

*Riunione Annuale*

# **GIM** GRUPPO ITALIANO MAMMELLA

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**26-27 SETTEMBRE 2025 BERGAMO**

**HOTEL EXCELSIOR SAN MARCO**

PIAZZA DELLA REPUBBLICA, 6

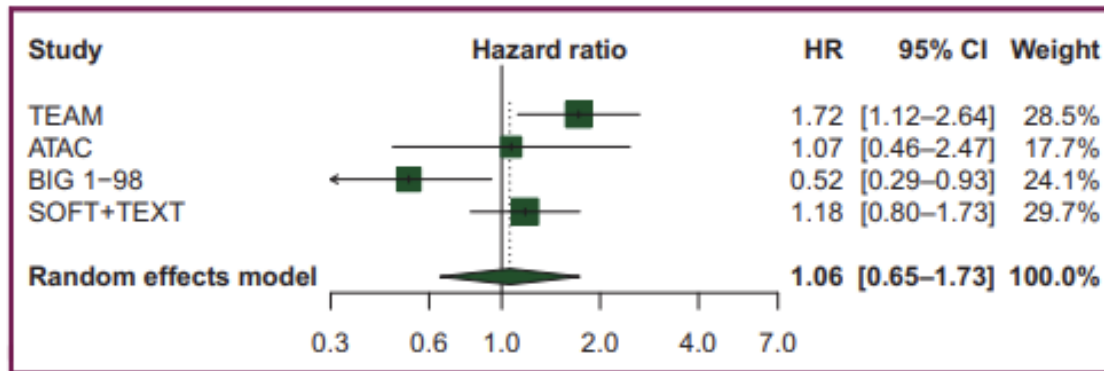
# TAHER

## Optimal Adjuvant Endocrine Therapy in premenopausal patients with HR+/HER2+ Early Breast Cancer: A Randomized Phase III Trial of Tamoxifen versus Aromatase Inhibitors

**Principal Investigator: Michelino De Laurentiis, S.C. Oncologia Clinica Sperimentale di Senologia, Istituto Nazionale Tumori IRCCS “Fondazione G. Pascale”, Naples, Italy**

### Background and rationale

- HER2+ BC: 15–20% of all breast cancers; approximately 50% are HR+/HER2+.
- Unique biology driven by ER–HER2 crosstalk.
- AIs usually preferred in HR+ disease, but benefit in HR+/HER2+ is uncertain.
- Need to define the optimal endocrine therapy to improve survival, adherence, and QoL



**Figure 3. Odds ratio for disease-free survival of tamoxifen versus aromatase inhibitors in all included randomized controlled trials excluding ALTO trial (the size of the squares is proportional to the weight of each study).**

AI, aromatase inhibitors; CI, confidence intervals; HR, hazard ratio; OR, odds ratio.

Peleg Hasson S, Brezis MR, Shachar E, Shachar SS, Wolf I, Sonnenblick A. Adjuvant endocrine therapy in HER2-positive breast cancer patients: systematic review and meta-analysis. *ESMO Open*. 2021 Apr;6(2):100088. doi: 10.1016/j.esmoop.2021.100088. Epub 2021 Mar 16. Erratum in: *ESMO Open*. 2021 Jun;6(3):100158. doi: 10.1016/j.esmoop.2021.100158. PMID: 33735801; PMCID: PMC7988286

# Project Plan

## Stratification factors:

- Nodal status (positive vs negative)
- Type/duration of HER2-targeted therapy (trastuzumab ± pertuzumab; 1 vs >1 year)

## Key eligibility criteria:

- ✓ Premenopausal patients aged  $\geq 18$  years
- ✓ Histologically confirmed HR+ (ER and/or PR  $\geq 1\%$ ) and HER2+ (IHC 3+ or FISH amplified) early-stage breast cancer
- ✓ Curative-intent surgery completed (BCS or mastectomy)

Random. 1:1

Sample size 1898

Tamoxifen + OFS

Aromatase inhibitor + OFS

## Recruitment period:

36 months

## Additional follow-up:

60 months

- Clinical visits every 6 months for 5 years, then annually up to 8 years
- Assessments: physical exam, labs, imaging per guidelines, toxicity (CTCAE v5.0), QoL (EORTC QLQ-C30, QLQ-BR23)

## PRIMARY OBJECTIVE

- ✓ To evaluate whether AI + OFS provides superior 5-year invasive disease-free survival (iDFS) compared with tamoxifen + OFS in premenopausal patients with HR+/HER2+ early breast cancer.

## SECONDARY OBJECTIVES

- ✓ Overall survival (OS), Distant DFS (DDFS), Safety, Adherence, Quality of life
- ✓ Subgroup analyses by menopausal status, nodal involvement, and type/duration of HER2-targeted therapy.

## Statistical considerations

- **Sample size:** A total of **1,898 patients**, with **949 in each group**.
- **Statistical power:** The study has **80% power** to detect a meaningful difference between groups.
- **Expected effect:** We expect treatment with AI to reduce the risk of disease recurrence by **28%** compared to tamoxifene  
This corresponds to a **hazard ratio (HR) of 0.72**.
- **Absolute benefit:** This translates into an increase in 5-year IDFS from **86% in the tamoxifene group to 90% in the AI group** (a 4% absolute improvement).
- **Significance level (alpha):** The chance of a false positive is set at **5% (two-sided test)**.
- **Events needed:** To confirm the expected treatment effect, we need to observe **247 IDFS events** (recurrences, metastases, or deaths).
- **Enrollment & follow-up:** Patients will be enrolled over **36 months**, Followed for up to **60 months** after enrollment. Total study duration: **~96 months (8 years)**
- **Interim analysis:**  
One **interim analysis** is planned when **~148 events** have occurred (about **5 years** in).
- **Final analysis:**  
Will take place once **247 events** are reached or at the **end of the study**.

Grazie per l'attenzione

