

# OUTCOMES OF THE SPANISH COHORT OF EARLY ACCESS TO PERTUZUMAB AND TRASTUZUMAB EMTANSINE (KNOWHER STUDY)

**First published:** 30/01/2017

**Last updated:** 03/09/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS17462

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### Study ID

17463

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### DARWIN EU® study

No

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### Study countries

Spain

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### Study description

Currently, four targeted anti-HER2 agents are available in the EU for the treatment of advanced HER2+ breast cancer: trastuzumab (a humanized monoclonal antibody that targets subdomain IV of HER2), lapatinib (a HER1/HER2 dual tyrosine kinase inhibitor) and, more recently, pertuzumab (a humanized monoclonal antibody that targets domain II of HER2) and trastuzumab emtansine (an antibody-drug conjugate). Three of these agents have been approved in combination with chemotherapy: trastuzumab, lapatinib (also authorized in combination with trastuzumab), and pertuzumab.

Trastuzumab emtansine (T-DM1) is the only targeted agent currently approved as monotherapy. The addition of pertuzumab (Perjeta®) to trastuzumab plus chemotherapy (docetaxel) in first line treatment of HER2-positive metastatic breast cancer obtains a significant and clinically relevant increase in median PFS of 6.1 months. Both Kadcylla® and Perjeta® were available under those special access systems. In order to be eligible for CU of Trastuzumab emtansine (T-DM1) or Pertuzumab, patients had to meet the some prespecified criteria. After the EU approval, oncologists could prescribe the product to specific patients through the Early Access Program, provided that the local or regional responsible people accept payment. In order to evaluate the effectiveness and safety of Trastuzumab emtansine (T-DM1) and Pertuzumab in HER2-positive metastatic breast cancer under real-world disease conditions, is proposed a retrospective observational cohort non-comparative study / registry in Spain.

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## **Study status**

Finalised

## Research institutions and networks

### Institutions

## Puerta de Hierro-Majadahonda University Hospital

**First published:** 01/02/2024

**Last updated:** 01/02/2024

**Institution**

## Clinical Pharmacology Service, Puerta de Hierro-Majadahonda University Hospital (HUPHM)

Spain

**First published:** 26/12/2012

**Last updated:** 20/08/2024

**Institution**

**Educational Institution**

**Hospital/Clinic/Other health care facility**

## Clinical Pharmacology Department, Area del Medicament, Hospital Clínic de Barcelona

Spain

**First published:** 29/03/2010

**Last updated:** 24/08/2023

**Institution**

**Hospital/Clinic/Other health care facility**

**ENCePP partner**

## Contact details

### **Study institution contact**

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**Study contact**

[mariabelen.ruiz@salud.madrid.org](mailto:mariabelen.ruiz@salud.madrid.org)

### **Primary lead investigator**

Avendaño-Sola Cristina

**Primary lead investigator**

## Study timelines

### **Date when funding contract was signed**

Planned: 01/12/2016

Actual: 01/12/2016

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### **Study start date**

Planned: 03/04/2017

Actual: 30/01/2017

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### **Data analysis start date**

Planned: 03/07/2017

Actual: 30/01/2017

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### **Date of final study report**

Planned: 31/10/2017

Actual: 30/01/2017

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

Roche Farma, S.A

## Study protocol

[Study protocol ML29844 V2.0\\_25\\_11\\_2016.pdf](#) (769.45 KB)

## Regulatory

### **Was the study required by a regulatory body?**

No

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### **Is the study required by a Risk Management Plan (RMP)?**

Not applicable

## Other study registration identification numbers and links

ClinicalTrials.gov Identifier: NCT03025711

<https://clinicaltrials.gov/ct2/show/NCT03025711?term=NCT03025711&rank=1>

## Methodological aspects

### Study type

### Study type list

**Study topic:**

Disease /health condition  
Human medicinal product

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**Study type:**

Non-interventional study

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**Scope of the study:**

Drug utilisation  
Effectiveness study (incl. comparative)

**Data collection methods:**

Secondary use of data

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**Main study objective:**

To evaluate the effectiveness of Trastuzumab emtansine (T-DM1) and Pertuzumab in patients with HER2-positive MBC treated under compassionate use or early access program.

## Study Design

**Non-interventional study design**

Other

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**Non-interventional study design, other**

Case-series

## Study drug and medical condition

**Study drug International non-proprietary name (INN) or common name**

PERTUZUMAB

TRASTUZUMAB EMTANSINE

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**Medical condition to be studied**

HER2 positive breast cancer

## Population studied

**Short description of the study population**

Adult patients (age  $\geq$  18 years at enrolment) from the Spain with HER2-positive metastatic or locally recurrent unresectable breast cancer and who were treated with Trastuzumab emtansine (T-DM1) and Pertuzumab under compassionate use or early access program.

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**Age groups**

- Adults (18 to < 46 years)
  - Adults (46 to < 65 years)
  - Adults (65 to < 75 years)
  - Adults (75 to < 85 years)
  - Adults (85 years and over)
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**Special population of interest**

Other

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**Special population of interest, other**

Breast cancer patients

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**Estimated number of subjects**

## Study design details

### Outcomes

Overall survival. Defined as the time between the date of start of treatment and the date of death. For subjects without documentation of death, OS will be censored on the last date the subject was known to be alive, •Progression free survival. •Best overall response rate•Duration of response •Time to treatment failure •Time to Objective Response•Time to change treatment•Time to next treatment

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### Data analysis plan

The analysis of the present study will primarily make use of descriptive statistical methods (i.e. number, mean, median, standard deviation, rate, range, and IC95% for the estimated parameters).Where possible, and if allowed by the number of enrolled patients receiving different treatment regimens, a comparative analysis of the outcomes across various groups will also be performed.If applicable, it will be calculated IC 95% for the estimated parameters in relevant subgroups, analysis of variance (t test or F test) or non-parametric testing, such as Wilcoxon's rank-sum test or Kruskal-Wallis test, will be used to test group differences on the continuous variables. All test performed will be two-sided and carried out with a 5%  $\alpha$ -error rate without correction for multiplicity.Categorical variables will be summarized by numbers and proportions, and, where applicable, chi-squared testing will be used to test group differences.

## Data management

## ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

## Data sources

### Data sources (types)

[Drug registry](#)

## Use of a Common Data Model (CDM)

### CDM mapping

No

## Data quality specifications

### Check conformance

Unknown

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### Check completeness

Unknown

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### Check stability

Unknown

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### Check logical consistency

Unknown

## Data characterisation

## **Data characterisation conducted**

Unknown