Protocol Plain Language Summary

A clinical study of treatment with doravirine and islatravir for people with HIV-1 who have not been treated before (MK-8591A-053)

Protocol title: A Phase 3, Randomized, Active-Controlled, Double-Blind Clinical Study to Evaluate the Antiretroviral Activity, Safety, and Tolerability of Doravirine/Islatravir (DOR/ISL 100 mg/0.25 mg) Once-Daily in HIV-1 Infected Treatment-Naïve Participants

Why is this study needed?

Researchers are looking for new treatments for all people living with **HIV-1** (Human Immunodeficiency Virus Type 1). HIV-1 is the most common type of HIV, which is a virus that attacks cells of the immune system.

HIV-1 treatments, called **ART** (antiretroviral therapy), involve taking medicines to lower the amount of HIV-1 virus in the body. **Standard ART** helps people live longer but includes up to three medicines and may affect other health problems. New ART is needed that is safe and works well. In addition, new ART is needed that can be taken for a long time without creating or worsening other medical conditions and that does not interact with other medicine a person takes. The **study ART** combines 2 medicines and is taken once a day.

The purpose of this study is to see if **study ART** works as well as a **standard ART** to treat HIV-1.

Who will take part in this study?

About 500 people with HIV-1 will take part in this study. They will be at least 18 years old and:

- Have not been treated with any ART
- Not have HIV-2 (a different type of HIV virus)

How is this study designed?

This study has 2 treatment groups. People will be assigned by equal chance to Group 1 or Group 2:

- **Group 1** will take the **study ART** for 96 weeks (about 2 years)
- **Group 2** will take one type of **standard ART** for 96 weeks (about 2 years)

A person will be in the study for about 2 years. Neither the people in the study nor the researchers will know which treatment a person is taking (double-blind study).

A person will give urine samples, have blood and imaging tests and physical examinations, and answer questions during the study.

What treatments are being given during the study?

During this study, people will take either:

- **Study ART** – 2 medicines combined in a single pill called **DOR/ISL** (doravirine and islatravir)
- **Standard ART** – 3 medicines combined in a single pill called **BIC/FTC/TAF** (bictegravir, emtricitabine, and tenofovir alafenamide)

In addition to their assigned ART, each person in the study will also take a **placebo** that looks like the other ART but does not contain any medicine. This way, the person and the researchers will not know which treatment a person is taking. Using a placebo helps researchers better understand the real effects of the study medicine.

People will take their assigned treatment and placebo by mouth once a day.

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What are the goals of this study and how will they be measured?

Main goal	How it will be measured
To compare if DOR/ISL works as well as BIC/FTC/TAF to treat HIV-1	At Week 48, the number of people who have a HIV-1 viral load of less than 50 copies in a milliliter (mL) of blood. A lower viral load of HIV-1 in the blood is better. The viral load is measured as the number of "**copies**" in a small amount of blood (1 mL).
To learn about the **safety** and how well people **tolerate** DOR/ISL compared to BIC/FTC/TAF	By Week 48, the number of people who: • Had an **adverse event (AE)**. An AE is a health problem that happens or worsens during a study • Stopped ART due to an AE
Other goals	**How they will be measured**
To learn how well DOR/ISL works to treat HIV-1 compared to BIC/FTC/TAF	The number of people who have a HIV-1 viral load of: • Less than 50 copies at Week 96 • Less than 200 copies at Week 48 • Less than 200 copies at Week 96
To learn if the number of immune system cells called **CD4+ T-cells** has changed during the study for people who took DOR/ISL compared to people who took BIC/FTC/TAF. **CD4+ T-cells** help fight HIV-1 infection	The average change in the number of CD4+ T-cells in the blood from before treatment to: • Week 48 • Week 96
To learn if DOR/ISL or BIC/FTC/TAF stops working for people	**Resistance testing** will be done during certain times of the study for people whose ART stops working for them. Resistance testing of a blood sample can show which ART may not work to control a person's HIV-1.
To compare if people who took DOR/ISL gained less weight than people who took BIC/FTC/TAF	The average change in people's weight from the start of the study to: • Week 48 • Week 96
To learn if the treatment is safe and how well people tolerate DOR/ISL compared to BIC/FTC/TAF	During the study, the number of people who: • Had an AE • Stopped ART due to an AE

What are the possible benefits and risks?

People may or may not benefit from the treatment received during the study. This study has a Data Monitoring Committee that oversees the study's overall risk and benefit. If this committee decides that the study treatment is not safe or does not show benefit, the study can be stopped.

More information about the benefits and risks is in the Investigator Brochure, Protocol, and Informed Consent documents.