Table S1. Dose comparison between monotherapy and combination arms of clinical trials analyzed. Related to Figures 1, 4, and S5.

Treatment	Arm #1 dose	Arm #2 dose	Combination dose	Dose comparison
Figure 1, Untreated metastatic melanoma, ipilimumab plus nivolumab (Larkin et al., 2015)				
Ipilimumab	4 cycles of 3 mg/kg every 3 weeks		4 cycles of 3 mg/kg every 3 weeks	No difference in design
Nivolumab		3 mg/kg every 2 weeks	First 2 cycles of 1 mg/kg every 3 weeks Second 2 cycles of 3 mg/kg every 3 weeks Followed by maintenance 3 mg/kg every 2 weeks	67% reduction during first 2 cycles, No difference in dose in cycles 3, 4, and during maintenance.
Figure 4A, Recurrent platinum sensitive ovarian cancer, chemotherapy plus olaparib (Liu et al., 2014; Oza et al., 2015)				
Paclitaxel	6 cycles of 175 mg/m^2 every 3 weeks		6 cycles of 175 mg/m^2 every 3 weeks	No difference in design
Carboplatin	6 cycles of AUC = 6 mg/mL/min every 3 weeks		6 cycles of AUC = 4 mg/mL/min every 3 weeks	33% reduction in dose
Olaparib		400 mg twice daily until progression	During chemotherapy cycles 200 mg twice daily, followed by 400 mg twice daily until progression	50% reduction in dose during chemotherapy cycles, followed by a maintenance dose which is equal to the monotherapy arm.
Figure 4B, HER2-positive metastatic breast cancer, chemotherapy plus trastuzumab (Slamon et al., 2001; Vogel et al., 2002)				
Anthracycline	6 cycles of 60mg/m^2 doroxubicin *or* 75mg/m^2 epirubucin every 3 weeks		6 cycles of 60mg/m^2 doroxubicin *or* 75mg/m^2 epirubucin every 3 weeks	No difference in design
Cyclophosphamide	6 cycles of 600 mg/m^2 every 3 weeks		6 cycles of 600 mg/m^2 every 3 weeks	No difference in design
Paclitaxel (in place of AC for patients who received adjuvant anthracycline)	6 cycles of 175 mg/m^2 every 3 weeks		6 cycles of 175 mg/m^2 every 3 weeks	No difference in design
Trastuzumab		Loading dose of 4 mg/kg, followed by 2 mg/kg weekly (52% of patients), *or* loading dose of 8 mg/kg, followed by 4 mg/kg weekly (48% of patients). No statistically significant difference in response rate and overall survival between doses.	Loading dose of 4 mg/kg, followed by 2 mg/kg weekly	48% of patients in trastuzumab monotherapy study received double dose, but this change produced no statistically significant difference in response rate or overall survival.
Figure 4C, Advanced pancreatic cancer, gemcitabine plus erlotinib (Moore et al., 2007; Renouf et al., 2014)				
Gemcitabine	1,000 mg/m^2 on days 1, 8, 15, 22, 29, 36, and 43 followed by a 1-week rest in cycle one (8 weeks), and on days 1, 8 and 15 in all subsequent 4-week cycles		1,000 mg/m^2 on days 1, 8, 15, 22, 29, 36, and 43 followed by a 1-week rest in cycle one (8 weeks), and on days 1, 8 and 15 in all subsequent 4-week cycles	No difference in design
Erlotinib		150 mg/day. Dose-escalation to 200-300 mg/day possible in 9 of 49 patients.	100 to 150 mg/day. 100 mg/day in initial safety evaluation phase, increased to 150 mg/day in subsequent cohorts.	Majority of patients have dose difference ≤ 33%. Only 9 patients receiving Erlotinib monotherapy have 50% or more dose difference.
Figure 4D, BRAF-mutant metastatic melanoma, dabrafenib plus trametinib (Kim et al., 2013; Long et al., 2014)				
Dabrafenib	150 mg twice daily		150 mg twice daily	No difference in design
Trametinib		2 mg once daily	2 mg once daily	No difference in design

Figure 4E, Recurrent platinum-sensitive ovarian cancer, chemotherapy plus bevacizumab (Aghajanian et al., 2012; Burger et al., 2007)				
Gemcitabine	6 cycles (up to 10 if responding) of 1000 mg/m^2 on days 1 and 8 of every 3 weeks		6 cycles (up to 10 if responding) of 1000 mg/m^2 on days 1 and 8 of every 3 weeks	No difference in design
Carboplatin	6 cycles (up to 10 if responding) of AUC = 4 mg/mL/min every 3 weeks		6 cycles (up to 10 if responding) of AUC = 4 mg/mL/min every 3 weeks	No difference in design
Bevacizumab		15 mg/kg every 21 days	15 mg/kg every 21 days	No difference in design
Figure 4F, Previously treated colorectal cancer, FOLFOX4 plus bevacizumab (Giantonio et al., 2007)				
Oxaliplatin	Every 2 weeks, 85 mg/m^2		Every 2 weeks, 85 mg/m^2	No difference in design
Leucovorin	Every 2 weeks, 200 mg/m^2 on days 1 and 2		Every 2 weeks, 200 mg/m^2 on days 1 and 2	No difference in design
5-Fluorouracil	Every 2 weeks, 400 mg/m^2 bolus then 600 mg/m^2 infusion on days 1 and 2		Every 2 weeks, 400 mg/m^2 bolus then 600 mg/m^2 infusion on days 1 and 2	No difference in design
Bevacizumab		Every 2 weeks, 10 mg/kg	Every 2 weeks, 10 mg/kg	No difference in design
Figure 4G, Advanced pancreatic cancer, 5-fluorouracil plus oxaliplatin (Ducreux et al., 2004)				
5-Fluorouracil	Every 3 weeks, 1000 mg/m^2/day on days 1-4		Every 3 weeks, 1000 mg/m^2/day on days 1-4	No difference in design
Oxaliplatin		Every 3 weeks, 130 mg/m^2	Every 3 weeks, 130 mg/m^2	No difference in design
Figure 4H, KRAS-wildtype metastatic colorectal carcinoma, chemotherapy plus cetuximab (Bokemeyer et al., 2009; Bokemeyer et al., 2012; Karapetis et al., 2008; Van Cutsem et al., 2009)				
FOLFIRI (CRYSTAL trial)	Every 2 weeks: Irinotecan 180 mg/m^2; leucovorin 200 mg/m^2 L-form, or 400 mg/m^2 racemic; fluorouracil 400 mg/m^2 bolus then 2400 mg/m^2 infusion		Every 2 weeks: Irinotecan 180 mg/m^2; leucovorin 200 mg/m^2 L-form, or 400 mg/m^2 racemic; fluorouracil 400 mg/m^2 bolus then 2400 mg/m^2 infusion	No difference in design
FOLFOX-4 (OPUS trial)	Every 2 weeks: Oxaliplatin 85 mg/m^2; leucovorin 200 mg/m^2; fluorouracil 400 mg/m^2 bolus then 600 mg/m^2 infusion on days 1 and 2		Every 2 weeks: Oxaliplatin 85 mg/m^2; leucovorin 200 mg/m^2; fluorouracil 400 mg/m^2 bolus then 600 mg/m^2 infusion on days 1 and 2	No difference in design
Cetuximab		Loading dose of 400mg/m^2, followed by 250 mg/m^2 weekly	Loading dose of 400mg/m^2, followed by 250 mg/m^2 weekly	No difference in design
Supplementary Figure S5B, Low grade oligodendroglioma, chemotherapy plus radiation (Buckner et al., 2016; Taal et al., 2015)				
Procarbazine	6 cycles of 60 mg/m^2 on days 8-21, every 6 weeks		6 cycles of 60 mg/m^2 on days 8-21, every 8 weeks	No difference in dose, but 8 week instead of 6 week cycles
Lomustine	6 cycles of 110 mg/m^2, on day 1, every 6 weeks		6 cycles of 110 mg/m^2, on day 1, every 8 weeks	No difference in dose, but 8 week instead of 6 week cycles
Vincristine	6 cycles of 1.4 mg/m^2 on days 8 and 29, every 6 weeks		6 cycles of 1.4 mg/m^2 on days 8 and 29, every 8 weeks	No difference in dose, but 8 week instead of 6 week cycles
Radiation		54 Gy total, in 30 fractions of 1.8 Gy each over 6 weeks	54 Gy total, in 30 fractions of 1.8 Gy each over 6 weeks	No difference in design