Development of AntiRetroviral Therapy in Africa (DART) study post hoc safety data analysis comparing safety outcomes of study participants with baseline creatinine clearance of 30-49 mL/min vs participants with creatinine clearance of ≥50 mL/min

First published: 18/06/2018

Last updated: 02/04/2024

Study Finalised

Administrative details

EU PAS number

EUPAS24473

Study ID

48250

DARWIN EU® study

No

Study countries

Uganda

Zimbabwe

Study description

This report describes the ViiV Healthcare initiated post-hoc analyses for the 96 week safety outcome comparison of study participants with baseline creatinine clearance (CLcr) of 30-49 mL/min vs participants with CLcr of ≥50 mL/min from the completed open-label interventional Development of AntiRetroviral Therapy in Africa trial (DART), a randomized study where 3316 participants received an antiretroviral therapy regimen containing 150 mg twice daily dose of lamivudine, dosed as a fixed dose combination of lamivudine and zidovudine (COMBIVIR) plus a third antiretroviral drug of either tenofovir, abacavir or nevirapine, the original protocol for the completed DART study has been supplied with results from the ViiV Healthcare post hoc analysis.

Study status

Finalised

Research institutions and networks

Institutions

ViiV Healthcare

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Institution

Contact details

Study institution contact

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Study contact

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Primary lead investigator

GSK Clinical Disclosure Advisor GSK Clinical Disclosure Advisor

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 09/02/2017

Actual: 09/02/2017

Study start date

Planned: 14/02/2017

Actual: 14/02/2017

Date of final study report

Planned: 12/03/2018

Actual: 16/04/2018

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

ViiV Healthcare

Study protocol

viiv-208674-protocol-redact.pdf (1.18 MB)

Regulatory

Was the study required by a regulatory body?

No

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

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Not applicable

If ‘other’, further details on the scope of the study

Post-hoc analyses of 96 week safety outcome comparison of study participants with baseline creatinine clearance (CLcr) of 30-49 mL/min vs participants with CLcr of ≥50 mL/min from the open-label Development of AntiRetroviral Therapy in Africa trial

Main study objective:

To describe the post-hoc analyses for the 96 week safety outcome comparison of study participants with baseline creatinine clearance (CLcr) of 30-49 mL/min vs participants with CLcr of ≥50 mL/min from the open-label Development of AntiRetroviral Therapy in Africa trial (DART).

Study drug and medical condition

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

LAMIVUDINE

ZIDOVUDINE

ABACAVIR

NEVIRAPINE

TENOFOVIR

Medical condition to be studied

HIV infection

Population studied

Short description of the study population

Patients aged 18 years or older with HIV infection in Africa.

Inclusion criteria:

1. Documentation of HIV-1 infection: antibody positive serology by ELISA test (confirmed by licensed second ELISA or Western Blot).
2. Age > 18 years
3. Symptomatic WHO stage 2, 3 or 4 HIV disease and CD4 < 200 cells/mm3
4. ART naïve (except for ART use during pregnancy for the prevention of mother-to-child HIV transmission).
5. Agreement and documented informed consent to be randomised to CMO or LCM and to STI or continuous ART, if eligible.
6. Life expectancy of at least 3 months

Exclusion criteria:

1. Cannot, or unlikely to attend regularly (e.g. usual residence too far from Study Centre)
2. Likelihood of poor compliance
3. Presence of acute infection (e.g. malaria, acute hepatitis, pneumococcal pneumonia, non-typhoid salmonella septicaemia, cryptococcal meningitis). Patients may be admitted after recovery of an acute infection. Patients with tuberculosis (TB) will not be enrolled while on the intensive phase of anti-tuberculosis therapy, but should be re-evaluated after the intensive phase and a decision made then about starting ART. Patients starting ART whilst on anti-tuberculosis therapy after the intensive phase will not receive NVP, nor will they be randomised into the NORA substudy.
4. On chemotherapy for malignancy
5. Laboratory abnormalities which are a contra-indication for the patient to start ART (e.g. Haemoglobin <8g/dl, neutrophils <0.50x109/l, AST or ALT >5 x the upper limit of normal (ULN), grade 3 renal dysfunction - creatinine >360 mol/l

and/or urea >5 x

ULN).

6. Pregnancy or breast-feeding

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

Immunocompromised

Other

Special population of interest, other

Patients with HIV infection

Estimated number of subjects

3316

Study design details

Outcomes

Safety events, effect of ART initiation on renal function over 96 weeks.

Data analysis plan

Descriptive statistics were used to compare safety outcomes over a period of 96 weeks for study participants that entered the study with baseline renal function of CLcr 30-49 mL/min to those with baseline CLcr ≥50 mL/min. The

adverse event rates for common adverse events for participants treated with any antiretroviral drug with baseline CLcr 30-49 mL/min and those with baseline CLcr ≥50 mL/min) were evaluated and the relative risk and 95% confidence intervals were presented. This was not a powered study and no multiple comparisons were adjusted.

Documents

Study results

viiv-208674-clinical-study-report-redact.pdf (4.68 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 sources (types)

Other

Data sources (types), other

Post hoc analysis of specific safety outcomes obtained from the previously completed Medical Research Council Sponsored DART 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

No