

Supplementary Material 8

Deviations

D.9 Deviations

Table S331 shows summary statistics for the number of deviations reported per patient.

Table S331: Summary statistics for number of deviations per patient.

Number of deviations	
Mean	6.26
Median	6
Range	(1,11)
IQR	(4.5,8.5)

From table S331 all patients experienced at least one deviation, with the maximum number of deviations experienced by any one patient being 11.

Table S332 shows the number of deviations by patient, given as an overall number and categorised according to deviation type.

Table S332: Number of deviations by patient and deviation type.

PAT_TNO	Deviation Type				Total
	Deviation from treatment	Other deviation	Patient found to be ineligible post registration	Scheduled assessment not performed	
1	0 (0.00%)	1 (2.17%)	0 (0.00%)	7 (8.05%)	8 (5.56%)
2	1 (11.11%)	0 (0.00%)	0 (0.00%)	7 (8.05%)	8 (5.56%)
3	0 (0.00%)	1 (2.17%)	0 (0.00%)	9 (10.34%)	10 (6.94%)
4	1 (11.11%)	1 (2.17%)	0 (0.00%)	7 (8.05%)	9 (6.25%)
5	0 (0.00%)	0 (0.00%)	0 (0.00%)	10 (11.49%)	10 (6.94%)
6	1 (11.11%)	1 (2.17%)	1 (50.00%)	0 (0.00%)	3 (2.08%)
7	0 (0.00%)	1 (2.17%)	0 (0.00%)	1 (1.15%)	2 (1.39%)
8	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (4.60%)	4 (2.78%)
9	0 (0.00%)	1 (2.17%)	0 (0.00%)	5 (5.75%)	6 (4.17%)
10	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	1 (0.69%)
11	0 (0.00%)	4 (8.70%)	0 (0.00%)	1 (1.15%)	5 (3.47%)
12	0 (0.00%)	6 (13.04%)	0 (0.00%)	0 (0.00%)	6 (4.17%)
13	0 (0.00%)	1 (2.17%)	0 (0.00%)	9 (10.34%)	10 (6.94%)
14	0 (0.00%)	3 (6.52%)	0 (0.00%)	2 (2.30%)	5 (3.47%)
15	3 (33.33%)	1 (2.17%)	0 (0.00%)	3 (3.45%)	7 (4.86%)
16	1 (11.11%)	3 (6.52%)	0 (0.00%)	4 (4.60%)	8 (5.56%)
17	0 (0.00%)	3 (6.52%)	0 (0.00%)	2 (2.30%)	5 (3.47%)
18	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.15%)	1 (0.69%)
19	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (2.30%)	2 (1.39%)
20	1 (11.11%)	5 (10.87%)	0 (0.00%)	1 (1.15%)	7 (4.86%)
21	0 (0.00%)	2 (4.35%)	0 (0.00%)	4 (4.60%)	6 (4.17%)
22	1 (11.11%)	9 (19.57%)	0 (0.00%)	0 (0.00%)	10 (6.94%)
23	0 (0.00%)	3 (6.52%)	0 (0.00%)	8 (9.20%)	11 (7.64%)
Total	9 (100.00%)	46 (100.00%)	2 (100.00%)	87 (100.00%)	144 (100.00%)

Table S333 provides a line listing of all deviations.

Table S333: Line listing of all deviations.

Patient	Deviation Date	Deviation Type	Treatment Deviation	Deviation Type Details	Details
1	2015-07-14	Scheduled assessment not performed		Biochemistry screening visit 1	Aspartate Transaminase was not recorded on the blood report.
1	2015-09-03	Scheduled assessment not performed		Biochemistry screening visit 2	Total protein was not recorded on the blood report
1	2015-09-10	Scheduled assessment not performed		Biochemistry visit 3, post dose	Alanine transferase, Aspartate transaminase, Potassium were not assayed.
1	2015-09-18	Scheduled assessment not performed		Biochemistry visit 4, post dose	ALT, AST, potassium, haemolysed and were unable to be reported on.
1	2015-10-01	Other deviation		IBD diary completed early, not 7 days pre treatment as per protocol.	patient error
1	2015-10-02	Scheduled assessment not performed		Haematology visit 5 pre and post dose	INR and APTT ratio were not reported on both occasions because there was insufficient samples.
1	2015-10-16	Scheduled assessment not performed		Biochemistry visit 6 pre dose	The Total protein result was not recorded on the blood report form.
1	2015-11-12	Scheduled assessment not performed		Haematology visit 8 post dose	APTT was not recorded on the blood report
2	2015-10-13	Scheduled assessment not performed		Physical Examination screening visit 1	Gastrointestinal Tract, Liver, Spleen, Urogenital system, Nervous system and Endocrine system observations were not performed because they were missed from the checklist in error.
2	2015-10-13	Scheduled assessment not performed		height and weight not completed	missed in error

Table S333: Line listing of all deviations. (continued)

Patient	Deviation Date	Deviation Type	Treatment Deviation	Deviation Type Details	Details
2	2015-12-02	Scheduled assessment not performed		Biochemistry screening visit 2	Results for Direct bilirubin, Indirect bilirubin, and GGT were not recorded on the report form.
2	2015-12-09	Scheduled assessment not performed		Physical examination visit 3	Gastrointestinal Tract, Liver, Spleen, Urogenitalsystem, Nervous system and Endocrine system were not observed because were missed off the nursing checklist in error.
2	2016-01-05	Scheduled assessment not performed		Physical examination visit 10	Urogenital system, Nervous system and Endocrine system were not observed because they were left off the nursing checklist in error.
2	2016-01-20	Deviation from treatment	Treatment stopped early		MRI scan visit 11 not done. Patient withdrew from trial 10-Dec-2015 at an unscheduled visit after visit 3. No further treatment took place. Engaged in two follow up visits 5-Jan-2016 and 20-Jan-2016
2	2016-01-20	Scheduled assessment not performed		Physical examination visit 11	Urogenital system, Nervous system were not observed because they were left off the nursing checklist in error.
2	2016-01-20	Scheduled assessment not performed		Biochemistry visit 11	AST result was not recorded on the report form.
3	2016-01-13	Other deviation		Patient possibly allergic to cetirizine so decision made to give loratidine instead for all of this patient's visits as agreed with Dr Hirshfield	Patient possibly allergic to cetirizine so decision made to give loratidine instead for all of this patient's visits as agreed with Dr Hirshfield
3	2016-01-13	Scheduled assessment not performed		Biochemistry visit 3 post dose	GGT result was not recorded on the blood report form.

Table S333: Line listing of all deviations. (continued)

Patient	Deviation Date	Deviation Type	Treatment Deviation	Deviation Type Details	Details
3	2016-01-21	Scheduled assessment not performed		Vital signs visit 4	90 minute observations missed by mistake.
3	2016-02-18	Scheduled assessment not performed		Vital signs visit 6	90 minute observations done early, and 120 minute observations missed by mistake.
3	2016-03-03	Scheduled assessment not performed		Vital signs visit 7	Observations missed at 120 minutes in error.
3	2016-03-17	Scheduled assessment not performed		Biochemistry visit 8 pre-dose	Alanine transaminase, Total bilirubin, Total protein were not recorded on the blood report.
3	2016-03-31	Scheduled assessment not performed		Biochemistry visit 9 pre dose	Total protein result was not recorded on the blood report.
3	2016-03-31	Scheduled assessment not performed		Haematology pre dose	APTT result was not recorded on the blood test report.
3	2016-04-21	Scheduled assessment not performed		Biochemistry visit 10	Alanine transaminase, Total protein were not recorded on the blood report.
3	2016-05-12	Scheduled assessment not performed		Biochemistry visit 11	Results for AST, GGT were not recorded on the blood report.
4	2015-11-18	Scheduled assessment not performed		Physical examination screening visit 1	Urogenital system and Nervous system observations were not taken because they were missed of the nursing checklist in error.
4	2016-01-13	Deviation from treatment	Incorrect timing of treatment		Due to logistical reasons, patient was unable to have first infusion by 14th Jan so discussion taken to delay first infusion to 18-Jan-2016, as discussed and agreed with Dr Hirschfield.

Table S333: Line listing of all deviations. (continued)

Patient	Deviation Date	Deviation Type	Treatment Deviation	Deviation Type Details	Details
4	2016-01-18	Scheduled assessment not performed		Physical examination visit 3	Urogenital system and Nervous system observations were not made because they were missed off the nursing checklist in error.
4	2016-01-25	Other deviation		not all tests for biochemistry blood sample were taken	the specimen haemolysed
4	2016-02-08	Scheduled assessment not performed		Physical examination visit 5	Urogenital system, Nervous system and Endocrine system observations were not taken because they were missed off the nursing checklist in error.
4	2016-03-07	Scheduled assessment not performed		Physical examination visit 7	Urogenital system, Nervous system were not observed because they were missed off the nursing checklist in error.
4	2016-04-04	Scheduled assessment not performed		Physical examination, visit 9	Head (including ENT and Eyes), Urogenital system, were missed from the observations. Skin and Other Connective Tissue, Muscular and Skeletal System were not performed because the patient reported no symptoms.
4	2016-04-25	Scheduled assessment not performed		Physical examination, visit 10	Head (including ENT and Eyes) and Urogenital system were missed from the observations.
4	2016-05-18	Scheduled assessment not performed		Physical examination, visit 11	Head (including ENT and Eyes), Lymphatic System, Urogenital system and Endocrine System were missed from the observations.
5	2015-12-16	Scheduled assessment not performed		Vital Signs, Screening visit 1	The Respiratory Rate (bpm) does not appear on the ECG printout.

Table S333: Line listing of all deviations. (continued)

Patient	Deviation Date	Deviation Type	Treatment Deviation	Deviation Type Details	Details
5	2016-02-18	Scheduled assessment not performed		Visit 4, vital signs post infusion	Vital signs 90 minutes post infusion were left off the nursing checklist in error and so not observed.
5	2016-03-17	Scheduled assessment not performed		Biochemistry visit 6, pre dose	The result for AST was not entered on the report form.
5	2016-03-31	Scheduled assessment not performed		Biochemistry, Visit 7, pre dose	The results for ALT, AST, Potassium, Calcium, Total Protein were not reported because the specimen haemolysed.
5	2016-03-31	Scheduled assessment not performed		Biochemistry, visit 7, post dose	AST result was not reported because the specimen haemolysed.
5	2016-04-14	Scheduled assessment not performed		Biochemistry visit 8, pre dose	The result for total protein did not appear on the Report form.
5	2016-04-28	Scheduled assessment not performed		Biochemistry visit 9, pre dose	ALT, AST, Potassium results were not reported because the specimen haemolysed.
5	2016-05-19	Scheduled assessment not performed		Biochemistry visit 10, follow up	AST result was not recorded on the report form.
5	2016-05-31	Scheduled assessment not performed		Haematology visit 7, pre dose	The result for the INR test was not entered on the report form.
5	2016-06-09	Scheduled assessment not performed		Biochemistry visit 11, follow up	The result for AST was not recorded on the report form.
6	2016-05-20	Patient found to be ineligible post registration		Raised ALP	Patient had minor fluctuation in ALP. It was just >25% and was an oversight and 'not' clinically significant.

Table S333: Line listing of all deviations. (continued)

Patient	Deviation Date	Deviation Type	Treatment Deviation	Deviation Type Details	Details
6	2016-07-14	Deviation from treatment	Incorrect timing of treatment		Infusion was administered on 18-Jul-2016 due to temp exceed in pharmacy fridge. Was awaiting advice from sponsor.
6	2016-08-29	Other deviation		Visit 10 delayed by a week	Visit 10 was late/delayed by a week due to work commitments. Patient is due to return on 08-sep-2016 for visit 10.
7	2016-07-20	Scheduled assessment not performed		Biochemistry visit 6, post dose	The GGT result was not recorded on the blood report form.
7	2016-08-03	Other deviation		BTT1023 Dosing visit 7 delay	Infusion started 20 minutes after the 2 hour post pre-med time limit as cannula had to be replaced.
8	2017-01-31	Scheduled assessment not performed		Biochemistry screening visit	The results for Calcium and Total protein were not recorded on the blood report form.
8	2017-02-28	Scheduled assessment not performed		Biochemistry screening visit 2	The results for Calcium and Total protein were not recorded on the blood report form.
8	2017-04-11	Scheduled assessment not performed		Haematology visit 6, pre dose	the result for APTT was not recorded on the blood report form.
8	2017-04-25	Scheduled assessment not performed		Biochemistry visit 7, post dose	The result for AST was not possible because the specimen haemolysed.
9	2017-01-12	Scheduled assessment not performed		APPT result is missing	APTT not reported by the labs

Table S333: Line listing of all deviations. (continued)

Patient	Deviation Date	Deviation Type	Treatment Deviation	Deviation Type Details	Details
9	2017-03-08	Scheduled assessment not performed		Post infusion sodium and Potassium bloods were not collected from ward Fridge in a timely manner, therefore when the bloods were received at the labs they were not able to process them . Therefore there are no haematology results this visit	Because bloods were not received at the Labs in time
9	2017-03-29	Scheduled assessment not performed		no APTT result	No lab results
9	2017-04-12	Scheduled assessment not performed		Pre and post APTT results not available	no lab report unknown reason
9	2018-04-26	Scheduled assessment not performed		total protein result not reported	not reported from labs reasons unknown
9		Other deviation		sildenafil added to con med	patient started sildenafil in 2010 so was on this at baseline
10	2017-05-08	Patient found to be ineligible post registration		Patient was registered and then found to be ineligible. This was reported to the trials office immediately.	Eligibility criteria checked. 25% change for ALP checked, however ALP not high enough on second screening, which was overlooked.

Table S333: Line listing of all deviations. (continued)

Patient	Deviation Date	Deviation Type	Treatment Deviation	Deviation Type Details	Details
11	2017-05-10	Other deviation		<ul style="list-style-type: none"> TNO 11 last underwent colonoscopy on 21-Mar-2016, and although this confirmed "no evidence of active inflammation throughout the colon", it was more than a year prior to registration 	This was an error by site. Discussed with PI who said "As patient has not been having any symptoms from his IDB and the patient has now agreed to have a colonoscopy which has been requested for August 2017 this has no impact on patient safety"
11	2017-05-10	Other deviation		pk taken 16.25 when it should have been taken at 17.25	unknown
11	2017-06-14	Scheduled assessment not performed		post dose bloods were not processed	Bloods were taken at 15.00 and were taking down to the pathology labs by hand . when checked the labs said that they had not received these blood samples
11	2017-07-05	Other deviation		MRI carried out outside the window	unknown
11		Other deviation		Patients IBD diary for visit 6 was posted to Birmingham clinical trials unit but has got lost in transit, unfortunately a copy was not kept at our site.	Diary is not available
12	2017-05-16	Other deviation			Patient declined to complete Quality of life form for visit 3
12	2017-06-20	Other deviation			Quality of life questionnaire form visit 6 has been lost
12	2017-06-20	Other deviation		Calcium result not reported	Labs did not receive sample
12	2017-07-18	Other deviation		missing data	source data for vital signs missing for visit 8

Table S333: Line listing of all deviations. (continued)

Patient	Deviation Date	Deviation Type	Treatment Deviation	Deviation Type Details	Details
12	2018-05-23	Other deviation		APTT not processed at our site	Sample lost
12	2018-05-23	Other deviation		APTT was not processed at our site	Sample lost
13	2017-03-30	Scheduled assessment not performed		Direct and indirect bilirubin results not done/available	Unfortunately, another nurse (who has left the team) performed this visit so I don't know why this was not done.
13	2017-05-12	Scheduled assessment not performed		Total protein not completed for Visit 3 post dose	Unfortunately another study nurse (who has now left the team) performed this visit, so I am unsure why these were not performed.
13	2017-05-18	Scheduled assessment not performed		GGT and calcium not assessed both pre and post dose	Unfortunately another study nurse (who has now left the team) performed this visit, so I am unsure why these were not performed.
13	2017-06-29	Scheduled assessment not performed		Total protein not assessed.	The result wasn't processed by the lab - reason unknown.
13	2017-07-27	Scheduled assessment not performed		Total protein not assessed.	The lab did not process the result - reason unknown
13	2018-06-07	Other deviation		PBMC and serum samples missing from site.	The following serum samples BRS2853, BRS2849 and BRS2851 are missing from the site. PBMCs are missing from visits 2, 6 and 10. Unfortunately the reason is unknown. We will keep looking for them at the site. Date deviation occurred is the date that we shipped the samples.

Table S333: Line listing of all deviations. (continued)

Patient	Deviation Date	Deviation Type	Treatment Deviation	Deviation Type Details	Details
13	2019-03-30	Scheduled assessment not performed		GGT, Calcium and Total Protein not completed	Unfortunately another study nurse (who has now left the team) performed this visit, so I am unsure why these were not performed.
13	2019-05-05	Scheduled assessment not performed		Calcium and Total protein not assessed	Unfortunately another study nurse (who has now left the team) performed this visit, so I am unsure why these were not performed.
13		Scheduled assessment not performed		On visits 7 and 11, urogenital system not done on physical examination	Reason unknown
13		Scheduled assessment not performed		APTT ratio not performed at any visit	The local labs did not perform the APTT ratio - reason unknown.
14	2017-06-13	Other deviation			Specimen haemolysed, so not all results reported.
14	2017-06-13	Scheduled assessment not performed		Vital signs 90 minutes post end of infusion were not observed.	unknown as to why observations were not recorded
14	2017-06-27	Other deviation			specimen haemolysed
14	2017-08-10	Scheduled assessment not performed		ECG visit 8, pre-infusion	The trace was too poor to calculate QT, QTc.
14	2017-09-12	Other deviation		The Mayo PSC Risk Score for visit 10 could not be calculated.	as a consequence of the AST result having not been reported by the labs the Mayo PSC Risk Score for visit 10 was unable to be calculated.
15	2017-08-31	Deviation from treatment			BTT1023 dosing visit 4. Dose amended to 48ml as only 8 vials of BTT1023 available.

15 2017-09-14 Scheduled assessment
not performed

Biochemistry visit 5 pre-dose.

AST not result not reported because the specimen
haemolysed.

Table S333: Line listing of all deviations. (continued)

Patient	Deviation Date	Deviation Type	Treatment Deviation	Deviation Type Details	Details
15	2017-09-28	Scheduled assessment not performed		Haematology visit 6, post dose.	APTT result was not recorded on the report form.
15	2017-10-12	Other deviation		did not attend Visit7 scheduled for 12-oct-2017	Unwell with flu-like symptoms
15	2017-10-26	Deviation from treatment	Incorrect timing of treatment		Difficulty in cannulating patient. Infusion due to start by 13:21 (pre-medication given @ 11:21). Infusion actually started @ 13:48
15	2017-10-26	Deviation from treatment	Other:treatment stopped late		Patient complained of tingling and numb fingers to arm where infusion was sited. PI suggested the infusion be slowed down and then restarted again at normal rate if tolerated by patient. Therefore infusion slowed down for a period of time, restarted at normal rate for a period of time, then slowed down again. Start time 13:48, finish time 15:53. All infusion given.
15	2017-11-19	Scheduled assessment not performed		Haematology visit 9, post dose.	INR, APTT results were not reported because the sample clotted.
16	2017-09-04	Other deviation		TB spot test performed at Screening Visit 2	Original sample from Screening Visit 1 was lost in the post so test was performed again at Screening Visit 2.
16	2017-09-08	Scheduled assessment not performed		15 mins PIS serum sample not obtained	Cannula unfortunately failed so sample could not be obtained
16	2017-09-15	Other deviation		Serum samples for visits 3 and 4	

ent as ambient as opposed to on
dry ice

Samples sent in error. Trial nursing team have all read
the updated lab manual (dated 18-Sep-2017)

Table S333: Line listing of all deviations. (continued)

Patient	Deviation Date	Deviation Type	Treatment Deviation	Deviation Type Details	Details
16	2017-09-28	Deviation from treatment	Other:Infusion stopped at 12:05 and restarted at 12:20		Cannula tissue and replaced.
16	2017-10-12	Scheduled assessment not performed		Total protein not assessed both pre and post dose.	Total protein not performed by the local lab - reason unknown.
16	2018-06-07	Other deviation		Serum samples missing from the site.	Serum samples from visits 1 and 2 are missing from the site. Unfortunately the reason is unknown. We will keep looking for the samples. Date deviation occurred is the date that we shipped the samples.
16		Scheduled assessment not performed		On visits 1, 3, 5, 7 and 9 urogenital system not done on physical examination. On visit 7 endocrine system not done on physical examination.	Reason unknown
16		Scheduled assessment not performed		APTT ratio not performed at any visits	The local labs did not perform the APTT ratio - reason unknown.
17	2017-09-21	Scheduled assessment not performed		Biochemistry sample was not received by the laboratory	The haematology was received by the laboratory, but the Biochemistry sample was taken but not received by the pathology laboratory on 21-sep-2017 and therefore the sample was retaken on 25-sep-2017.
17	2017-10-05	Other deviation		change in hydrocortizone amount	50mg hydrocortizone given rather than 100mg due to high Blood sugar post visit 3 infusion
17	2017-11-30	Scheduled assessment not performed		direct and indirect bilirubin not performed	missed in error

Table S333: Line listing of all deviations. (continued)

Patient	Deviation Date	Deviation Type	Treatment Deviation	Deviation Type Details	Details
17	2018-01-04	Other deviation		Health Questionnaire visit 10	The Pruritus Visual Analogue Scale (VAS) was not completed
17	2018-02-01	Other deviation			Haematology taken on 25-jan-2018 but not reported by the labs therefore patient returned 01-feb-2018 to recheck and retake bloods. Haematology samples discarded by local labs
18		Scheduled assessment not performed		APTT ratio not assessed for all visits.	APTT ratio not performed by local labs - reason unknown.
19		Scheduled assessment not performed		On visits 1 and 5, urogenital system not done on physical examination	Reason unknown
19		Scheduled assessment not performed		APTT ratio not performed on any visit	The local lab didn't perform the APTT ratio - reason unknown.
20	2018-02-06	Scheduled assessment not performed		Full blood count taken but not analysed at screening visit 01	Haematology taken but not analysed at screening visit 01, therefore all samples were retaken on 06-feb-2018. Haematology bloods discarded by local labs.
20	2018-02-26	Other deviation		screening visit 1 was done 4 weeks and 4 days prior to treatment visit and not between 5-7 weeks prior to first treatment in error.	scheduling error
20	2018-03-19	Other deviation		Biochemistry sample taken pre dose. Sent to local labs. AST not performed by labs in error, all other results performed.	Biochemistry sample taken pre dose. Sent to local labs. AST not performed by labs in error, all other results performed.

Table S333: Line listing of all deviations. (continued)

Patient	Deviation Date	Deviation Type	Treatment Deviation	Deviation Type Details	Details
20	2018-04-03	Deviation from treatment			treatment temporarily stopped for 10 minutes as patient needed to be recannulated
20	2018-04-30	Other deviation		many blood results were missing from Biochemistry Visit 8, pre dose	The specimen haemolysed
20	2018-06-01	Other deviation			visit performed outside of visit window. patient usually attends study visits on a Monday- but due to bank holiday and doctor availability, the visit had to be rescheduled.
20	2018-06-21	Other deviation			study visit outside of visit window due to the MRI machine only being available on a Thursday. Therefore had to reschedule visit to fit a Thursday.
21	2018-01-25	Scheduled assessment not performed		Full Blood Count was not analysed at screening visit 01	Haemotology was not analysed at screening visit, therefore all samples were retaken on 05-feb-2018. Haemotology discarded by local labs
21	2018-01-25	Scheduled assessment not performed		Physical examination of Urogenital and Endocrine system not performed.	not completed by co investigator
21	2018-03-08	Other deviation		only one day of IBD diary was filled out	The patient did not fully complete the IBD diary
21	2018-04-27	Scheduled assessment not performed			not performed
21	2018-05-10	Scheduled assessment			

Biochemistry Results not
all the blood results were possible
because the

specimen haemolysed
AST and GGT missed in error

Table S333: Line listing of all deviations. (continued)

Patient	Deviation Date	Deviation Type	Treatment Deviation	Deviation Type Details	Details
21	2018-05-24	Other deviation		Haematology results pre dose were incomplete	Only INR and APTT reported on. Explanation from laboratories is , "no specimen received with request"
22	2018-05-24	Other deviation		180 minutes postinfusion Pk sample were taken at 16.50. the next sample should have been taken 3 hours later but were taken 1 hour later.	unknown
22	2018-06-01	Deviation from treatment	Other:60 minute post infusion Pharmacokinetic bloods was omitted in error		I misread the protocol & didn't take the 60 minute post infusion Pharmacokinetic bloods .
22	2018-06-24	Other deviation			Potassium blood sample was delayed in arriving at the hospital laboratories causing the blood sample to become haemolysed
22	2018-06-28	Other deviation			Some of the Biochemistry samples had haemolysed on reaching the lab. These were: AST Bilirubin (direct) Potassium
22	2018-06-28	Other deviation			The anticoagulation sample had haemolysed on reaching the lab.
22	2018-06-28	Other deviation			Aspartate transaminase blood sample was delayed in arriving at the hospital laboratories causing the blood sample to become haemolysed.

Table S333: Line listing of all deviations. (continued)

Patient	Deviation Date	Deviation Type	Treatment Deviation	Deviation Type Details	Details
22	2018-06-28	Other deviation			INR blood sample was delayed in arriving at the hospital laboratories causing the blood sample to become haemolysed
22	2018-06-28	Other deviation			APTT blood sample was delayed in arriving at the hospital laboratories causing the blood sample to become haemolysed
22	2018-06-28	Other deviation			Direct Bilirubin blood sample was delayed in arriving at the hospital laboratories causing the blood sample to become haemolysed. As we did not have the result of the direct bilirubin we were unable to calculate the result of the indirect bilirubin
22	2018-08-30	Other deviation			Subject was unable to attend for his Visit 10 on the 30-AUG-2018 for personal reasons. He attended for his Visit 10 on the 06-SEP-2018
23	2018-05-14	Scheduled assessment not performed		Urogenital Physical assessment, screening visit	Urogenital not done and no reason indicated by Sub I performing the physical assessment
23	2018-06-26	Other deviation		The APTT was collected and results not processed- Lab comment states that unable to process APTT, no reason provided. This was for visit 3	The APTT was collected and results not processed- Lab comment states that unable to process APTT, no reason provided. this was for visit 3
23	2018-06-26	Scheduled assessment not performed		Urogenital Physical assessment not done- Visit 3 Day 1	Urogenital not done and no reason indicated by Sub I performing the physical assessment

Table S333: Line listing of all deviations. (continued)

Patient	Deviation Date	Deviation Type	Treatment Deviation	Deviation Type Details	Details
23	2018-07-17	Scheduled assessment not performed		Sodium, potassium, Urea and eGFR were requested but no results available from lab	Results not available by lab, at the time it was noticed it was sample was unsuitable for the tests to be added , this was post dose visit 5 biochemistry
23	2018-07-17	Scheduled assessment not performed		Urogenital physical assessment for Visit 5, day 22 not done	Urogenital not done and no reason indicated by Sub I performing the physical assessment
23	2018-07-31	Other deviation		APTT ratio not reported for Visit 6	APTT ratio not reported for Visit 6, Actual APPT not requested but normal CS requested
23	2018-08-22	Other deviation		-80 freezer temperature excursion	The temperature was showing -50C, the door wasn't shut and we were unable to close it due to a large build-up of ice around the main door & on the doors to the shelves. This was on the 22nd August. I checked the Buteo samples and they were still frozen but we have to inform the sponsors of the temperature excursion We have all the samples for subject 05/01 TNO23. Samples in Freezer at the time were from Visit 1 to visit 7. Thanks .
23	2018-09-11	Scheduled assessment not performed		Urogenital investigation not completed for visit 9 day 78	Urogenital not done and no reason indicated by Sub I performing the physical assessment
23	2018-10-02	Scheduled assessment not performed		Urogenital investigation not completed for visit 10, day 99	Urogenital not done and no reason indicated by Sub I performing the physical assessment
23	2018-10-23	Scheduled assessment not performed		Urogenital investigation not completed for visit 11, day 120	Urogenital not done and no reason indicated by Sub I performing the physical assessment
23	2019-08-14	Scheduled assessment not performed		Urogenital assessment not performed for Visit 7, day 50	Urogenital not done and no reason indicated by Sub I performing the physical assessment

