Supplementary File 2

Specific dose modifications for cisplatin and capecitabine

Haematological toxicity

ANC x 10^9/L (on day of chemotherapy)	
0.5 to less than 1.5	Delay treatment until recovery
less than 0.5	Delay treatment until recovery and consider reducing cisplatin and capecitabine by 25% for subsequent cycles
Febrile neutropenia	Delay treatment until recovery and consider reducing cisplatin and capecitabine by 25% for subsequent cycles
Platelets x10^9/L (at any stage of the cycle)	
50 to less than 100	Delay treatment until recovery
less than 50	Delay treatment until recovery and consider reducing cisplatin and capecitabine by 25% for subsequent cycles

Renal impairment

eGFR (Cockcroft Gault) (mL/min)*	
greater than or equal to 70	No dose modifications necessary
50 to less than 70	Reduce cisplatin by 25%
30 to less than 50	Reduce capecitabine by 25% and cisplatin by 50%
less than 30	Withhold treatment

Hepatic impairment

Hepatic dysfunction	
Mild	No dose modifications necessary
Moderate	Reduce capecitabine by 25%
Severe	Reduce capecitabine by 50%
Treatment related Grade 3 or 4 Hyperbilirubinaemia	Delay treatment until toxicity resolves to Grade 2 or less

Peripheral neuropathy

CTC grading	
Grade 2, Grade 3 or Grade 4	Omit cisplatin

Mucositis & stomatitis

CTC grading	
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follow: 1st occurrence: No dose reduction 2nd occurrence: Reduce cisplatin and capecitabine by 25% 3rd occurrence: Reduce cisplatin and capecitabine by 50% 4th occurrence: Omit cisplatin and capecitabine
Grade 3 or Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follow: 1st occurrence: Reduce cisplatin and capecitabine by 50% 2nd occurrence: Omit cisplatin and capecitabine

Diarrhoea

CTC grading	
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follow: 1st occurrence: No dose reduction 2nd occurrence: Reduce capecitabine 25% 3rd occurrence: Reduce capecitabine by 50% 4th occurrence: Omit capecitabine
Grade 3 or Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follow: 1st occurrence: Reduce capecitabine by 50% 2nd occurrence: Omit capecitabine

Hand and foot syndrome (Palmar-plantar erythrodysesthesia syndrome)

CTC grading	
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follow: 1st occurrence: No dose reduction

	2nd occurrence: Reduce capecitabine 25% 3rd occurrence: Reduce capecitabine by 50% 4th occurrence: Omit capecitabine
Grade 3	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follow: 1st occurrence: Reduce capecitabine by 50% 2nd occurrence: Omit capecitabine