Supplementary Table 1. MP1U Dosing Regimens

Chemical Agent	Brand name(s)	Dose (mpk)	Route	Schedule	Notes
ABT-888 (Veliparib)	NA	100	PO	continuous in food or bid	Doses were based upon literature review.
AZD-6244 (Selumetinib)	NA	100	PO	continuous in food or qd	Literature review suggested a dose of 75 mpk PO in food. While this was efficacious in the acute setting, younger C3-Tag females suffered severe toxicity around 28 days. Weight loss and body composition score suggested a 50% reduction in dose to 37 mpk PO-food.
BEZ235	NA	100	PO	continuous in food or qd	Single agent doses were recommended by Novartis.
AZD6244/BEZ235	NA	18/25	PO	continuous in food or qd	Initially full single agent doses were used (37 and 50 mpk respectively). Severe toxicity was noted after 17 days in the Neu model. The dose was cut to 75% of single agents and found again to be toxic in the acute setting using MMTV-Neu. The combination was cut to a final tolerable dose of 50% of single agents.
BKM120	NA	100	PO	continuous in food or qd	Single agent doses were recommended by Novartis
BTG226	NA	100	PO	continuous in food or qd	Single agent doses were recommended by Novartis
Capecitabine	Xeloda	300	PO	continuous in food	Doses were based upon literature review.
Carboplatin	Carbo	100	Parenteral	qw	Carboplatin was dosed in a range from 50-75 mpk as a single agent. A dose of 50mpk was determined to illicit a tumor response and was tolerable for overall survival.
Cyclophosphamide	Cytoxan	30	Parenteral	qw	Doses were based upon literature review.
Dasatinib	Spyrcel	30	PO	continuous in food or qd	Doses of 15 and 30 mpk were tried in the acute response setting. No tumor effect was noted and plasma was drawn from mice treated with 30mpk to confirm the presence of metabolites of the drug.
Doxorubicin	Dox	10	Parenteral	qw	Doxorubicin was dosed at 10, 7, 5 mpk IP. 10 mpk caused severe toxicity in the acute setting and significant death in the long term setting after only 4 doses. 7 mpk, while suitable for 21-day assessment caused severe toxicity in long term survival. A dose of 5mpk was used in both the acute response and the overall survival studies. While weight loss continued to be a problem it was not severely limiting.
Erlotinib	Tarceva	75	PO	continuous in food or qd	Doses were based upon literature review.
Gemcitabine	Gemzar	125	Parenteral	qw	Doses were based upon literature review.
Lapatinib	Tykerb	220	PO	continuous in food or qd	Drug was first dosed on the targeted model Neu at 75 mpk PO in food. Stable disease was reached in 21 days but no toxicity was noted. The dose was escalated systematically to 220 mpk. This dose caused tumor complete regression in the Neu model within 14 days and was tolerated very well with mild toxicity only showing in some animals after 120 days of continuous treatment. Plasma was drawn to confirm drug presence.
Lonafarnib	Sarosar	60	PO	bid	Dose and schedule provided by Schering-Plough.
Paclitaxel	Taxol	10	Parenteral	qw	Drug was dosed by tail IV at 10 and 20 mpk and IP at 10 mpk. IV 20 mpk caused moderate skin lesions on the tail around 28 days. IV and IP 10 mpk were well tolerated and no tumor response differences between IV and IP were noted. Significant differences were found in a PK study comparing IP and IV administration of 10 mpk Taxol. The IP route was pursued for all subsequent studies due to the ease of administration.
PD0332991	NA	100-150	PO	continuous in food or qd	Based on PK analysis and published studies, 100 mpk dose was used for long-term continuous treatment of mice as an anti-neoplastic. .
Sorafenib	Nexavar	300	PO	continuous in food or qd	A range of doses were used from 10-300 mpk on the Neu model. Peak efficacy was seen at 50 mpk with an OS of 137 days but stable disease and no regression. Dose was escalated to 300 mpk with no adverse side effects noted nor increased efficacy. 50 and 100 mpk were used in the C3Tag with no immediate change to OS. A final dose of 50 mpk was used.
Sunitinib	Sutent	40	PO	continuous in food or qd	Sutent dosing was based on literature review. However when combined with Carboplatin significant dose finding of the combination was performed. The dose of Carboplatin was given at a range of 10-50 mpk and was only tolerable at the lowest dose for overall survival.
Temozolomide	Temodar	66	PO	continuous in food	Temozolomide was initially dosed at 200 mpk by oral gavage x 5 days, however due to lack of efficacy, toxicity and practical concerns delivery was changed continuous delivery in food and dose was tapered down to 66 mpk.

Abbreviations: bid, twice daily; mpk, mg per kilogram; PO, by mouth; qd, once daily; qw, once weekly.