Supplemental Material

Patient Eligibility Criteria

Patients were eligible for enrollment if they were ≥ 18 years old with histologically proven colorectal cancer, measurable metastatic disease (at least one lesion ≥ 2 cm diameter on CT), expected survival ≥ 4 months, Eastern Cooperative Oncology Group performance status 0-2, and able to give valid informed consent. Adequate blood parameters required were: Neutrophil count ≥ 1.5 x 10^9/L, platelet count ≥ 150 x 10^9/L, serum bilirubin ≤ 34 μmol/L, and a calculated creatinine clearance >50 ml/ min (Cockcroft and Gault formula). Patients were excluded from the study if they had active central nervous system disease, >50% liver involvement by metastatic disease, had received prior capecitabine, or had received other chemotherapy, radiation therapy, or immunotherapy within 4 weeks prior to study entry. Prior external beam irradiation was an exclusion criteria with the exception of standard adjuvant pelvic radiation for rectal cancer, localized irradiation for skin cancer, or if the sum total of all previous external beam irradiation port areas was <25% of the total red marrow. Other serious illnesses, concomitant treatment with systemic corticosteroids, and previous antibody treatment with a positive huA33 HAHA titre were also amongst the exclusion criteria.

Patient Evaluability

All patients who received the therapy dose of ^{131}I-huA33 and either experienced DLT or completed the study to at least six weeks of after the therapy dose of ^{131}I-huA33 were evaluable for safety. All patients who received at least the scout dose of ^{131}I-

huA33 were evaluable for HAHA. All patients who received at least one complete cycle of capecitabine were evaluable for tumor response.

Enrolled patients withdrawn from the study within six weeks of receiving the therapy dose of ^{131}I-huA33 for reasons other than toxicity were replaced.

Dose-Limiting Toxicities (DLT)

All adverse events (as defined in Section 9.1.1) were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE v3.0). DLT was defined as any of the following events occurring within 6 weeks of the first ^{131}I-huA33 therapy infusion.

- Any grade 2 or greater allergic reaction related to huA33 antibody protein.

- Any grade ≥ 3 non-haematological toxicity related to ^{131}I-huA33 or capecitabine. These toxicities include palmar plantar erythema, but skin rash thought to be related to huA33 protein was not a DLT as previous studies had shown no relation of this toxicity to dose of huA33 or radioiodine dose.

- Any grade ≥ 4 neutropenia ≥ 7 days in duration or any thrombocytopenia with a platelet count < 10 x 10^9/L.

To be dose-limiting, an adverse event was required to be definitely, probably, or possibly related to the administration of the investigational agent.

Maximum Tolerated Dose (MTD)

The maximum tolerated dose was defined as the highest safely tolerated dose level where at most 1 of 6 patients experiences a dose limiting toxicity with the next higher dose level having at least 2 of 6 patients who experience a dose limiting toxicity.

Supplemental Table 1. Commonest toxicity encountered: Number of patients with maximal CTCAE grade, study related toxicity

System Organ Class (MedDRA v9)	Toxicity	Number of patients with maximal CTCAE grade, study related toxicity				
		Total	G1	G2	G3	G4
Blood and lymphatic system disorders	Anemia	**2**	2	0	0	0
	Febrile neutropenia	**1**	0	0	1	0
	Leukopenia	**11**	1	5	5	0
	Lymphopenia	**6**	0	2	3	1
	Neutropenia	**13**	3	4	5	1
	Thrombocytopenia	**14**	1	6	6	1
Cardiac disorders	Chest pain - cardiac	**1**	0	0	1	0
	Retrosternal Chest Pain	**1**	1	0	0	0
Gastrointestinal disorders	Diarrhea	**6**	3	2	1	0
	Constipation	**1**	1	0	0	0
	Nausea	**14**	14	0	0	0
	Vomiting	**4**	1	3	0	0
	Stomatitis	**1**	1	0	0	0
	Gastroesophageal reflux/indigestion	**3**	3	0	0	0
	Bloating, flatulence	**2**	2	0	0	0
	Rectal bleeding	**1**	1	0	0	0
General disorders and administration site conditions	Fever	**1**	0	1	0	0
	Lethargy	**11**	10	1	0	0
Hepatobiliary disorders	Hyperbilirubinaemia	**10**	7	2	1	0
Infections and infestations	Cold sore mouth	**1**	1	0	0	0
	Oral thrush	**1**	0	1	0	0
Metabolism and nutrition disorders	Anorexia	**7**	7	0	0	0
Musculoskeletal and connective tissue disorders	Hand/foot pain	**2**	2	0	0	0

Nervous system disorders	Dizziness	**1**	1	0	0	0
	Headache	**1**	1	0	0	0
	Paresthesia distal	**1**	1	0	0	0
	Smell loss	**1**	1	0	0	0
Respiratory, thoracic and mediastinal disorders	Epistaxis	**1**	1	0	0	0
Skin and subcutaneous tissue disorders	Desquamation/dry skin	**3**	2	1	0	0
	Palmar-plantar erythema	**2**	2	0	0	0
	Pruritis	**1**	0	1	0	0
	Rash	**5**	4	1	0	0
	Skin tenderness	**1**	1	0	0	0