

## LBA11

### Individual patient data meta-analysis of 5 non-inferiority RCTs of reduced duration single agent adjuvant trastuzumab in the treatment of HER2 positive early breast cancer

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## Background

We planned an individual patient data (IPD) meta-analysis of non-inferiority (NI) RCTs to determine if a duration of less than the standard of 12 months (m) of adjuvant trastuzumab is non-inferior for treatment outcomes in HER-2 positive early breast cancer patients.

## Methods

A systematic review identified five NI RCTs, and trial groups agreed a meta-analysis collaboration. PERSEPHONE, PHARE and HORG compared 12m v 6m; SOLD and Short-HER compared 12m v 9weeks[w]. Primary outcome was invasive disease-free survival (IDFS). Secondary outcomes were distant relapse-free survival (DRFS); overall survival (OS) and breast cancer specific survival (BCSS). Analysis was intention-to-treat (ITT). Random effects modelling evaluated prognostic effects of patient and tumour characteristics, treatment and trial. Heterogeneity between studies was assessed using the Cochran's Q statistic. For the comparison of 12m v less (n≈11,500 pts), a 1-sided 2.5% significance was used. For the analyses of 12m v 6m (n≈8,000 pts) and 12m v 9w (n≈3,500 pts), 1-sided 5% significance was utilised.

## Results

To date, IPD has been obtained from 4 trials and published data has been used from PHARE. For ITT analysis of the primary outcome of IDFS, non-inferiority limits for absolute 2% margins were calculated as 1.19 for all 5 trials, 1.20 for 3 trials comparing 12m v 6m and 1.25 for 2 trials comparing 12m v 9w. For 12m v less (all 5 trials combined), 5-year IDFS rates were 88.46% and 86.87% respectively. The adjusted HR for treatment was 1.14 (95% credibility interval (CI) 0.88-1.47), non-inferiority p=0.37. For 12m v 6m, 5-year IDFS rates were 89.26% and 88.56% respectively. The adjusted HR for treatment was 1.07 (90% CI 0.98-1.17), non-inferiority p=0.02. For 12m v 9w, 5-year IDFS rates were 91.40% and 89.22% respectively. The adjusted HR for treatment was 1.27 (90% CI 1.07-1.49), non-inferiority p=0.56. Cochran's Q is 5.5 for all 5 trials, 0.91 for the 3 trials comparing 12m v 6m and 1.1 for the 2 trials comparing 12m v 9w.

## Conclusions

Six months trastuzumab is non-inferior to 12months, although nine weeks is not.

## Legal entity responsible for the study

The authors.

## Funding

## Disclosure

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