About the Oral Investigational Drug

The investigational medication (DOR/ISL) is a once-daily, oral agent combining 2 medications, islatravir—the first in a new class of antiretroviral therapies (ART)—with doravirine. Some of the characteristics of DOR/ISL are potency, a high barrier to resistance, a favorable drug resistance profile, and a long half-life.

- Islatravir is the first nucleoside reverse transcriptase translocation inhibitor (NRTTI). It works through 2 different mechanisms—*translocation inhibition* and *delayed chain termination*—to prevent HIV replication
- Doravirine, a recently approved non-nucleoside reverse transcriptase inhibitor (NNRTI), has demonstrated efficacy, good tolerability, and a low likelihood of selection for viral resistance *in vivo*

Based on early clinical data, this novel, once-daily combination of 2 ARTs may provide patients with an efficacy profile comparable to the current 3-drug standard of care for HIV-1, along with a high barrier to resistance.

Comparator Treatment	Randomization Goal
Placebo (only in part 1)	Approximately 100

For more information, or to refer a patient, please contact:

[SITE NAME]

[SITE ADDRESS]

[SITE PHONE NUMBER]

ILLUMINATE HTE

For more information, or to refer a patient, please contact:

[SITE NAME]

[SITE ADDRESS]

[SITE PHONE NUMBER]

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ILLUMINATE HTE

Together we can advance HIV research

Learn about a clinical research study evaluating an oral investigational medication for people living with HIV-1.

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Illuminate HTE Study

The Illuminate HTE Study is a Phase 3, randomized clinical trial evaluating a once-daily, oral investigational medication, a fixed-dose combination of doravirine/islatravir (DOR/ISL), in participants with HIV-1 who are heavily treatment experienced and failing on their current antiretroviral therapy (ART).

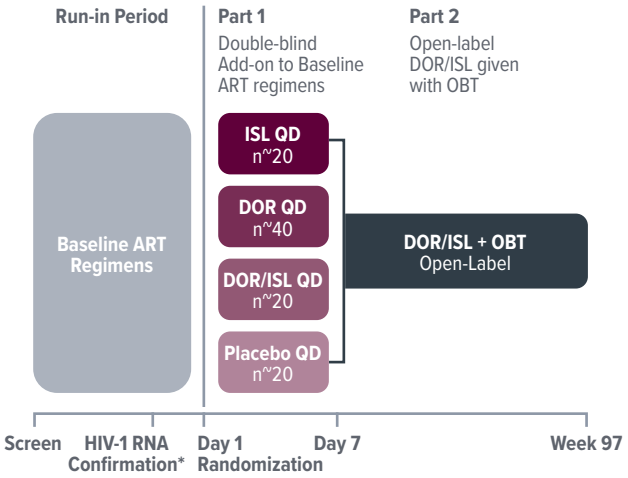
ILLUMINATE HTE

Key Eligibility Criteria

1. Is male or female; pediatric participants <18 years of age must weigh ≥35 kg. There is no weight requirement for adults ≥18 years. (Participants under the age of majority need parent/guardian consent.)
2. HIV-1 positive with plasma HIV-1 RNA ≥500 copies/mL
3. Has been receiving the same baseline ART for ≥3 months
4. Has at least triple-class resistance (NRTI, NNRTI, and resistance to at least 1 other class [ie, resistance to at least 1 drug in each class])
5. Has ≤1 fully active antiretroviral remaining that can be effectively combined to form a viable regimen based on resistance, tolerability, safety, drug access, or acceptability to participant
6. Use contraception to prevent pregnancy (women of childbearing potential only)
7. No HIV-2
8. No HBV coinfection and is not currently being treated for HBV
   - **A.** Participants coinfected with HBV who are currently taking oral antiviral treatment for hepatitis B (eg, tenofovir, entecavir, telbivudine, adefovir, lamivudine, etc) are eligible for enrollment and should remain on the same treatment for their HBV throughout the study
   - **B.** Chronic HCV infection and treatment with direct-acting antiviral therapies are not exclusionary, provided the participant has stable liver function tests and no significant hepatic synthetic dysfunction
9. Cannot be taking or anticipate requiring systemic immunosuppressive therapy or immune modulators (Time-limited courses of corticosteroids [eg, for asthma exacerbation] are permitted)
10. Cannot be taking strong and moderate cytochrome P450 3A (CYP3A) inducers
11. Cannot be taking pentostatin
12. Cannot be taking doravirine as part of the current failing antiretroviral regimen
13. Cannot be taking efavirenz, etravirine, or nevirapine

Note: NRTI=nucleoside reverse transcriptase inhibitor, NNRTI=non-nucleoside reverse transcriptase inhibitor

Study Design



Participation will last about 112 weeks and include up to 17 visits to the study site.

After a screening phase of up to 60 days, each participant will receive blinded intervention for 1 week.

Participants will be randomized 1:2:1:1 into 4 groups:

Group 1: ISL QD + failing baseline ART

Group 2: DOR QD + failing baseline ART

Group 3: DOR/ISL QD + failing baseline ART

Group 4: Placebo QD + failing baseline ART

Then all participants will receive open-label intervention for 96 weeks: DOR/ISL QD + optimized background therapy (OBT).

ART=antiretroviral therapy; DOR=doravirine; HIV-1=Human Immunodeficiency Virus Type 1; ISL=islatravir; n=number of participants per group; OBT=optimized background therapy; QD=once daily; RNA=ribonucleic acid.

*HIV-1 RNA testing will be repeated during the Run-in Period to confirm eligibility for randomization (defined as HIV-1 RNA ≥500 copies/mL). Participants with ≥500 copies/mL on confirmation testing but with ≥0.5 $\log_{10}$ decline in HIV-1 RNA from the Screening Visit (Visit 1) will have an additional HIV-1 RNA confirmation test within 7 to 14 days. Participants with further decline in HIV-1 RNA ≥0.3 $\log_{10}$ compared to the previous confirmation test will be excluded from the study.

Note: Participants are treated with open-label DOR/ISL + OBT for 96 weeks in Part 2.