# Additional Pharmacovigilance Study to Evaluate the Risks of Major Hemorrhage With the Administration of IMBRUVICA® (ibrutinib)

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Study Finalised

## Administrative details

**EU PAS number**

EUPAS27376

**Study ID**

27377

**DARWIN EU® study**

No

**Study countries**

United States

**Study description**

HaemorrhageSince for technical reasons haemorrhage is not in the MedDRA PT for selection and no more than 10 MedDRA Lower Level Terms (LLTs) can be selected, the most important terms from the available list of terms are provided (broader terms (PT or HLT) in that field,Cerebral, Subdural, and Subarachnoid hemorrhage

**Study status**

Finalised

# Research institutions and networks

## Institutions

NA, retrospective database analysis

# Contact details


**Study institution contact**

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**Study contact**

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**Primary lead investigator**

Maria Cleveland-Jones

**Primary lead investigator**


# Study timelines

**Date when funding contract was signed**
Planned: 28/01/2016

Actual: 28/01/2016

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**Study start date**
Planned: 25/02/2009

Actual: 03/10/2008

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**Date of final study report**
Planned: 12/12/2018

Actual: 13/12/2018

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

Janssen Research & Development

## Regulatory

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

Yes

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

EU RMP category 3 (required)

# 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:**

Assessment of risk minimisation measure implementation or effectiveness

**Data collection methods:**

Secondary use of data

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**Main study objective:**

Primary objective: to characterize the risks of major hemorrhage associated with ibrutinibtherapy in various patient populations from all completed clinical trials and postmarketingsources. Secondary objective: To evaluate the risks of major hemorrhagic events and theirpotential association with the concomitant use of anti-platelet and/or anticoagulant drugs.

## Study Design

**Non-interventional study design**

Cohort

Other

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**Non-interventional study design, other**

Case-series, Retrospective analysis of clinical trials data (cohort study) and post-marketing safety data (case series).

## Study drug and medical condition

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

IBRUTINIB

**Anatomical Therapeutic Chemical (ATC) code**

(L01XE27) ibrutinib

ibrutinib

**Medical condition to be studied**

Subarachnoid haemorrhage

Subdural haemorrhage

Cerebral haemorrhage

# Population studied

**Short description of the study population**

Patients treated with ibrutinib therapy.

**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**

2838

# Study design details

**Outcomes**

major hemorrhage(MH) incidence. Clinical studies:MH defined as G3+ non-serious AEs,SAEs, or any-grade CNS hemorrhage terms that mapped to MedDRA v 21.0 'Haemorrhageterms (excluding laboratory terms)' sub-SMQ. GSD: MH defined as any SAE terms thatmapped to MedDRA v21.0 SMQ of 'Haemorrhages', incl sub-SMQs of 'Haemorrhagelaboratory terms' and 'Haemorrhage terms (excluding laboratory terms)'. The relative risk (RR) of MH associated with concomitant use of antiplatelet (AP) and/oranticoagulant (AC) was evaluated with both the crude incidence and AC and/or APexposure-adjusted incidence rates (EAIRs).

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**Data analysis plan**

Demographics and baseline characteristics were summarized using descriptive statistics.Major hemorrhage incidence was summarized by system organ class, preferred term, and maximum NCI-CTCAE toxicity grade. Exposure-adjusted incidence rate (per subject, per preferred term, per system organ class, and on a global level) was calculated usingpatient-months as denominator. Cox-regression analysis was used to perform univariate and multivariate analysis of risk factors including baseline characteristics and time-dependent variables for developing major hemorrhage. All analyses were performed for Total Ibrutinib Pool and Randomized Controlled Trial Pool separately.

# 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**

Ibrutinib clinical trials database, Ibrutinib Global Safety Database

# 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

Unknown