Trial	DOC + PLAT	GEM + PLAT	PAX + PLAT	PEM + PLAT	VNB + PLAT	GEF
Kelly 2001[48]			PAX + CARB 15% discontinued therapy because of toxicity. Overall, 27% completed therapy as planned. The every-3-weeks schedule of PAX + CARB was more convenient than weekly VNB with CIS. In the PAX + CARB arm, patients received 97% and 94% of the planned PAX and CARB doses, respectively		VNB + CIS More patients (28%) discontinued therapy because of toxicity ($p = 0.001$). Overall, 15% of patients on the VNB arm completed therapy as planned ($p = 0.008$). Over six cycles, patients treated with VNB and CIS received 78% of the intended CIS dose and 65% of the intended VNB dose	
Scagliotti 2002[43]		Total number cycles delivered for GEM + CIS arm was 825 (mean per patient 4.0 cycles). Dose reductions and omissions were 12% and 6%. Actual dose intensities were 90.6% for GEM and 100% for CIS (with GEM)	Total number cycles delivered for PAX + CARB arm was 851 (mean per patient 4.2 cycles). Dose reductions and omissions were 13% and 0%. Actual dose intensities were 94.7% for PAX and 99.2% for CARB		Total number cycles delivered = 653 (mean per patient 3.2 cycles). Dose reductions (17%) and omissions (19%), mainly because of haematological toxicities. Actual dose intensities were 77.4% for VNB and 94.8% for CIS (with VNB)	
Schiller 2002[47]	NR	NR	NR			
Fossella 2003[44]	DOC + CIS Median number treatment cycles delivered = 5.0 (over 15 weeks) combined RDI = 0.94; completed at least six cycles = 49.8%; treatment delays = 11.8% DOC + CARB Median number treatment cycles delivered = six (18 weeks) combined RDI = 0.93; completed at least six cycles = 51.4%; treatment delays = 11.2%				Median number treatment cycles delivered = 4.0 (16 weeks) combined RDI = 0.78; completed at least six cycles = 33.6%; treatment delays = 16.1%	

Trial	DOC + PLAT	GEM + PLAT	PAX + PLAT	PEM + PLAT	VNB + PLAT	GEF
Gebbia 2003[49]		Total of 610 cycles with a mean of 4.3 cycles per patient. Programmed dose intensity of 25 mg/m^2/week for CIS, 700 mg/m^2/week for GEM (estimated for four cycles). Actual delivered dose intensities = 22.5 mg/m^2/week for CIS (90%) and 590 mg/m^2/week for GEM (84%), mainly due to myelosuppression, asthenia and mild renal toxicity			Total of 659 cycles, mean of 4.7 cycles per patient. Programmed dose intensity of 25 mg/m^2/week for CIS and 12.5 mg/m^2/week for VNB. Actual delivered dose intensity of CIS and VNB calculated in patients who received four cycles of chemotherapy = 22.7 mg/m^2/week (91%) and 11.5 mg/m^2/week (92%), respectively. Overall, dose reduction was performed in 19% of cycles owing to toxicity, which was mainly represented by myelosuppression, neurological and mild renal side effects	
Gridelli 2003[45]		NR			NR	
Smit 2003[46]		Median number of cycles = 5.0, RDI was not different between the treatment arms	Median number of cycles = 5.0, RDI was not different between the treatment arms			
Chen 2004[51]			281 cycles; mean 4.01 cycles; mean percentage dose administered was 95.3% scheduled PAX dose on day 1, 90% on day 8, and 85.2% on day 15, and 88.9% scheduled CIS dose on day 15		307 cycles; mean 4.39 cycles; mean percentage dose administered was 93.1% scheduled VNB dose on day 1, 95.3% on day 8, and 83.3% on day 15, and 87.6% of the scheduled CIS dose on day 15	

Trial	DOC + PLAT	GEM + PLAT	PAX + PLAT	PEM + PLAT	VNB + PLAT	GEF
Douillard 2005[53]	Total of 544 combination cycles were given as first line with a median of 6.0 (range: 1–6) cycles; median dose intensity = >98% of planned dose for both drugs; majority of combination therapy cycles were administered on time (93%); 38 cycles (7%) were delayed because of haematological (14 cycles), non-haematological toxicities (14 cycles) and for other reasons unrelated to treatment (10 cycles). During combination therapy, the dose of DOC was reduced in 13 cycles (2.4%) and in 17 (3.1%) cycles for CIS				Total of 519 combination cycles were given as first line with a median of 6.0 (range: 1–6) cycles; median dose intensity was 88% (VNB) to 90% (CIS) of planned dose; majority of combination therapy cycles were administered on time (73.4%); 138 (26.6%) cycles were delayed for haematological (92 cycles, 66.7%) and non-haematological toxicities (27 cycles, 19.6%), and one cycle for both types of toxicity and 18 (13%) for other reasons. VNB was reduced in 34 cycles (6.6%) and CIS was reduced in 53 (10.2%) cycles	
Martoni 2005[54]		Median number cycles per patient = 6.0 (range: 1–7); mean percentages of doses actually administered as compared with the planned dose in the scheduled time intervals during the administration of the CIS combinations were 88.9% for GEM and 98.9% for CIS (with GEM)			Median number cycles per patient = 6.0 (range: 1–10); mean percentages of doses actually administered as compared with the planned dose in the scheduled time intervals during the administration of the CIS combinations were 86.8% for VNB and 96.6% for CIS (with VNB)	

Trial	DOC + PLAT	GEM + PLAT	PAX + PLAT	PEM + PLAT	VNB + PLAT	GEF
Thomas 2006[58]		Total of 190 cycles were administered with a median of 4.0 cycles per patient. Dose intensity was 84.9% for GEM and 99.8% for CARB. Treatment was delayed for 13.7% of cycles; median number of days per cycle was 21. The ratio between theoretical duration of chemotherapy and real duration calculated is 95.1%			Total of 172 cycles were administered, median of 3.0 cycles per patient. Dose intensity was 97.7% for CIS and 67.7% for VNB. Treatment delayed 19.2% of cycles; median number of days per cycle was 21. The ratio between theoretical duration of chemotherapy and real duration calculated is 93.8%	
Chen 2007[52]	209 cycles (median 5)				230 cycles (median five)	
Helbekkmo 2007[55]		Mean number of cycles = 2.6. 167 (78%) received all three cycles, 17 (8%) two cycles, 26 (12%) one cycle and 4 (2%) no chemotherapy. Delayed or cancelled GEM at day 8 due to haematological toxicity = 18.1% (delayed 10.2%; not given 7.9%) ($p = 0.03$). Time exceeding 24 days between the main chemotherapy courses = 23% ($p = 0.06$)			Mean number of cycles = 2.7. 180 patients (83%) received all three cycles, 21 (10%) two cycles, 15 (7%) one cycle and 2 (1%) no chemotherapy. Delayed or cancelled VNB at day 8 due to haematological toxicity = 9.3% (delayed 4.6%; not given 4.8%) ($p = 0.03$). Time exceeding 24 days between the main chemotherapy courses = 15% ($p = 0.06$)	
Langer 2007[56]		Median number of cycles administered = three per arm, 31% of 47 treated patients completed all six cycles, 10% received more than six cycles, and 46% received at least four	Median number of cycles administered = three per arm, 27% of 51 patients completed all six cycles, 11% received more than six cycles, and 49% received at least four			
Ohe 2007[57]		NR	NR		NR	

Trial	DOC + PLAT	GEM + PLAT	PAX + PLAT	PEM + PLAT	VNB + PLAT	GEF
Chang 2008[50]	Of the 73 eligible patients, 160 courses were administered to 34 patients. The mean number of courses = 4.7; number of courses administered per patient did not differ significantly between the two arms ($p = 0.221$). 60% of patients received the full-schedule chemotherapy doses without dose modification or delay. Compliance was insignificantly ($p = 0.062$) favorable for the GEM + CIS arm				166 courses administered to 39 patients, mean number of courses = 4; 34% of patients received the full-schedule chemotherapy doses without dose modification or delay	
Scagliotti 2008[61]		Median number of cycles = 5.0, GEM + CIS dose reductions were most commonly attributable to neutropenia, thrombocytopenia, febrile neutropenia and leucopenia. On day 8, 339 GEM doses (9.3%) were omitted. Delivered dose intensities were higher for PEM + CIS (95.0% and 94.8%, respectively) than for GEM + CIS (93.5% and 85.8%, respectively)		Median number of cycles = 5.0, dose adjustments (delays, reductions, and omissions) were less frequent in patients treated with PEM + CIS compared with GEM + CIS, even when considering the more frequent GEM dosing (days 1 and 8 for GEM vs only day 1 for PEM). On day 1, PEM + CIS dose reductions were much less frequent (CIS, $n = 64$; PEM, $n = 54$ vs CIS, $n = 154$; GEM, $n = 362$), mainly caused by neutropenia Delivered dose intensities were higher for PEM + CIS (95.0% and 94.8%, respectively) than for GEM + CIS (93.5% and 85.8%, respectively)		

Trial	DOC + PLAT	GEM + PLAT	PAX + PLAT	PEM + PLAT	VNB + PLAT	GEF
Gronberg 2009[62]		Mean number cycles = 3.1; GEM on day 8 was omitted in 79 (12%) of 675 cycles; chemotherapy discontinued as a result of toxicity in 5% of the patients (PEM + CARB: 4%, GEM + CARB: 6%; $p = 0.51$)		Mean number of cycles = 3.3 ($p = 0.037$). Significantly more patients completed four cycles (PEM + CARB: 72%, GEM + CARB: 62%; $p = 0.030$), four cycles without delays (PEM + CARB: 58%, GEM + CARB: 44%; $p = 0.004$), and four cycles without dose reductions (PEM + CARB: 50%, GEM + CARB: 20%; $p < 0.001$)		
Mok 2009[15] and Fukuoka 2011[64]			Mean duration of treatment = 3.4 months (median 4.1 months; range 0.7–5.8 months). Median number of treatment cycles = 6.0, all patients had discontinued study treatment at data cut-off			Mean duration of treatment = 6.4 months (median 5.6 months; range 0.1–22.8 months). 24.5% of the patients continued to receive study treatment at data cut-off

Trial	DOC + PLAT	GEM + PLAT	PAX + PLAT	PEM + PLAT	VNB + PLAT	GEF
Tan 2009[59]	807 cycles were delivered, without delay in 90.5% cycles. Reasons for cycle delays for haematological/ non-haematological toxicity were reported in 8.8%/20.0% of cycles. At least one dose reduction during the trial was reported in 30 (15.7%) patients. Number of doses reduced for related haematological toxicity on day 1 of the cycle was similar in both arms. Among 172 patients receiving second cycle, 122 cycles (70.9%) were given with escalated doses. Planned six cycles of treatment were delivered in 98 of 191 patients; mean numbers of cycles = 4.4, with 129 patients having completed four cycles in both arms. RDI = 96.3% for DOC and 96.6% for CIS				807 cycles were delivered without delay in 81.3% cycles; reasons for cycle delays for haematological/ non-haematological toxicity were reported in 48.3%/6.6% of cycles. 708 cycles of oral VNB were delivered on day 8 with or without delay for 97.7%. Reason for the day 8 delay was haematological toxicity in 9 of 16 affected cycles (56.3%). At least one dose reduction during the trial was reported in 37 (19.5%) patients. Planned six cycles of treatment were delivered in 85 of 190 patients; the mean numbers of cycles = 4.2 with 124 patients having completed four cycles in both arms. RDI = 92% for i.v. VNB, 83.6% for oral VNB and 93.7% for CIS	
Maemondo 2010[63]			NR			NR
Mitsudomi 2010[65]	Median number of cycles = 4, or 64 days (range 1–6 cycles, or 1–106 days)					Median exposure = 165 days (range 22–1100 days)

Trial	DOC + PLAT	GEM + PLAT	PAX + PLAT	PEM + PLAT	VNB + PLAT	GEF
Treat 2010[60]		Median number of cycles administered = 4.0, mean number of cycles administered = 3.9, percentage of patients receiving a maximum six cycles = 36.5%, median RDI = 82.9% for GEM and 94.6% for CARB, percentage of patients receiving dose adjustments = 75.8% for GEM and 62.1% for CARB. During therapy, the rates of discontinuation due to excessive complication or toxicity were 12.4%	Median number of cycles administered = 4.0, mean number of cycles administered = 3.7, percentage of patients receiving a maximum six cycles = 30.6%, median RDI = 98.2% for PAX and 95.2% for CARB, percentage of patients receiving dose adjustments = 32.2% for PAX and 33.9% for CARB. During therapy, the rates of discontinuation due to excessive complication or toxicity were 15.3%			

NR, not reported.