

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Valle J, Wasan H, Palmer DH, et al. Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. *N Engl J Med* 2010;362:1273-81.

Table of contents

Supplementary table 1: Reasons for treatment discontinuation (ABC-02 patients only)	Page 2
Supplementary table 2: Treatment compliance and reasons for non-compliance for patients in the Gem arm	Page 3
Supplementary table 3: Treatment compliance and reasons for non-compliance for patients in the CisGem arm	Page 5
Supplementary table 4: Tumour response for all evaluable patients, and split by tumour site	Page 7

Supplementary table 1: Reasons for treatment discontinuation (ABC-02 patients only)

	Treatment arm	
	Gem (N=162)	CisGem (N=162)
Disease progression	49	26
Death	26	17
Co-morbidity	14	6
Toxicity	14	17
Withdrew consent	8	8
Clinician's decision	3	2
Unknown	4	7
Completed treatment	40	75
Never received trial treatment	4	4

Supplementary table 2: Treatment compliance and reasons for non-compliance for patients in the Gem arm

Cycle 1 (N=200)	Toxicity	Comorbid condition	Patient decision	Logistical	Evidence of PD	Non treatment death	Other	Unknown
Cycle outcome								
Treated as per protocol: 152 (76.0%)								
Treatment modifications: 48 (24.0%)								
Delayed	5 (2.5)	3 (1.5)	1 (0.5)	2 (1.0)	0 (0)	0 (0)	5 (2.5)	0 (0)
Reduced	9 (4.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (2.0)	1 (0.5)
Delayed & reduced	3 (1.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Omitted	5 (2.5)	4 (2.0)	1 (0.5)	0 (0)	0 (0)	0 (0)	3 (1.5)	1 (0.5)
Cycle 2 (N=187)								
Cycle outcome								
Treated as per protocol: 122 (65.2%)								
Treatment modifications: 65 (34.8%)								
Delayed	11 (5.9)	0 (0)	2 (1.1)	6 (3.2)	0 (0)	0 (0)	4 (2.1)	0 (0)
Reduced	9 (4.8)	0 (0)	1 (0.5)	0 (0)	0 (0)	0 (0)	2 (1.1)	4 (2.1)
Delayed & reduced	7 (3.7)	1 (0.5)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.5)	0 (0)
Omitted	1 (0.5)	2 (1.1)	2 (1.1)	0 (0)	2 (1.1)	0 (0)	4 (2.1)	6 (3.2)
Cycle 3 (N=176)								
Cycle outcome								
Treated as per protocol: 117 (66.5%)								
Treatment modifications: 59 (33.5%)								
Delayed	13 (7.4)	3 (1.7)	0 (0)	3 (1.7)	0 (0)	0 (0)	5 (2.8)	0 (0)
Reduced	4 (2.3)	0 (0)	1 (0.6)	0 (0)	0 (0)	1 (0.6)	4 (2.3)	0 (0)
Delayed & reduced	2 (1.1)	1 (0.6)	0 (0)	0 (0)	0 (0)	0 (0)	2 (1.1)	0 (0)
Omitted	4 (2.3)	2 (1.1)	2 (1.1)	0 (0)	1 (0.6)	0 (0)	1 (0.6)	10 (5.7)
Cycle 4 (N=161)								
Cycle outcome								
Treated as per protocol: 91 (56.5%)								
Treatment modifications: 70 (43.5%)								
Delayed	1 (0.6)	2 (1.2)	2 (1.2)	6 (3.7)	0 (0)	0 (0)	3 (1.9)	0 (0)
Reduced	16 (9.9)	0 (0)	1 (0.6)	0 (0)	0 (0)	0 (0)	2 (1.2)	4 (2.5)
Delayed & reduced	4 (2.5)	0 (0)	0 (0)	1 (0.6)	0 (0)	0 (0)	0 (0)	1 (0.6)
Omitted	10 (6.2)	2 (1.2)	2 (1.2)	0 (0)	3 (1.9)	0 (0)	6 (3.7)	4 (2.5)

Cycle 5 (N=126)	Toxicity	Comorbid condition	Patient decision	Logistical	Evidence of PD	Non treatment death	Other	Unknown
Cycle outcome								
Treated as per protocol: 69 (54.8%)								
Treatment modifications: 57 (45.2%)								
Delayed	8 (6.4)	1 (0.8)	2 (1.6)	6 (4.8)	0 (0)	0 (0)	6 (4.8)	0 (0)
Reduced	11 (8.7)	0 (0)	1 (0.8)	0 (0)	0 (0)	0 (0)	2 (1.6)	2 (1.6)
Delayed & reduced	3 (2.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.8)	0 (0)
Omitted	4 (3.2)	0 (0)	2 (1.6)	1 (0.8)	0 (0)	0 (0)	2 (1.6)	5 (4.0)
Cycle 6 (N=120)								
Cycle outcome								
Treated as per protocol: 71 (59.2%)								
Treatment modifications: 49 (40.8%)								
Delayed	6 (5.0)	1 (0.8)	1 (0.8)	6 (5.0)	0 (0)	0 (0)	0 (0)	0 (0)
Reduced	9 (7.5)	0 (0)	1 (0.8)	0 (0)	0 (0)	0 (0)	4 (3.3)	3 (2.5)
Delayed & reduced	2 (1.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.8)	0 (0)
Omitted	2 (1.7)	2 (1.7)	2 (1.7)	0 (0)	2 (1.7)	0 (0)	3 (2.5)	4 (3.3)
Cycle 7 (N=108)								
Cycle outcome								
Treated as per protocol: 64 (59.3%)								
Treatment modifications: 44 (40.7%)								
Delayed	5 (4.6)	0 (0)	0 (0)	1 (0.9)	1 (0.9)	0 (0)	3 (2.8)	0 (0)
Reduced	13 (12.0)	1 (0.9)	0 (0)	0 (0)	0 (0)	0 (0)	2 (1.9)	4 (3.7)
Delayed & reduced	3 (2.8)	0 (0)	0 (0)	1 (0.9)	0 (0)	0 (0)	1 (0.9)	0 (0)
Omitted	5 (4.6)	0 (0)	1 (0.9)	0 (0)	1 (0.9)	0 (0)	0 (0)	2 (1.9)
Cycle 8 (N=98)								
Cycle outcome								
Treated as per protocol: 52 (53.1%)								
Treatment modifications: 46 (46.9%)								
Delayed	3 (3.1)	0 (0)	1 (1.0)	1 (1.0)	0 (0)	0 (0)	4 (4.1)	0 (0)
Reduced	8 (8.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (4.1)	5 (5.1)
Delayed & reduced	5 (5.1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Omitted	3 (3.1)	0 (0)	2 (2.0)	0 (0)	2 (2.0)	0 (0)	3 (3.1)	5 (5.1)

Supplementary table 3: Treatment compliance and reasons for non-compliance for patients in the CisGem arm

Cycle 1 (N=202)	Toxicity	Comorbid condition	Patient decision	Logistical	Evidence of PD	Non treatment death	Other	Unknown
Cycle outcome								
Treated as per protocol: 123 (60.9%)								
Treatment modifications: 79 (29.1%)								
Delayed	13 (6.4)	5 (2.5)	1 (0.5)	4 (2.0)	0 (0)	0 (0)	2 (1.0)	0 (0)
Reduced	28 (13.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	7 (3.5)
Delayed & reduced	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.5)	0 (0)
Omitted	4 (2.0)	2 (1.0)	1 (0.5)	0 (0)	2 (1.0)	0 (0)	7 (3.5)	2 (1.0)
Cycle 2 (N=180)								
Cycle outcome								
Treated as per protocol: 115 (63.9%)								
Treatment modifications: 65 (36.1%)								
Delayed	5 (2.8)	1 (0.6)	4 (2.2)	3 (1.7)	0 (0)	0 (0)	8 (4.4)	0 (0)
Reduced	9 (5.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.6)	5 (2.8)
Delayed & reduced	1 (0.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Omitted	8 (4.4)	4 (2.2)	1 (0.6)	2 (1.1)	2 (1.1)	2 (1.1)	5 (2.8)	4 (2.2)
Cycle 3 (N=154)								
Cycle outcome								
Treated as per protocol: 93 (60.4%)								
Treatment modifications: 61 (39.6%)								
Delayed	8 (5.2)	3 (2.0)	1 (0.7)	2 (1.3)	0 (0)	0 (0)	2 (1.3)	1 (0.7)
Reduced	14 (9.1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.7)	6 (3.9)
Delayed & reduced	2 (1.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Omitted	6 (3.9)	5 (3.3)	0 (0)	0 (0)	1 (0.7)	0 (0)	4 (2.6)	5 (3.3)
Cycle 4 (N=104)								
Cycle outcome								
Treated as per protocol: 62 (59.6%)								
Treatment modifications: 42 (40.4%)								
Delayed	8 (7.7)	1 (1.0)	1 (1.0)	4 (3.9)	0 (0)	0 (0)	2 (1.9)	0 (0)
Reduced	10 (9.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (1.9)	4 (3.9)
Delayed & reduced	3 (2.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Omitted	1 (1.0)	1 (1.0)	0 (0)	0 (0)	1 (1.0)	0 (0)	2 (1.9)	2 (1.9)

Cycle 5 (N=89)	Toxicity	Comorbid condition	Patient decision	Logistical	Evidence of PD	Non treatment death	Other	Unknown
Cycle outcome								
Treated as per protocol: 46 (51.7%)								
Treatment modifications: 43 (48.3%)								
Delayed	5 (5.6)	1 (1.1)	3 (3.4)	3 (3.4)	0 (0)	0 (0)	4 (4.5)	1 (1.1)
Reduced	9 (10.1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (3.4)
Delayed & reduced	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Omitted	4 (4.5)	1 (1.1)	2 (2.3)	0 (0)	3 (3.4)	0 (0)	4 (4.5)	0 (0)
Cycle 6 (N=73)								
Cycle outcome								
Treated as per protocol: 41 (56.2%)								
Treatment modifications: 32 (43.8%)								
Delayed	2 (2.7)	1 (1.4)	0 (0)	2 (2.7)	0 (0)	0 (0)	0 (0)	0 (0)
Reduced	7 (9.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (5.5)
Delayed & reduced	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Omitted	3 (4.1)	2 (2.7)	4 (5.5)	0 (0)	2 (2.7)	1 (1.4)	2 (2.7)	2 (2.7)

Supplementary table 4: Tumour response for all evaluable patients, and split by tumour site

	Treatment arm		p value
	Gem	CisGem	
All evaluable patients	N=142	N=161	
Complete response	1 (0.7)	1 (0.6)	
Partial response	21 (14.8)	41 (25.5)	
Stable disease	80 (56.3)	89 (55.3)	
Progressive disease	40 (28.2)	30 (18.6)	
Tumour control (CR+PR+SD)	102 (71.8)	131 (81.4)	0.049
Difference (95% CI)	9.5% (0.1, 19.0)		
Gallbladder tumours	N=56	N=61	
Complete response	0 (0)	0 (0)	
Partial response	12 (21.4)	23 (37.7)	
Stable disease	31 (55.4)	29 (47.5)	
Progressive disease	13 (23.2)	9 (14.8)	
Tumour control (CR+PR+SD)	43 (76.8)	52 (85.2)	0.242
Difference (95% CI)	8.5% (-5.7, 22.7)		
Bile duct and ampullary tumours	N=86	N=100	
Complete response	1 (1.2)	1 (1.0)	
Partial response	9 (10.5)	18 (18.0)	
Stable disease	49 (57.0)	60 (60.0)	
Progressive disease	27 (31.4)	21 (21.0)	
Tumour control (CR+PR+SD)	59 (68.6)	79 (79.0)	0.106
Difference (95% CI)	10.4% (-2.2, 23.0)		