LAPaL
THE LONG-ACTING THERAPEUTICS PATENTS AND LICENCES DATABASE

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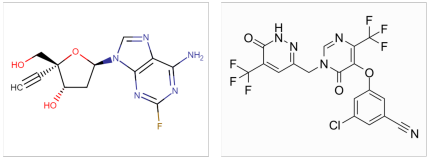


MK-8591B (islatravir + ulonivirine)

Developer(s)

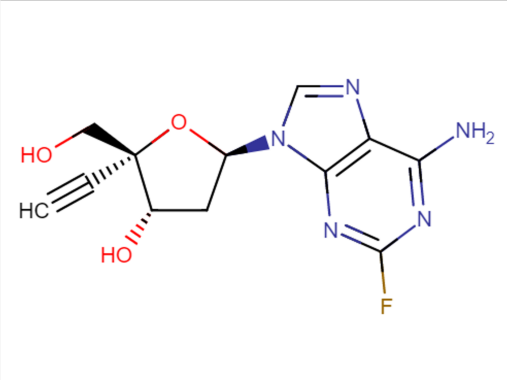
Merck & Co., Inc.

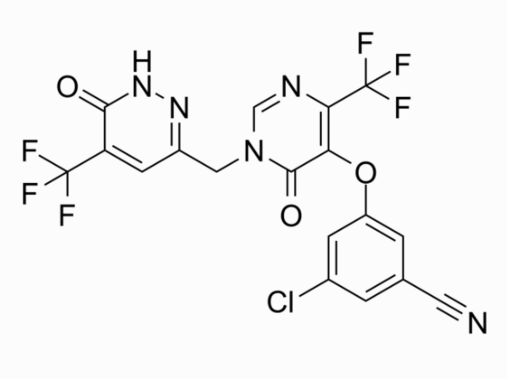
Originator

https://www.merck.com/research/product-pipeline/

United States

Drug structure





islatravir and ulonivirine

Drug information

Associated long-acting platforms

Oral solid form

Administration route

Oral

Therapeutic area(s)

HIV

Use case(s)

Treatment

Use of drug

Ease of administration

Self-administered

User acceptance

Not provided

Dosage

Available dose and strength

Not provided

Frequency of administration

Not provided

Maximum dose

Not provided

Recommended dosing regimen

Not provided

Additional comments

Not provided

Dosage link(s)

Not provided

Drug information

Drug's link(s)

Not provided

Generic name

Not provided

Brand name

Not provided

Compound type

Small molecule

Summary

Not provided

Approval status

Unknown

Regulatory authorities

Unknown

Delivery device(s)

No delivery device

Scale-up and manufacturing prospects

Scale-up prospects

Not provided

Tentative equipment list for manufacturing

Not provided

Manufacturing

Not provided

Specific analytical instrument required for characterization of formulation

Not provided

Clinical trials

8591-013

Identifier

NCT04564547

Link

https://clinicaltrials.gov/study/NCT04564547

Phase

Phase II

Status

Completed

Sponsor

Merck Sharp & Dohme LLC

More details

This is a randomized, controlled, double-blind, study to evaluate the safety and tolerability of islatravir (ISL) + ulonivirine based on review of the accumulated safety data, in adult participants with human immunodeficiency virus type 1 (HIV-1) who have been virologically suppressed for ≥6 months on bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) once-daily.

Purpose

Dose Ranging, Switch Study of Islatravir (ISL) and Ulonivirine (MK-8507) Once-Weekly in Virologically-Suppressed Adults With Human Immunodeficiency Virus Type 1 (HIV-1)

[MK-8591-013]

Interventions

Intervention 1

ISL+ULO

Dosage: 20mg+100mg QW

Intervention 2

ISL+ULO

Dosage: 20mg+200mg QW

Intervention 3

ISL+ULO

Dosage: 20mg+400mg QW

Intervention 4

BIC/FTC/TAF

Dosage: 50 mg/200 mg/25 mg QD

Countries

United States of America

France

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2021-03-09

Anticipated Date of Last Follow-up

2025-02-10

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2025-01-30

Actual Completion Date

2025-01-30

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Is HIV-1 positive with plasma HIV-1 RNA \<50 copies/mL at screening * Has been virologically suppressed on BIC/FTC/TAF for ≥6 months * Has a

screening CD4+ T-cell count \>200 cells/mm\^3 (completed by the central laboratory) * Is male or female, at least 18 years of age, at the time of signing the informed consent * female participant is eligible to participate if she is not pregnant or breastfeeding, and at least one of the following conditions applies: * Is not a woman of childbearing potential (WOCBP) * Is a WOCBP and using a contraceptive method that is highly effective (with a failure rate of \<1% per year), or be abstinent from heterosexual intercourse as their preferred and usual lifestyle (abstinent on a long term and persistent basis) Exclusion Criteria: *

Health status

Positive to : HIV
Negative to : HBV, HCV
Other health status: Virologically supressed individuals

Study type

Interventional (clinical trial)

Enrollment

161

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Triple-blind masking

Masking description

Not provided

Frequency of administration

Weekly

Studied LA-formulation(s)

Tablet

Studied route(s) of administration

Oral

Use case

Treatment

Key results

Type of key results	Title	Website link
Article	Protocol Plain Language Summary	https://trialstransparency.merckclinicalt 511041- 19_for%20pub_01May2024_V1- 0_MK-8591-013-04.pdf

8591B-060

Identifier

NCT06891066

Link

https://clinicaltrials.gov/study/NCT06891066

Phase

Phase II

Status

Recruiting

Sponsor

Merck Sharp & Dohme LLC

More details

Investigators are trying to find better treatments for people with HIV-1. In this clinical study, investigators want to see how well a new treatment called ISL+ULO, taken once a week, works compared to an existing treatment called BIC/FTC/TAF, which is taken every day. Investigators will check how many people still have a high level of the virus in their blood after 24 weeks. The investigators also want to understand if the new treatment, MK-8591B, is safe and how well people can handle it.

Purpose

A Study of Islatravir (ISL) and Ulonivirine (ULO) Once Weekly (QW) in Virologically Suppressed Adults With Human Immunodeficiency Virus Type 1 (HIV-1) (MK-8591B-060)

Interventions

Intervention 1

ISL+ULO weekly

Dosage: 2mg (2x1mg capsules)+200mg (2x100mg tablets)

Intervention 2

ISL+ULO weekly (switched from B/F/TAF)

Dosage: 2mg (2x1mg capsules)+200mg (2x100mg tablets)

Intervention 3

BIC/FTC/TAF daily

Dosage: BIC 50mg oral tablet/FTC 200mg oral tablet/TAF 25 mg oral tablet

Countries

United States of America

Puerto Rico

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2025-04-14

Anticipated Date of Last Follow-up

2025-05-10

Estimated Primary Completion Date

2027-09-24

Estimated Completion Date

2027-09-24

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion: The main inclusion criteria include but are not limited to the following: - Has been receiving Bictegravir/Emtricitabine/Tenofovir alafenamide (BIC/FTC/TAF) therapy with documented viral suppression \[Human immunodeficiency virus type 1 (HIV-1) ribonucleic acid (RNA) \<50 copies/mL\] for ≥6 months prior to providing documented informed consent and has no history of prior virologic treatment failure on any past or current regimen. Exclusion: The main exclusion criteria include but are not limited to the following: * Has Human immunodeficiency virus type 2 (HIV-2) infection. * Has a diagnosis of an active Acquired immune deficiency syndrome (AIDS)-defining opportunistic infection. * Has active hepatitis C virus (HCV) coinfection. * Has hepatitis B virus (HBV) coinfection. * H

Health status

Positive to : HIV
Negative to : HBV, HCV

Study type

Interventional (clinical trial)

Enrollment

150

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Weekly

Studied LA-formulation(s)

Tablet

Studied route(s) of administration

Oral

Use case

Treatment

Key results

Not provided

Excipients

Proprietary excipients used

Not provided

Novel excipients or existing excipients at a concentration above Inactive Ingredients Database (IID) for the specified route of administration

Not provided

Residual solvents used

Not provided

Patent info

There are either no relevant patents or these were not yet submitted to LAPaL

Supporting material

Publications

Matthews RP, Patel M, Liu W, Liu Y, Rondón JC, Vargo RC, Stoch SA, Iwamoto M.2025.

Pharmacokinetics of islatravir in participants with moderate hepatic impairment.

Antimicrob Agents Chemother69:e01553-24.https://doi.org/10.1128/aac.01553-24

Islatravir (ISL) is a nucleoside reverse transcriptase translocation inhibitor in development for the treatment of HIV-1 infection. People living with HIV are at risk of liver disease. ISL is metabolized by adenosine deaminase (ADA), which is expressed in the liver; thus, ISL pharmacokinetics (PK) may be affected by hepatic impairment. This study evaluated the effect of moderate hepatic impairment on ISL PK. This nonrandomized, open-label, phase 1 study (MK-8591-030) evaluated the effects of a single oral dose of ISL 60 mg in HIV-seronegative adults with moderate hepatic insufficiency (n = 6) and matched healthy adult participants (n = 6). Blood samples for plasma ISL and 4′-ethynyl-2-fluoro-2′deoxyinosine (M4) and peripheral blood mononuclear cell (PBMC) ISL-triphosphate (ISL-TP) were collected at multiple time points through 672 h, and safety was monitored throughout. Modest decreases in maximum measured concentration (Cmax) and area under the concentration-time curve (AUC) of plasma ISL and AUC of PBMC ISL-TP were observed in participants with moderate hepatic impairment versus matched healthy participants, while ISL-TP C max was relatively unchanged. In contrast, plasma M4 was modestly increased in the moderate hepatic impairment group, suggesting that hepatic impairment may result in increased metabolism of ISL to M4 via ADA. The clinical relevance of the overall modest changes in M4, ISL, and ISL-TP levels with moderate hepatic impairment will be contextualized once exposure response data from ongoing clinical studies are available to elucidate the thresholds for clinical efficiency. A single oral dose of ISL 60 mg was generally well tolerated in both groups.

Additional documents

- A clinical study of islatravir and MK-8507 for people with HIV-1 (MK-8591-013) - Protocol Plain Language Summary

Useful links

There are no additional links

Access principles

Collaborate for development

Consider on a case by case basis, collaborating on developing long acting products with potential significant public health impact, especially for low- and middle-income countries (LMICs), utilising the referred to long-acting technology

Not provided

Share technical information for match-making assessment

Provide necessary technical information to a potential partner, under confidentiality agreement, to enable preliminary assessment of whether specific medicines of public health importance in LMICs might be compatible with the referred to long-acting technology to achieve a public health benefit

Not provided

Work with MPP to expand access in LMICs

In the event that a product using the referred to long-acting technology is successfully developed, the technology IP holder(s) will work with the Medicines Patent Pool towards putting in place the most appropriate strategy for timely and affordable access in low and middle-income countries, including through licensing

Not provided

Comment & Information

Not provided