Single-arm studies with external comparators for cancer drug development: a statistical methodology study to evaluate External Comparator Arm (ECA) study results versus Randomised Controlled Trial (RCT) results

First published: 14/10/2021

Last updated: 09/01/2025

Study Finalised

Administrative details

EU PAS number

EUPAS43709

Study ID

50418

DARWIN EU® study

No

Study countries

☐ Netherlands

Study description

Randomised controlled trials (RCTs) are generally considered by regulators to be the gold standard for establishing a causal relationship between medications and patient outcomes. Several new clinical trial designs have been introduced in oncology drug development based on clinical scientific insights. This is related to the fact that for many cancers, or their (biomarker-selected) subtypes, the target populations are relatively small and/or there is a high unmet medical need. An example of this are trial designs without a parallel randomised control group, such as single-arm trials (SATs), which can be contextualised by providing an external comparator group. The purpose of this statistical methodology study is to advance the knowledge around using SATs with external comparators for cancer drug development, and to develop recommendations on the best practice to incorporate external comparators in the analysis. The results of this study, using data from RCTs and real-world data (RWD), are intended to contribute to the development of recommendations regarding methodologies to be applied and characteristics of situations where evidence generated from a SAT with an external comparator can form a basis for drug approval.

Study status

Finalised

Research institutions and networks

Institutions

IQVIA

United Kingdom

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Last updated: 22/04/2024

Institution | Non-Pharmaceutical company | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Rippin Gerd

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 23/11/2020

Actual: 23/11/2020

Study start date

Planned: 01/04/2021

Actual: 16/07/2021

Date of final study report

Planned: 01/09/2022

Actual: 14/11/2022

Sources of funding

- EMA

Regulatory

Was the study required by a regulatory body?

No

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

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Other

Study topic, other:

Disease/Epidemiology study

Study type:

Not applicable

If ‘other’, further details on the scope of the study

A statistical methodology study to evaluate External Comparator Arm (ECA) study results versus Randomised Controlled Trial (RCT) results

Main study objective:

The aim of this study is to evaluate External Comparator Arm (ECA) study results versus RCT results and evaluate statistical methods and potential sources of bias in the oncology therapeutic area.

Population studied

Short description of the study population

N/A

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)

Estimated number of subjects

0

Study design details

Data analysis plan

The primary analyses from the selected RCTs will be re-derived following the analysis specified in their respective study protocols and statistical analysis plans (SAPs). To emulate an ECA study, the data from the experimental arm of the RCT will then be used as if it was a SAT where it will be analysed together with the RWD using propensity score methods, such as inverse probability of treatment weighting, to account for the imbalance of potential confounders between the experimental treatment arm of the RCT and the external control arm. As it is expected that the RWD has a higher degree of missingness, multiple imputation will be used to derive a complete set of baseline covariates for each patient. Sensitivity analyses will be conducted to assess the robustness of the findings. In addition, simulation studies will be performed using realistic assumptions based on the selected RCTs and RWD sources.

Summary results

See link to publication (Study publications section).

Documents

Study publications

Rippin G, Sanz H, Hoogendoorn WE, Ballarini NM, Largent JA, Demas E, Postmus D,...

Data management

Data sources

Data sources (types)

Other

Data sources (types), other

Data from RCTs and EMR data from patients from a network of community hospitals

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No