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





### Administrative details

#### **EU PAS number**

**EUPAS43709** 

Study ID

50418

**DARWIN EU® study** 

No

**Study countries** 

	Netherlands
- 1	

### 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** 



## Contact details

### **Study institution contact**

Gerd Rippin Gerd.Rippin@iqvia.com

Study contact

Gerd.Rippin@iqvia.com

### **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

### **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)**

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**

## **Check logical consistency**

Unknown

## Data characterisation

### **Data characterisation conducted**

No