Once-Weekly Oral Islatravir/Lenacapavir Versus Daily Standard of Care Across Participant Subgroups Through Week 48 in the Phase 3 ISLEND-2 Trial

P049

ISLEND-2

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Conclusions

- In the Phase 3 ISLEND-2 trial, safety and efficacy of islatravir/lenacapavir (ISL/LEN) were similar across sex, age, race, and ethnicity subgroups, and by baseline antiretroviral therapy (ART), CD4+ T-cell count, or presence of M184V/I mutation in this diverse population
- There was a high rate of virologic suppression and a favorable safety profile through Week 48 in all participant subgroups
- These results support the potential of ISL/LEN to be the first complete, once-weekly, oral single-tablet regimen (STR) for people with HIV-1

Plain Language Summary

- In the ongoing ISLEND-2 trial, researchers studied a new treatment for HIV called islatravir/lenacapavir (ISL/LEN). Participants took one ISL/LEN tablet once a week. The treatment was as good at controlling HIV as commonly used daily HIV medicines (standard of care)
- In this analysis, researchers looked at whether sex, age, race, ethnicity, or the HIV medicines that participants were taking before starting ISL/LEN affected how well ISL/LEN worked or how safe it was. They found that these factors did not affect how well ISL/LEN worked or its safety
- The results suggest that once-weekly ISL/LEN may be a suitable treatment for many different people with HIV

Introduction

- Long-acting oral HIV-1 treatments could broaden treatment options for people seeking alternatives to daily oral and long-acting injectable ART, and address preferences for enhanced privacy, convenience, and fewer reminders of HIV status[1-4]
- The combination of ISL, a nucleoside reverse transcriptase translocation inhibitor,[5,6] and LEN, a capsid inhibitor,[7] is being developed as a complete once-weekly oral STR for virologically suppressed people with HIV-1
- In a diverse population of people with HIV-1 in the Phase 3 ISLEND-2 trial, switching to once-weekly oral ISL/LEN demonstrated noninferior efficacy to continuing daily oral standard of care (SOC) in maintaining high rates of virologic suppression through Week 48, and was well tolerated
  - 1/314 (0.3%) participants on ISL/LEN and 4/312 (1.3%) participants receiving SOC had HIV-1 RNA ≥ 50 copies/mL (difference: -1.0% [95.002% CI: -3.0%, 1.1%])

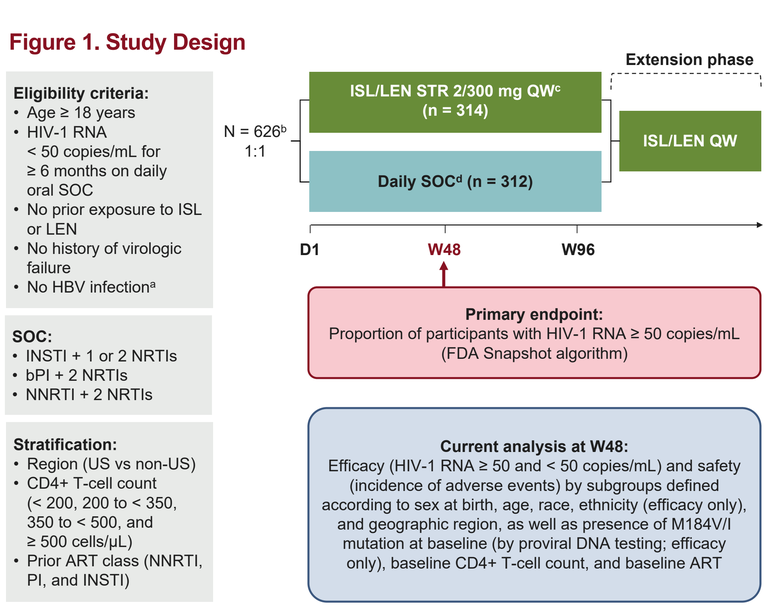
Objective

- To present ISLEND-2 Week 48 analyses by subgroups based on baseline demographic and clinical characteristics

Methods

- ISLEND-2 was a Phase 3, open-label, active-controlled noninferiority study in virologically suppressed people with HIV-1[8] (**Figure 1**)

Figure 1. Study Design



[a]Defined as hepatitis B surface antigen positive or hepatitis B core antibody positive and surface antibody negative.
[b]Randomized: N = 634, dosed: N = 626.
[c]Participants received two oral tablets (initiation dose), each containing 0.5 mg ISL and 300 mg LEN on D1 and D2, then one oral tablet of ISL/LEN 2/300 mg QW from D8, without regard to food.
[d]All SOC treatments were taken once daily, including fixed-dose combinations and STRs, except for raltegravir, which could be taken once or twice daily.
ART, antiretroviral therapy; (b)PI, boosted protease inhibitor; CD4, cluster of differentiation 4; D, Day; FDA, US Food and Drug Administration; HBV, hepatitis B virus; INSTI, integrase strand-transfer inhibitor; ISL, islatravir; LEN, lenacapavir; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; QW, once weekly; SOC, standard of care; STR, single-tablet regimen; W, Week.

Results

- Baseline demographic and clinical characteristics were similar between groups in this diverse study population (**Table 1**)

Table 1. Baseline Demographic and Clinical Characteristics

Participants, n (%)		ISL/LEN QW n = 314	Daily SOC n = 312
Sex assigned at birth	Male	209 (67)	206 (66)
	Female	105 (33)	106 (34)
Age	≥ 50 years	180 (57)	184 (59)
	≥ 65 years	47 (15)	42 (13)
Race[a]	Black	94 (30)	99 (32)
	White	130 (41)	134 (43)
	Other[b]	78 (25)	68 (22)

Results (cont.)

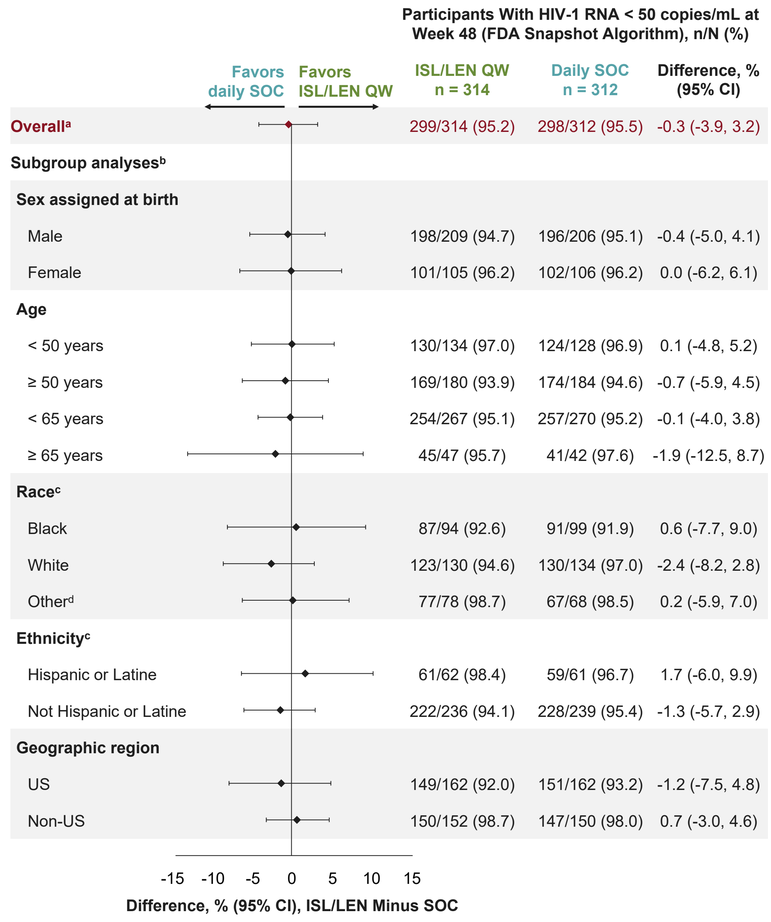
Table 1. Baseline Demographic and Clinical Characteristics (cont.)

Participants, n (%)		ISL/LEN QW n = 314	Daily SOC n = 312
Ethnicity[a]	Hispanic or Latine	62 (20)	61 (20)
	Not Hispanic or Latine	236 (75)	239 (77)
Geographic region	US	162 (52)	162 (52)
	Non-US	152 (48)	150 (48)
M184V/I mutation[c]	Yes	18 (6)	19 (6)
	No	277 (88)	277 (89)
CD4+ T-cell count[d]	< 500 cells/μL	60 (19)	66 (21)
	≥ 500 cells/μL	254 (81)	246 (79)
ART	NNRTI	43 (14)	52 (17)
	PI	26 (8)	27 (9)
	INSTI	245 (78)	233 (75)
Select comorbidities	Dyslipidemia	135 (43)	137 (44)
	Hypertension	115 (37)	103 (33)
	Hyperglycemia/new-onset diabetes mellitus	67 (21)	73 (23)
	Chronic kidney disease	17 (5)	21 (7)

[a]In some countries, local regulators did not allow the collection of race or ethnicity information (race: ISL/LEN, n = 12 [4%]; SOC, n = 11 [4%]; ethnicity: ISL/LEN, n = 16 [5%]; SOC, n = 12 [4%]).
[b]Includes Asian, American Indian or Alaska Native, Native Hawaiian or Pacific Islander, and other.
[c]Baseline genotypic data were unavailable for 19 (6%) ISL/LEN participants and 16 (5%) SOC participants.
[d]8 (1%) participants had baseline CD4+ T-cell counts < 200 cells/μL (ISL/LEN, n = 3 [1%]; SOC, n = 5 [2%]).
ART, antiretroviral therapy; CD4, cluster of differentiation 4; INSTI, integrase strand-transfer inhibitor; ISL/LEN, islatravir/lenacapavir; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; QW, once weekly; SOC, standard of care.

- Rates of virologic suppression were high and comparable between the treatment groups across demographic subgroups, including in people assigned female at birth and older adults (**Figure 2**)

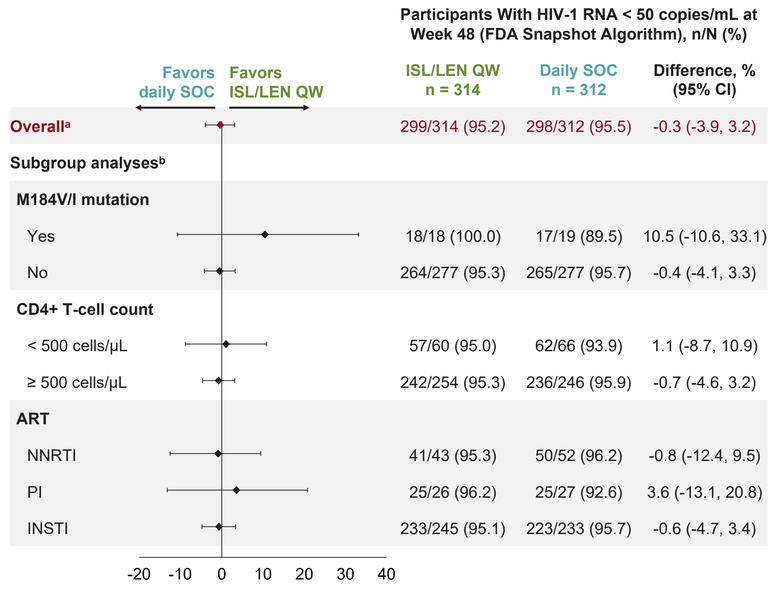
Figure 2. HIV-1 RNA < 50 copies/mL at Week 48 by Baseline Demographics



[a]Between-group differences (ISL/LEN minus SOC) in percentages of participants and two-sided 95% CIs were constructed based on stratum-adjusted Mantel-Haenszel proportion and adjusted by geographic region. A total of 14 and 10 participants had missing data in the Week 48 window in the ISL/LEN QW and daily SOC groups, respectively.
[b]Between-group differences (ISL/LEN minus SOC) in percentages of participants and 95% CIs were calculated based on an unconditional exact method using two inverted one-sided tests.
[c]In some countries, local regulators did not allow collection of race or ethnicity information (race: ISL/LEN, n = 12 [4%]; SOC, n = 11 [4%]; ethnicity: ISL/LEN, n = 16 [5%]; SOC, n = 12 [4%]).
[d]Includes Asian, American Indian or Alaska Native, Native Hawaiian or Pacific Islander, and other.
FDA, US Food and Drug Administration; ISL/LEN, islatravir/lenacapavir; QW, once weekly; SOC, standard of care.

- Rates of virologic suppression were high and comparable between the treatment groups across subgroups defined by baseline clinical characteristics (**Figure 3**)

Figure 3. HIV-1 RNA < 50 copies/mL at Week 48 by Baseline Clinical Characteristics



[a]Between-group differences (ISL/LEN minus SOC) in percentages of participants and two-sided 95% CIs were constructed based on stratum-adjusted Mantel-Haenszel proportion and adjusted by geographic region. A total of 14 and 10 participants had missing data in the Week 48 window in the ISL/LEN QW and daily SOC groups, respectively.
[b]Between-group differences (ISL/LEN minus SOC) in percentages of participants and 95% CIs were calculated based on an unconditional exact method using two inverted one-sided tests.
ART, antiretroviral therapy; CD4, cluster of differentiation 4; FDA, US Food and Drug Administration; INSTI, integrase strand-transfer inhibitor; ISL/LEN, islatravir/lenacapavir; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; QW, once weekly; SOC, standard of care.

- The safety profile was consistent with previously reported data[8] and similar across the subgroups; no new safety concerns were identified (**Table 2**)

Table 2. Adverse Events – Overall Incidence at Week 48 by Treatment Group and Subgroup

Any Adverse Event, n/N (%)		ISL/LEN QW n = 314	Daily SOC n = 312
All participants		**249/314 (79)**	**241/312 (77)**
Sex assigned at birth	Male	174/209 (83)	160/206 (78)
	Female	75/105 (71)	81/106 (76)
Age	≥ 50 years	138/180 (77)	142/184 (77)
	≥ 65 years	35/47 (74)	35/42 (83)
Race[a]	Black	73/94 (78)	70/99 (71)
	White	111/130 (85)	107/134 (80)
	Other[b]	55/78 (71)	53/68 (78)
Geographic region	US	129/162 (80)	119/162 (73)
	Non-US	120/152 (79)	122/150 (81)
Baseline CD4+ T-cell count	< 500 cells/μL	52/60 (87)	44/66 (67)
	≥ 500 cells/μL	197/254 (78)	197/246 (80)
Baseline ART	NNRTI	36/43 (84)	43/52 (83)
	PI	20/26 (77)	18/27 (67)
	INSTI	193/245 (79)	180/233 (77)

[a]In some countries, local regulators did not allow the collection of race or ethnicity information (race: ISL/LEN, n = 12 [4%]; SOC, n = 11 [4%]).
[b]Includes Asian, American Indian or Alaska Native, Native Hawaiian or Pacific Islander, and other.
ART, antiretroviral therapy; CD4, cluster of differentiation 4; INSTI, integrase strand-transfer inhibitor; ISL/LEN, islatravir/lenacapavir; n, number of participants with the event; N, number of participants in the subgroup of interest; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; QW, once weekly; SOC, standard of care.

- Safety and efficacy findings were consistent with those of the subgroup analysis of the Phase 3 ISLEND-1 study comparing once-weekly ISL/LEN and daily bictegravir/emtricitabine/tenofovir alafenamide (Poster P050)

References: 1. Derrick CB, et al. *Open Forum Infect Dis.* 2018;5:ofy247. **2.** Graham SM, et al. *J Int AIDS Soc.* 2023;26 (Suppl 2):e26099. **3.** Stout JA, et al. *AIDS Behav.* 2024;28:3315-25. **4.** Nachega JB, et al. *Lancet HIV.* 2023;10:e332-42. **5.** Michailidis E, et al. *J Biol Chem.* 2014;289:24533-48. **6.** Salie ZL, et al. *Proc Natl Acad Sci U S A.* 2016;113:9274-9. **7.** Link JO, et al. *Nature.* 2020;584:614-18. **8.** Colson AE, et al. *Lancet.* 2026;408:821-32.

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Disclosures (cont.): **OO** received honoraria from ViiV Healthcare; and served on advisory boards for Gilead Sciences, Inc., MSD, and ViiV Healthcare. **JG** received grants (paid to their institution) from Gilead Sciences, Inc. and ViiV Healthcare; consulting fees from Gilead Sciences, Inc. and MSD; honoraria from Gilead Sciences, Inc.; and holds stock options in, and receives deferred income from, Gilead Sciences, Inc. **RK** received grants from Gilead Sciences, Inc. (for training by the Desmond Tutu Health Foundation). **HW**, **FS**, **EB**, and **HD-S** are employees and shareholders of Gilead Sciences, Inc. **KC**, **TLD**, and **CL** are employees and shareholders of Merck Sharp & Dohme LLC, Rahway, NJ, USA. **DSG** is an employee and shareholder of Gilead Sciences, Inc.; Co-Chair of the IAS HIV Cure Industry Collaborative Group; board member of the San Francisco AIDS Foundation; and advisory council member of the California HIV Research Program. **AEC** received consulting fees from Gilead Sciences, Inc. and MSD; and honoraria from Gilead Sciences, Inc.

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