Study title	An observational study to describe the population of patients treated with extended adjuvant neratinib.
Disease 	Breast cancer
Treatment(s) observed 	Neratinib (Nerlynx®)
Participants 	Adult patients with HER2+ early breast cancer who have been treated in the Early Access Program (EAP) with extended adjuvant neratinib in Europe from August 01, 2017 until December 31, 2020.
Study dates 	Collection of data takes place from July 2022 to January 2023.
Study Locations 	Belgium, Croatia, France, Italy, and Spain.
We do research to improve patient care. By participating in an observational study, one helps to answer important scientific questions for the benefit of all.	

This document is a summary of study results and conclusions written for public and people who took part in the study.

This summary was finalized on 28 August 2024. The information in this summary does not include additional information available after this date.

For people who took part in the study, Pierre Fabre Pharmaceutical group would like to say THANK YOU

We hope this document helps you understand and feel proud of your key role in medical research. If you have questions about the results, please speak with the doctor or staff at your study site.

To learn about the study and its conduct

- What was the purpose of the study?
- What were the objectives and how were they evaluated?
- How was the study carried out?

To get a summary of study results:

- What were the results of the study?

What was the purpose of the study?	HER2+ breast cancer is a subtype of breast cancer which represents approximately 15% to 25% of breast cancer worldwide. In patients with early-stage HER2+ breast cancer, a pivotal clinical study demonstrated that the use neratinib (Nerlynx®), following an adjuvant trastuzumab based therapy, improves clinical outcomes of patients. In this context, the purpose of this observational retrospective study named "NEAR" is to describe the population of patients in Europe who were treated with extended adjuvant neratinib after having received an adjuvant trastuzumab based therapy*. *Trastuzumab based therapy = treatment with trastuzumab combined with chemotherapy, with or without pertuzumab, or treatment with trastuzumab emtansine and being part of the reference treatment for adjuvant (= post-surgery) therapy of HER2+ breast cancer.
What were the objectives of the study and how are they evaluated?	The primary objective of the study was to describe demographic and clinical characteristics of patients with HER2+ breast cancer treated with neratinib by collecting information such as age, gender, history of disease, … The secondary objectives of NEAR were: • To describe neratinib treatment patterns (e.g., dose, treatment duration, discontinuation …). • To describe breast cancer treatment history before neratinib initiation. • To describe the side effects in patients with breast cancer using neratinib.
How was the study carried out ?	Patients were retrospectively enrolled from 23 active participating sites across 5 European countries (France, Belgium, Italy, Spain and Croatia). The study period was from 01 August 2017 until 31 December 2020, with a follow-up of the patients until 05 July 2022 (*i.e.* the date of the first eligible patient in the retrospective study). The study data collection period was initiated on 05 July 2022 and was completed on 30 January 2023 (last patient enrolled in the retrospective study).

	The present study observation period was defined as the period during all relevant data for each patient were collected (from baseline [*i.e.* before neratinib initiation] till study entry date [*i.e.* 05 July 2022]). As this study was retrospective, the decision to prescribe neratinib was taken prior to and independent of the proposal to select a patient for this study.

❖ Demographic and clinical characteristics of the patients at neratinib treatment initiation

This study enrolled 111 patients. Among them 108 patients were analysed. These patients had HER2+ early-stage breast cancer who were treated with neratinib as extended adjuvant therapy.

In the results presented hereafter the percentages are calculated on the total of 108 patients, unless otherwise specified.

The median age was 48 years, and all patients except one were female. Female were premenopausal (37.4%) or perimenopausal (4.7%), and the others were postmenopausal, or had amenorrhea for other reasons, or the information was unavailable.

At primary breast cancer diagnosis, the median age of patients was 46.0 years. Clinical American Joint Committee on Cancer (AJCC) stage at primary breast cancer diagnosis was available for 90.7% of the patients. Among these patients, 62.2% were diagnosed at stage IIB to IIIC.

Most patients (84.3%) were estrogen receptor positive and/or progesterone receptor positive (68.5%).

Most of the patients (90.4%) had a good performance status: they were fully active, able to carry on all pre-disease performance without restriction.

❖ Neratinib treatment patterns

Among 108 patients, the median time from breast cancer diagnosis to neratinib initiation was 20.4 months, and the median time from completion of adjuvant trastuzumab-based therapy to neratinib initiation was 4.6 months.

The initial daily neratinib dose was 240 mg for 87.0% of patients.
The median duration of neratinib treatment was 12.3 months.

About one third of the patients had neratinib treatment modifications, mostly due to physician's decision and side effects.

A total of 22.2% of the patients had neratinib temporary treatment interruption, mostly due to side effects.

As of 05 July 2022, 97.2% of the patients discontinued the treatment, and 2.8% of the patients were lost to follow-up. Main reasons for discontinuation were the completion of the treatment period (73.3%) and the occurrence of side effects (17.1%).

❖ Breast cancer treatment history before neratinib initiation

Neoadjuvant therapy

Among patients, 58.3% (63/108 patients) received neoadjuvant therapy with a median duration of 4.9 months, and 25.4% of these patients had a complete response with the treatment.

Among the 63 patients who received neoadjuvant therapy, most common neoadjuvant therapy combinations received were: chemotherapy + trastuzumab + pertuzumab (+/- endocrine therapy) (57.1% out of 63 patients), followed by chemotherapy + trastuzumab (+/- endocrine therapy) (31.7% out of 63 patients).

Most patients who received neoadjuvant therapy were treated with anti-HER2 therapy (90.5%, *i.e.* 57 patients). Anti-HER2 therapy was trastuzumab as a monotherapy (35.1% of these patients), and trastuzumab in combination with pertuzumab for 64.9%.
The median duration of neoadjuvant anti-HER2 therapy was 3.5 months. Almost all patients (98.2%) who received neoadjuvant therapy completed this treatment as initially planned.

Adjuvant therapy

All patients received after their surgery an adjuvant therapy. Chemotherapy + trastuzumab (+/-endocrine) were commonly received (34.3%). Most of the patients received endocrine therapy (65.7%), mostly represented by tamoxifen (47.9% = 37/71 patients).
Most of the patients (90.7%) received adjuvant (post neoadjuvant or adjuvant only) anti-HER2 therapy with a median duration of 10.5 months.

Overall, trastuzumab as a monotherapy was the main adjuvant anti-HER2 treatment received (87.8% of the patients) and 8.2% of patients received trastuzumab in combination with pertuzumab.
Regarding previous setting therapy, 41.7% of the patients received adjuvant treatment only and 58.3% received neoadjuvant as well as post neoadjuvant treatment.

❖ Side effects reported during the study

Among the 108 patients, relevant side effects (66.7%) included the following:

- Any side effect of interest (63.0%),
- Any serious side effect (11.1%),
- Side effects leading to treatment discontinuation (permanently and temporarily) (48.6%),
- Side effects leading to treatment dose decreased (22.2%).

The most commonly side effect of interest reported was diarrhoea (58.3%), followed by other Gastrointestinal disorders (29.6%). Among Gastrointestinal disorders, most frequently reported side effects were nausea (16.7%), abdominal pain (9.3%), and vomiting (7.4%).
Other side effects were asthenia (5.6%), decreased appetite (2.8%), and gastroenteritis (1.9%).
Most of the events were non-severe, and 9.3% of patients had Gastrointestinal disorders side effects considered as severe, mostly diarrhoea: 8.3%.
Diarrhoea was considered as related to neratinib treatment for most of the patients (96.8).
Diarrhoea led to neratinib treatment discontinuation (permanently or temporarily) in about one third of the patients, and permanent discontinuation in 10.5% of the patients.
Most of the patients recovered from diarrhoea (76.2%).

Prophylactic treatment for diarrhoea was received by about forty percent of the patients. In these patients, diarrhoea led to a lower proportion of severe diarrhoea, of neratinib treatment discontinuation (permanently and temporarily) compared to patients who did not receive it.

Of the 108 patients, 3 patients died, 2 were due to the breast cancer and one from an unknow cause.

Glossary	
Adjuvant	A treatment whose objective it is to prevent or stop the spread of cancer to other parts of the body. Often used after surgical removal of the primary lesion. These can include chemotherapy, immunotherapy, targeted therapy, radiation, and vaccine therapy. An Extended adjuvant therapy is provided following another adjuvant. A Neo-adjuvant therapy is provided before primary treatment and before surgery.
Early Access Program (EAP)	Program that gives access to investigational drugs outside of the clinical trial space and before the commercial launch of the drug, to patients with life-threatening diseases having no treatment options available. EAP offer ethical, compliant and controlled mechanisms.
HER2+ breast cancer	Breast cancer that expresses a protein called human epidermal growth factor receptor 2 (HER2)
Median	The median separates equally the low values and the high values
Pivotal clinical study	Clinical study intended to demonstrate and confirm the safety and efficacy of a treatment.
Post-authorization safety study	Any study relating to an authorized medicinal product conducted with the aim of identifying, characterizing or quantifying a safety hazard, confirming the safety profile of the medicinal product, or of measuring the effectiveness of risk management measures.
Relevant side effects	Relevant side effects are defined as any serious side effects (meaning: life-threatening, needs hospital care, or causes lasting problems) or a side effect leading to dose adaptation or treatment discontinuation, or side effects of interest.
Retrospective study	Study in which participants with known outcomes are assessed based on data collected before the study.
Side effects	Side effects are unwanted medical events (such as headache) that happen during the study and that are related or possibly related to study treatment.
Side effects of interest	The side effects were defined in the study protocol as follows: • Diarrhoea, • Gastrointestinal disorders (nausea, vomiting, abdominal pain, constipation), • Hepatic disorders, • Cardiac disorders, • Pulmonary disorders, • Pancreatitis: which is an inflammation of the pancreas • Reproductive and developmental disorders