Appendix Three: Trastuzumab (Herceptin) Clinical Trial Summaries

	Sequential treatment trials, long duration (12 month)[1] regimens		Concurrent treatment trials, long duration (12 month) regimens			Concurrent treatment trials with short duration regimens	
	HERA Trial	**N9831 (Arm B)**	**N9831 (Arm C)**	**BCIRG006[2]**	**B31**	**FinHer Trial**	**E2198[3]**
Patient Numbers	Observation: 1,693 Trastuzumab (1 yr): 1,694 Trastuzumab (2 yr):[1] 1,694	Observation: 979 Trastuzumab: 985	Observation: 979 Trastuzumab: 840	Observation: 1,073 Trastuzumab: 1,074	Observation: 1,024 Trastuzumab: 1,019	Observation: (116) vinorelbine – 58 docetaxel – 58 Trastuzumab: (116) docetaxel - 54 vinorelbine - 62	Short duration : 115 patients Long duration: 112 patients
Intervention	1 loading dose (8mg/kg) trastuzumab, then 6mg/kg every 3 weeks for one year or two years (17 or 35 infusions, respectively).	1 loading dose (4mg/kg) trastuzumab, then 2mg/kg every week for 52 weeks	1 loading dose (4mg/kg) trastuzumab, then 2mg/kg every week for 52 weeks	1 loading dose (4mg/kg) trastuzumab, then 2mg/kg every week for 52 weeks	1 loading dose (4mg/kg) trastuzumab, then 2mg/kg every week for 52 weeks	9 trastuzumab infusions at 1 week intervals. First dose 4mg/kg (90min infusion), remaining doses 2mg/kg (30 min infusion)	Short duration: 10 trastuzumab infusions at 1 week intervals. Trastuzumab given in combination with paclitaxel– Loading dose 4mg/kg followed by 9 weeks 2mg/kg Long duration: As above but with further 52 weeks of trastuzumab at 2mg/kg per week.
Timing of treatment	Sequential (after completion of all chemotherapy – anthracycline chemotherapy[4] and taxane treatment[5])		Concurrent with taxane (paclitaxel), after completion of anthracycline chemotherapy			Concurrent with taxane (docetaxel) treatment, before anthracycline chemotherapy[2]	Short duration: Concurrent with taxane treatment, before anthracycline chemotherapy[2] Long duration: concurrent and sequential
Disease free survival Hazard Ratio (95% confidence interval)	12-mth median f/up: 0.54 (0.43-0.67) 23-mth median f/up: 0.64 (0.54-0.76)	0.87 (0.67-1.13)	0.55 (CI not reported[6])	23-mth median f/up: 0.49 (0.37-0.79) 36-mth median f/up: 0.61 (0.48-0.76)	0.45 (CI not reported[3])	36-mth median f/up: 0.42 (0.21-0.83)	DFS at 5 yrs: 76% short duration 75% long duration Note that a pilot study, not designed to report efficacy[3]
Overall DFS HR	0.70 (0.61-0.81) (2-yr HERA f/u)		0.53 (0.46-0.62) (3-yr BCIRG006 f/u)			0.42 (0.21.0.83)	N/A – placebo group data not reported
Overall survival (95% CI)	12-mth median f/up: 0.76 (0.47-1.23) 23-mth median f/up: 0.66 (0.47-0.91)	0.85 (0.55-1.33)	Not reported (joint analysis with B31 = 0.67 (0.48-0.93))	36-mth median f/up: 0.59 (0.42-0.85)	Not reported (joint analysis with N9831 arm C = 0.67 (0.48-0.93))	36-mth median f/up: 0.41 (0.16-1.08)	OS at 5 yrs: 89% short duration 83% long duration Note that E2198 is a pilot study, not designed to report efficacy[3]
Overall OS HR (95% CI)	0.72 (0.55-0.94)		0.63 (0.50-0.80)			0.41 (0.16-1.08)	N/A – placebo group data not reported

[1] No evidence is available on the outcomes of the 2 year trastuzumab treatment arm in the HERA trial.
[2] Note that there was also an arm to BCIRG006 ('arm TCH') that consisted of 6 cycles of docetaxel and carboplatin with concurrent trastuzumab (i.e. no anthracycline chemotherapy). However, because this regimen is not comparable to the other regimens, these results are not presented in this table. For further information regarding BCIRG006 see Appendix One: Minutes of the relevant clinical advisory committee meetings.
[3] The E2198 study (Sledge et al, poster presentation at ASCO 2006) was not designed to test efficacy, and was not powered to determine equivalence, and results comparing the treatment arms to the control arm have yet to be reported. However, the results supported the efficacy of short duration concurrent trastuzumab therapy when administered before anthracycline containing chemotherapy, as demonstrated in the FinHer study (Appendix One: Minutes of the relevant clinical advisory committee meetings).
[4] Anthracycline containing chemotherapy regimens (FEC or FAC).
[5] The HERA trial allowed several different chemotherapy regimens.
[6] Note that N9831 Arm C and trial B31 data were only published as a joint analysis (Romond, 2005) without stating the hazard ratios' confidence intervals for the individual trials. Confidence limits for the disease recurrence HR for N9831 Arm B were stated in the 2005 conference presentation on the ASCO website.