.12	(0.54, 0.99)
Randomisation Allocation	.	.	
DFIS vs CCS	0.03	0.05	(-0.06, 0.13)
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	
Intermediate risk (1-2 factors) vs. Poor risk (> = 3 factors)	0.49	0.10	(0.28, 0.69)
Favourable risk (0 factors) vs Poor risk (> = 3 factors)	0.82	0.12	(0.59, 1.05)
Randomised Under Stratification Factor: Sex	.	.	
Female vs Male	-0.07	0.05	(-0.17, 0.03)
Randomised Under Stratification Factor: Age Group	.	.	
<60 vs >=60	-0.07	0.05	(-0.18, 0.03)
Randomised Under Stratification Factor: Disease Status	.	.	
Locally advanced s Metastatic	-0.09	0.16	(-0.41, 0.23)
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	
No vs Yes	-0.14	0.07	(-0.28, 0.01)
Randomised Under Stratification Factor: TKI Received	.	.	
Pazopanib vs Sunitinib	-0.10	0.05	(-0.20, -0.01)

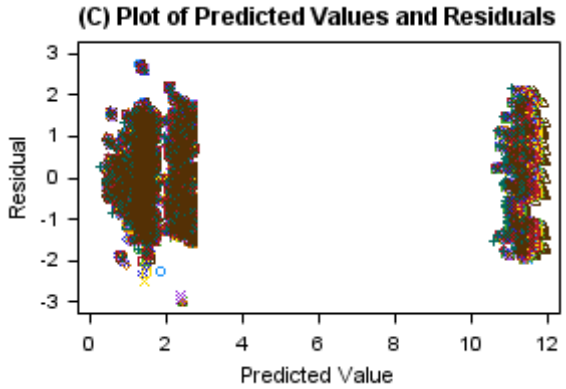
Supplementary Figure 56:Finite Mixture Model Diagnostics – QALYs, Calculated up to 36 Months Post-Randomisation, Sensitivity Analysis – (A) Histogram of Residuals (P2f_QALYs_SensitivityAnalysis_36m)



Supplementary Figure 57:Finite Mixture Model Diagnostics – QALYs, Calculated up to 36 Months Post-Randomisation, Sensitivity Analysis – (B) QQ-Plot of Residuals (P2f_QALYs_SensitivityAnalysis_36m)



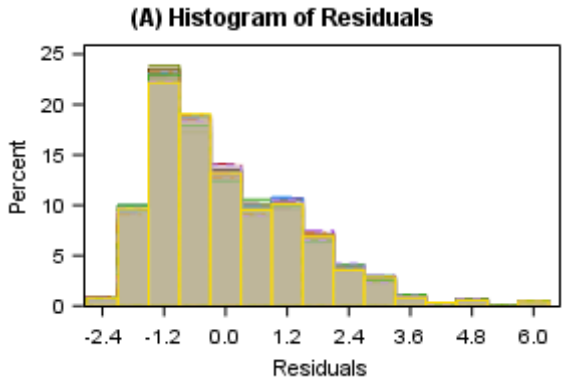
Supplementary Figure 58: Finite Mixture Model Diagnostics – QALYs, Calculated up to 36 Months Post-Randomisation, Sensitivity Analysis – (C) Plot of Predicted Values and Residuals (P2f_QALYs_SensitivityAnalysis_36m)



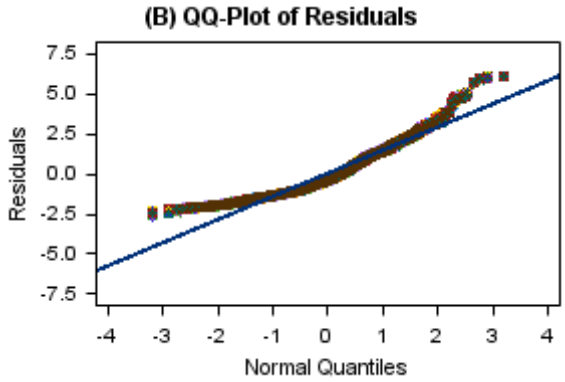
Supplementary Table 48: Combined Multivariate Linear Regression Results for QALYs in the PP population (P2i_QALYs_SensitivityAnalysis_Linear)

	Estimate	Standard Error	95% Confidence Interval
Intercept	1.53	0.38	(0.79, 2.27)
Randomisation Allocation	.	.	
DFIS vs. CCS	0.07	0.10	(-0.13, 0.26)
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.43	0.12	(-0.66, -0.21)
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-1.15	0.22	(-1.59, -0.72)
Randomised Under Stratification Factor: Sex	.	.	
Female vs Male	-0.16	0.11	(-0.38, 0.06)
Randomised Under Stratification Factor: Age Group	.	.	
>=60 vs <60	0.04	0.11	(-0.19, 0.26)
Randomised Under Stratification Factor: Disease Status	.	.	
Metastatic vs Locally advanced	0.35	0.33	(-0.30, 1.00)
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	
Yes vs No	0.29	0.14	(0.02, 0.56)
Randomised Under Stratification Factor: TKI Received	.	.	
Pazopanib vs Sunitinib	-0.08	0.10	(-0.28, 0.11)

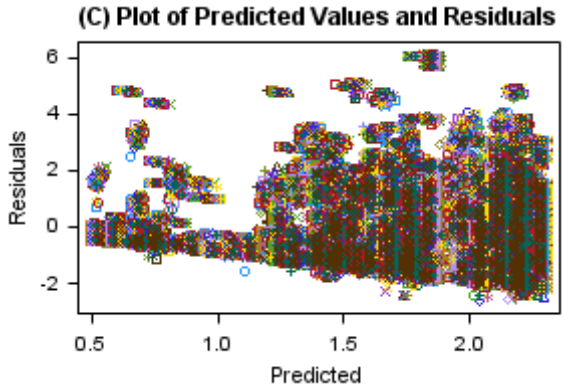
Supplementary Figure 59: Multivariate Linear Regression Model Diagnostics - in each Imputed Dataset – (A) Histogram of Residuals (P2i_QALYs_SensitivityAnalysis_Linear)



Supplementary Figure 60: Multivariate Linear Regression Model Diagnostics - in each Imputed Dataset – (B) QQ-Plot of Residuals (P2i_QALYs_SensitivityAnalysis_Linear)



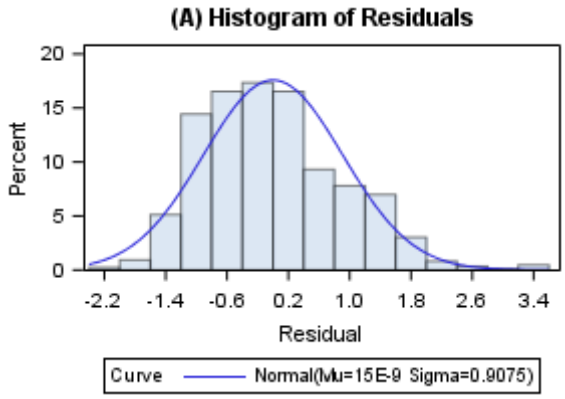
Supplementary Figure 61: Multivariate Linear Regression Model Diagnostics - in each Imputed Dataset – (C) Plot of Predicted Values and Residuals (P2i_QALYs_SensitivityAnalysis_Linear)



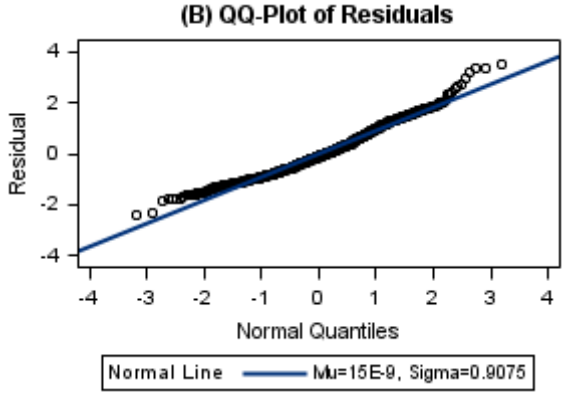
Supplementary Table 49: Marginal Model results for a finite mixture model with two components for QALYs over the lifetime of the trial - complete case data (P2j_QALYs_SensitivityAnalysis_Complete)

	Estimate	Standard Error	Confidence Interval
Intercept	1.36	0.25	(0.87, 1.85)
Randomisation Allocation	.	.	
DFIS vs. CCS	0.02	0.08	(-0.15, 0.18)
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	
Intermediate risk (1-2 factors) vs. Poor risk (> = 3 factors)	0.40	0.23	(-0.05, 0.85)
Favourable risk (0 factors) vs. Poor risk (> = 3 factors)	0.53	0.25	(0.04, 1.03)
Randomised Under Stratification Factor: Sex	.	.	
Female vs Male	-0.24	0.09	(-0.42, -0.06)
Randomised Under Stratification Factor: Age Group	.	.	
<60 vs >=60	0.06	0.10	(-0.14, 0.25)
Randomised Under Stratification Factor: Disease Status	.	.	
Locally advanced vs Metastatic	-0.20	0.33	(-0.85, 0.44)
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	
No vs Yes	-0.32	0.13	(-0.57, -0.07)
Randomised Under Stratification Factor: TKI Received	.	.	
Pazopanib vs Sunitinib	-0.19	0.09	(-0.36, -0.02)

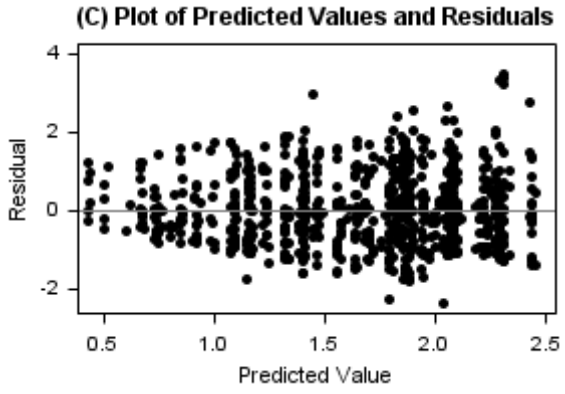
Supplementary Figure 62: Finite Mixture Model Diagnostics - QALY Complete Case Analysis – (A) Histogram of Residuals (P2j_QALYs_SensitivityAnalysis_Complete)



Supplementary Figure 63: Finite Mixture Model Diagnostics - QALY Complete Case Analysis – (B) QQ-Plot of Residuals (P2j_QALYs_SensitivityAnalysis_Complete)



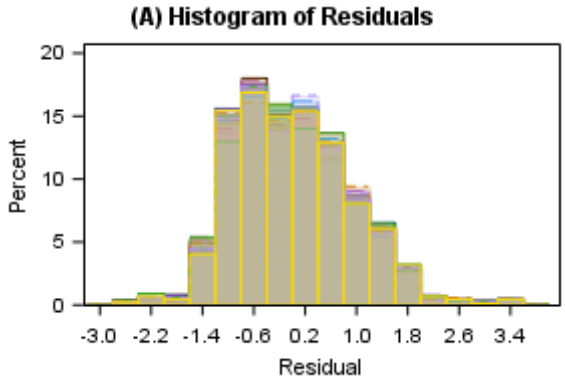
Supplementary Figure 64: Finite Mixture Model Diagnostics - QALY Complete Case Analysis – (C) Plot of Predicted Values and Residuals (P2j_QALYs_SensitivityAnalysis_Complete)



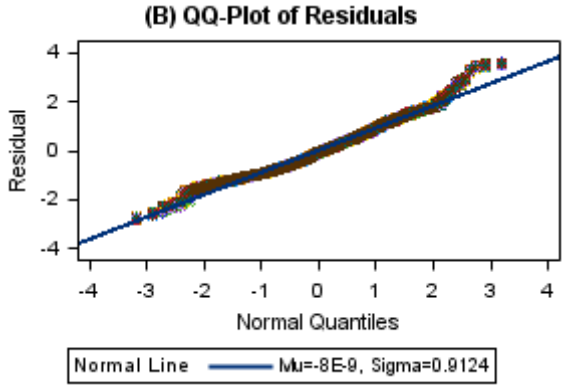
Supplementary Table 50: Combined Marginal Effects of the Finite Mixture Model with Two Components for QALYs, over trial and follow-up, in the PP population - MNAR Scenario 1 (P2l_EQ5D_SensitivityImputation_WorstCase)

	Estimate	Standard Error	95% Confidence Interval
Intercept	1.30	0.24	(0.82, 1.78)
Randomisation Allocation	.	.	
DFIS vs CCS	0.04	0.09	(-0.13, 0.21)
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	
Intermediate risk (1-2 factors) vs. Poor risk (> = 3 factors)	0.52	0.22	(0.08, 0.96)
Favourable risk (0 factors) vs Poor risk (> = 3 factors)	0.65	0.25	(0.17, 1.13)
Randomised Under Stratification Factor: Sex	.	.	
Female vs Male	-0.16	0.10	(-0.36, 0.04)
Randomised Under Stratification Factor: Age Group	.	.	
<60 vs >=60	0.05	0.10	(-0.16, 0.25)
Randomised Under Stratification Factor: Disease Status	.	.	
Locally advanced s Metastatic	-0.16	0.32	(-0.79, 0.47)
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	
No vs Yes	-0.30	0.14	(-0.56, -0.03)
Randomised Under Stratification Factor: TKI Received	.	.	
Pazopanib vs Sunitinib	-0.11	0.09	(-0.29, 0.06)

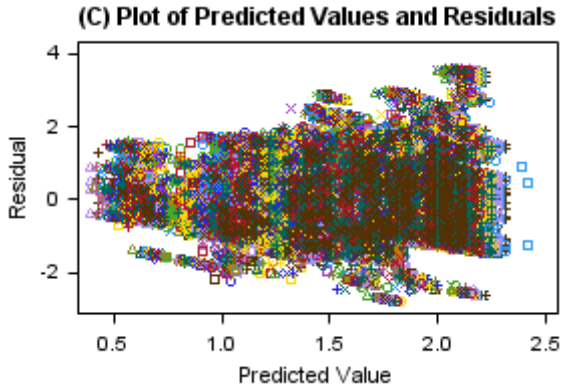
Supplementary Figure 65: Finite Mixture Model Diagnostics - QALY, MNAR Scenario 1, Sensitivity Analysis – (A) Histogram of Residuals (P2l_EQ5D_SensitivityImputation_WorstCase)



Supplementary Figure 66: Finite Mixture Model Diagnostics - QALY, MNAR Scenario 1, Sensitivity Analysis – (B) QQ-Plot of Residuals (P2l_EQ5D_SensitivityImputation_WorstCase)

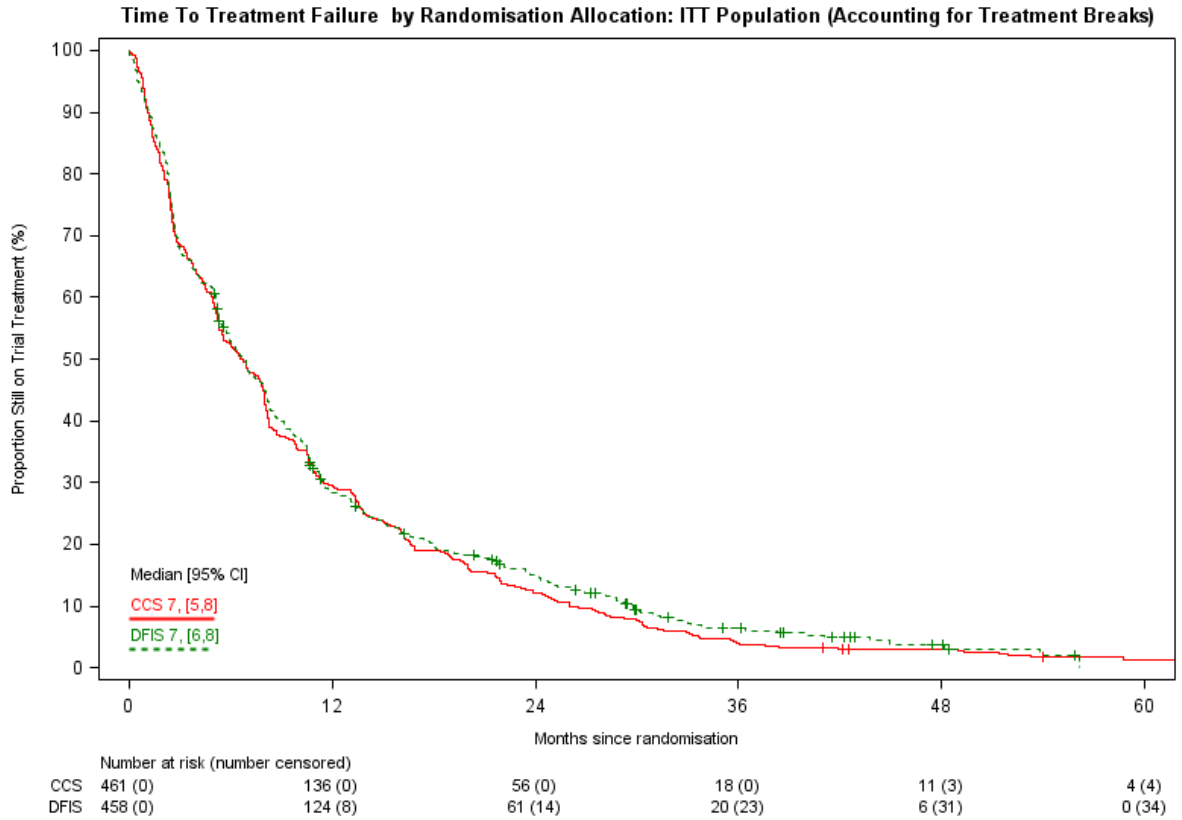


Supplementary Figure 67: Finite Mixture Model Diagnostics - QALY, MNAR Scenario 1, Sensitivity Analysis – (C) Plot of Predicted Values and Residuals (P2l_EQ5D_SensitivityImputation_WorstCase)



2.10 Ancillary Analysis of Secondary Endpoints

Supplementary Figure 68: Kaplan-Meier Figure for Time to Treatment Failure by Randomisation Allocation in the Intention-To-Treat Population



Supplementary Table 51: Cox Regression Analysis Results for Time To Treatment Failure in the ITT population - Accounting for Treatment Breaks (S2b_TTF_Sensitivity)

	DF	Estimate	Standard Error	Hazard Ratio Estimate (HR)	95% CI for HR	Test Statistic	p-value
Randomisation treatment	1	.	.	.		0.27	0.604
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	.	-0.04	0.07	0.97	[0.85, 1.10]	.	.
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	2	.	.	.		14.30	<.001
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	.	0.21	0.08	1.23	[1.06, 1.44]	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	.	0.57	0.16	1.77	[1.29, 2.41]	.	.
Randomised Under Stratification Factor: Sex	1	.	.	.		6.58	0.010
Female vs. Male	.	0.19	0.08	1.22	[1.05, 1.41]	.	.
Randomised Under Stratification Factor: Age Group	1	.	.	.		0.93	0.335
>=60 vs. <60	.	0.07	0.08	1.08	[0.93, 1.25]	.	.
Randomised Under Stratification Factor: Disease Status	1	.	.	.		0.89	0.347

	DF	Estimate	Standard Error	Hazard Ratio Estimate (HR)	95% CI for HR	Test Statistic	p-value
Metastatic vs. Locally advanced	.	-0.22	0.23	0.80	[0.51, 1.27]	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	1	.	.	.		0.21	0.646
Yes vs. No	.	-0.04	0.10	0.96	[0.79, 1.15]	.	.
Randomised Under Stratification Factor: TKI Received	1	.	.	.		0.33	0.563
Pazopanib vs. Sunitinib	.	0.04	0.07	1.04	[0.91, 1.19]	.	.

Supplementary Table 52: Results of mixed modelling for the FKSI total score, measured up to 12 months post-randomisation (Week 54) (S6_FKSI15)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 4057	.	.	.	.	.
Intercept	16.54	2.18	.	.	.
Quality of Life Timepoint	0.10	0.06	1, 645	10.55	0.001
FKSI Total Score at Baseline	0.59	0.03	1, 2627	463.79	<.001
Randomisation treatment	.	.	1, 2627	0.79	0.374
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.46	0.52	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.09	0.09	1, 2627	1.16	0.281
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 2627	0.55	0.575
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.33	0.53	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-1.15	1.11	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 2627	0.57	0.450

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Female vs. Male	-0.39	0.52	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 2627	0.04	0.850
>=60vs. <60	0.10	0.52	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 2627	1.03	0.310
Metastatic vs. Locally advanced	1.67	1.64	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 2627	3.28	0.070
Yes vs. No	-1.17	0.64	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 2627	10.27	0.001
Pazopanib vs. Sunitinib	-1.48	0.46	.	.	.

Supplementary Table 53: Results of mixed modelling for the FKIS-DRS score, measured up to 12 months post-randomisation (Week 54) (S6_FKSI15)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 4060	.	.	.	.	.
Intercept	11.48	1.28	.	.	.
Quality of Life Timepoint	0.03	0.04	1, 645	5.18	0.023
FKSI-DRS Score at Baseline	0.56	0.03	1, 2631	453.10	<.001
Randomisation treatment	.	.	1, 2631	0.86	0.355
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.28	0.30	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.05	0.05	1, 2631	0.88	0.349
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 2631	0.62	0.537
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	0.21	0.30	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-0.31	0.63	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 2631	0.37	0.544
Female vs. Male	-0.18	0.29	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 2631	0.05	0.821

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
>=60vs. <60	-0.07	0.29	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 2631	0.46	0.500
Metastatic vs. Locally advanced	0.63	0.93	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 2631	0.55	0.458
Yes vs. No	-0.27	0.36	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 2631	6.25	0.013
Pazopanib vs. Sunitinib	-0.65	0.26	.	.	.

Supplementary Table 54: Results of mixed modelling for the FKSI total score, measured up to 24 months post-randomisation (Week 102) (S6_FKSI15)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 5651	.	.	.	.	.
Intercept	16.45	2.18	.	.	.
Quality of Life Timepoint	0.08	0.04	1, 645	5.38	0.021
FKSI Total Score at Baseline	0.59	0.03	1, 4221	463.36	<.001
Randomisation treatment	.	.	1, 4221	3.41	0.065
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.90	0.49	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.05	0.05	1, 4221	0.77	0.380
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 4221	0.78	0.459
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.39	0.53	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-1.37	1.11	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 4221	0.59	0.444

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Female vs. Male	-0.40	0.52	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 4221	0.10	0.750
>=60vs. <60	0.17	0.52	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 4221	1.12	0.289
Metastatic vs. Locally advanced	1.74	1.65	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 4221	3.00	0.083
Yes vs. No	-1.12	0.64	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 4221	10.14	0.001
Pazopanib vs. Sunitinib	-1.47	0.46	.	.	.

Supplementary Table 55: Results of mixed modelling for the FKIS-DRS score, measured up to 24 months post-randomisation (Week 102) (S6_FKSI15)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 5653	.	.	.	.	.
Intercept	11.35	1.28	.	.	.
Quality of Life Timepoint	0.04	0.02	1, 645	1.18	0.277
FKSI-DRS Score at Baseline	0.56	0.03	1, 4224	457.66	<.001
Randomisation treatment	.	.	1, 4224	4.14	0.042
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.57	0.28	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.05	0.03	1, 4224	2.09	0.148
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 4224	0.63	0.535
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	0.16	0.30	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-0.42	0.63	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 4224	0.39	0.532

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Female vs. Male	-0.18	0.30	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 4224	0.01	0.918
>=60vs. <60	-0.03	0.29	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 4224	0.45	0.501
Metastatic vs. Locally advanced	0.63	0.93	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 4224	0.38	0.535
Yes vs. No	-0.23	0.36	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 4224	5.84	0.016
Pazopanib vs. Sunitinib	-0.63	0.26	.	.	.

Supplementary Table 56: Results of mixed modelling for the FKSI total score, measured up to 36 months post-randomisation (Week 156) (S6_FKSI15)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 6633	.	.	.	.	.
Intercept	16.45	2.18	.	.	.
Quality of Life Timepoint	0.07	0.03	1, 646	0.98	0.322
FKSI Total Score at Baseline	0.59	0.03	1, 5203	464.60	<.001
Randomisation treatment	.	.	1, 5203	5.45	0.020
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	1.11	0.48	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.09	0.04	1, 5203	4.58	0.032
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 5203	0.92	0.400
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.48	0.53	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-1.45	1.12	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 5203	0.54	0.464

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Female vs. Male	-0.38	0.52	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 5203	0.10	0.747
>=60vs. <60	0.17	0.52	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 5203	1.19	0.275
Metastatic vs. Locally advanced	1.80	1.65	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 5203	2.98	0.084
Yes vs. No	-1.12	0.65	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 5203	10.57	0.001
Pazopanib vs. Sunitinib	-1.51	0.46	.	.	.

Supplementary Table 57: Results of mixed modelling for the FKIS-DRS score, measured up to 36 months post-randomisation (Week 156) (S6_FKSI15)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 6635	.	.	.	.	.
Intercept	11.34	1.28	.	.	.
Quality of Life Timepoint	0.03	0.02	1, 645	0.01	0.910
FKSI-DRS Score at Baseline	0.56	0.03	1, 5205	458.72	<.001
Randomisation treatment	.	.	1, 5205	5.53	0.019
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.64	0.27	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.06	0.03	1, 5205	5.80	0.016
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 5205	0.56	0.573
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	0.11	0.30	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-0.47	0.63	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 5205	0.39	0.534

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Female vs. Male	-0.18	0.30	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 5205	0.00	0.953
>=60vs. <60	-0.02	0.29	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 5205	0.51	0.477
Metastatic vs. Locally advanced	0.66	0.93	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 5205	0.39	0.532
Yes vs. No	-0.23	0.36	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 5205	5.88	0.015
Pazopanib vs. Sunitinib	-0.63	0.26	.	.	.

Supplementary Table 58: Results of mixed modelling for the FACT-G total score, measured up to 12 months post-randomisation (Week 54) (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 3864	.	.	.	.	.
Intercept	23.45	3.60	.	.	.
Quality of Life Timepoint	0.15	0.10	1, 621	6.16	0.013
FACTG Total Score at Baseline	0.68	0.02	1, 2487	735.69	<.001
Randomisation treatment	.	.	1, 2487	0.11	0.743
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.27	0.81	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.04	0.13	1, 2487	0.07	0.786
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 2487	1.24	0.291
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-1.24	0.86	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-2.10	1.77	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 2487	0.79	0.373
Female vs. Male	-0.75	0.84	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 2487	0.85	0.356
>=60vs. <60	0.78	0.85	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 2487	1.61	0.204
Metastatic vs. Locally advanced	3.42	2.69	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 2487	3.28	0.070
Yes vs. No	-1.89	1.04	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 2487	3.09	0.079
Pazopanib vs. Sunitinib	-1.32	0.75	.	.	.

Supplementary Table 59: Results of mixed modelling for the FACT-G Physical Well-Being Subscale, measured up to 12 months post-randomisation (Week 54) (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 3915	.	.	.	.	.
Intercept	7.17	1.32	.	.	.
Quality of Life Timepoint	0.04	0.04	1, 625	14.15	<.001
FACT-G Physical Well-Being Subscale at Baseline	0.57	0.03	1, 2529	327.63	<.001
Randomisation treatment	.	.	1, 2529	0.09	0.762
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.10	0.32	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.10	0.05	1, 2529	4.13	0.042
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 2529	1.39	0.249
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.26	0.32	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-1.10	0.66	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 2529	1.00	0.318
Female vs. Male	-0.31	0.31	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 2529	3.65	0.056
>=60vs. <60	0.59	0.31	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 2529	1.42	0.234
Metastatic vs. Locally advanced	1.18	0.99	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 2529	2.21	0.137
Yes vs. No	-0.57	0.38	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 2529	4.01	0.045
Pazopanib vs. Sunitinib	-0.55	0.28	.	.	.

Supplementary Table 60: Results of mixed modelling for the FACT-G Social/Family Well-Being Subscale, measured up to 12 months post-randomisation (Week 54) (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 3927	.	.	.	.	.
Intercept	9.80	0.97	.	.	.
Quality of Life Timepoint	-0.00	0.03	1, 623	0.41	0.520
FACT-G Social/Family Well-Being Subscale at Baseline	0.56	0.02	1, 2544	588.91	<.001
Randomisation treatment	.	.	1, 2544	1.35	0.245
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.27	0.23	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.03	0.04	1, 2544	0.41	0.522
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 2544	0.17	0.840
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.10	0.24	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	0.10	0.50	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 2544	0.02	0.882
Female vs. Male	0.04	0.24	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 2544	1.54	0.215
>=60vs. <60	0.30	0.24	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 2544	0.93	0.334
Metastatic vs. Locally advanced	0.75	0.77	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 2544	0.05	0.825
Yes vs. No	-0.07	0.30	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 2544	3.71	0.054
Pazopanib vs. Sunitinib	-0.41	0.21	.	.	.

Supplementary Table 61: Results of mixed modelling for the FACT-G Emotional Well-Being Subscale, measured up to 12 months post-randomisation (Week 54) (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 3920	.	.	.	.	.
Intercept	8.52	0.89	.	.	.
Quality of Life Timepoint	0.09	0.03	1, 623	13.80	<.001
FACT-G Emotional Well-Being Subscale at Baseline	0.56	0.02	1, 2541	611.86	<.001
Randomisation treatment	.	.	1, 2541	0.49	0.486
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.16	0.23	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.05	0.04	1, 2541	1.59	0.207
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 2541	1.17	0.311
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.34	0.23	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-0.44	0.47	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 2541	2.97	0.085
Female vs. Male	-0.39	0.23	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 2541	2.41	0.121
>=60vs. <60	0.35	0.23	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 2541	0.51	0.477
Metastatic vs. Locally advanced	0.51	0.72	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 2541	2.02	0.155
Yes vs. No	-0.39	0.28	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 2541	0.00	0.978
Pazopanib vs. Sunitinib	0.01	0.20	.	.	.

Supplementary Table 62: Results of mixed modelling for the FACT-G Functional Well-Being Subscale, measured up to 12 months post-randomisation (Week 54) (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 3929	.	.	.	.	.
Intercept	6.26	1.35	.	.	.
Quality of Life Timepoint	0.05	0.05	1, 624	3.57	0.059
FACT-G Functional Well-Being Subscale at Baseline	0.61	0.03	1, 2548	581.56	<.001
Randomisation treatment	.	.	1, 2548	0.37	0.545
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.22	0.36	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.01	0.06	1, 2548	0.04	0.833
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 2548	2.61	0.073
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.65	0.36	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-1.53	0.75	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 2548	0.49	0.485
Female vs. Male	-0.25	0.35	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 2548	0.14	0.708
>=60vs. <60	0.13	0.35	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 2548	0.59	0.442
Metastatic vs. Locally advanced	0.87	1.13	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 2548	2.48	0.116
Yes vs. No	-0.69	0.44	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 2548	1.21	0.272
Pazopanib vs. Sunitinib	-0.35	0.32	.	.	.

Supplementary Table 63: Results of mixed modelling for the FACT-G total score, measured up to 24 months post-randomisation (Week 102) (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 5372	.	.	.	.	.
Intercept	23.45	3.61	.	.	.
Quality of Life Timepoint	0.11	0.06	1, 621	1.22	0.269
FACTG Total Score at Baseline	0.68	0.03	1, 3995	730.29	<.001
Randomisation treatment	.	.	1, 3995	0.97	0.325
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.76	0.77	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.13	0.08	1, 3995	2.64	0.104
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 3995	1.29	0.274
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-1.20	0.86	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-2.36	1.78	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 3995	0.69	0.407
Female vs. Male	-0.70	0.85	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 3995	0.86	0.353
>=60vs. <60	0.79	0.85	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 3995	1.79	0.181
Metastatic vs. Locally advanced	3.61	2.70	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 3995	3.39	0.066
Yes vs. No	-1.93	1.05	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 3995	3.25	0.072
Pazopanib vs. Sunitinib	-1.36	0.75	.	.	.

Supplementary Table 64: Results of mixed modelling for the FACT-G Physical Well-Being Subscale, measured up to 24 months post-randomisation (Week 102) (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 5446	.	.	.	.	.
Intercept	7.00	1.32	.	.	.
Quality of Life Timepoint	0.05	0.02	1, 626	9.92	0.002
FACT-G Physical Well-Being Subscale at Baseline	0.57	0.03	1, 4058	332.40	<.001
Randomisation treatment	.	.	1, 4058	2.24	0.135
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.44	0.30	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.02	0.03	1, 4058	0.40	0.526
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 4058	1.46	0.232
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.29	0.32	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-1.12	0.66	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 4058	0.65	0.419
Female vs. Male	-0.25	0.31	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 4058	3.19	0.074
>=60vs. <60	0.55	0.31	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 4058	1.49	0.222
Metastatic vs. Locally advanced	1.21	0.99	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 4058	1.58	0.210
Yes vs. No	-0.48	0.38	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 4058	4.15	0.042
Pazopanib vs. Sunitinib	-0.56	0.28	.	.	.

Supplementary Table 65: Results of mixed modelling for the FACT-G Social/Family Well-Being Subscale, measured up to 24 months post-randomisation (Week 102) (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 5459	.	.	.	.	.
Intercept	9.76	0.98	.	.	.
Quality of Life Timepoint	0.01	0.02	1, 623	0.66	0.416
FACT-G Social/Family Well-Being Subscale at Baseline	0.56	0.02	1, 4075	584.76	<.001
Randomisation treatment	.	.	1, 4075	1.78	0.182
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.29	0.22	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.04	0.02	1, 4075	2.37	0.123
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 4075	0.17	0.844
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.12	0.25	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	0.06	0.50	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 4075	0.06	0.807
Female vs. Male	0.06	0.24	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 4075	1.47	0.226
>=60vs. <60	0.29	0.24	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 4075	0.98	0.323
Metastatic vs. Locally advanced	0.77	0.78	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 4075	0.07	0.793
Yes vs. No	-0.08	0.30	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 4075	3.20	0.074
Pazopanib vs. Sunitinib	-0.38	0.22	.	.	.

Supplementary Table 66: Results of mixed modelling for the FACT-G Emotional Well-Being Subscale, measured up to 24 months post-randomisation (Week 102) (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 5448	.	.	.	.	.
Intercept	8.59	0.89	.	.	.
Quality of Life Timepoint	0.06	0.02	1, 623	10.18	0.001
FACT-G Emotional Well-Being Subscale at Baseline	0.56	0.02	1, 4069	612.24	<.001
Randomisation treatment	.	.	1, 4069	0.52	0.473
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.15	0.21	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.05	0.02	1, 4069	5.38	0.020
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 4069	1.10	0.332
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.33	0.23	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-0.44	0.47	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 4069	2.95	0.086
Female vs. Male	-0.39	0.23	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 4069	2.49	0.114
>=60vs. <60	0.36	0.23	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 4069	0.48	0.489
Metastatic vs. Locally advanced	0.50	0.72	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 4069	1.86	0.172
Yes vs. No	-0.38	0.28	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 4069	0.00	0.954
Pazopanib vs. Sunitinib	-0.01	0.20	.	.	.

Supplementary Table 67: Results of mixed modelling for the FACT-G Functional Well-Being Subscale , measured up to 24 months post-randomisation (Week 102) (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 5463	.	.	.	.	.
Intercept	6.27	1.35	.	.	.
Quality of Life Timepoint	0.02	0.03	1, 624	0.07	0.785
FACT-G Functional Well-Being Subscale at Baseline	0.61	0.03	1, 4082	578.89	<.001
Randomisation treatment	.	.	1, 4082	1.01	0.315
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.33	0.33	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.02	0.04	1, 4082	0.42	0.516
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 4082	2.79	0.062
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.62	0.36	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-1.64	0.75	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 4082	0.42	0.518
Female vs. Male	-0.23	0.35	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 4082	0.17	0.682
>=60vs. <60	0.14	0.35	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 4082	0.77	0.380
Metastatic vs. Locally advanced	1.00	1.13	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 4082	2.57	0.109
Yes vs. No	-0.71	0.44	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 4082	1.38	0.240
Pazopanib vs. Sunitinib	-0.37	0.32	.	.	.

Supplementary Table 68: Results of mixed modelling for the FACT-G total score, measured up to 36 months post-randomisation (Week 156) (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 6298	.	.	.	.	.
Intercept	23.75	3.61	.	.	.
Quality of Life Timepoint	0.10	0.05	1, 621	0.00	0.981
FACTG Total Score at Baseline	0.68	0.03	1, 4922	727.92	<.001
Randomisation treatment	.	.	1, 4922	1.86	0.172
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	1.04	0.76	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.20	0.07	1, 4922	8.20	0.004
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 4922	1.58	0.206
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-1.36	0.86	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-2.52	1.78	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 4922	0.55	0.459
Female vs. Male	-0.63	0.85	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 4922	0.83	0.361
>=60vs. <60	0.78	0.85	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 4922	1.75	0.185
Metastatic vs. Locally advanced	3.58	2.70	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 4922	3.26	0.071
Yes vs. No	-1.89	1.05	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 4922	3.76	0.052
Pazopanib vs. Sunitinib	-1.46	0.75	.	.	.

Supplementary Table 69: Results of mixed modelling for the FACT-G Physical Well-Being Subscale, measured up to 36 months post-randomisation (Week 156) (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 6389	.	.	.	.	.
Intercept	6.96	1.32	.	.	.
Quality of Life Timepoint	0.04	0.02	1, 625	3.73	0.054
FACT-G Physical Well-Being Subscale at Baseline	0.57	0.03	1, 5002	333.72	<.001
Randomisation treatment	.	.	1, 5002	3.70	0.054
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.56	0.29	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.04	0.02	1, 5002	3.87	0.049
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 5002	1.58	0.207
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.31	0.32	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-1.17	0.66	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 5002	0.66	0.417
Female vs. Male	-0.25	0.31	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 5002	3.07	0.080
>=60vs. <60	0.54	0.31	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 5002	1.65	0.199
Metastatic vs. Locally advanced	1.28	0.99	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 5002	1.57	0.210
Yes vs. No	-0.48	0.38	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 5002	4.12	0.042
Pazopanib vs. Sunitinib	-0.56	0.28	.	.	.

Supplementary Table 70: Results of mixed modelling for the FACT-G Social/Family Well-Being Subscale, measured up to 36 months post-randomisation (Week 156)(S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 6402	.	.	.	.	.
Intercept	9.91	0.99	.	.	.
Quality of Life Timepoint	0.01	0.02	1, 623	0.14	0.707
FACT-G Social/Family Well-Being Subscale at Baseline	0.56	0.02	1, 5019	567.31	<.001
Randomisation treatment	.	.	1, 5019	1.45	0.229
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.26	0.22	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.03	0.02	1, 5019	2.55	0.111
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 5019	0.28	0.757
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.17	0.25	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	0.00	0.51	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 5019	0.05	0.829
Female vs. Male	0.05	0.24	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 5019	1.88	0.170
>=60vs. <60	0.33	0.24	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 5019	0.85	0.357
Metastatic vs. Locally advanced	0.72	0.78	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 5019	0.21	0.646
Yes vs. No	-0.14	0.30	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 5019	3.56	0.059
Pazopanib vs. Sunitinib	-0.41	0.22	.	.	.

Supplementary Table 71: Results of mixed modelling for the FACT-G Emotional Well-Being Subscale, measured up to 36 months post-randomisation (Week 156) (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 6380	.	.	.	.	.
Intercept	8.69	0.89	.	.	.
Quality of Life Timepoint	0.05	0.01	1, 624	7.58	0.006
FACT-G Emotional Well-Being Subscale at Baseline	0.56	0.02	1, 4999	604.22	<.001
Randomisation treatment	.	.	1, 4999	0.40	0.525
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.13	0.20	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.06	0.02	1, 4999	9.54	0.002
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 4999	1.33	0.266
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.36	0.23	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-0.49	0.47	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 4999	2.74	0.098
Female vs. Male	-0.38	0.23	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 4999	2.49	0.115
>=60vs. <60	0.36	0.23	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 4999	0.49	0.485
Metastatic vs. Locally advanced	0.50	0.72	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 4999	1.87	0.171
Yes vs. No	-0.38	0.28	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 4999	0.02	0.892
Pazopanib vs. Sunitinib	-0.03	0.20	.	.	.

Supplementary Table 72: Results of mixed modelling for the FACT-G Functional Well-Being Subscale, measured up to 36 months post-randomisation (Week 156) (S7_FACTG)

	Estimate	Standard Error	Degrees of Freedom	Test Statistic	P-value
Number of Observation used: 6397	.	.	.	.	.
Intercept	6.27	1.35	.	.	.
Quality of Life Timepoint	0.01	0.02	1, 625	0.85	0.358
FACT-G Functional Well-Being Subscale at Baseline	0.61	0.03	1, 5014	576.85	<.001
Randomisation treatment	.	.	1, 5014	2.16	0.142
Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	0.48	0.33	.	.	.
Quality of Life Timepoint for Drug-Free Interval Strategy (DFIS) vs. Conventional Continuation Strategy (CCS)	-0.06	0.03	1, 5014	3.49	0.062
Randomised Under Stratification Factor: Motzer/MSKCC prognostic group	.	.	2, 5014	2.98	0.051
Intermediate risk (1-2 factors) vs. Favourable risk (0 factors)	-0.66	0.36	.	.	.
Poor risk (> = 3 factors) vs. Favourable risk (0 factors)	-1.68	0.75	.	.	.
Randomised Under Stratification Factor: Sex	.	.	1, 5014	0.36	0.550
Female vs. Male	-0.21	0.36	.	.	.
Randomised Under Stratification Factor: Age Group	.	.	1, 5014	0.16	0.694
>=60vs. <60	0.14	0.35	.	.	.
Randomised Under Stratification Factor: Disease Status	.	.	1, 5014	0.82	0.364
Metastatic vs. Locally advanced	1.03	1.14	.	.	.
Randomised Under Stratification Factor: Previous Nephrectomy	.	.	1, 5014	2.46	0.117
Yes vs. No	-0.69	0.44	.	.	.
Randomised Under Stratification Factor: TKI Received	.	.	1, 5014	1.62	0.203
Pazopanib vs. Sunitinib	-0.40	0.32	.	.	.

2.11 Harms

Supplementary Table 73: Number of participants experiencing each type of AE (S5a_Toxicity_AEs)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
Hypertension									
Yes	135 (66.5%)	110 (60.8%)	245 (63.8%)	197 (69.9%)	192 (76.8%)	389 (73.1%)	332 (68.5%)	302 (70.1%)	634 (69.2%)
No	68 (33.5%)	71 (39.2%)	139 (36.2%)	85 (30.1%)	58 (23.2%)	143 (26.9%)	153 (31.5%)	129 (29.9%)	282 (30.8%)
Haemorrhage/Bleeding/Coagulopathy									
Yes	36 (17.7%)	43 (23.8%)	79 (20.6%)	33 (11.7%)	41 (16.4%)	74 (13.9%)	69 (14.2%)	84 (19.5%)	153 (16.7%)
No	167 (82.3%)	138 (76.2%)	305 (79.4%)	249 (88.3%)	209 (83.6%)	458 (86.1%)	416 (85.8%)	347 (80.5%)	763 (83.3%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
Venus Thrombosis									
Yes	2 (1.0%)	4 (2.2%)	6 (1.6%)	14 (5.0%)	13 (5.2%)	27 (5.1%)	16 (3.3%)	17 (3.9%)	33 (3.6%)
No	201 (99.0%)	177 (97.8%)	378 (98.4%)	268 (95.0%)	237 (94.8%)	505 (94.9%)	469 (96.7%)	414 (96.1%)	883 (96.4%)
Arterial Thrombosis									
Yes	3 (1.5%)	0 (0.0%)	3 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (0.6%)	0 (0.0%)	3 (0.3%)
No	200 (98.5%)	181 (100.0%)	381 (99.2%)	282 (100.0%)	250 (100.0%)	532 (100.0%)	482 (99.4%)	431 (100.0%)	913 (99.7%)
Neutropenia									

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
Yes	71 (35.0%)	49 (27.1%)	120 (31.3%)	35 (12.4%)	24 (9.6%)	59 (11.1%)	106 (21.9%)	73 (16.9%)	179 (19.5%)
No	132 (65.0%)	132 (72.9%)	264 (68.8%)	247 (87.6%)	226 (90.4%)	473 (88.9%)	379 (78.1%)	358 (83.1%)	737 (80.5%)
Thrombocytopenia									
Yes	59 (29.1%)	54 (29.8%)	113 (29.4%)	41 (14.5%)	46 (18.4%)	87 (16.4%)	100 (20.6%)	100 (23.2%)	200 (21.8%)
No	144 (70.9%)	127 (70.2%)	271 (70.6%)	241 (85.5%)	204 (81.6%)	445 (83.6%)	385 (79.4%)	331 (76.8%)	716 (78.2%)
Fatigue									
Yes	180 (88.7%)	163 (90.1%)	343 (89.3%)	251 (89.0%)	215 (86.0%)	466 (87.6%)	431 (88.9%)	378 (87.7%)	809 (88.3%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
No	23 (11.3%)	18 (9.9%)	41 (10.7%)	31 (11.0%)	35 (14.0%)	66 (12.4%)	54 (11.1%)	53 (12.3%)	107 (11.7%)
Anaemia									
Yes	105 (51.7%)	94 (51.9%)	199 (51.8%)	99 (35.1%)	111 (44.4%)	210 (39.5%)	204 (42.1%)	205 (47.6%)	409 (44.7%)
No	98 (48.3%)	87 (48.1%)	185 (48.2%)	183 (64.9%)	139 (55.6%)	322 (60.5%)	281 (57.9%)	226 (52.4%)	507 (55.3%)
Hand-foot syndrome									
Yes	118 (58.1%)	87 (48.1%)	205 (53.4%)	81 (28.7%)	69 (27.6%)	150 (28.2%)	199 (41.0%)	156 (36.2%)	355 (38.8%)
No	85 (41.9%)	94 (51.9%)	179 (46.6%)	201 (71.3%)	181 (72.4%)	382 (71.8%)	286 (59.0%)	275 (63.8%)	561 (61.2%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
Hepatotoxicity									
Yes	41 (20.2%)	45 (24.9%)	86 (22.4%)	130 (46.1%)	132 (52.8%)	262 (49.2%)	171 (35.3%)	177 (41.1%)	348 (38.0%)
No	162 (79.8%)	136 (75.1%)	298 (77.6%)	152 (53.9%)	118 (47.2%)	270 (50.8%)	314 (64.7%)	254 (58.9%)	568 (62.0%)
Nausea / Vomiting									
Yes	132 (65.0%)	109 (60.2%)	241 (62.8%)	174 (61.7%)	163 (65.2%)	337 (63.3%)	306 (63.1%)	272 (63.1%)	578 (63.1%)
No	71 (35.0%)	72 (39.8%)	143 (37.2%)	108 (38.3%)	87 (34.8%)	195 (36.7%)	179 (36.9%)	159 (36.9%)	338 (36.9%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
Pyrexia									
Yes	20 (9.9%)	16 (8.8%)	36 (9.4%)	18 (6.4%)	27 (10.8%)	45 (8.5%)	38 (7.8%)	43 (10.0%)	81 (8.8%)
No	183 (90.1%)	165 (91.2%)	348 (90.6%)	264 (93.6%)	223 (89.2%)	487 (91.5%)	447 (92.2%)	388 (90.0%)	835 (91.2%)
Dyspepsia / Indigestion									
Yes	98 (48.3%)	91 (50.3%)	189 (49.2%)	69 (24.5%)	79 (31.6%)	148 (27.8%)	167 (34.4%)	170 (39.4%)	337 (36.8%)
No	105 (51.7%)	90 (49.7%)	195 (50.8%)	213 (75.5%)	171 (68.4%)	384 (72.2%)	318 (65.6%)	261 (60.6%)	579 (63.2%)
Diarrhoea									

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
Yes	134 (66.0%)	107 (59.1%)	241 (62.8%)	189 (67.0%)	158 (63.2%)	347 (65.2%)	323 (66.6%)	265 (61.5%)	588 (64.2%)
No	69 (34.0%)	74 (40.9%)	143 (37.2%)	93 (33.0%)	92 (36.8%)	185 (34.8%)	162 (33.4%)	166 (38.5%)	328 (35.8%)
Constipation									
Yes	83 (40.9%)	64 (35.4%)	147 (38.3%)	78 (27.7%)	93 (37.2%)	171 (32.1%)	161 (33.2%)	157 (36.4%)	318 (34.7%)
No	120 (59.1%)	117 (64.6%)	237 (61.7%)	204 (72.3%)	157 (62.8%)	361 (67.9%)	324 (66.8%)	274 (63.6%)	598 (65.3%)
Mucositis/Stomatitis									
Yes	146 (71.9%)	111 (61.3%)	257 (66.9%)	126 (44.7%)	110 (44.0%)	236 (44.4%)	272 (56.1%)	221 (51.3%)	493 (53.8%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
No	57 (28.1%)	70 (38.7%)	127 (33.1%)	156 (55.3%)	140 (56.0%)	296 (55.6%)	213 (43.9%)	210 (48.7%)	423 (46.2%)
Thyroid dysfunction									
Yes	63 (31.0%)	50 (27.6%)	113 (29.4%)	66 (23.4%)	59 (23.6%)	125 (23.5%)	129 (26.6%)	109 (25.3%)	238 (26.0%)
No	140 (69.0%)	131 (72.4%)	271 (70.6%)	216 (76.6%)	191 (76.4%)	407 (76.5%)	356 (73.4%)	322 (74.7%)	678 (74.0%)
Anorexia									
Yes	122 (60.1%)	102 (56.4%)	224 (58.3%)	155 (55.0%)	131 (52.4%)	286 (53.8%)	277 (57.1%)	233 (54.1%)	510 (55.7%)
No	81 (39.9%)	79 (43.6%)	160 (41.7%)	127 (45.0%)	119 (47.6%)	246 (46.2%)	208 (42.9%)	198 (45.9%)	406 (44.3%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
Altered taste									
Yes	121 (59.6%)	113 (62.4%)	234 (60.9%)	148 (52.5%)	135 (54.0%)	283 (53.2%)	269 (55.5%)	248 (57.5%)	517 (56.4%)
No	82 (40.4%)	68 (37.6%)	150 (39.1%)	134 (47.5%)	115 (46.0%)	249 (46.8%)	216 (44.5%)	183 (42.5%)	399 (43.6%)
Change in hair and skin colour									
Yes	71 (35.0%)	66 (36.5%)	137 (35.7%)	108 (38.3%)	95 (38.0%)	203 (38.2%)	179 (36.9%)	161 (37.4%)	340 (37.1%)
No	132 (65.0%)	115 (63.5%)	247 (64.3%)	174 (61.7%)	155 (62.0%)	329 (61.8%)	306 (63.1%)	270 (62.6%)	576 (62.9%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
Hypersensitivity									
Yes	7 (3.4%)	5 (2.8%)	12 (3.1%)	3 (1.1%)	10 (4.0%)	13 (2.4%)	10 (2.1%)	15 (3.5%)	25 (2.7%)
No	196 (96.6%)	176 (97.2%)	372 (96.9%)	279 (98.9%)	240 (96.0%)	519 (97.6%)	475 (97.9%)	416 (96.5%)	891 (97.3%)
Dyspnoea									
Yes	55 (27.1%)	61 (33.7%)	116 (30.2%)	75 (26.6%)	64 (25.6%)	139 (26.1%)	130 (26.8%)	125 (29.0%)	255 (27.8%)
No	148 (72.9%)	120 (66.3%)	268 (69.8%)	207 (73.4%)	186 (74.4%)	393 (73.9%)	355 (73.2%)	306 (71.0%)	661 (72.2%)
Reduced cardiac function									
Yes	3 (1.5%)	2 (1.1%)	5 (1.3%)	4 (1.4%)	5 (2.0%)	9 (1.7%)	7 (1.4%)	7 (1.6%)	14 (1.5%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
No	200 (98.5%)	179 (98.9%)	379 (98.7%)	278 (98.6%)	245 (98.0%)	523 (98.3%)	478 (98.6%)	424 (98.4%)	902 (98.5%)
Proteinuria/nephrotic syndrome									
Yes	12 (5.9%)	8 (4.4%)	20 (5.2%)	17 (6.0%)	19 (7.6%)	36 (6.8%)	29 (6.0%)	27 (6.3%)	56 (6.1%)
No	191 (94.1%)	173 (95.6%)	364 (94.8%)	265 (94.0%)	231 (92.4%)	496 (93.2%)	456 (94.0%)	404 (93.7%)	860 (93.9%)

Supplementary Table 74: Maximum CTCAE grade experienced per participant for each type of AE (S5a_Toxicity_AEs)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
Hypertension									
0	68 (33.5%)	71 (39.2%)	139 (36.2%)	85 (30.1%)	58 (23.2%)	143 (26.9%)	153 (31.5%)	129 (29.9%)	282 (30.8%)
1	46 (22.7%)	30 (16.6%)	76 (19.8%)	38 (13.5%)	44 (17.6%)	82 (15.4%)	84 (17.3%)	74 (17.2%)	158 (17.2%)
2	43 (21.2%)	36 (19.9%)	79 (20.6%)	81 (28.7%)	65 (26.0%)	146 (27.4%)	124 (25.6%)	101 (23.4%)	225 (24.6%)
3	45 (22.2%)	42 (23.2%)	87 (22.7%)	78 (27.7%)	83 (33.2%)	161 (30.3%)	123 (25.4%)	125 (29.0%)	248 (27.1%)
4	1 (0.5%)	2 (1.1%)	3 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	2 (0.5%)	3 (0.3%)
Haemorrhage/Bleeding/Coagulopathy									

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
0	167 (82.3%)	138 (76.2%)	305 (79.4%)	249 (88.3%)	209 (83.6%)	458 (86.1%)	416 (85.8%)	347 (80.5%)	763 (83.3%)
1	21 (10.3%)	32 (17.7%)	53 (13.8%)	18 (6.4%)	26 (10.4%)	44 (8.3%)	39 (8.0%)	58 (13.5%)	97 (10.6%)
2	11 (5.4%)	3 (1.7%)	14 (3.6%)	5 (1.8%)	8 (3.2%)	13 (2.4%)	16 (3.3%)	11 (2.6%)	27 (2.9%)
3	3 (1.5%)	8 (4.4%)	11 (2.9%)	7 (2.5%)	5 (2.0%)	12 (2.3%)	10 (2.1%)	13 (3.0%)	23 (2.5%)
4	1 (0.5%)	0 (0.0%)	1 (0.3%)	2 (0.7%)	1 (0.4%)	3 (0.6%)	3 (0.6%)	1 (0.2%)	4 (0.4%)
5	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.4%)	1 (0.4%)	2 (0.4%)	1 (0.2%)	1 (0.2%)	2 (0.2%)
Venus Thrombosis									
0	201 (99.0%)	177 (97.8%)	378 (98.4%)	268 (95.0%)	237 (94.8%)	505 (94.9%)	469 (96.7%)	414 (96.1%)	883 (96.4%)
1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (1.2%)	3 (0.6%)	0 (0.0%)	3 (0.7%)	3 (0.3%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
2	2 (1.0%)	1 (0.6%)	3 (0.8%)	8 (2.8%)	4 (1.6%)	12 (2.3%)	10 (2.1%)	5 (1.2%)	15 (1.6%)
3	0 (0.0%)	3 (1.7%)	3 (0.8%)	6 (2.1%)	6 (2.4%)	12 (2.3%)	6 (1.2%)	9 (2.1%)	15 (1.6%)
Arterial Thrombosis									
0	200 (98.5%)	181 (100.0%)	381 (99.2%)	282 (100.0%)	250 (100.0%)	532 (100.0%)	482 (99.4%)	431 (100.0%)	913 (99.7%)
2	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	0 (0.0%)	1 (0.1%)
3	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	0 (0.0%)	1 (0.1%)
4	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	0 (0.0%)	1 (0.1%)
Neutropenia									
0	132 (65.0%)	132 (72.9%)	264 (68.8%)	247 (87.6%)	226 (90.4%)	473 (88.9%)	379 (78.1%)	358 (83.1%)	737 (80.5%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
1	35 (17.2%)	25 (13.8%)	60 (15.6%)	22 (7.8%)	11 (4.4%)	33 (6.2%)	57 (11.8%)	36 (8.4%)	93 (10.2%)
2	18 (8.9%)	18 (9.9%)	36 (9.4%)	12 (4.3%)	10 (4.0%)	22 (4.1%)	30 (6.2%)	28 (6.5%)	58 (6.3%)
3	16 (7.9%)	5 (2.8%)	21 (5.5%)	1 (0.4%)	2 (0.8%)	3 (0.6%)	17 (3.5%)	7 (1.6%)	24 (2.6%)
4	2 (1.0%)	1 (0.6%)	3 (0.8%)	0 (0.0%)	1 (0.4%)	1 (0.2%)	2 (0.4%)	2 (0.5%)	4 (0.4%)
Thrombocytopenia									
0	144 (70.9%)	127 (70.2%)	271 (70.6%)	241 (85.5%)	204 (81.6%)	445 (83.6%)	385 (79.4%)	331 (76.8%)	716 (78.2%)
1	38 (18.7%)	30 (16.6%)	68 (17.7%)	36 (12.8%)	40 (16.0%)	76 (14.3%)	74 (15.3%)	70 (16.2%)	144 (15.7%)
2	13 (6.4%)	14 (7.7%)	27 (7.0%)	4 (1.4%)	5 (2.0%)	9 (1.7%)	17 (3.5%)	19 (4.4%)	36 (3.9%)
3	7 (3.4%)	8 (4.4%)	15 (3.9%)	0 (0.0%)	1 (0.4%)	1 (0.2%)	7 (1.4%)	9 (2.1%)	16 (1.7%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
4	1 (0.5%)	2 (1.1%)	3 (0.8%)	1 (0.4%)	0 (0.0%)	1 (0.2%)	2 (0.4%)	2 (0.5%)	4 (0.4%)
Fatigue									
0	23 (11.3%)	18 (9.9%)	41 (10.7%)	31 (11.0%)	35 (14.0%)	66 (12.4%)	54 (11.1%)	53 (12.3%)	107 (11.7%)
1	81 (39.9%)	64 (35.4%)	145 (37.8%)	138 (48.9%)	101 (40.4%)	239 (44.9%)	219 (45.2%)	165 (38.3%)	384 (41.9%)
2	81 (39.9%)	65 (35.9%)	146 (38.0%)	92 (32.6%)	85 (34.0%)	177 (33.3%)	173 (35.7%)	150 (34.8%)	323 (35.3%)
3	17 (8.4%)	34 (18.8%)	51 (13.3%)	21 (7.4%)	28 (11.2%)	49 (9.2%)	38 (7.8%)	62 (14.4%)	100 (10.9%)
4	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.4%)	1 (0.2%)	1 (0.2%)	1 (0.2%)	2 (0.2%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
Anaemia									
0	98 (48.3%)	87 (48.1%)	185 (48.2%)	183 (64.9%)	139 (55.6%)	322 (60.5%)	281 (57.9%)	226 (52.4%)	507 (55.3%)
1	75 (36.9%)	55 (30.4%)	130 (33.9%)	63 (22.3%)	72 (28.8%)	135 (25.4%)	138 (28.5%)	127 (29.5%)	265 (28.9%)
2	16 (7.9%)	26 (14.4%)	42 (10.9%)	26 (9.2%)	31 (12.4%)	57 (10.7%)	42 (8.7%)	57 (13.2%)	99 (10.8%)
3	14 (6.9%)	13 (7.2%)	27 (7.0%)	10 (3.5%)	8 (3.2%)	18 (3.4%)	24 (4.9%)	21 (4.9%)	45 (4.9%)
Hand-foot syndrome									
0	85 (41.9%)	94 (51.9%)	179 (46.6%)	201 (71.3%)	181 (72.4%)	382 (71.8%)	286 (59.0%)	275 (63.8%)	561 (61.2%)
1	59 (29.1%)	41 (22.7%)	100 (26.0%)	52 (18.4%)	55 (22.0%)	107 (20.1%)	111 (22.9%)	96 (22.3%)	207 (22.6%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
2	40 (19.7%)	30 (16.6%)	70 (18.2%)	23 (8.2%)	9 (3.6%)	32 (6.0%)	63 (13.0%)	39 (9.0%)	102 (11.1%)
3	19 (9.4%)	16 (8.8%)	35 (9.1%)	6 (2.1%)	5 (2.0%)	11 (2.1%)	25 (5.2%)	21 (4.9%)	46 (5.0%)
Hepatotoxicity									
0	162 (79.8%)	136 (75.1%)	298 (77.6%)	152 (53.9%)	118 (47.2%)	270 (50.8%)	314 (64.7%)	254 (58.9%)	568 (62.0%)
1	30 (14.8%)	28 (15.5%)	58 (15.1%)	64 (22.7%)	66 (26.4%)	130 (24.4%)	94 (19.4%)	94 (21.8%)	188 (20.5%)
2	5 (2.5%)	11 (6.1%)	16 (4.2%)	17 (6.0%)	24 (9.6%)	41 (7.7%)	22 (4.5%)	35 (8.1%)	57 (6.2%)
3	6 (3.0%)	4 (2.2%)	10 (2.6%)	44 (15.6%)	39 (15.6%)	83 (15.6%)	50 (10.3%)	43 (10.0%)	93 (10.2%)
4	0 (0.0%)	1 (0.6%)	1 (0.3%)	4 (1.4%)	2 (0.8%)	6 (1.1%)	4 (0.8%)	3 (0.7%)	7 (0.8%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
5	0 (0.0%)	1 (0.6%)	1 (0.3%)	1 (0.4%)	1 (0.4%)	2 (0.4%)	1 (0.2%)	2 (0.5%)	3 (0.3%)
Nausea/Vomiting									
0	71 (35.0%)	72 (39.8%)	143 (37.2%)	108 (38.3%)	87 (34.8%)	195 (36.7%)	179 (36.9%)	159 (36.9%)	338 (36.9%)
1	78 (38.4%)	67 (37.0%)	145 (37.8%)	104 (36.9%)	104 (41.6%)	208 (39.1%)	182 (37.5%)	171 (39.7%)	353 (38.5%)
2	45 (22.2%)	29 (16.0%)	74 (19.3%)	66 (23.4%)	46 (18.4%)	112 (21.1%)	111 (22.9%)	75 (17.4%)	186 (20.3%)
3	9 (4.4%)	12 (6.6%)	21 (5.5%)	4 (1.4%)	13 (5.2%)	17 (3.2%)	13 (2.7%)	25 (5.8%)	38 (4.1%)
5	0 (0.0%)	1 (0.6%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Pyrexia									

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
0	183 (90.1%)	165 (91.2%)	348 (90.6%)	264 (93.6%)	223 (89.2%)	487 (91.5%)	447 (92.2%)	388 (90.0%)	835 (91.2%)
1	12 (5.9%)	14 (7.7%)	26 (6.8%)	16 (5.7%)	25 (10.0%)	41 (7.7%)	28 (5.8%)	39 (9.0%)	67 (7.3%)
2	7 (3.4%)	0 (0.0%)	7 (1.8%)	1 (0.4%)	2 (0.8%)	3 (0.6%)	8 (1.6%)	2 (0.5%)	10 (1.1%)
3	1 (0.5%)	2 (1.1%)	3 (0.8%)	1 (0.4%)	0 (0.0%)	1 (0.2%)	2 (0.4%)	2 (0.5%)	4 (0.4%)
Dyspepsia / Indigestion									
0	105 (51.7%)	90 (49.7%)	195 (50.8%)	213 (75.5%)	171 (68.4%)	384 (72.2%)	318 (65.6%)	261 (60.6%)	579 (63.2%)
1	58 (28.6%)	62 (34.3%)	120 (31.3%)	53 (18.8%)	64 (25.6%)	117 (22.0%)	111 (22.9%)	126 (29.2%)	237 (25.9%)
2	39 (19.2%)	29 (16.0%)	68 (17.7%)	15 (5.3%)	15 (6.0%)	30 (5.6%)	54 (11.1%)	44 (10.2%)	98 (10.7%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
3	1 (0.5%)	0 (0.0%)	1 (0.3%)	1 (0.4%)	0 (0.0%)	1 (0.2%)	2 (0.4%)	0 (0.0%)	2 (0.2%)
Diarrhoea									
0	69 (34.0%)	74 (40.9%)	143 (37.2%)	93 (33.0%)	92 (36.8%)	185 (34.8%)	162 (33.4%)	166 (38.5%)	328 (35.8%)
1	80 (39.4%)	67 (37.0%)	147 (38.3%)	112 (39.7%)	89 (35.6%)	201 (37.8%)	192 (39.6%)	156 (36.2%)	348 (38.0%)
2	41 (20.2%)	30 (16.6%)	71 (18.5%)	59 (20.9%)	59 (23.6%)	118 (22.2%)	100 (20.6%)	89 (20.6%)	189 (20.6%)
3	13 (6.4%)	9 (5.0%)	22 (5.7%)	18 (6.4%)	9 (3.6%)	27 (5.1%)	31 (6.4%)	18 (4.2%)	49 (5.3%)
4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.4%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
5	0 (0.0%)	1 (0.6%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
Constipation									
0	120 (59.1%)	117 (64.6%)	237 (61.7%)	204 (72.3%)	157 (62.8%)	361 (67.9%)	324 (66.8%)	274 (63.6%)	598 (65.3%)
1	65 (32.0%)	44 (24.3%)	109 (28.4%)	67 (23.8%)	73 (29.2%)	140 (26.3%)	132 (27.2%)	117 (27.1%)	249 (27.2%)
2	18 (8.9%)	16 (8.8%)	34 (8.9%)	10 (3.5%)	19 (7.6%)	29 (5.5%)	28 (5.8%)	35 (8.1%)	63 (6.9%)
3	0 (0.0%)	4 (2.2%)	4 (1.0%)	1 (0.4%)	1 (0.4%)	2 (0.4%)	1 (0.2%)	5 (1.2%)	6 (0.7%)
Mucositis/Stomatitis									
0	57 (28.1%)	70 (38.7%)	127 (33.1%)	156 (55.3%)	140 (56.0%)	296 (55.6%)	213 (43.9%)	210 (48.7%)	423 (46.2%)
1	86 (42.4%)	52 (28.7%)	138 (35.9%)	92 (32.6%)	85 (34.0%)	177 (33.3%)	178 (36.7%)	137 (31.8%)	315 (34.4%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
2	47 (23.2%)	49 (27.1%)	96 (25.0%)	33 (11.7%)	17 (6.8%)	50 (9.4%)	80 (16.5%)	66 (15.3%)	146 (15.9%)
3	13 (6.4%)	10 (5.5%)	23 (6.0%)	1 (0.4%)	7 (2.8%)	8 (1.5%)	14 (2.9%)	17 (3.9%)	31 (3.4%)
4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.4%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Thyroid dysfunction									
0	140 (69.0%)	131 (72.4%)	271 (70.6%)	216 (76.6%)	191 (76.4%)	407 (76.5%)	356 (73.4%)	322 (74.7%)	678 (74.0%)
1	39 (19.2%)	32 (17.7%)	71 (18.5%)	44 (15.6%)	42 (16.8%)	86 (16.2%)	83 (17.1%)	74 (17.2%)	157 (17.1%)
2	23 (11.3%)	18 (9.9%)	41 (10.7%)	22 (7.8%)	17 (6.8%)	39 (7.3%)	45 (9.3%)	35 (8.1%)	80 (8.7%)
3	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	0 (0.0%)	1 (0.1%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
Anorexia									
0	81 (39.9%)	79 (43.6%)	160 (41.7%)	127 (45.0%)	119 (47.6%)	246 (46.2%)	208 (42.9%)	198 (45.9%)	406 (44.3%)
1	74 (36.5%)	65 (35.9%)	139 (36.2%)	96 (34.0%)	80 (32.0%)	176 (33.1%)	170 (35.1%)	145 (33.6%)	315 (34.4%)
2	47 (23.2%)	29 (16.0%)	76 (19.8%)	55 (19.5%)	42 (16.8%)	97 (18.2%)	102 (21.0%)	71 (16.5%)	173 (18.9%)
3	1 (0.5%)	8 (4.4%)	9 (2.3%)	4 (1.4%)	9 (3.6%)	13 (2.4%)	5 (1.0%)	17 (3.9%)	22 (2.4%)
Altered taste									
0	82 (40.4%)	68 (37.6%)	150 (39.1%)	134 (47.5%)	115 (46.0%)	249 (46.8%)	216 (44.5%)	183 (42.5%)	399 (43.6%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
1	92 (45.3%)	83 (45.9%)	175 (45.6%)	123 (43.6%)	105 (42.0%)	228 (42.9%)	215 (44.3%)	188 (43.6%)	403 (44.0%)
2	29 (14.3%)	29 (16.0%)	58 (15.1%)	23 (8.2%)	30 (12.0%)	53 (10.0%)	52 (10.7%)	59 (13.7%)	111 (12.1%)
3	0 (0.0%)	1 (0.6%)	1 (0.3%)	2 (0.7%)	0 (0.0%)	2 (0.4%)	2 (0.4%)	1 (0.2%)	3 (0.3%)
Change in hair and skin colour									
0	132 (65.0%)	115 (63.5%)	247 (64.3%)	174 (61.7%)	155 (62.0%)	329 (61.8%)	306 (63.1%)	270 (62.6%)	576 (62.9%)
1	63 (31.0%)	59 (32.6%)	122 (31.8%)	93 (33.0%)	82 (32.8%)	175 (32.9%)	156 (32.2%)	141 (32.7%)	297 (32.4%)
2	7 (3.4%)	6 (3.3%)	13 (3.4%)	15 (5.3%)	10 (4.0%)	25 (4.7%)	22 (4.5%)	16 (3.7%)	38 (4.1%)
3	1 (0.5%)	1 (0.6%)	2 (0.5%)	0 (0.0%)	1 (0.4%)	1 (0.2%)	1 (0.2%)	2 (0.5%)	3 (0.3%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.8%)	2 (0.4%)	0 (0.0%)	2 (0.5%)	2 (0.2%)
Hypersensitivity									
0	196 (96.6%)	176 (97.2%)	372 (96.9%)	279 (98.9%)	240 (96.0%)	519 (97.6%)	475 (97.9%)	416 (96.5%)	891 (97.3%)
1	6 (3.0%)	3 (1.7%)	9 (2.3%)	3 (1.1%)	8 (3.2%)	11 (2.1%)	9 (1.9%)	11 (2.6%)	20 (2.2%)
2	1 (0.5%)	2 (1.1%)	3 (0.8%)	0 (0.0%)	2 (0.8%)	2 (0.4%)	1 (0.2%)	4 (0.9%)	5 (0.5%)
Dyspnoea									
0	148 (72.9%)	120 (66.3%)	268 (69.8%)	207 (73.4%)	186 (74.4%)	393 (73.9%)	355 (73.2%)	306 (71.0%)	661 (72.2%)
1	28 (13.8%)	34 (18.8%)	62 (16.1%)	47 (16.7%)	27 (10.8%)	74 (13.9%)	75 (15.5%)	61 (14.2%)	136 (14.8%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
2	18 (8.9%)	22 (12.2%)	40 (10.4%)	18 (6.4%)	27 (10.8%)	45 (8.5%)	36 (7.4%)	49 (11.4%)	85 (9.3%)
3	9 (4.4%)	5 (2.8%)	14 (3.6%)	9 (3.2%)	10 (4.0%)	19 (3.6%)	18 (3.7%)	15 (3.5%)	33 (3.6%)
4	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.4%)	0 (0.0%)	1 (0.2%)	1 (0.2%)	0 (0.0%)	1 (0.1%)
Reduced cardiac function									
0	200 (98.5%)	179 (98.9%)	379 (98.7%)	278 (98.6%)	245 (98.0%)	523 (98.3%)	478 (98.6%)	424 (98.4%)	902 (98.5%)
1	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (1.4%)	2 (0.8%)	6 (1.1%)	4 (0.8%)	2 (0.5%)	6 (0.7%)
2	1 (0.5%)	1 (0.6%)	2 (0.5%)	0 (0.0%)	1 (0.4%)	1 (0.2%)	1 (0.2%)	2 (0.5%)	3 (0.3%)
3	2 (1.0%)	1 (0.6%)	3 (0.8%)	0 (0.0%)	1 (0.4%)	1 (0.2%)	2 (0.4%)	2 (0.5%)	4 (0.4%)
4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.4%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=203) N (%)	**DFIS (n=181) N (%)**	**Total (n=384) N (%)**	**CCS (n=282) N (%)**	**DFIS (n=250) N (%)**	**Total (n=532) N (%)**	**CCS (n=485) N (%)**	**DFIS (n=431) N (%)**	**Total (n=916) N (%)**
Proteinuria/nephrotic syndrome									
0	191 (94.1%)	173 (95.6%)	364 (94.8%)	265 (94.0%)	231 (92.4%)	496 (93.2%)	456 (94.0%)	404 (93.7%)	860 (93.9%)
1	9 (4.4%)	3 (1.7%)	12 (3.1%)	7 (2.5%)	8 (3.2%)	15 (2.8%)	16 (3.3%)	11 (2.6%)	27 (2.9%)
2	3 (1.5%)	3 (1.7%)	6 (1.6%)	9 (3.2%)	8 (3.2%)	17 (3.2%)	12 (2.5%)	11 (2.6%)	23 (2.5%)
3	0 (0.0%)	2 (1.1%)	2 (0.5%)	0 (0.0%)	3 (1.2%)	3 (0.6%)	0 (0.0%)	5 (1.2%)	5 (0.5%)
4	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.4%)	0 (0.0%)	1 (0.2%)	1 (0.2%)	0 (0.0%)	1 (0.1%)

Supplementary Table 75: Other AEs categorised by grade (S5a_Toxicity_AEs)

	CCS N (%)	DFIS N (%)	Total N (%)
Overall			
1	4881 (73.5%)	4567 (71.8%)	9448 (72.6%)
2	1249 (18.8%)	1290 (20.3%)	2539 (19.5%)
3	341 (5.1%)	368 (5.8%)	709 (5.5%)
4	35 (0.5%)	30 (0.5%)	65 (0.5%)
5	10 (0.2%)	16 (0.3%)	26 (0.2%)
Unable to grade	127 (1.9%)	93 (1.5%)	220 (1.7%)
Total	6643 (100%)	6364 (100%)	13007 (100%)
Sunitinib			
1	2073 (71.2%)	2283 (71.3%)	4356 (71.3%)
2	565 (19.4%)	666 (20.8%)	1231 (20.1%)
3	168 (5.8%)	175 (5.5%)	343 (5.6%)
4	20 (0.7%)	15 (0.5%)	35 (0.6%)
5	5 (0.2%)	8 (0.2%)	13 (0.2%)
Unable to grade	80 (2.7%)	55 (1.7%)	135 (2.2%)
Total	2911 (100%)	3202 (100%)	6113 (100%)
Pazopanib			
1	2808 (75.2%)	2284 (72.2%)	5092 (73.9%)
2	684 (18.3%)	624 (19.7%)	1308 (19.0%)
3	173 (4.6%)	193 (6.1%)	366 (5.3%)
4	15 (0.4%)	15 (0.5%)	30 (0.4%)

	CCS N (%)	DFIS N (%)	Total N (%)
5	5 (0.1%)	8 (0.3%)	13 (0.2%)
Unable to grade	47 (1.3%)	38 (1.2%)	85 (1.2%)
Total	3732 (100%)	3162 (100%)	6894 (100%)

Supplementary Table 76: Other AEs with grade 3 or above by CTCAE term (S5a_Toxicity_AEs)

	Sunitinib			Pazopanib			Overall		
	CCS (n=193) N (%)	**DFIS (n=198) N (%)**	**Total (n=391) N (%)**	**CCS (n=193) N (%)**	**DFIS (n=216) N (%)**	**Total (n=409) N (%)**	**CCS (n=386) N (%)**	**DFIS (n=414) N (%)**	**Total (n=800) N (%)**
Back pain	8 (4.1%)	11 (5.6%)	19 (4.9%)	13 (6.7%)	4 (1.9%)	17 (4.2%)	21 (5.4%)	15 (3.6%)	36 (4.5%)
Lung infection	11 (5.7%)	5 (2.5%)	16 (4.1%)	10 (5.2%)	10 (4.6%)	20 (4.9%)	21 (5.4%)	15 (3.6%)	36 (4.5%)
Abdominal pain	5 (2.6%)	5 (2.5%)	10 (2.6%)	14 (7.3%)	8 (3.7%)	22 (5.4%)	19 (4.9%)	13 (3.1%)	32 (4.0%)
Pain in extremity	11 (5.7%)	5 (2.5%)	16 (4.1%)	4 (2.1%)	10 (4.6%)	14 (3.4%)	15 (3.9%)	15 (3.6%)	30 (3.8%)
Hyponatremia	5 (2.6%)	2 (1.0%)	7 (1.8%)	1 (0.5%)	18 (8.3%)	19 (4.6%)	6 (1.6%)	20 (4.8%)	26 (3.3%)
Pleural effusion	10 (5.2%)	6 (3.0%)	16 (4.1%)	5 (2.6%)	3 (1.4%)	8 (2.0%)	15 (3.9%)	9 (2.2%)	24 (3.0%)
Urinary tract infection	2 (1.0%)	8 (4.0%)	10 (2.6%)	9 (4.7%)	5 (2.3%)	14 (3.4%)	11 (2.8%)	13 (3.1%)	24 (3.0%)
Pain	5 (2.6%)	9 (4.5%)	14 (3.6%)	6 (3.1%)	2 (0.9%)	8 (2.0%)	11 (2.8%)	11 (2.7%)	22 (2.8%)
Dyspnea	8 (4.1%)	7 (3.5%)	15 (3.8%)	3 (1.6%)	3 (1.4%)	6 (1.5%)	11 (2.8%)	10 (2.4%)	21 (2.6%)
Hypophosphatemia	3 (1.6%)	16 (8.1%)	19 (4.9%)	2 (1.0%)	0 (0.0%)	2 (0.5%)	5 (1.3%)	16 (3.9%)	21 (2.6%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=193) N (%)	**DFIS (n=198) N (%)**	**Total (n=391) N (%)**	**CCS (n=193) N (%)**	**DFIS (n=216) N (%)**	**Total (n=409) N (%)**	**CCS (n=386) N (%)**	**DFIS (n=414) N (%)**	**Total (n=800) N (%)**
Hematuria	4 (2.1%)	6 (3.0%)	10 (2.6%)	6 (3.1%)	4 (1.9%)	10 (2.4%)	10 (2.6%)	10 (2.4%)	20 (2.5%)
Tumor pain	15 (7.8%)	1 (0.5%)	16 (4.1%)	1 (0.5%)	1 (0.5%)	2 (0.5%)	16 (4.1%)	2 (0.5%)	18 (2.3%)
Acute kidney injury	7 (3.6%)	2 (1.0%)	9 (2.3%)	3 (1.6%)	5 (2.3%)	8 (2.0%)	10 (2.6%)	7 (1.7%)	17 (2.1%)
Syncope	4 (2.1%)	7 (3.5%)	11 (2.8%)	2 (1.0%)	4 (1.9%)	6 (1.5%)	6 (1.6%)	11 (2.7%)	17 (2.1%)
Thromboembolic event	6 (3.1%)	4 (2.0%)	10 (2.6%)	1 (0.5%)	6 (2.8%)	7 (1.7%)	7 (1.8%)	10 (2.4%)	17 (2.1%)
Headache	3 (1.6%)	2 (1.0%)	5 (1.3%)	0 (0.0%)	9 (4.2%)	9 (2.2%)	3 (0.8%)	11 (2.7%)	14 (1.8%)
Musculoskeletal and connective tissue disorder - Other, specify	4 (2.1%)	2 (1.0%)	6 (1.5%)	2 (1.0%)	6 (2.8%)	8 (2.0%)	6 (1.6%)	8 (1.9%)	14 (1.8%)
Blood bilirubin increased	0 (0.0%)	0 (0.0%)	0 (0.0%)	10 (5.2%)	3 (1.4%)	13 (3.2%)	10 (2.6%)	3 (0.7%)	13 (1.6%)
Hypercalcemia	2 (1.0%)	2 (1.0%)	4 (1.0%)	6 (3.1%)	3 (1.4%)	9 (2.2%)	8 (2.1%)	5 (1.2%)	13 (1.6%)
Non-cardiac chest pain	3 (1.6%)	0 (0.0%)	3 (0.8%)	6 (3.1%)	3 (1.4%)	9 (2.2%)	9 (2.3%)	3 (0.7%)	12 (1.5%)
Hyperkalemia	2 (1.0%)	5 (2.5%)	7 (1.8%)	0 (0.0%)	4 (1.9%)	4 (1.0%)	2 (0.5%)	9 (2.2%)	11 (1.4%)
Arthralgia	1 (0.5%)	3 (1.5%)	4 (1.0%)	3 (1.6%)	3 (1.4%)	6 (1.5%)	4 (1.0%)	6 (1.4%)	10 (1.3%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=193) N (%)	DFIS (n=198) N (%)	Total (n=391) N (%)	CCS (n=193) N (%)	DFIS (n=216) N (%)	Total (n=409) N (%)	CCS (n=386) N (%)	DFIS (n=414) N (%)	Total (n=800) N (%)
Bone pain	2 (1.0%)	3 (1.5%)	5 (1.3%)	1 (0.5%)	4 (1.9%)	5 (1.2%)	3 (0.8%)	7 (1.7%)	10 (1.3%)
Dehydration	3 (1.6%)	3 (1.5%)	6 (1.5%)	0 (0.0%)	4 (1.9%)	4 (1.0%)	3 (0.8%)	7 (1.7%)	10 (1.3%)
Creatinine increased	6 (3.1%)	1 (0.5%)	7 (1.8%)	0 (0.0%)	2 (0.9%)	2 (0.5%)	6 (1.6%)	3 (0.7%)	9 (1.1%)
Edema limbs	1 (0.5%)	0 (0.0%)	1 (0.3%)	5 (2.6%)	3 (1.4%)	8 (2.0%)	6 (1.6%)	3 (0.7%)	9 (1.1%)
Fall	0 (0.0%)	1 (0.5%)	1 (0.3%)	3 (1.6%)	5 (2.3%)	8 (2.0%)	3 (0.8%)	6 (1.4%)	9 (1.1%)
Sepsis	1 (0.5%)	3 (1.5%)	4 (1.0%)	3 (1.6%)	2 (0.9%)	5 (1.2%)	4 (1.0%)	5 (1.2%)	9 (1.1%)
Confusion	2 (1.0%)	3 (1.5%)	5 (1.3%)	1 (0.5%)	2 (0.9%)	3 (0.7%)	3 (0.8%)	5 (1.2%)	8 (1.0%)
GGT increased	3 (1.6%)	1 (0.5%)	4 (1.0%)	3 (1.6%)	1 (0.5%)	4 (1.0%)	6 (1.6%)	2 (0.5%)	8 (1.0%)
Infections and infestations - Other, specify	2 (1.0%)	2 (1.0%)	4 (1.0%)	1 (0.5%)	3 (1.4%)	4 (1.0%)	3 (0.8%)	5 (1.2%)	8 (1.0%)
Alkaline phosphatase increased	2 (1.0%)	1 (0.5%)	3 (0.8%)	1 (0.5%)	2 (0.9%)	3 (0.7%)	3 (0.8%)	3 (0.7%)	6 (0.8%)
Hypoalbuminemia	0 (0.0%)	5 (2.5%)	5 (1.3%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	5 (1.2%)	6 (0.8%)
Intracranial hemorrhage	2 (1.0%)	0 (0.0%)	2 (0.5%)	1 (0.5%)	3 (1.4%)	4 (1.0%)	3 (0.8%)	3 (0.7%)	6 (0.8%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=193) N (%)	DFIS (n=198) N (%)	Total (n=391) N (%)	CCS (n=193) N (%)	DFIS (n=216) N (%)	Total (n=409) N (%)	CCS (n=386) N (%)	DFIS (n=414) N (%)	Total (n=800) N (%)
Ascites	1 (0.5%)	0 (0.0%)	1 (0.3%)	2 (1.0%)	2 (0.9%)	4 (1.0%)	3 (0.8%)	2 (0.5%)	5 (0.6%)
Flank pain	1 (0.5%)	0 (0.0%)	1 (0.3%)	1 (0.5%)	3 (1.4%)	4 (1.0%)	2 (0.5%)	3 (0.7%)	5 (0.6%)
Investigations - Other, specify	0 (0.0%)	3 (1.5%)	3 (0.8%)	2 (1.0%)	0 (0.0%)	2 (0.5%)	2 (0.5%)	3 (0.7%)	5 (0.6%)
Skin ulceration	1 (0.5%)	1 (0.5%)	2 (0.5%)	3 (1.6%)	0 (0.0%)	3 (0.7%)	4 (1.0%)	1 (0.2%)	5 (0.6%)
Abdominal distension	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.0%)	2 (0.9%)	4 (1.0%)	2 (0.5%)	2 (0.5%)	4 (0.5%)
Alanine aminotransferase increased	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	3 (1.4%)	4 (1.0%)	1 (0.3%)	3 (0.7%)	4 (0.5%)
Depression	1 (0.5%)	1 (0.5%)	2 (0.5%)	0 (0.0%)	2 (0.9%)	2 (0.5%)	1 (0.3%)	3 (0.7%)	4 (0.5%)
Fracture	0 (0.0%)	2 (1.0%)	2 (0.5%)	1 (0.5%)	1 (0.5%)	2 (0.5%)	1 (0.3%)	3 (0.7%)	4 (0.5%)
Hypotension	0 (0.0%)	2 (1.0%)	2 (0.5%)	0 (0.0%)	2 (0.9%)	2 (0.5%)	0 (0.0%)	4 (1.0%)	4 (0.5%)
Malaise	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	3 (1.4%)	4 (1.0%)	1 (0.3%)	3 (0.7%)	4 (0.5%)
Skin and subcutaneous tissue disorders - Other, specify	1 (0.5%)	1 (0.5%)	2 (0.5%)	1 (0.5%)	1 (0.5%)	2 (0.5%)	2 (0.5%)	2 (0.5%)	4 (0.5%)
Skin infection	1 (0.5%)	1 (0.5%)	2 (0.5%)	2 (1.0%)	0 (0.0%)	2 (0.5%)	3 (0.8%)	1 (0.2%)	4 (0.5%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=193) N (%)	DFIS (n=198) N (%)	Total (n=391) N (%)	CCS (n=193) N (%)	DFIS (n=216) N (%)	Total (n=409) N (%)	CCS (n=386) N (%)	DFIS (n=414) N (%)	Total (n=800) N (%)
Upper respiratory infection	1 (0.5%)	1 (0.5%)	2 (0.5%)	1 (0.5%)	1 (0.5%)	2 (0.5%)	2 (0.5%)	2 (0.5%)	4 (0.5%)
Agitation	0 (0.0%)	3 (1.5%)	3 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (0.7%)	3 (0.4%)
Anxiety	0 (0.0%)	2 (1.0%)	2 (0.5%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	3 (0.7%)	3 (0.4%)
Bronchial infection	1 (0.5%)	1 (0.5%)	2 (0.5%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	1 (0.3%)	2 (0.5%)	3 (0.4%)
Chest pain - cardiac	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.0%)	1 (0.5%)	3 (0.7%)	2 (0.5%)	1 (0.2%)	3 (0.4%)
Cholecystitis	1 (0.5%)	0 (0.0%)	1 (0.3%)	2 (1.0%)	0 (0.0%)	2 (0.5%)	3 (0.8%)	0 (0.0%)	3 (0.4%)
Cough	0 (0.0%)	1 (0.5%)	1 (0.3%)	1 (0.5%)	1 (0.5%)	2 (0.5%)	1 (0.3%)	2 (0.5%)	3 (0.4%)
Dizziness	0 (0.0%)	1 (0.5%)	1 (0.3%)	1 (0.5%)	1 (0.5%)	2 (0.5%)	1 (0.3%)	2 (0.5%)	3 (0.4%)
Fatigue	1 (0.5%)	1 (0.5%)	2 (0.5%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	1 (0.3%)	2 (0.5%)	3 (0.4%)
Generalized muscle weakness	0 (0.0%)	1 (0.5%)	1 (0.3%)	1 (0.5%)	1 (0.5%)	2 (0.5%)	1 (0.3%)	2 (0.5%)	3 (0.4%)
Hoarseness	2 (1.0%)	0 (0.0%)	2 (0.5%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	2 (0.5%)	1 (0.2%)	3 (0.4%)
Hypomagnesemia	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	2 (0.9%)	2 (0.5%)	0 (0.0%)	3 (0.7%)	3 (0.4%)
Hypoxia	1 (0.5%)	2 (1.0%)	3 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	2 (0.5%)	3 (0.4%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=193) N (%)	DFIS (n=198) N (%)	Total (n=391) N (%)	CCS (n=193) N (%)	DFIS (n=216) N (%)	Total (n=409) N (%)	CCS (n=386) N (%)	DFIS (n=414) N (%)	Total (n=800) N (%)
Insomnia	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	2 (0.9%)	2 (0.5%)	0 (0.0%)	3 (0.7%)	3 (0.4%)
Muscle weakness lower limb	1 (0.5%)	0 (0.0%)	1 (0.3%)	1 (0.5%)	1 (0.5%)	2 (0.5%)	2 (0.5%)	1 (0.2%)	3 (0.4%)
Rash maculo-papular	1 (0.5%)	0 (0.0%)	1 (0.3%)	1 (0.5%)	1 (0.5%)	2 (0.5%)	2 (0.5%)	1 (0.2%)	3 (0.4%)
Small intestinal perforation	0 (0.0%)	1 (0.5%)	1 (0.3%)	2 (1.0%)	0 (0.0%)	2 (0.5%)	2 (0.5%)	1 (0.2%)	3 (0.4%)
Stroke	2 (1.0%)	1 (0.5%)	3 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.5%)	1 (0.2%)	3 (0.4%)
Acute coronary syndrome	0 (0.0%)	1 (0.5%)	1 (0.3%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	1 (0.2%)	2 (0.3%)
Aspiration	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.9%)	2 (0.5%)	0 (0.0%)	2 (0.5%)	2 (0.3%)
Chills	0 (0.0%)	2 (1.0%)	2 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.5%)	2 (0.3%)
Chronic kidney disease	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	1 (0.3%)	1 (0.2%)	2 (0.3%)
Conduction disorder	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	2 (0.5%)	2 (0.3%)
Dental caries	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	2 (0.5%)	2 (0.3%)
Dysphasia	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	1 (0.3%)	1 (0.2%)	2 (0.3%)
Ejection fraction decreased	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.9%)	2 (0.5%)	0 (0.0%)	2 (0.5%)	2 (0.3%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=193) N (%)	DFIS (n=198) N (%)	Total (n=391) N (%)	CCS (n=193) N (%)	DFIS (n=216) N (%)	Total (n=409) N (%)	CCS (n=386) N (%)	DFIS (n=414) N (%)	Total (n=800) N (%)
Fever	2 (1.0%)	0 (0.0%)	2 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.5%)	0 (0.0%)	2 (0.3%)
Flu like symptoms	0 (0.0%)	1 (0.5%)	1 (0.3%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	1 (0.2%)	2 (0.3%)
Gait disturbance	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.9%)	2 (0.5%)	0 (0.0%)	2 (0.5%)	2 (0.3%)
Gallbladder pain	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.0%)	0 (0.0%)	2 (0.5%)	2 (0.5%)	0 (0.0%)	2 (0.3%)
Gastric hemorrhage	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.5%)	2 (0.5%)	1 (0.3%)	1 (0.2%)	2 (0.3%)
Kidney infection	1 (0.5%)	0 (0.0%)	1 (0.3%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	2 (0.5%)	0 (0.0%)	2 (0.3%)
Myocardial infarction	1 (0.5%)	0 (0.0%)	1 (0.3%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	2 (0.5%)	0 (0.0%)	2 (0.3%)
Neck pain	1 (0.5%)	0 (0.0%)	1 (0.3%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	2 (0.5%)	0 (0.0%)	2 (0.3%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) - Other, specify	0 (0.0%)	1 (0.5%)	1 (0.3%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	1 (0.2%)	2 (0.3%)
Neuralgia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.9%)	2 (0.5%)	0 (0.0%)	2 (0.5%)	2 (0.3%)
Pain of skin	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.0%)	0 (0.0%)	2 (0.5%)	2 (0.5%)	0 (0.0%)	2 (0.3%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=193) N (%)	DFIS (n=198) N (%)	Total (n=391) N (%)	CCS (n=193) N (%)	DFIS (n=216) N (%)	Total (n=409) N (%)	CCS (n=386) N (%)	DFIS (n=414) N (%)	Total (n=800) N (%)
Paresthesia	0 (0.0%)	1 (0.5%)	1 (0.3%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	1 (0.2%)	2 (0.3%)
Pericardial effusion	1 (0.5%)	1 (0.5%)	2 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	1 (0.2%)	2 (0.3%)
Peripheral motor neuropathy	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	1 (0.3%)	1 (0.2%)	2 (0.3%)
Psychosis	2 (1.0%)	0 (0.0%)	2 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.5%)	0 (0.0%)	2 (0.3%)
Scrotal infection	1 (0.5%)	0 (0.0%)	1 (0.3%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	2 (0.5%)	0 (0.0%)	2 (0.3%)
Upper gastrointestinal hemorrhage	1 (0.5%)	1 (0.5%)	2 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	1 (0.2%)	2 (0.3%)
Urinary incontinence	2 (1.0%)	0 (0.0%)	2 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.5%)	0 (0.0%)	2 (0.3%)
Vascular disorders - Other, specify	2 (1.0%)	0 (0.0%)	2 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.5%)	0 (0.0%)	2 (0.3%)
Abdominal infection	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Anal fistula	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Anal pain	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Anorexia	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Appendicitis	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=193) N (%)	DFIS (n=198) N (%)	Total (n=391) N (%)	CCS (n=193) N (%)	DFIS (n=216) N (%)	Total (n=409) N (%)	CCS (n=386) N (%)	DFIS (n=414) N (%)	Total (n=800) N (%)
Arthritis	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Ataxia	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Atrial flutter	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Bladder infection	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Blood and lymphatic system disorders - Other, specify	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Blurred vision	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Bronchial obstruction	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Bronchopulmonary hemorrhage	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Bruising	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Cardiac arrest	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Cardiac disorders - Other, specify	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Cataract	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=193) N (%)	DFIS (n=198) N (%)	Total (n=391) N (%)	CCS (n=193) N (%)	DFIS (n=216) N (%)	Total (n=409) N (%)	CCS (n=386) N (%)	DFIS (n=414) N (%)	Total (n=800) N (%)
Colitis	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Colonic perforation	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Constipation	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Depressed level of consciousness	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Dry skin	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Duodenal ulcer	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Dysarthria	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Edema cerebral	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Epistaxis	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Eye disorders - Other, specify	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Facial muscle weakness	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Gastrointestinal disorders - Other, specify	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=193) N (%)	DFIS (n=198) N (%)	Total (n=391) N (%)	CCS (n=193) N (%)	DFIS (n=216) N (%)	Total (n=409) N (%)	CCS (n=386) N (%)	DFIS (n=414) N (%)	Total (n=800) N (%)
Gastrointestinal pain	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
General disorders and administration site conditions - Other, specify	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Hallucinations	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Heart failure	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Hematoma	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Hemoglobin increased	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Hepatobiliary disorders - Other, specify	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Hip fracture	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Hyperglycemia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Hyperuricemia	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Hypocalcemia	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Hypokalemia	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.1%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=193) N (%)	DFIS (n=198) N (%)	Total (n=391) N (%)	CCS (n=193) N (%)	DFIS (n=216) N (%)	Total (n=409) N (%)	CCS (n=386) N (%)	DFIS (n=414) N (%)	Total (n=800) N (%)
INR increased	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Kidney anastomotic leak	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Mania	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Meningitis	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Muscle weakness left-sided	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Nervous system disorders - Other, specify	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Neutrophil count decreased	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Optic nerve disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Osteonecrosis of jaw	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Palmar-plantar erythrodysesthesia syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Periorbital edema	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.1%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=193) N (%)	DFIS (n=198) N (%)	Total (n=391) N (%)	CCS (n=193) N (%)	DFIS (n=216) N (%)	Total (n=409) N (%)	CCS (n=386) N (%)	DFIS (n=414) N (%)	Total (n=800) N (%)
Personality change	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Platelet count decreased	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Pleuritic pain	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Presyncope	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Productive cough	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Pruritus	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Pulmonary edema	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Rectal hemorrhage	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Rectal pain	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Retinal detachment	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Retinal tear	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Sinus bradycardia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Skin induration	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=193) N (%)	DFIS (n=198) N (%)	Total (n=391) N (%)	CCS (n=193) N (%)	DFIS (n=216) N (%)	Total (n=409) N (%)	CCS (n=386) N (%)	DFIS (n=414) N (%)	Total (n=800) N (%)
Spinal fracture	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Stomach pain	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Tooth infection	1 (0.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Toothache	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Transient ischemic attacks	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Urinary retention	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Urticaria	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Vasovagal reaction	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Vertigo	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Visceral arterial ischemia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Voice alteration	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Weight loss	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Wound infection	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=193) N (%)	**DFIS (n=198) N (%)**	**Total (n=391) N (%)**	**CCS (n=193) N (%)**	**DFIS (n=216) N (%)**	**Total (n=409) N (%)**	**CCS (n=386) N (%)**	**DFIS (n=414) N (%)**	**Total (n=800) N (%)**
Unable to code	4 (2.1%)	7 (3.5%)	11 (2.8%)	2 (1.0%)	2 (0.9%)	4 (1.0%)	6 (1.6%)	9 (2.2%)	15 (1.9%)

Supplementary Table 77: Line-Listing of Other AEs (Grade 3 or above) with no CTCAE recoding, by treatment (S5a_Toxicity_AEs)

Sunitinib		Pazopanib	
CCS	**DFIS**	**CCS**	**DFIS**
Turp	brain metastases	subcapsular orchidectomy	
Vertebroplasty	Hospitalisation for deterioration of condition	Lytic lesion left femur	
Lymphangitis carcinomatosis	hydronephrosis		
Lymphangitis Carcinomatosis	Brain met		
	Brain mets		
	hemiarthroplasty		
	Metastatic lesion right frontal lobe of brain		
	Brain Metastases		
	Metabolism - electrolyte imbalance		

Supplementary Table 78: SAE by CTCAE grade (S5b_Toxicity_SAEs)

	CCS N (%)	DFIS N (%)	Total N (%)
Overall			
1	18 (5.2%)	19 (4.7%)	37 (5.0%)
2	91 (26.5%)	106 (26.4%)	197 (26.5%)
3	190 (55.4%)	214 (53.4%)	404 (54.3%)
4	26 (7.6%)	24 (6.0%)	50 (6.7%)
5	14 (4.1%)	20 (5.0%)	34 (4.6%)
Unable to grade	4 (1.2%)	18 (4.5%)	22 (3.0%)
Total	343 (100%)	401 (100%)	744 (100%)
Sunitinib			
1	8 (5.3%)	7 (4.2%)	15 (4.7%)
2	39 (26.0%)	39 (23.5%)	78 (24.7%)
3	86 (57.3%)	87 (52.4%)	173 (54.7%)
4	9 (6.0%)	12 (7.2%)	21 (6.6%)
5	6 (4.0%)	9 (5.4%)	15 (4.7%)
Unable to grade	2 (1.3%)	12 (7.2%)	14 (4.4%)
Total	150 (100%)	166 (100%)	316 (100%)
Pazopanib			
1	10 (5.2%)	12 (5.1%)	22 (5.1%)
2	52 (26.9%)	67 (28.5%)	119 (27.8%)
3	104 (53.9%)	127 (54.0%)	231 (54.0%)
4	17 (8.8%)	12 (5.1%)	29 (6.8%)

	CCS N (%)	DFIS N (%)	Total N (%)
5	8 (4.1%)	11 (4.7%)	19 (4.4%)
Unable to grade	2 (1.0%)	6 (2.6%)	8 (1.9%)
Total	193 (100%)	235 (100%)	428 (100%)

Supplementary Table 79: SAR by CTCAE grade (S5c_Toxicity_SARs)

	CCS N (%)	DFIS N (%)	Total N (%)
Overall			
1	5 (4.7%)	6 (5.0%)	11 (4.9%)
2	30 (28.0%)	39 (32.8%)	69 (30.5%)
3	60 (56.1%)	54 (45.4%)	114 (50.4%)
4	7 (6.5%)	10 (8.4%)	17 (7.5%)
5	3 (2.8%)	9 (7.6%)	12 (5.3%)
Unable to code	2 (1.9%)	1 (0.8%)	3 (1.3%)
Total	107 (100%)	119 (100%)	226 (100%)
Sunitinib			
1	0 (0.0%)	2 (3.4%)	2 (1.8%)
2	17 (32.1%)	18 (30.5%)	35 (31.3%)
3	29 (54.7%)	29 (49.2%)	58 (51.8%)
4	4 (7.5%)	7 (11.9%)	11 (9.8%)
5	1 (1.9%)	2 (3.4%)	3 (2.7%)
Unable to code	2 (3.8%)	1 (1.7%)	3 (2.7%)
Total	53 (100%)	59 (100%)	112 (100%)
Pazopanib			
1	5 (9.3%)	4 (6.7%)	9 (7.9%)
2	13 (24.1%)	21 (35.0%)	34 (29.8%)
3	31 (57.4%)	25 (41.7%)	56 (49.1%)
4	3 (5.6%)	3 (5.0%)	6 (5.3%)

	CCS N (%)	DFIS N (%)	Total N (%)
5	2 (3.7%)	7 (11.7%)	9 (7.9%)
Total	54 (100%)	60 (100%)	114 (100%)

Supplementary Table 80: SAE by MedDRA (S5b_Toxicity_SAEs)

	Sunitinib			Pazopanib			Overall		
	CCS (n=150) N (%)	**DFIS (n=166) N (%)**	**Total (n=316) N (%)**	**CCS (n=193) N (%)**	**DFIS (n=235) N (%)**	**Total (n=428) N (%)**	**CCS (n=343) N (%)**	**DFIS (n=401) N (%)**	**Total (n=744) N (%)**
Gastrointestinal disorders	23 (15.3%)	26 (15.7%)	49 (15.5%)	33 (17.1%)	33 (14.0%)	66 (15.4%)	56 (16.3%)	59 (14.7%)	115 (15.5%)
Infections and infestations	17 (11.3%)	29 (17.5%)	46 (14.6%)	26 (13.5%)	40 (17.0%)	66 (15.4%)	43 (12.5%)	69 (17.2%)	112 (15.1%)
Respiratory, thoracic and mediastinal disorders	24 (16.0%)	20 (12.0%)	44 (13.9%)	24 (12.4%)	21 (8.9%)	45 (10.5%)	48 (14.0%)	41 (10.2%)	89 (12.0%)
Musculoskeletal and connective tissue disorders	14 (9.3%)	15 (9.0%)	29 (9.2%)	15 (7.8%)	20 (8.5%)	35 (8.2%)	29 (8.5%)	35 (8.7%)	64 (8.6%)
Renal and urinary disorders	11 (7.3%)	13 (7.8%)	24 (7.6%)	16 (8.3%)	19 (8.1%)	35 (8.2%)	27 (7.9%)	32 (8.0%)	59 (7.9%)
Nervous system disorders	12 (8.0%)	11 (6.6%)	23 (7.3%)	6 (3.1%)	23 (9.8%)	29 (6.8%)	18 (5.2%)	34 (8.5%)	52 (7.0%)
Neoplasms benign, malignant and unspecified (including cysts and polyps)	5 (3.3%)	14 (8.4%)	19 (6.0%)	12 (6.2%)	9 (3.8%)	21 (4.9%)	17 (5.0%)	23 (5.7%)	40 (5.4%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=150) N (%)	**DFIS (n=166) N (%)**	**Total (n=316) N (%)**	**CCS (n=193) N (%)**	**DFIS (n=235) N (%)**	**Total (n=428) N (%)**	**CCS (n=343) N (%)**	**DFIS (n=401) N (%)**	**Total (n=744) N (%)**
Vascular disorders	4 (2.7%)	3 (1.8%)	7 (2.2%)	11 (5.7%)	15 (6.4%)	26 (6.1%)	15 (4.4%)	18 (4.5%)	33 (4.4%)
Blood and lymphatic system disorders	12 (8.0%)	10 (6.0%)	22 (7.0%)	5 (2.6%)	4 (1.7%)	9 (2.1%)	17 (5.0%)	14 (3.5%)	31 (4.2%)
General disorders and administration site conditions	4 (2.7%)	6 (3.6%)	10 (3.2%)	9 (4.7%)	10 (4.3%)	19 (4.4%)	13 (3.8%)	16 (4.0%)	29 (3.9%)
Investigations	4 (2.7%)	2 (1.2%)	6 (1.9%)	6 (3.1%)	16 (6.8%)	22 (5.1%)	10 (2.9%)	18 (4.5%)	28 (3.8%)
Cardiac disorders	4 (2.7%)	7 (4.2%)	11 (3.5%)	7 (3.6%)	9 (3.8%)	16 (3.7%)	11 (3.2%)	16 (4.0%)	27 (3.6%)
Hepatobiliary disorders	2 (1.3%)	4 (2.4%)	6 (1.9%)	5 (2.6%)	5 (2.1%)	10 (2.3%)	7 (2.0%)	9 (2.2%)	16 (2.2%)
Metabolism and nutrition disorders	3 (2.0%)	2 (1.2%)	5 (1.6%)	5 (2.6%)	5 (2.1%)	10 (2.3%)	8 (2.3%)	7 (1.7%)	15 (2.0%)
Injury, poisoning and procedural complications	4 (2.7%)	2 (1.2%)	6 (1.9%)	4 (2.1%)	4 (1.7%)	8 (1.9%)	8 (2.3%)	6 (1.5%)	14 (1.9%)
Skin and subcutaneous tissue disorders	3 (2.0%)	0 (0.0%)	3 (0.9%)	2 (1.0%)	1 (0.4%)	3 (0.7%)	5 (1.5%)	1 (0.2%)	6 (0.8%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=150) N (%)	**DFIS (n=166) N (%)**	**Total (n=316) N (%)**	**CCS (n=193) N (%)**	**DFIS (n=235) N (%)**	**Total (n=428) N (%)**	**CCS (n=343) N (%)**	**DFIS (n=401) N (%)**	**Total (n=744) N (%)**
Endocrine disorders	2 (1.3%)	1 (0.6%)	3 (0.9%)	2 (1.0%)	0 (0.0%)	2 (0.5%)	4 (1.2%)	1 (0.2%)	5 (0.7%)
Eye disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.0%)	1 (0.4%)	3 (0.7%)	2 (0.6%)	1 (0.2%)	3 (0.4%)
Psychiatric disorders	1 (0.7%)	1 (0.6%)	2 (0.6%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	2 (0.6%)	1 (0.2%)	3 (0.4%)
Ear and labyrinth disorders	1 (0.7%)	0 (0.0%)	1 (0.3%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	2 (0.6%)	0 (0.0%)	2 (0.3%)
Reproductive system and breast disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.2%)	1 (0.3%)	0 (0.0%)	1 (0.1%)

Supplementary Table 81: SAR by MedDRA (S5c_Toxicity_SARs)

	Sunitinib			Pazopanib			Overall		
	CCS (n=53) N (%)	**DFIS (n=59) N (%)**	**Total (n=112) N (%)**	**CCS (n=54) N (%)**	**DFIS (n=60) N (%)**	**Total (n=114) N (%)**	**CCS (n=107) N (%)**	**DFIS (n=119) N (%)**	**Total (n=226) N (%)**
Gastrointestinal disorders	18 (34.0%)	16 (27.1%)	34 (30.4%)	18 (33.3%)	18 (30.0%)	36 (31.6%)	36 (33.6%)	34 (28.6%)	70 (31.0%)
Infections and infestations	4 (7.5%)	8 (13.6%)	12 (10.7%)	4 (7.4%)	7 (11.7%)	11 (9.6%)	8 (7.5%)	15 (12.6%)	23 (10.2%)
Vascular disorders	2 (3.8%)	3 (5.1%)	5 (4.5%)	7 (13.0%)	8 (13.3%)	15 (13.2%)	9 (8.4%)	11 (9.2%)	20 (8.8%)
Blood and lymphatic system disorders	8 (15.1%)	8 (13.6%)	16 (14.3%)	1 (1.9%)	2 (3.3%)	3 (2.6%)	9 (8.4%)	10 (8.4%)	19 (8.4%)
Respiratory, thoracic and mediastinal disorders	4 (7.5%)	3 (5.1%)	7 (6.3%)	5 (9.3%)	4 (6.7%)	9 (7.9%)	9 (8.4%)	7 (5.9%)	16 (7.1%)
Renal and urinary disorders	3 (5.7%)	6 (10.2%)	9 (8.0%)	2 (3.7%)	4 (6.7%)	6 (5.3%)	5 (4.7%)	10 (8.4%)	15 (6.6%)
Nervous system disorders	3 (5.7%)	3 (5.1%)	6 (5.4%)	3 (5.6%)	4 (6.7%)	7 (6.1%)	6 (5.6%)	7 (5.9%)	13 (5.8%)
Cardiac disorders	2 (3.8%)	3 (5.1%)	5 (4.5%)	3 (5.6%)	2 (3.3%)	5 (4.4%)	5 (4.7%)	5 (4.2%)	10 (4.4%)

	Sunitinib			Pazopanib			Overall		
	CCS (n=53) N (%)	**DFIS (n=59) N (%)**	**Total (n=112) N (%)**	**CCS (n=54) N (%)**	**DFIS (n=60) N (%)**	**Total (n=114) N (%)**	**CCS (n=107) N (%)**	**DFIS (n=119) N (%)**	**Total (n=226) N (%)**
Hepatobiliary disorders	1 (1.9%)	2 (3.4%)	3 (2.7%)	2 (3.7%)	3 (5.0%)	5 (4.4%)	3 (2.8%)	5 (4.2%)	8 (3.5%)
Musculoskeletal and connective tissue disorders	3 (5.7%)	2 (3.4%)	5 (4.5%)	2 (3.7%)	0 (0.0%)	2 (1.8%)	5 (4.7%)	2 (1.7%)	7 (3.1%)
General disorders and administration site conditions	2 (3.8%)	0 (0.0%)	2 (1.8%)	1 (1.9%)	3 (5.0%)	4 (3.5%)	3 (2.8%)	3 (2.5%)	6 (2.7%)
Investigations	0 (0.0%)	1 (1.7%)	1 (0.9%)	2 (3.7%)	2 (3.3%)	4 (3.5%)	2 (1.9%)	3 (2.5%)	5 (2.2%)
Metabolism and nutrition disorders	1 (1.9%)	1 (1.7%)	2 (1.8%)	1 (1.9%)	1 (1.7%)	2 (1.8%)	2 (1.9%)	2 (1.7%)	4 (1.8%)
Eye disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (3.7%)	1 (1.7%)	3 (2.6%)	2 (1.9%)	1 (0.8%)	3 (1.3%)
Neoplasms benign, malignant and unspecified (including cysts and polyps)	0 (0.0%)	3 (5.1%)	3 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.5%)	3 (1.3%)
Endocrine disorders	2 (3.8%)	0 (0.0%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.9%)	0 (0.0%)	2 (0.9%)
Skin and subcutaneous tissue disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.9%)	1 (1.7%)	2 (1.8%)	1 (0.9%)	1 (0.8%)	2 (0.9%)

Supplementary Table 82: Outcome of SAEs (S5b_Toxicity_SAEs)

	CCS N (%)	DFIS N (%)	Total N (%)
Overall			
Recovered	233 (67.9%)	245 (61.1%)	478 (64.2%)
Recovered with sequelae	53 (15.5%)	65 (16.2%)	118 (15.9%)
Condition improving	1 (0.3%)	5 (1.2%)	6 (0.8%)
Condition still present and unchanged	3 (0.9%)	5 (1.2%)	8 (1.1%)
Death	14 (4.1%)	21 (5.2%)	35 (4.7%)
Ongoing at the time of death	39 (11.4%)	60 (15.0%)	99 (13.3%)
Total	343 (100%)	401 (100%)	744 (100%)
Sunitinib			
Recovered	114 (76.0%)	102 (61.4%)	216 (68.4%)
Recovered with sequelae	19 (12.7%)	32 (19.3%)	51 (16.1%)
Condition improving	0 (0.0%)	2 (1.2%)	2 (0.6%)
Death	6 (4.0%)	10 (6.0%)	16 (5.1%)
Ongoing at the time of death	11 (7.3%)	20 (12.0%)	31 (9.8%)
Total	150 (100%)	166 (100%)	316 (100%)
Pazopanib			
Recovered	119 (61.7%)	143 (60.9%)	262 (61.2%)
Recovered with sequelae	34 (17.6%)	33 (14.0%)	67 (15.7%)
Condition improving	1 (0.5%)	3 (1.3%)	4 (0.9%)

	CCS N (%)	DFIS N (%)	Total N (%)
Condition still present and unchanged	3 (1.6%)	5 (2.1%)	8 (1.9%)
Death	8 (4.1%)	11 (4.7%)	19 (4.4%)
Ongoing at the time of death	28 (14.5%)	40 (17.0%)	68 (15.9%)
Total	193 (100%)	235 (100%)	428 (100%)

Supplementary Table 83: Outcome of SARs (S5c_Toxicity_SARs)

	CCS N (%)	DFIS N (%)	Total N (%)
Overall			
Recovered	85 (79.4%)	84 (70.6%)	169 (74.8%)
Recovered with sequelae	10 (9.3%)	19 (16.0%)	29 (12.8%)
Condition improving	0 (0.0%)	2 (1.7%)	2 (0.9%)
Condition still present and unchanged	3 (2.8%)	1 (0.8%)	4 (1.8%)
Death	3 (2.8%)	9 (7.6%)	12 (5.3%)
Ongoing at the time of death	6 (5.6%)	4 (3.4%)	10 (4.4%)
Total	107 (100%)	119 (100%)	226 (100%)
Sunitinib			
Recovered	46 (86.8%)	41 (69.5%)	87 (77.7%)
Recovered with sequelae	5 (9.4%)	11 (18.6%)	16 (14.3%)
Condition improving	0 (0.0%)	2 (3.4%)	2 (1.8%)
Death	1 (1.9%)	2 (3.4%)	3 (2.7%)

	CCS N (%)	DFIS N (%)	Total N (%)
Ongoing at the time of death	1 (1.9%)	3 (5.1%)	4 (3.6%)
Total	53 (100%)	59 (100%)	112 (100%)
Pazopanib			
Recovered	39 (72.2%)	43 (71.7%)	82 (71.9%)
Recovered with sequelae	5 (9.3%)	8 (13.3%)	13 (11.4%)
Condition still present and unchanged	3 (5.6%)	1 (1.7%)	4 (3.5%)
Death	2 (3.7%)	7 (11.7%)	9 (7.9%)
Ongoing at the time of death	5 (9.3%)	1 (1.7%)	6 (5.3%)
Total	54 (100%)	60 (100%)	114 (100%)

Supplementary Table 84: SAE seriousness criteria – non-mutually exclusive (S5b_Toxicity_SAEs)

	CCS N (%)	DFIS N (%)	Total N (%)
Overall			
Participant died	14 (3.8%)	21 (4.9%)	35 (4.4%)
Life threatening	7 (1.9%)	10 (2.3%)	17 (2.1%)
Required / prolonged hospitalisation	330 (89.9%)	384 (89.5%)	714 (89.7%)
Persistent or significant disability/incapacity	6 (1.6%)	3 (0.7%)	9 (1.1%)
Jeopardised participant / required intervention to prevent one of the above	0 (0.0%)	2 (0.5%)	2 (0.3%)
Other important medical event	10 (2.7%)	9 (2.1%)	19 (2.4%)
Total	367 (100%)	429 (100%)	796 (100%)
Sunitinib			
Participant died	6 (3.7%)	10 (5.5%)	16 (4.7%)
Life threatening	3 (1.9%)	5 (2.8%)	8 (2.3%)
Required / prolonged hospitalisation	145 (89.5%)	160 (88.4%)	305 (88.9%)
Persistent or significant disability/incapacity	4 (2.5%)	1 (0.6%)	5 (1.5%)
Jeopardised participant / required intervention to prevent one of the above	0 (0.0%)	1 (0.6%)	1 (0.3%)
Other important medical event	4 (2.5%)	4 (2.2%)	8 (2.3%)
Total	162 (100%)	181 (100%)	343 (100%)
Pazopanib			
Participant died	8 (3.9%)	11 (4.4%)	19 (4.2%)

	CCS N (%)	DFIS N (%)	Total N (%)
Life threatening	4 (2.0%)	5 (2.0%)	9 (2.0%)
Required / prolonged hospitalisation	185 (90.2%)	224 (90.3%)	409 (90.3%)
Persistent or significant disability/incapacity	2 (1.0%)	2 (0.8%)	4 (0.9%)
Jeopardised participant / required intervention to prevent one of the above	0 (0.0%)	1 (0.4%)	1 (0.2%)
Other important medical event	6 (2.9%)	5 (2.0%)	11 (2.4%)
Total	205 (100%)	248 (100%)	453 (100%)

Supplementary Table 85: SAR Seriousness criteria – non-mutually exclusive (S5c_Toxicity_SARs)

	CCS N (%)	DFIS N (%)	Total N (%)
Overall			
Participant died	3 (2.7%)	9 (7.1%)	12 (5.0%)
Life threatening	2 (1.8%)	4 (3.1%)	6 (2.5%)
Required / prolonged hospitalisation	104 (92.9%)	108 (85.0%)	212 (88.7%)
Persistent or significant disability/incapacity	1 (0.9%)	0 (0.0%)	1 (0.4%)
Other important medical event	2 (1.8%)	6 (4.7%)	8 (3.3%)
Total	112 (100%)	127 (100%)	239 (100%)
Sunitinib			
Participant died	1 (1.8%)	2 (3.3%)	3 (2.6%)
Life threatening	1 (1.8%)	1 (1.6%)	2 (1.7%)
Required / prolonged hospitalisation	51 (92.7%)	54 (88.5%)	105 (90.5%)
Persistent or significant disability/incapacity	1 (1.8%)	0 (0.0%)	1 (0.9%)
Other important medical event	1 (1.8%)	4 (6.6%)	5 (4.3%)
Total	55 (100%)	61 (100%)	116 (100%)
Pazopanib			
Participant died	2 (3.5%)	7 (10.6%)	9 (7.3%)
Life threatening	1 (1.8%)	3 (4.5%)	4 (3.3%)
Required / prolonged hospitalisation	53 (93.0%)	54 (81.8%)	107 (87.0%)
Other important medical event	1 (1.8%)	2 (3.0%)	3 (2.4%)

	CCS N (%)	DFIS N (%)	Total N (%)
Total	57 (100%)	66 (100%)	123 (100%)

Supplementary Table 86: Line Listing of all SUSARs (S5e_Toxicity_LineListings)

Observation number	Randomisation allocation	MedDRA System Organ Class	SUSAR Medical Description	SUSAR Case Description	CTCAE grade	Associated symptoms
1	Conventional Continuation Strategy (CCS)	Cardiac disorders	Myocardinal Infarction	Worsening shortness of breath. Patient taken to local A&E, ECG demonstrated acute MI, chest X-ray showed right sided pleural effusion	3	
2	Conventional Continuation Strategy (CCS)	Eye disorders	Detached retina	Patient noticed his eye sight had deteriorated - went to A&E and was diagnosed with a detached retina. New info rec 18/06/2015: Fix with op on 24/07/2014.	3	Loss of sight L eye
3	Conventional Continuation Strategy (CCS)	Musculoskeletal and connective tissue disorders	Avascular necrosis	Admitted via clinic in severe pain, demonstrating extreme side effects from a concoction of analgesics. Admitted. MRI scan left hip - Avascular Necrosis. Declined surgery for medical management.	2	Severe Pain
4	Conventional Continuation Strategy (CCS)	Respiratory, thoracic and mediastinal disorders	?Gastric Perforation (abdo pain)	Admitted to Whipps X Hospital with abdominal - epigastric pain radiating to the back. Bloods showed CRP 40 and amylase 167. CT showed air-fluid collection suspicious for contained perforation at level of pylorus. Treated with IV antibiotics, fluids and analgesics. Discharged well on 01/11/2013.	3	

Observation number	Randomisation allocation	MedDRA System Organ Class	SUSAR Medical Description	SUSAR Case Description	CTCAE grade	Associated symptoms
5	Conventional Continuation Strategy (CCS)	Renal and urinary disorders	Acute renal failure	Patient admitted for IV fluids following abnormal renal function test results. Now recovering.	3	
6	Drug-Free Interval Strategy (DFIS)	Renal and urinary disorders	Pain R flank	Patient admitted into accident and emergency with 2 day history of R flank pain 7/10 which developed into acute pain on inspiration on 19/05/2014. They also experienced grade 2 fatigue contributing to him spending >50% time in bed. On admission they commenced IV tazocin and began investigations to rule out pulmonary embolus - awaiting results. New info received 30/05/2014: Not pulmonary embolus. Pain from tumour as final diagnosis - CT confirms slight increase in size of tumour suggestive of responserather than recurrence. Confirmed as SUSAR. Pain now resolving and pain relief prescribed (Oramorph 1.75-2.5mg PRN). Sutent on hold until review on 06/06/2014.	2	

Observation number	Randomisation allocation	MedDRA System Organ Class	SUSAR Medical Description	SUSAR Case Description	CTCAE grade	Associated symptoms
7	Drug-Free Interval Strategy (DFIS)	Vascular disorders	Abdominal aortic aneurysm	AAA that has leaked increase size to 5.8cm from 5.3cm	5	Sharp abdominal pain
8	Drug-Free Interval Strategy (DFIS)	Blood and lymphatic system disorders	Autoimmune thrombocytopenia	Platelets 3 after 2 weeks. Given platelet transfusions with no benefit. Platelets remain under 10. Commenced steroids and immunoglobulins. New info rec 07/11/2014: Discharged 25/06/2013 - platelets 13. Platelets 296 01/08/2013.	4	
9	Drug-Free Interval Strategy (DFIS)	Nervous system disorders	Multifocal intracranial haemorrhage	Seen 20/03 in clinic with staggering gait and subtle neurology. CT head showed bleed. MRI arranged which shows multifocal intracranial haemorrhage. BP has been high, platelets 80-95.	2	
10	Drug-Free Interval Strategy (DFIS)	Vascular disorders	Bowel Ischaemia	Acute deterioration within 24 hours of admission. Patient died. Post mortem results requested from coroner 25/07/2016	5	

Observation number	Randomisation allocation	MedDRA System Organ Class	SUSAR Medical Description	SUSAR Case Description	CTCAE grade	Associated symptoms
11	Drug-Free Interval Strategy (DFIS)	Neoplasms benign, malignant and unspecified (including cysts and polyps)	New primary squamous cell	Lesions removed from temple. Diagnosed as new primary squamous cell	4	
12	Drug-Free Interval Strategy (DFIS)	Hepatobiliary disorders	Hepatorenal syndrome	Patient admitted with deranged liver function. 03/02/2015 ultrasound kidney; no obstruction demonstrated. 04/02/2015 US abdomen; fatty liver, no hydronephrosis. Kidneys failed. Died.	5	
13	Drug-Free Interval Strategy (DFIS)	Cardiac disorders	Sudden death syndrome	c/o being unwell on 04/10/2016 but had not sought medical attention. Family found her unresponsive on 05/10/2016 evening. Paramedic called and declared dead.	5	

Supplementary Table 87: Line Listing of all SUSARs (S5e_Toxicity_LineListings) cont.

Observation number	Other relevant medical conditions	Date of randomisation	Onset date	Date event became a SUSAR	Treatment cycle SUSAR occurred	Seriousness Criteria
1	Controlled Hypertension, left radical nephrectomy (2010), right adrenalectomy (2011), hypercholesterolclaemia	06/06/2012	04/10/2012	04/10/2012	3	Required / prolonged hospitalisation
2		29/10/2013	17/07/2014	19/07/2014	7	Required / prolonged hospitalisation
3	Benign essential hypertension, TIA x7, COPD, Type 2 diabetic diet control, Ischaemic heart disease	25/02/2015	28/10/2015	29/10/2015	7	Required / prolonged hospitalisation
4		11/07/2013	24/10/2013	27/10/2013	3	Required / prolonged hospitalisation

Observation number	Other relevant medical conditions	Date of randomisation	Onset date	Date event became a SUSAR	Treatment cycle SUSAR occurred	Seriousness Criteria
5		24/07/2014	18/09/2014	18/09/2014	2	Required / prolonged hospitalisation
6		09/05/2014	17/05/2014	19/05/2014	1	Required / prolonged hospitalisation
7	Metastatic renal cell carcinoma. Abdominal aortic aneurysm. Hypertension. Colitis. Asthma. Renal stones.	11/08/2015	06/01/2020	06/01/2020	38	Participant died + Life threatening
8		21/05/2013	06/06/2013	13/06/2013	1	Required / prolonged hospitalisation
9	Hypertension (start date not known)	14/01/2014	20/03/2014	02/04/2014	2	Life threatening

Observation number	Other relevant medical conditions	Date of randomisation	Onset date	Date event became a SUSAR	Treatment cycle SUSAR occurred	Seriousness Criteria
10	Ischaemic heart disease - MI and coronary angioplasty 2012	08/04/2015	17/07/2016	17/07/2016	12	Participant died
11		25/10/2013	16/02/2016	16/02/2016	21	Other important medical event
12	Metastatic breast cancer 2014, pulmonary metastases, bony metastases, history of hepatic impairement.	19/03/2014	03/02/2015	04/02/2015	8	Required / prolonged hospitalisation + Participant died
13	Ischemic heart disease	29/09/2016	05/10/2016	05/10/2016	1	Participant died

Supplementary Table 88: Line Listing of all SUSARs (S5e_Toxicity_LineListings) cont.

Observation number	Outcome	Place of SUSAR	Recovery date	Date of death	Other causality?	Causality if other illness	Causality if other reason	First ever trial medication	Start date of 1st dose	First dose (mg/day)	Date most recent dose	Most recent dose (mg/day)
1	Recovered	Hospital	08/10/2012	.	Other illness	Previously known hypertension	Ex - smoker	Sunitinib	06/06/2012	50	25/09/2012	50
2	Recovered	Home	24/07/2014	.	.			Pazopanib	29/10/2013	800	21/07/2014	400
3	Ongoing at the time of death	Home	.	.	.			Pazopanib	25/02/2015	800	29/10/2015	400
4	Recovered	Home	01/11/2013	.	Renal cancer			Pazopanib	12/07/2013	800	24/10/2013	800
5	Recovered	Home	23/09/2014	.	.			Pazopanib	24/07/2014	800	19/08/2014	800

Observation number	Outcome	Place of SUSAR	Recovery date	Date of death	Other causality?	Causality if other illness	Causality if other reason	First ever trial medication	Start date of 1st dose	First dose (mg/day)	Date most recent dose	Most recent dose (mg/day)
6	Recovered with sequelae	Home	23/05/2014	.	Renal cancer			Sunitinib	09/05/2014	50	18/05/2014	50
7	Death	Hospital	.	08/01/2020	Other illness	Idiopathic abdominal aortic aneurysm		Pazopanib	12/08/2015	800	06/01/2020	800
8	Recovered	Hospital	01/08/2013	.	.			Sunitinib	21/05/2013	50	03/06/2013	50
9	Recovered	Home	16/05/2014	.	Other illness	Hypertension		Pazopanib	15/01/2014	800	19/03/2014	400
10	Death	Home	.	18/07/2016	Renal cancer	Ischaemic heart disease		Pazopanib	08/04/2015	800	17/07/2016	400

Observation number	Outcome	Place of SUSAR	Recovery date	Date of death	Other causality?	Causality if other illness	Causality if other reason	First ever trial medication	Start date of 1st dose	First dose (mg/day)	Date most recent dose	Most recent dose (mg/day)
11	Recovered with sequelae	.	22/02/2016	.	Other		Age and sundamage	Sunitinib	25/10/2013	50	16/02/2016	37.5
12	Death	Home	.	13/02/2015	Other illness	Unknown		Pazopanib	20/03/2014	800	03/02/2015	400
13	Death	Home	.	05/10/2016	Other illness	Ischemic heart disease		Pazopanib	29/09/2016	800	04/10/2016	800

Supplementary Table 89: Confirmed cases of Osteonecrosis of the Jaw (S5g_ONJ)

Observation Number	TKI Received	Randomisation Allocation	Date of last treatment dose	Date of first symptom	Date ONJ confirmed	History of invasive dental procedures	Dental work whilst on trial	Oral bisphosphonates	Previous radiotherapy to the jaw	Palate	Maxilla	Mandible
1	Sunitinib	Drug-Free Interval Strategy (DFIS)	21/12/2014	05/01/2015	14/04/2015	No	No	Yes	No	No	No	Yes
2	Sunitinib	Drug-Free Interval Strategy (DFIS)	21/01/2015	05/12/2014	12/02/2016	No	Yes	No	No	No	No	Yes
3	Sunitinib	Conventional Continuation Strategy (CCS)	01/05/2016	02/05/2016	29/07/2016	No	Yes	Yes	No	No	Yes	No
4	Sunitinib	Conventional Continuation Strategy (CCS)	27/02/2018	16/10/2017	01/03/2018	Yes	Yes	Yes	No	.	.	.

Supplementary Table 90: Confirmed cases of Osteonecrosis of the Jaw (S5g_ONJ) cont.

Observation Number	Localized to side	Relationship to teeth	Necrotic bone visible	Ulceration	Bleeding	Discharge	Size	Other	Other details	Date of Conservative resection	Date of Operative resection	Response to treatment	Further action
1	No	No	Yes	Yes	Yes	Yes	1cm	Yes	scabby areas	.	.	No	antibiotics only at this stage
2	No	No	No	No	No	Yes	8cm	No		.	.	Yes	
3	No	Yes	Yes	Yes	Yes	Yes	1	Yes	Blister on upper hard pallate	29/07/2016	03/11/2016	Yes	
4	.	.	.	.	.	.		No		.	.	.	