HARMONIA SOLTI-2101 / AFT-58: A head-to-head phase III study comparing ribociclib (RIB) and palbociclib (PAL) in patients (pts) with hormone receptor-positive/HER2-negative/HER2-Enriched (HR+/HER2−/ HER2E) advanced breast cancer (ABC)

HARMONIA (NCT02570799) is an international, multicenter, randomized, open-label, phase III study, using prospective pre-screening based on tumor biology in pts with HR+/HER2−/ ABC. Pts will undergo a molecular pre-screening to determine intrinsic subtype by Prosigna IHC test.

**Methods and design**

**Primary Objective**

- To compare PFS of RIB+ET vs PAL+ET in pts with HR+/HER2−/ ABC.

**Secondary Objectives**

1. **Overall survival**
2. **Overall response and clinical benefit as defined by RECIST 1.1**
3. **Time to response and duration of response per RECIST 1.1**
4. **Safety and tolerability in terms of occurrence frequency of AEs, laboratory abnormalities, discontinuation rates, dose reductions/interruptions**
5. **Time to 10% deterioration in the global health status/QOL scale score of the EORTC QLQ-C30**
6. **Change from baseline in the global health status/QOL scale score of the EORTC QLQ-C30**
7. **Change from baseline in the fatigue scale score of the FACT-G scale of FACT Fatigue Scale (Version 4)**

**Endpoints**

- **Progression-free survival using RECIST 1.1 criteria, as assessed by local radiologists/investigators**

**Key eligibility criteria**

- **HER2-E cohort with**
  - HR IHC < 100%
  - ER IHC < 100%
  - HER2 IHC 1-3+
  - Basal-like classification
  - Luminal B sub-type

**Figure 1.** DSMB subtypes

**Figure 2.** Subtypes switching under normal disease progression**

**Figure 3.** Study Design

**Statistical analysis**

To evaluate the primary endpoint progression-free survival (PFS) a total of 456 patients will be randomized into the HER2-E cohort. Using a 1:1 randomization ratio, the sample size provides at least 80% power to demonstrate statistical significance of treatment differences on PFS under the study hypothesis. To assess the hypothesis testing a one-sided stratified log-rank test will be used. The endpoint will be conducted at an overall 5% level of significance. One interim analysis and one final analysis are planned for PFS. The trial will be stopped for efficacy if the key assumption according to Lan-Dawson with an O’Brien-Fleming-like boundaries has been used to control the overall type I error.

**Current status**

- HARMONIA has started enrollment in March 2022.
- As of 29th of August 2022, 74 pts have been treated and 8 pts enrolled.
- A total of 80 sites will participate globally, 40 sites in Spain and 5 sites in Portugal within SOLTI network, and 35 sites in USA within AFT network.
- Interim analysis is estimated to be conducted in Q2 2025 and the final analysis in Q2 2026.

**References**

7. IHC scanning

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**Scan to see HARMONIA study explainer video**

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