An Observational Post-Authorization Safety Study of Temodar® (Temozolomide) and Severe Acute Liver Injury in the HealthCore Integrated Research Environment (MK-7365-295)

First published: 16/10/2014

Last updated: 27/02/2024

Study Finalised

Administrative details

EU PAS number

EUPAS7622

Study ID

22860

DARWIN EU® study

No

Study countries

☐ United States

Study description

This is a is a retrospective case-control study nested within a cohort of patients (age 18-99 years) with malignant brain cancer using a healthcare claims database, augmented with information obtained from medical records, to assess the relation, if any, between temozolomide exposure and severe acute liver injury (SALI).

Study status

Finalised

Research institutions and networks

Institutions

Merck Sharp & Dohme LLC

United States

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Last updated: 08/07/2025

Institution | Pharmaceutical company

Contact details

Study institution contact

Clinical Trials Disclosure Merck Sharp & Dohme Corp.
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Study contact

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Primary lead investigator

Stephan Lanes

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 22/05/2014

Study start date

Actual: 24/09/2014

Data analysis start date

Planned: 02/11/2015

Actual: 26/10/2015

Date of final study report

Planned: 16/12/2015

Actual: 07/12/2015

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Merck Sharp & Dohme Corp.

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)

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

To assess the relation, if any, between temozolomide exposure and severe acute liver injury (SALI)

Study Design

Non-interventional study design

Case-control

Cohort

Other

Non-interventional study design, other

Post-Authorization Safety Study

Study drug and medical condition

Name of medicine, other

Temodar

Population studied

Short description of the study population

The source study population will include adult patients with two diagnoses of brain cancer (ICD-9-CM codes 191.xx) on different dates between 01 January 2006 through 30 September 2013 (or the most recent date for which sufficiently complete claims are available). The primary reason for requiring two diagnoses is because cancer diagnoses often appear as rule-out diagnoses, and a patient with only one diagnosis is less likely to be a true brain cancer case.

This criterion could be relaxed to increase the number of cases, but it is anticipated this population will provide sufficient study size (Section 7.3 and Feasibility Assessment Report). Any patients exposed to temozolomide and who also have an inpatient diagnosis consistent with SALI after one diagnosis of brain cancer will not fulfil criteria for inclusion in the cohort but will be identified and enumerated. The index date for each patient will be defined as the latter of (1) the day after the second brain cancer diagnosis after six months of continuous enrollment with both medical and pharmacy coverage, or (2) completion of six months of continuous enrollment containing at least two brain cancer diagnoses. Subjects will be required to have at least six months of continuous enrollment prior to and including the index date in order to identify covariates including co-morbidities and medication use. Patients with more than two baseline brain cancer diagnoses before the index date will be included and classified as prevalent cases. Subjects with a potential SALI diagnosis during the six months prior to or including the index date, and patients aged less than 18 years or 100 years or greater on the index date will be excluded.

Inclusion Criteria

• At least two diagnoses of brain cancer on different dates during the study period from 01 January 2006 through 30 September 2013 (or most recent data available).

Exclusion Criteria

• Potential SALI diagnosis within six months prior to or including the index date.

• Less tha

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)

Special population of interest

Other

Special population of interest, other

Brain cancer patients

Estimated number of subjects

875

Study design details

Outcomes

To assess the relation, if any, between temozolomide exposure andSALI. Provide case narratives for temozolomide-exposed cases of SALI (e.g. demographics, clinical and pathological factors, comorbidities, and brain cancer treatment characteristics).

Data analysis plan

This study will have two rounds of data analysis using data from the HealthCore Integrated Research Database (HIRD, Andover MA, US). An interim data analysis will occur after confirmed cases and their controls have been identified, this analysis will include effect estimation using exposure and covariate data available from automated claims data. Concurrently, a round of medical record reviews will be done to obtain information on certain covariates pertaining primarily to brain cancer and its treatment. After this information is obtained, it will be added to analytic files and effect estimation will be repeated on the expanded database. Effect estimation will be conducted using multivariate logistic regression models. All statistical analyses will be performed using

Statistical Analysis Software (SAS) version 9.4 (SAS Institute, Cary, NC, US) and/or Stata® version 11.1 (Stata Corporation, College Station, TX, US).

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 source(s), other

HealthCore Integrated Research Database℠ (HIRD)

Data sources (types)

Administrative healthcare records (e.g., claims)

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