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PROOFS-Registry – Pre-/perimenopausal patients with HR+/HER2- early breast cancer with intermediate to high clinical and low genomic risk, optimally treated by endocrine treatment plus ovarian function (OFS) or chemotherapy followed by endocrine treatment

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WSG Westdeutsche Studiengruppe West German Study Group

Background & Methods

There is uncertainty about the optimal adjuvant treatment of pre-/perimenopausal women with hormone receptor-positive (HR+), HER2-negative early breast cancer (BC) with 0 to 3 positive lymph nodes in case of intermediate to high clinical and low genomic risk for recurrence. As the observed chemotherapy (CT) benefit might be attributed to CT-induced ovarian function suppression (OFS), endocrine therapy (ET) +/- ovarian function suppression (OFS) alone (without CT) might be sufficient for a subset of patients with endocrine sensitive disease. The **West German Study Group (WSG)** initiated the **PROOFS-Registry** to create a real-world database and to obtain clarification on how to optimally treat these patients.

Trial Synopsis

Indication: Pre-/perimenopausal, HR+/HER2- early breast cancer

Trial design: Open, prospective, multi-center, observational, non-interventional registry. Collection of data from clinical routine, no study specific measures, no investigational medicinal products, no extra visits.

Aim: Long-term follow-up of pre-/perimenopausal patients with an intermediate to high clinical and a low genomic risk for recurrence, regarding the 5-year distant recurrence-free interval (dRFI) under adjuvant treatment with ET (+/-OFS) alone (without CT)

Nr. of sites: Up to 100 sites in Germany
(24APR2023: 16 open for recruitment)

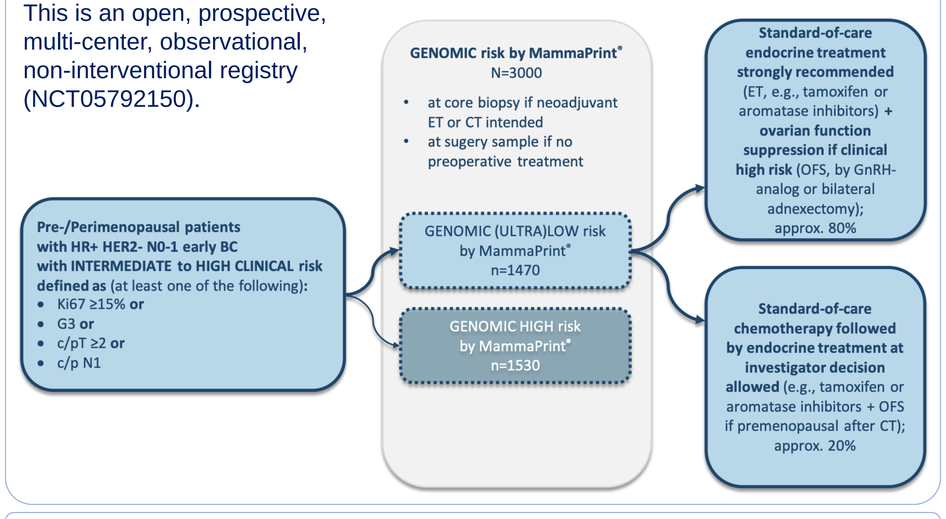
Nr. of patients: Planned: 3000 screened,
1470 included;
approximately 80% ET +/- OFS,
approximately 20% CT followed by ET +/- OFS
(24APR2023: 5 screened, 1 enrolled)

Recruitment: Q1 2023 - Q1 2025 (2.5 years)

Trial duration: 2035
(max. 10 years after last patient in)

Trial Design

This is an open, prospective, multi-center, observational, non-interventional registry (NCT05792150).



Eligibility Criteria

Pre-/perimenopausal women with HR+/HER2- early BC, with an **intermediate to high clinical risk** of recurrence and **low genomic risk** measured by MammaPrint® within a time frame of 3 months after primary diagnosis, with a planned or started treatment according to standard-of-care. Up to 30% of the study population may have nodal positive disease.

The PROOFS-Registry is aiming at the long-term follow-up of pre-/perimenopausal women with luminal early breast cancer with an intermediate to high clinical risk for recurrence and a low genomic risk measured by MammaPrint®. The registry seeks to give insides in the real-world use of ovarian function suppression (OFS) and to confirm an excellent outcome in patients treated by endocrine treatment (ET) +/- OFS alone (without chemotherapy). In addition it will capture the quality of life.

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Disclosure

No conflicts of interest to declare.

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Statistical Methods

There is one primary endpoint in this study (see below).
Cox regression models, Kaplan-Meier method and log-rank tests will be applied for survival analysis. The null hypothesis H(0) is: 5-year dRFI <92%.

Linear mixed models will be utilized to quantitatively describe the course of quality of life scores as well as therapy adherence, and to conduct group comparisons.

Objectives

The aim of the PROOFS-Registry is to confirm an excellent outcome in pre-/perimenopausal women with HR+/HER2- early BC with an intermediate to high clinical risk of recurrence and low genomic risk treated by endocrine treatment (+/- OFS) alone (without CT). The null hypothesis H(0) is: 5-year dRFI <92%.

Primary objective & endpoint:
To demonstrate

- **5-year distant recurrence-free interval** (dRFI, according to STEEP criteria) in all patients treated by (intensified) endocrine therapy alone (and with ovarian suppression in cases of enhanced clinical risk according to current AGO-recommendations).

Secondary objectives & endpoints:
Assessment of

- **10-year dRFI**, according to STEEP criteria, in all patients treated by (intensified) endocrine therapy alone (with ovarian suppression in cases with higher clinical risk)
- 5- and 10-year dRFI, according to STEEP criteria, in all patients treated by chemotherapy followed by ET+/-OFS
- 5- and 10-year distant disease free survival (**dDFS**), overall survival (**OS**) and breast cancer free interval (**BCFI**) in all patients, according to treatment group
- **Quality of life** (QLQ BR23 and QLQ-C30) at baseline, and after 3 months, 6 months, 12 months, 18 months, 2 years, 3 years, 4 years and 5 years
- **Adherence** to ET and OFS
- **Molecular subtype** according to BluePrint® and concordance with pathological immune-histochemistry results
- **Endocrine response** measured by post-endocrine Ki-67 (≤10% and/or relative change vs. baseline) in patients treated by preoperative ET according to MammaPrint® result
- 5- and 10-year iDFS in node-negative patients with ultralow MammaPrint® treated by shorter duration of ET (2-3 years at investigator decision)

Translational analyses

Patients optionally donate tumor material of the primary diagnosis or, if applicable, material of a tumor relapse for future biomedical research projects.