Efficacy and safety of subcutaneous trastuzumab and intravenous trastuzumab as part of adjuvant therapy for HER2-positive early breast cancer: Final analysis of the randomised, two-cohort PrefHer study

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Background

A 600-patient, double-blind randomised injection of subcutaneous trastuzumab (Hertraz®) or intravenous trastuzumab (Herceptin®) as part of adjuvant therapy for HER2-positive early breast cancer, given via hand-held syringe from an H SC Vial was approved following demonstration of non-inferiority compared with intravenous trastuzumab (Herceptin®) F Hoffmann-La Roche Ltd based on pathological complete response and severe toxic-trough in the HERA study.

• The international, open-label, randomised, crossover PrefHer study (NCT01401166) revealed overwhelming patient preferences for H SC, given by single-use injection device (SID) or hand-held syringe from an H IV Vial on an H IV adjuvant therapy for HER2-positive early breast cancer.

— Preferences were due to ‘time saving’ and ‘less pain/discomfort/side effects,’ driving 2 out of 5 patients to H SC (54.7%) and 1 out of 5 patients to H IV (19.3%) (Table 1).

3 (0.6) 13 (0.7) 5.0 85 (19.3)
11 (2.3) 33 (6.8) 0 9 (1.9) 0 0 4.0 0 12 (2.5) 1 (0.2) 2.0 17 (3.9) 5 (1.0)

Differences in AE rates between H SC and H IV periods during crossover administration of H SC trastuzumab. H SC trastuzumab was administered as 1 mg/kg every 3 weeks x 4 cycles.

Methods

• Patients with histologically confirmed primary invasive breast adenocarcinoma with no evidence of residual, locally recurrent or metastatic disease after completion of surgery and neoadjuvant or adjuvant chemotherapy or adjuvant chemotherapy (with or without H) were randomised to receive either one cycle of H IV every 3 weeks (cycle 1) then four cycles of H SC on the reverse sequence (Figure 1).

1. Overall study design?

• During the crossover period, patients in Cohort 1 received H IV at 1 mg/kg every 3 weeks x 4 cycles, followed by H SC at 6 mg/kg every 3 weeks x 4 cycles. Following the crossover, i.e., the H IV continuation period, it was planned for patients in Cohort 1 to receive H IV (unless participating in SID self-administration), and for patients in Cohort 2 to receive H SC (1 mg kg/ wk hand-held syringe from an H IV Vial).

• Patients could have had either H SC (on-cycle) or could have already started treatment for early breast cancer prior to study entry (off-cycle), but needed to receive at least eight more cycles to complete 1 year (18 cycles) of H treatment in the adjuvant setting.

• The primary endpoint, patient preference for H SC or H IV, has been reported previously, but needed to receive at least eight more cycles to complete 1 year (18 cycles) of H treatment in the adjuvant setting.

• The primary endpoint, patient preference for H SC or H IV, has been reported elsewhere as described in the Background section, along with safety data from the crossover period.16 We report here a secondary endpoint, 3-year event-free survival (EFS), defined as time from randomisation to local, regional or distant disease recurrence, contralateral breast cancer or death from any cause, as well as safety across both groups of the study in the crossover and H continuation periods.

• EFS was assessed using the Kaplan–Meier approach and is shown for the evaluable IPT population of both cohorts, and overall (Figure 2).

Event-free survival

• After median follow-up of 36.1 months, 3-year EFS across both groups in the evaluable IPT population was 91.4% overall (Figure 2A), 89.4% in Cohort 1 (Figure 2B) and 91.1% in Cohort 2 (Figure 2C).

Results

• The most common AEs across both cohorts (all grades) were arthralgia (13.5% of patients), and headache (10.4%), with no other AEs occurring in > 10% of patients.

— Differences in AEs between H SC and H IV periods during crossover administration of H SC trastuzumab. H SC trastuzumab was administered as 1 mg/kg every 3 weeks x 4 cycles.

Baseline characteristics were balanced between treatment groups, and the Hazard Ratio (HR) was 0.79 (95% CI 0.52–1.20), with a p value of 0.250.

• Overall, the 3-year EFS rates observed in both cohorts of the PrefHer study were consistent with those observed in previous clinical trials of H therapy for patients with HER2-positive early breast cancer.

— No new safety signals were identified with longer follow-up, with only one cycle SID, SAE reported in 478 patients.

— The overall safety profile during adjuvant treatment was acceptable.

— Cardiac events from both cohorts of PrefHer, combined with data from the HERA trial, demonstrate that H SC is a well-tolerated option for patients and healthcare professionals regardless of H SC delivery method (SID or hand-held syringe from an H IV Vial).

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Table 1. Summary of safety by treatment period (both cohorts combined)

Table 2. Cardiac AEs

Cardiac events

• Cardiac AEs are summarised in Table 2. Most Grade 1, or 2, or only one serious cardiac AE was reported (left ventricular dysfunction, above).

— Only four patients had Grade 3 cardiac AEs (three left ventricular dysfunction, one congestive heart failure).

— Congestive heart failure was reported in five patients (1.9%, none serious).

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References


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