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Herceptin (H) after adjuvant chemotherapy significantly improves disease-free survival (DFS) in HER2-positive early breast cancer (BC): HERA trial interim analysis

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HERA, an international, multi-centre, randomised, three-arm trial compared 1 year of 3 weekly H (8 mg/kg iv day 1; 6 mg/kg iv q 3 weeks thereafter) with observation and 2 years of 3 weekly H with observation in patients with HER2 overexpressing, node-negative (T size >1 cm) or node-positive BC who had completed at least 4 cycles of an acceptable (neo)adjuvant chemotherapy (CT) regimen. Adjuvant endocrine therapy (mostly tamoxifen) followed CT for patients with hormone receptor positive disease. Eligibility criteria included central confirmation of HER2 overexpression (3+) or amplification (FISH+) and baseline LVEF (echo or MUGA) ⩾55% following CT. Trial endpoints were 1) DFS (primary) 2) overall survival (OS), relapse-free survival (RFS), distant disease free survival (DDFS), overall safety and cardiac safety. The trial was designed to detect, with 80% power, a 23% reduction in the risk of a DFS event with H treatment after 951 DFS events with a total accrual of 4482 patients; 5090 patients have been enrolled by 478 institutions from Europe, Canada, South Africa, Israel, the Asia Pacific Region, Japan, and Latin America: median age = 49, node negative = 32%, hormone receptor negative = 49%, prior anthracyclines (A) = 68%, prior A *and* taxanes = 25%. At a median follow-up of 1 year, 475 events have been observed and have triggered the first and only interim analysis. The Independent Data Monitoring Committee recommended release of the results for the 1 year H arm (1694 pts; 127 events) versus observation (1693 pts; 220 events) presented in the table.

	DFS[a]	RFS	DDFS[b]	OS
HR	0.54	0.50	0.51	0.76
95%CI	0.43–0.67	0.40–0.63	0.40–0.66	0.47–1.23
p-value	<0.0001	<0.0001	<0.0001	0.26
events	127 vs. 220	113 vs. 209	98 vs. 179	29 vs. 37
2-year (%)	85.8 vs. 77.4	87.2 vs. 78.6	89.7 vs. 81.8	96.0 vs. 95.1

[a]Includes local, regional, distant recurrences, contralateral BC, 2nd malignancies, death without prior event.
[b]Includes distant recurrences, contralateral BC, 2nd malignancies.

H-treated patients had a higher incidence of primary cardiac endpoint [NYHA class III–IV congestive heart failure (cardiologist confirmed) LVEF drop of at least 10 EF points from baseline and to below 50% or cardiac death]: n = 9 (0.5%) with H versus n = 0 (without H). The 2 year H arm also improved DFS compared with observation ($p < 0.0001$). The trial will continue to assess the comparison of 2 years versus 1 year of H treatment and careful monitoring of potential late side effects.