197P: Clinical outcomes in patients with stage cT1/T2cN0 HER2[+] breast cancer treated with neoadjuvant trastuzumab and pertuzumab: an exploratory analysis from the PHERGain trial

2025 ESMO BREAST CANCER Annual Congress
MUNICH GERMANY
14-17 MAY 2025

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Background

- **The phase II PHERGain trial** validated the feasibility of a ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (PET)-guided, pathological complete response (pCR)-adapted strategy in patients with HER2[+] early-stage breast cancer (EBC) [1,2].
- **Dual primary endpoints achieved:**
  - 37.9% pCR rate in PET-responders (RX) from adaptive group B [1].
  - 94.8% 3-year invasive disease-free survival (3y-iDFS) rate for the entire adaptive group B [2].
- **Here, we retrospectively evaluated clinical outcomes in patients with cT1/T2cN0 tumors from the adaptive group B.**

Patients and Methods

Pathological evaluation of hormone receptor and HER2 status

- At baseline, estrogen receptor and progesterone receptor were locally assessed, whereas HER2 status was centrally evaluated according to the 2018 ASCO/CAP criteria.

Tumor size evaluation

- At baseline, PET target lesions were defined —per central assessment— as those lesions with a $SUV_{max} \geq 1.5 \times SUV_{mean}$ liver + 2 standard deviation and with a longest diameter ≥ 1.5 cm (MRI or ultrasound).

pCR definition and assessment

- pCR was defined as no residual invasive cancer in the breast and axillary nodes (ypT0/is ypN0), as determined by a local pathologist in accordance with the Breast International Group-North American Breast Cancer Group criteria [3].

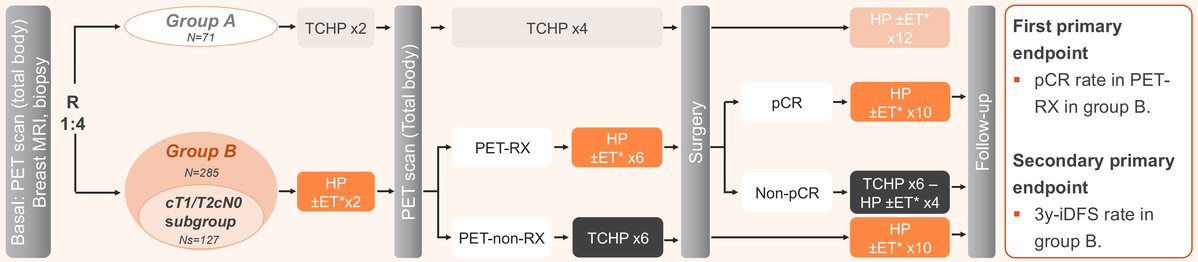
3y-iDFS definition

- 3-year iDFS was the percentage of patients alive without invasive recurrence, second non-breast primary cancer, or death from any cause three years post-surgery.

Study design

Figure 1. PHERGain scheme

- The analysis was performed in a cohort of 127 patients from PHERGain's adaptive group B with cT1/T2cN0 tumors.



First primary endpoint

- pCR rate in PET-RX in group B.

Secondary primary endpoint

- 3y-iDFS rate in group B.

KEY ELIGIBILITY CRITERIA

- Centrally confirmed HER2[+] stage I-IIIA EBC
- Tumor diameter ≥1.5 cm by MRI or ultrasound
- ≥1 breast PET-evaluable lesion

STRATIFICATION FACTOR

- Hormone receptor status

*Group A = control group. Group B = adaptive group. PET-RX were patients with maximum standard uptake value reduction of 40% or greater after cycle 2. *All hormonal receptor-positive patients received ET concomitantly with HP (except on chemotherapy).*

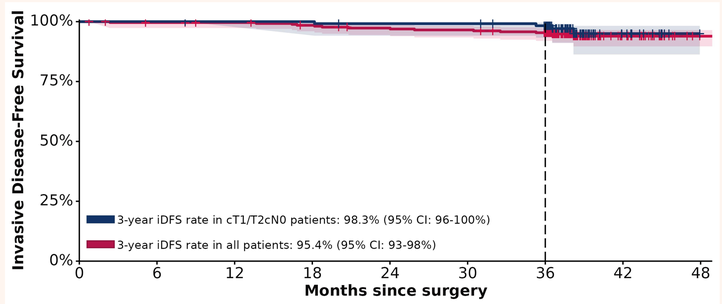
Results

- The adaptive group B included 285 patients, of whom **127 (44.6%) had cT1/T2cN0 tumors** (median tumor size: 26 mm, interquartile range: 20-35).
- A total of 105 (82.7%) patients were PET-RX and received exclusively neoadjuvant treatment with HP ± ET.
- Table 1 presents a summary of the **pCR data**.
- pCR rate was higher in patients with cT1/T2cN0 tumors who had HER2 IHC 3+ or hormone receptor negative status.
- The **3y-iDFS rate in patients with cT1/T2cN0 tumors** from adaptive group B (N=127) **was 98.3%** (95%CI 96%-100%), with only two (1.7%) recurrences: one locoregional and one distant (Figure 2).

Table 1. pCR data

% (n/N)	Adaptive group B	
	Entire group	cT1/T2cN0 subgroup
Overall	35.4 (101/285)	40.1 (51/127)
PET-RX	37.9 (86/227)	42.9 (45/105)
HER2 Expression		
2+ & ISH amplified	25.6 (11/43)	28.6 (6/21)
3+	40.8 (75/184)	46.4 (39/84)
HR Status		
Positive	35.0 (55/157)	34.2 (26/76)
Negative	44.3 (31/70)	65.5 (19/29)

Figure 2. 3y-iDFS rate



Conclusions

- The 3y-iDFS rate is exceptional in patients with cT1/T2cN0 tumors following a PET-guided, pCR-adapted strategy, positioning this subgroup as the most likely to benefit from this approach.
- Among patients with cT1/T2cN0 tumors, the rate of complete chemotherapy omission was 5% higher compared to the overall adaptive group B.
- Ongoing extended follow-up and upcoming PHERGain-2 trial results —which focuses on cT1/T2 (≤25 mm)cN0 HER2 IHC 3+ tumors— will further validate this chemotherapy-free strategy and help refine patient selection to maximize treatment benefit.

Acknowledgements

The PHERGain team is extremely grateful to all patients and their families. We warmly acknowledge all the trial teams of the participating sites, the trial unit staff at MEDSIR (study sponsor), and Hoffmann-La Roche (trial funder).

References

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Conflicts of interest of the presenting author:
Consulting/Advisor: Lilly, Roche, Pfizer, Novartis; Speaker's bureaus: Lilly, Astrazeneca, MSD, Pfizer, Novartis; Research support: Roche, Agendia, Lilly, Pfizer, Novartis, MSD, Gilead, Daiichi Sankyo; Stock: MAJ3 Capital & Initia-Research; Travel, accomodations, expenses: Roche, Pfizer, Astrazeneca, Steamline therapeutics, MSD; Patents: HER2 as a predictor of response to dual HER2 blockade in the absence of cytotoxic therapy. Aleix Prat, Antonio Llombart, Javier Cortés. US 2019/0338368 A1. *LICENSED*

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3y-iDFS: 3-year invasive disease-free survival; **CI**: confidence interval; **EBC:** early breast cancer; **ET:** endocrine therapy (letrozole post-menopausal/tamoxifen pre-menopausal); **HER2:** human epidermal growth factor receptor 2; **HP:** trastuzumab (subcutaneous) and pertuzumab (intravenous); **HR:** hormone receptor; **ISH:** *in situ* hybridization; **MRI:** magnetic resonance imaging; **n(%):** number of patients (percentage based on N); **N:** Number of patients in the population; **Ns:** number of patients in the cT1/T2cN0 subgroup; **pCR**: pathological complete response (ypT0/isN0); **PET:** ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography; **PET-RX:** PET-responders; **PET-non-RX:** PET non-responders; **TCHP:** docetaxel, carboplatin, trastuzumab and pertuzumab.