200TiP

ELEANOR: a multi-national, prospective, non-interventional study (NIS) in patients with human epidermal growth factor receptor (HER2) positive, early breast cancer (eBC) observing real-life extended adjuvant treatment with neratinib and concurrent use of the eHealth solution CANKADO

Nadia Harbeck[1], Diana Lüftner[2], Urs Breitenstein[3], Christian Jackisch[4], Volkmar Müller[5], Marcus Schmidt[6], Marija Balic[7], Gabriel Rinnerthaler[8], Michael Schwitter[9], Khalil Zaman[10], Denise Wrobel[11], Dagmar Guth[12], Jürgen Terhaag[13], Matthias Zaiss[14], Timo Schinköthe[15], Rupert Bartsch[16]

[1] Breast Center, Dept. OB&GYN, LMU University Hospital, Munich, Germany; [2] University Hospital Charité, Berlin, Germany; [3] Divison of Oncology, Brust-Zentrum Zürich, Switzerland; [4] Department of Gynecology and Obstetrics, Klinikum Offenbach, Offenbach, Germany; [5] Department of Gynecology and Obstetrics, University Hospital Hamburg-Eppendorf, Hamburg, Germany; [6] Dept. Gynecology, University Hospital Mainz, Mainz, Germany; [7] Divison of Oncology, Department of Internal Medicine, Medical University Graz, Austria; [8] Department of Internal Medicine III with Haematology, Medical Oncology, Haemostaseology, Infectiology and Rheumatology, Oncologic Center, Salzburg Cancer Research Institute – Laboratory for Immunological and Molecular Cancer Research (SCRI-LIMCR), Paracelsus Medical University, Salzburg, Austria; [9] Kantonsspital Graubünden, Chur, Switzerland; [10] Breast Center, Lausanne University Hospital CHUV, Lausanne, Switzerland; [11] Sozialstiftung Bamberg Klinikum am Bruderwald, Bamberg, Germany; [12] Gyneco-oncological practice Dr. Guth, Plauen, Germany; [13] Rottal/Inn Clinic, Eggenfelden, Germany; [14] Oncology Practice, Freiburg, Germany; [15] CANKADO Service GmbH, Kirchheim, Germany; [16] Department of Medicine I, Division of Oncology, Medical University of Vienna, Vienna, Austria

BACKGROUND

- The aim of (post-)/(neo)adjuvant chemotherapy and HER2-targeted therapy in HER2+ eBC is to prevent locoregional recurrences and development of distant metastases.
- HER2+ eBC is a heterogeneous disease[1,2]. Despite significant improvements of long-term clinical outcomes[3-6], (late) recurrences are still frequently observed with longer follow-up: up to 30% of patients are at risk of disease recurrence after 10 years[4], with distant metastases being predominant (ca. 18% after 11 years[4]).
- The subgroup of HER2+/hormone receptor-positive (HR+) patients has a specific risk profile with a higher risk for late recurrences (>5 years after diagnosis)[7,8].
- Neratinib is an irreversible pan-HER tyrosine kinase inhibitor registered in Europe as extended adjuvant treatment for patients with HR+, HER2+ eBC who completed adjuvant trastuzumab-based therapy less than one year ago („EMA-/Swissmedic-label" population)[9].
- By switching the mode of action from extracellular monoclonal antibodies in the adjuvant setting to an intracellular TKI, extended adjuvant neratinib can further reduce recurrence risk: a significant 42% relative risk reduction was demonstrated for neratinib vs. placebo in the ExteNET study (EMA-/Swissmedic-label population; HR 0.58, 95% CI 0.41-0.82)[10].
- According to explorative (post-hoc) analyses from ExteNET, the effect might be even more pronounced in patients with non-pCR after neoadjuvant trastuzumab treatment and/or in patients with completion of neratinib therapy (i.e. ≥11 months of neratinib treatment).[10-12]
- Diarrhea, a HER-TKI class effect, was the most common grade 3 adverse event in the absence of primary diarrhea prophylaxis (EMA-/Swissmedic-label population, neratinib arm: 39% grade 3 diarrhea, median cumulative duration 5 days; placebo: 1%; no grade 4 events)[10]. Diarrhea can generally be managed through adequate prophylaxis and treatment management[13].

RATIONALE

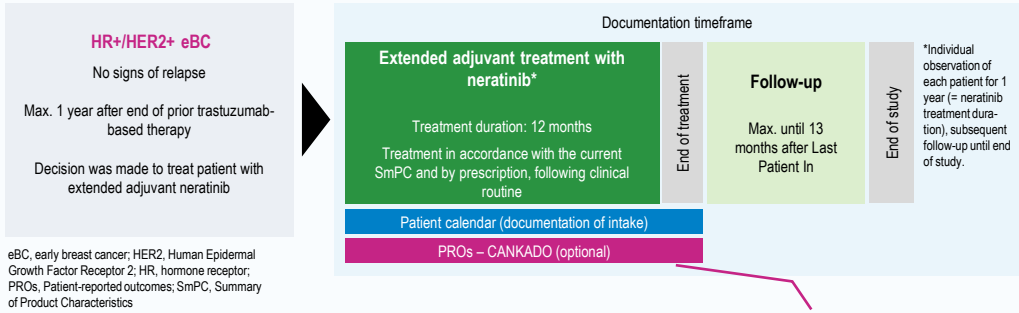
- So far, there is no data available on neratinib treatment of patients with HER2+ / HR+ eBC patients who completed adjuvant trastuzumab-based therapy less than one year ago, in the clinical routine setting.
- ExteNET patients were pre-treated with trastuzumab only. ELEANOR will include patients with different pre-treatments, representing modern treatment algorithms.
- Neratinib is an oral drug, providing the advantage of flexibility and patient autonomy, but also bearing the risk of non-adherence.
- ELEANOR will investigate patient adherence to neratinib, real-world use of neratinib in a modern therapy landscape and treatment management including neratinib dosing and concomitant medication.

REFERENCES

1. Vance GH et al. J Clin Oncol 2019;37(15_suppl):502; 3. Perez EA et al. J Clin Oncol 2014;32(33):3744-52; 4. Cameron D et al. Lancet 2017;389:1195-1205; 5. Piccart M et al. J Clin Oncol 2021;39:1448-1457; 6. Von Minckwitz G et al. N Engl J Med 2019;380(7):617-28; 7. Vaz-Luis I et al. Breast Cancer Res 2012;14(5):R129; 8. Strasser-Weippl K et al. Breast Cancer Res 2015;17(1):1-7; 9. Pierre Fabre Médicament. Neratinib (Nerlynx) Summary of Product Characteristics. May 2021. 10. Chan A et al. Clin Breast Cancer 2021;21(1):80–91; 11. Martin M et al. ESMO BC Virtual Meeting 2020, Abstract und Poster #83P; 12. Moy B et al. ASCO 2021, Abstract und Poster #540; 13. Barcenas CH et al. Ann Oncol 2020;9:1223-1230.

ePoster presented at: ESMO Congress, Sep 16-21 2021; Abstract #2367, Presentation Number 200TiP

Figure 1. STUDY DESIGN



eBC, early breast cancer; HER2, Human Epidermal Growth Factor Receptor 2; HR, hormone receptor; PROs, Patient-reported outcomes; SmPC, Summary of Product Characteristics

CANKADO

- Web- or app-based, multilingual online patient support system for patients with chronic diseases
- Developed to support patient/physician communication
- Registered as medical device in the EU
- Customized and adapted for ELEANOR, may be used optionally
- Automatic PRO-reports (questionnaires, health status, etc.) can be generated to facilitate visit preparation

One or more CANKADO modules can be used (optional):

QoL documentation*:
- EQ-5D-5L questionnaire
- Systemic Therapy-induced Diarrhea Assessment Tool (STIDAT)
- Patient's treatment satisfaction

Additional documentation may include:
- Digital patient diary
- Daily health status → triggered recommendations ("PRO-React", see **Figure 3**)

*If CANKADO is not used, PROs are evaluated using paper-based questionnaires

Figure 2. STATUS of PATIENT ENROLLMENT

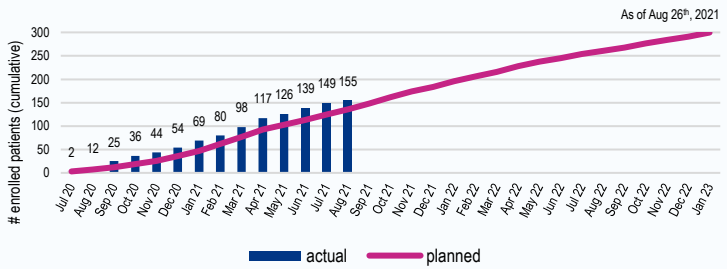
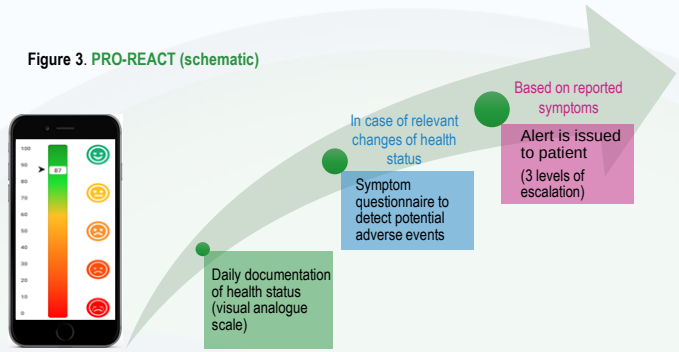


Figure 3. PRO-REACT (schematic)



PATIENT PROFILE

- Adult, female patients with early breast cancer stage I-III
- Hormone receptor positive and HER2-positive
- < 1 year after end of previous trastuzumab-based therapy
- Decision to treat patient with extended adjuvant neratinib has been made; neratinib treatment has not started yet
- Neratinib treatment is planned according to approval and Summary of Product Characteristics (SmPC), no contraindications according to SmPC present
- No signs of relapse
- No simultaneous participation in an interventional clinical trial

For full in- and exclusion criteria, please refer to the observational plan. Patient documentation may only start after written informed consent.

STUDY OBJECTIVES

Primary Objective

Patient treatment adherence: Rate of patients who take neratinib on at least 75% of the prescribed days, with the intake documented in a patient calendar

Secondary Objectives

- Patient and disease characteristics, including patients with different previous treatments
- Neratinib treatment: Dosages and dose modifications including reasons, concomitant medication
- Optional: PROs, quality of life, treatment satisfaction; optional use of CANKADO
- Safety and tolerability
- Disease recurrence

Table 1. SETTING AND MILESTONES

Study Size	
Planned total number of patients	300
Planned total number of active centers (Germany / Austria / Switzerland)	ca. 75 / 5-10 / 5-10
Milestones	
First Patient In actual	2nd July 2020
Last Patient In / End of Study planned	Q1 2023 / Q1 2024
Final Analysis planned (13 months after inclusion of last patient)	Q2 2024

Disclosure Statement: Nadia Harbeck reports personal fees from Agendia, Amgen, Astra Zeneca, BMS, Celgene, Daiichi-Sankyo, Genomic Health, Lilly, MSD, Novartis, Odonate, Pierre Fabre, Pfizer, Roche, Sandoz/Hexal, Seattle Genetics; stocks from WSG; institutional financial support in the context of clinical trials and non-financial leadership role in the AGO breast commission Germany.

This study is sponsored by Pierre Fabre Pharma GmbH (Freiburg, Germany) and Pierre Fabre Pharma AG (Allschwil, Switzerland) and its branch office Pierre Fabre Pharma Austria (Wels, Austria).