The influence of having bariatric surgery on the pharmacokinetics, safety and efficacy of the novel non-nucleoside reverse transcriptase inhibitor doravirine (LABRADOR)

Published: 16-02-2022
Last updated: 05-04-2024

Primary objective: • To assess the pharmacokinetics of DOR in patients prior to and after BSSecondary objectives: • To assess the safety of DOR in patients prior to and after undergoing BS• To assess the viral response to DOR in patients prior to...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON51582

Source
ToetsingOnline

Brief title
LABRADOR

Condition

- Other condition
- Viral infectious disorders
- Gastrointestinal therapeutic procedures

Synonym
HIV-infection, obesity-surgery

Health condition

obesitas

Research involving
Human

Sponsors and support

Primary sponsor: Afdeling Apotheek
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: bariatric surgery, doravirine, HIV, Pharmacokinetics

Outcome measures

Primary outcome

To investigate the influence of BS on the pharmacokinetics of DOR in HIV

patients represented by Geometric mean ratios (GMR) with 90% confidence

interval (CI) of PK parameters.

Secondary outcome

The percentage of patients showing a HIV VL >40 copy/ml will be reported.

Descriptive analysis will be provided for CD4 count pre- and post-BS as well as

safety data post-BS

Study description

Background summary

People living with HIV (PLWH) report high obesity trends similar to those to the general population [1]. Especially in PLWH, obesity is associated with a greater risk of morbidity and mortality compared to the general population, i.e. a higher incidence of cardiovascular diseases, diabetes and malignancies [2-4].
Bariatric surgery (BS), commonly sleeve gastrectomy (SG) and gastric bypass (GBP), is the most persistent and effective intervention when diet and lifestyle changes fail to achieve weight goals. BS improves obesity-related

comorbidities and overall quality of life despite high remission rates seen in the general population [5].
When patients undergo BS to prevent significant morbidity and mortality associated with overweight, this may have a profound impact on the pharmacokinetics (PK) of drugs that they are taking. Because of the manipulation of the gastrointestinal (GI) tract after BS, most likely absorption of drugs can be impaired, including absorption of antiretroviral agents (ARVs). In case inadequate absorption of ARVs occurs development of resistance may lead to treatment failure, which needs to be prevented [6-8].

Currently, there is either scarce or conflicting data regarding PK changes post-BS making it difficult to make any clinical recommendations. Also, HIV treating Guidelines such as HIV/AIDS Treatment and Prevention Guidelines (DHHS) and European AIDS Clinical Society (EACS) do not mention data on selection (and dosing) of ARVs in HIV-infected patients who have undergone BS.
Among several ARVs, the novel agent doravirine (DOR) might be an attractive candidate - on a theoretical basis - for patients to be used after BS. It meets a number of preferred PK properties [6], such as a good absorption profile that is independent from (fat) food and low gastric pH as well as a favourable interaction profile with post-surgery standard medications [9]. DOR has been demonstrated to be an effective switch regimen in the DRIVE-SHIFT trial where patients were virologically suppressed on various regimens [10]. Most likely, patients who are candidates for BS are also virologically suppressed, but most likely were not represented in the DRIVE-SHIFT trial.

We propose a multicentre phase IV study to collect evidence that a DOR-based regimen can be safely and effectively administered to virologically suppressed HIV-infected patients undergoing BS.

Study objective

Primary objective:
• To assess the pharmacokinetics of DOR in patients prior to and after BS

Secondary objectives:
• To assess the safety of DOR in patients prior to and after undergoing BS
• To assess the viral response to DOR in patients prior to and after undergoing BS

Study design

The study will include two full PK days before and after surgery in addition to two single PK samples on two other occasions. For full PK curves, 9 blood samples will be taken per PK day.
1st PK day: Between week -4 and week 0 before the surgery, a 24h PK curve will be recorded.

2nd PK day: After BS, a 2nd PK curve will be recorded at approximately week 12 post-BS.
To assist early and late effect on DOR PK levels, additional two trough PK samples at the end of the dosing interval (24h ± 4h) will be taken from each patient at week 4 and week 24 post BS.
Data on VL, HIV associated immune response (CD4 count), and safety data will be monitored and reported at each PK visit until week 24 post BS.

Study burden and risks

Patients who participate in the study will receive standard treatment.
Therefore the risk for participation in this study is regarded negligible.
The use of DOR is not mentioned to be contradicted with having bariatric surgery in the drug label.
Patients will not directly benefit from participating in this study. However, participants may benefit from the regular and optimized monitoring of their HIV response to medication (using HIV VL and CD4 count) after the surgery by their treating physicians, and thus, maybe protected from any small progression of their HIV status.

Contacts

Public
Selecteer

Geert Grooteplein 10
Nijmegen 6525 GA
NL
Scientific
Selecteer

Geert Grooteplein 10
Nijmegen 6525 GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Inclusion criteria:
- hiv-infected
- Viral load suppressed , below 40 copy/ml for at least 6 months, blips are allowed
- planned to have bariatric surgery (gastric bypass or Sleeve gastrectomy)
- Able to sign informed consent
- Age above or equal to 18 years
- Using doravirine for at least 4 weeks prior to bariatric surgery with no detectable viral load

Exclusion criteria

Exclusion criteria:
- History or current evidence of any condition, therapy, laboratory abnormality or other circumstance that might confound the results of the study or interfere with the subject*s participation
- Requires or is anticipated to require any of the prohibited medications known to contradict/interact with doravirine
- Has significant hypersensitivity or other contraindication to DOR
- Creatinine clearance below 40 ml/min
- Severe liver dysfunction (Diagnosed liver cirrhosis: Child-Pugh C)
- Pregnancy or planning to be pregnant during first 6 months post surgery.

Study design

Design

Study phase:	4
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-08-2022
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	(100 mg doravirine/ 300 mg Lamivudine/ 245 mg Tenofovir Disoproxil Fumarate)/Film-coated tablet
Generic name:	Delstrigo®
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	(100 mg doravirine) /Film-coated tablet
Generic name:	Pifeltro®
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	16-02-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-03-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-09-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2021-005347-79-NL
CCMO	NL79347.091.22

Study results

Date completed:	12-02-2024
Actual enrolment:	1