DARWIN EU® - Suicidality following exposure to doxycycline

First published: 25/07/2024

Last updated: 14/08/2026

Study Finalised

Administrative details

EU PAS number

EUPAS1000000280

Study ID

1000000280

DARWIN EU® study

Yes

Study countries

Netherlands

Spain

United Kingdom

Study description

There have been reports on a potential association between use of doxycycline and suicide. By means of a self-controlled case series and an active comparator cohort study, the study aims to assess the association between use of doxycycline and specific outcomes of interest (i.e. suicidality events).

Research questions

1. Is there an association between the use of doxycycline and suicide-related events?
2. Does the association between doxycycline use and completed suicide and suicide-related events vary by indication of use, compared to active comparators?

Objectives

1. To use a new-user cohort study to assess the association between doxycycline and completed suicide, composite suicide and suicide-related events (completed suicide, suicide ideation and suicide attempt, self-harm), composite suicide-related events (suicide ideation, suicide attempt, self-harm), depression and anxiety, compared to active comparators, stratified by indication of acne vulgaris, rosacea, chlamydia and lower respiratory tract infection (CAP or bronchitis)
2. To use a self-controlled case series study to assess the association between use of doxycycline and composite suicide-related events (including suicide ideation, suicide attempt, self-harm), depression and anxiety.

Research methods

Study design

New-user cohort study with active comparator (objective 1) and self-controlled case series (objective 2)

Population

The study population is new users of doxycycline (SCCS and cohort study) or the comparators (cohort). The new-user cohorts will be per indication: acne vulgaris: doxycycline, erythromycin or isotretinoin; rosacea: doxycycline, erythromycin or isotretinoin; chlamydia: doxycycline, azithromycin,

erythromycin or amoxicillin; and lower respiratory tract infection (CAP and bronchitis): doxycycline, azithromycin, or amoxicillin.

Study status

Finalised

Research institutions and networks

Institutions

Department of Medical Informatics - Health Data Science, Erasmus Medical Center (ErasmusMC)

Netherlands

First published: 03/11/2022

Last updated: 02/05/2024

Institution **Educational Institution** **ENCePP partner**

Contact details

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Primary lead investigator

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Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 16/05/2024

Actual: 16/05/2024

Study start date
Planned: 24/07/2024

Actual: 24/07/2024

Date of final study report
Planned: 15/08/2024

Actual: 11/11/2024

Sources of funding

- EMA

Study protocol

DARWIN EU_D2.2.3_Protocol_P3-C3-003_Suicidality exposure doxycycline_V4.pdf (863.74 KB)

Regulatory

Was the study required by a regulatory body?

Yes

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

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

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:

New-user cohort study with active comparator (objective 1) and self-controlled case series (objective 2)

Main study objective:

1. To use a new-user cohort study to assess the association between doxycycline and completed suicide, composite suicide and suicide-related events (completed suicide, suicide ideation and suicide attempt, self-harm), composite suicide-related events (suicide ideation, suicide attempt, self-harm), depression and anxiety, compared to active comparators, stratified by indication of acne vulgaris, rosacea, chlamydia and lower respiratory tract infection (CAP or bronchitis)
2. To use a self-controlled case series study to assess the association between use of doxycycline and composite suicide-related events (including suicide ideation, suicide attempt, self-harm), depression and anxiety.

Study Design

Non-interventional study design

Case-control

Cohort

Study drug and medical condition

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

DOXYCYCLINE

Anatomical Therapeutic Chemical (ATC) code

(J01AA02) doxycycline

doxycycline

Medical condition to be studied

Suicidal behaviour

Suicidal ideation

Suicide attempt

Suicide threat

Completed suicide

Depression suicidal

Depression

Anxiety

Population studied

Short description of the study population

The study population is new users of doxycycline (SCCS and cohort study) or the comparators (cohort). The new-user cohorts will be per indication: acne vulgaris: doxycycline, erythromycin or isotretinoin; rosacea: doxycycline, erythromycin or isotretinoin; chlamydia: doxycycline, azithromycin, erythromycin or amoxicillin; and lower respiratory tract infection (CAP and bronchitis): doxycycline, azithromycin, or amoxicillin.

Study design details

Setting

study was conducted using routinely collected data from 3 primary care data sources in 3 European countries

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Outcomes

The primary outcomes for the SCCS and the new-user cohort of the study were different. In the SCCS study, completed suicide was not included because this type of outcome affects subsequent follow-up time such as death breaches the assumptions of the SCCS study design.[28]

The new-user cohort design outcomes were as follows: Completed suicide

(condition record of suicide plus
death date in ±30 days); composite suicide-related events (includes completed suicide, suicide attempt, suicide ideation and self-harm); composite non-fatal suicide-related events (suicide attempt, suicide ideation and self-harm); depression (for general study population, not the subgroup with history of depression); and anxiety.
The outcomes for the SCCS study were as follows: composite non-fatal suicide-related events (suicide attempt, suicide ideation and self-harm); depression; and anxiety. Due to the risk of duplicate recording events, we only assessed the first outcome occurring after entry into the study.

Summary results

CONCLUSION

In this drug safety study using two study designs across three European electronic healthcare databases, we identified a two-fold increased association of suicide-related events with doxycycline use compared to erythromycin use in acne patients in the cohort study. However, these findings were not consistent and we
also found an increased risk of non-fatal suicide-related events in the pre-exposure period in the SCCS study, showing there is uncertainty around the causality of the association with non-fatal suicide-related events we find in doxycycline use. We found a smaller but increased association of anxiety with doxycycline use compared to erythromycin and isotretinoin, as well as an increased risk of depression with doxycycline use compared to erythromycin in patients with acne. We did not observe these increased associations for other indications in the cohort study, and in addition, many of the analyses remained blinded due to non passing of diagnostic tests. In contrast to the increased risk of psychiatric outcomes we found in acne patients, we observed a reduced risk of suicide-related events in doxycycline versus amoxicillin in LRTI patients in the cohort study. Although we observed an association between use of

doxycycline and suicide related events in individuals with acne, this could not be confirmed in the SCCS, where an increased risk in the pre-exposure period was observed. Studying the association between use of doxycycline and suicide related events in a population of individuals with acne might have been hindered by confounding. It is possible that conditions such as (severe) acne that impact self-esteem, especially in adolescents, might ultimately result in suicidal ideation and attempts.

Documents

Study report

DARWIN EU_Report_P3-C3-003_Doxycycline_suicidality_V5.pdf (6.9 MB)

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)

Clinical Practice Research Datalink (CPRD) GOLD

Integrated Primary Care Information (IPCI)

The Information System for Research in Primary Care (SIDIAP)

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

OMOP

CDM website

https://www.ohdsi.org/Data-standardization/

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

Unknown