

Evaluating Safety in Insulin-Requiring Diabetic Patients Receiving Inavolisib Plus Endocrine Therapy-Based Regimens in the Real World

First published: 01/10/2026

Last updated: 01/10/2026

Study

Planned

Administrative details

EU PAS number

EUPAS1000001124

Study ID

1000001124

DARWIN EU® study

No

Study countries



United States

Study description

This is a retrospective cohort study of eligible patients receiving inavolisib-based regimens in the Flatiron Health Network over a 3 to 4-year period from 01 January 2026 to 31 December 2029. The purpose of this real-world data (RWD) study is to evaluate inavolisib (Itovebi) in patients with hormone receptor positive (HR+)/ human epidermal growth factor receptor 2-negative (HER2-), phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha isoform (PIK3CA)-mutated metastatic breast cancer who have insulin-requiring diabetes (both type 1 and type 2). This RWD study will focus on the incidence, severity and complications, and management of hyperglycemia, stomatitis, and diarrhea, which are identified adverse events (AEs) for inavolisib.

Study status

Planned

Research institutions and networks

Institutions

F. Hoffmann-La Roche

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Sami Mahrus

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 30/03/2026

Actual: 30/03/2026

Study start date

Planned: 31/10/2026

Data analysis start date

Planned: 31/12/2029

Date of final study report

Planned: 31/12/2030

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Study protocol

[Protocol_-_GO46271_-_ITOVEBI_-_v2_-_GlobalCore_-_Published_Redacted.pdf](#)
(850.08 KB)

Regulatory

Was the study required by a regulatory body?

Yes

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

EU RMP category 3 (required)

Other study registration identification numbers and links

GO46271

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition
Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

Retrospective cohort study using secondary electronic health record (EHR) data from Flatiron Health network evaluating PIK3CA-mutated, HR+/HER2-metastatic breast cancer patients with insulin-requiring diabetes receiving inavolisib-based regimens over a 3 to 4-year study period.

Main study objective:

The main objective of this study is to describe clinical and demographic characteristics of insulin-requiring patients who receive inavolisib-based regimens in the real world (e.g., inavolisib plus fulvestrant plus palbociclib, inavolisib plus fulvestrant plus ribociclib, inavolisib plus fulvestrant, etc), and to describe the safety and tolerability of inavolisib-based regimens as it relates to hyperglycemia and associated complications (including diabetic ketoacidosis).

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

ITOVEBI

Anatomical Therapeutic Chemical (ATC) code

(L01EM06) inavolisib

inavolisib

Medical condition to be studied

Breast cancer

Additional medical condition(s)

PIK3CA-mutated, HR+/HER2- metastatic breast cancer; insulin-requiring diabetes (type 1 and type 2)

Population studied

Short description of the study population

The study population will consist of patients from United States of America who have insulin-requiring diabetes and are in the nationwide Flatiron Health network and who have PIK3CA-mutated, HR+/HER2- metastatic breast cancer and are taking inavolisib-based regimens in the real world.

Age groups

- **Adult and elderly population (≥ 18 years)**
 - Adults (18 to < 65 years)
 - Adults (18 to < 46 years)
 - Adults (46 to < 65 years)
 - Elderly (≥ 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

Special population of interest, other

Insulin-requiring diabetic patients (type 1 and type 2 diabetes)

Estimated number of subjects

50

Study design details

Setting

Inclusion criteria:

- Diagnosed with breast cancer International Classification of Diseases-Ninth Revision (ICD-9) (174.x or 175.x) or ICD-Tenth Revision (ICD-10) (C50.xx)
- Diagnosed with metastatic breast cancer (mBC) on or after 11/1/24 (FDA approval of inavolisib on 10 October 2024)
- ≥ 18 years of age at mBC diagnosis.
- HR+/HER2- (includes HER2-low and HER2-equivocal)
- Type 1 and type 2 diabetes patients who receive insulin for at least 6 months prior to the index date
- Patients receiving an inavolisib-based regimen, abstracted from the EHR between 01 January 2026 and 31 December 2029 (allowing for up to 6 cycles of inavolisib to collect real word adverse events [rwAEs]).

Exclusion criteria:

- Patients with diabetes and end organ damage (clinician notes for diabetic kidney disease, diabetic retinopathy, diabetic neuropathy, diabetic circulatory complications, diabetic foot ulcers)
 - Eastern Cooperative Oncology Group score = 3+
 - Inavolisib-based regimens in 4L or later
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Outcomes

Primary

- (1) Time to first diagnosis(es) of hyperglycemia following initiation of inavolisib therapy
- (2) Proportion of participants with hyperglycemia
- (3) Severity of hyperglycemia as assessed by date and discharge diagnosis of hospitalizations
- (4) Severity of hyperglycemia as assessed by date and results from laboratory tests (e.g., HbA1c and glucose)
- (5) Proportion of participants with complications from hyperglycemia
- (6) Proportion of participants who require management of hyperglycemia by changes in inavolisib dose, duration, discontinuations and holds along with concomitant medications.

Secondary

- (7) Time to first diagnosis of stomatitis following initiation of inavolisib therapy
- (8) Proportion of participants who require management of stomatitis by changes in inavolisib dose, duration, discontinuations and holds; and dates of concomitant medications.
- (9) Time to first instance/diagnosis of diarrhea following initiation of inavolisib therapy
- (10) Proportion of participants who require management of diarrhea by changes

in inavolisib dose, duration, discontinuations and holds; and dates of concomitant medications

Data analysis plan

All analyses will be descriptive in nature and there are no statistical tests of hypotheses, nor time to event outcomes.

In the descriptive analyses, frequencies and percentages will be reported for categorical variables. Missing values will be described as a separate category. For proportions of participants with an observed rwAE, the analyses will be conducted in several ways, by including: 1) all participants at baseline (defined as the start of the inavolisib-based regimen); 2) participants who have at least 2 visits during the inavolisib-based regimen; 3) participants who are followed up (e.g., have health care visits) during the entire inavolisib-based regimen. Medians with interquartile range (IQR), means with standard deviation (SD), minimum values, and maximum values will be reported for continuous variables.

Sensitivity analyses accounting for starting dose of inavolisib, line of therapy, history of diabetes, duration of insulin use, and type of diabetes (type 1 versus type 2) will be conducted, as is feasible based on sample size.

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)

[Electronic healthcare records \(EHR\)](#)

[Non-interventional study](#)

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