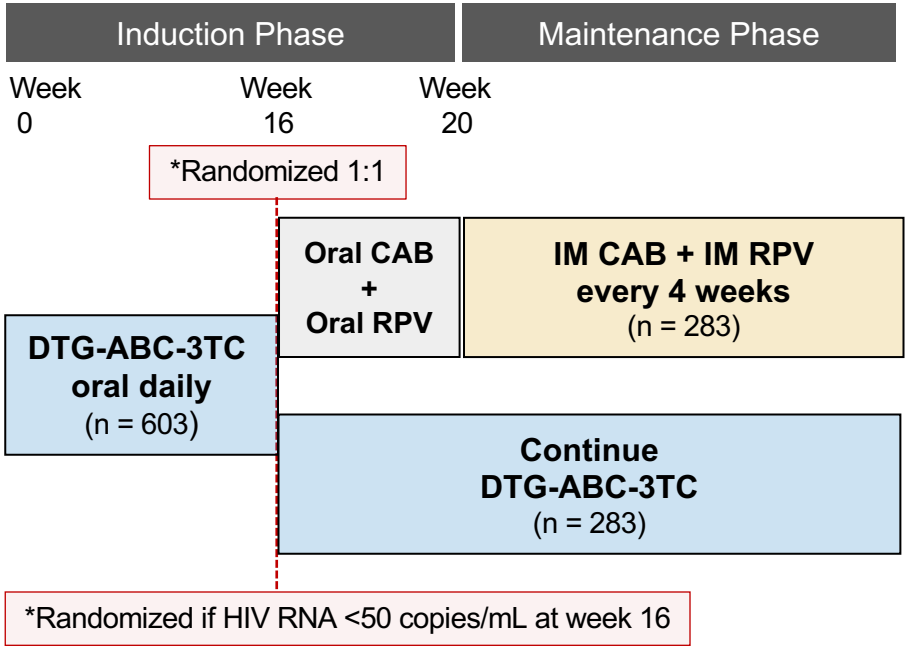
Long-Acting IM Cabotegravir and IM Rilpivirine after Oral Induction

FLAIR Study: 48-Week Data

Long-Acting IM Cabotegravir and IM Rilpivirine after Oral Induction FLAIR Study (48-Week Data): Design

- **Background**: Phase 3, randomized, open-label, trial assessing IM CAB + RPV after oral induction for treatment-naïve adults
- **Inclusion Criteria**
  - Age ≥18 years
  - Antiretroviral-naïve
  - HIV RNA ≥1,000 copies/mL
  - Any CD4 cell count
  - No chronic hepatitis B
  - No NNRTI resistance



Oral lead in dosing: cabotegravir 30 mg daily and rilpivirine 25 mg daily x 4 weeks
Loading injections: cabotegravir 600 mg IM and 900 mg rilpivirine IM x 1
Maintenance injections: cabotegravir 400 mg IM and 600 mg rilpivirine IM monthly

Source: Orkin C, et al. N Engl J Med. 2020;382:1124-35.

Long-Acting IM Cabotegravir and IM Rilpivirine after Oral Induction FLAIR Study (48-Week Data): Baseline Characteristics

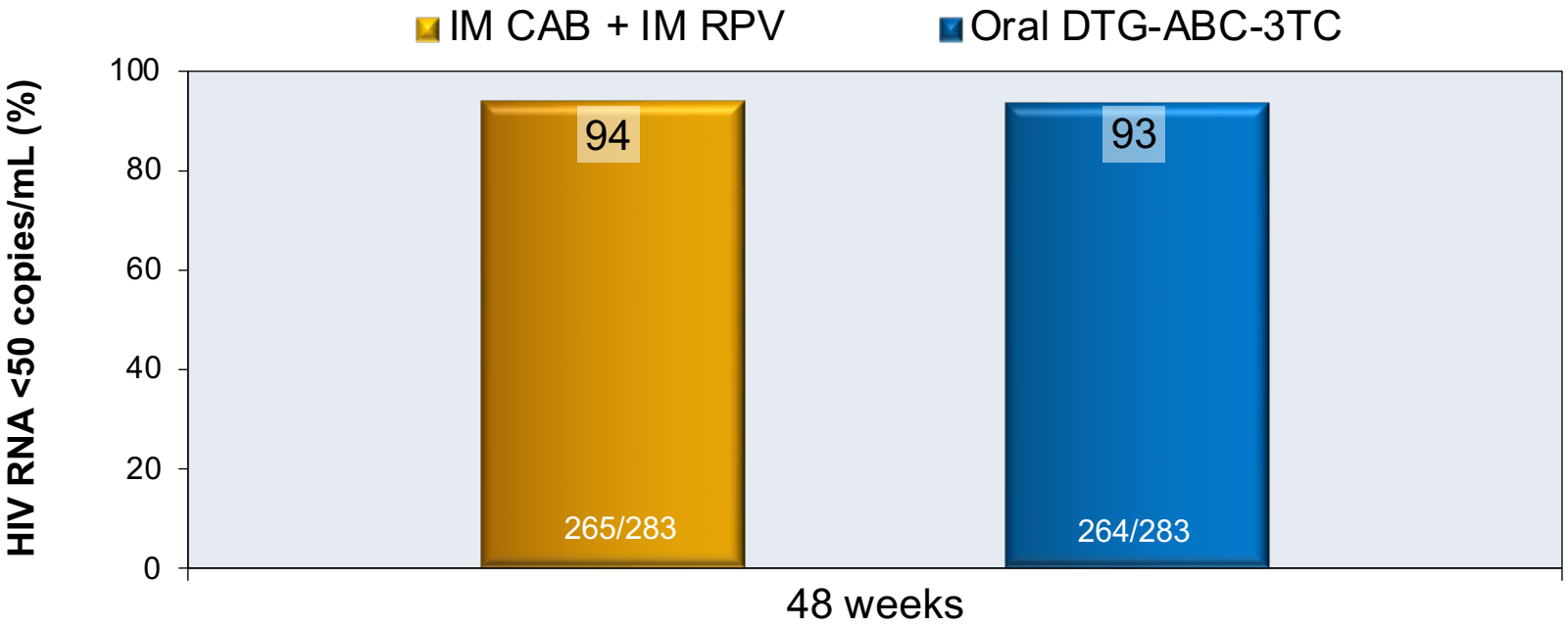
FLAIR: Baseline Characteristics

Characteristic	IM CAB + IM RPV (n = 283)	DTG-ABC-3TC (n = 283)	Overall (n = 566)
Age, years, median	34	34	34
Female, n, %	63 (22)	64 (23)	127 (22)
White, n, %	216 (76)	201 (71)	417 (74)
Black, n, %	47 (17)	56 (20)	103 (18)
Median body-mass index	24	24	24
CD4 count <200 cells/mm^3, n, %	16 (6)	23 (8)	39 (7)
CD4 count ≥500 cells/mm^3, n, %	108 (38)	108 (38)	216 (38)
HIV RNA ≥200k copies/mL, n, %	26 (9)	23 (8)	39 (7)
HIV RNA 10k-50k copies/mL, n, %	95 (34)	113 (40)	208 (37)

Source: Orkin C, et al. N Engl J Med. 2020;382:1124-35.

Long-Acting IM Cabotegravir and IM Rilpivirine after Oral Induction FLAIR Study (48-Week Data): Results

Weeks 48: Virologic Response by FDA Snapshot Analysis



*HIV RNA ≥50 copies/mL at 48 weeks: 2.1 % CAB-RPV, 2.5% DTG-ABC-3TC

Source: Orkin C, et al. N Engl J Med. 2020;382:1124-35.

Long-Acting Cabotegravir and IM Rilpivirine after Oral Induction FLAIR Study (48-Week Data): Results

Resistance Data for Participants in the IM CAB + IM RPV arm with Viral Rebound Meeting Protocol-Defined Criteria for Genotype Resistance Testing

Country; HIV-1 Subtype	At Baseline		At Virologic Failure	
	HIV RNA	INSTI RAMs	HIV RNA	INSTI RAMs
Russia; A1	54,000 copies/mL	L74I	456 copies/mL	L74I, Q148R
Russia; A1	23,000 copies/mL	L74I	299 copies/mL	L74I, G140R
Russia; A1	20,000 copies/mL	L74I	440 copies/mL	L74I, Q148R

There were no baseline NNRTI RAMs
There were also 3 virologic failures in the DTG-ABC-3TC arm; no new RAMs detected
Abbreviations: F = female; M = male; RAMs = resistance associated mutations

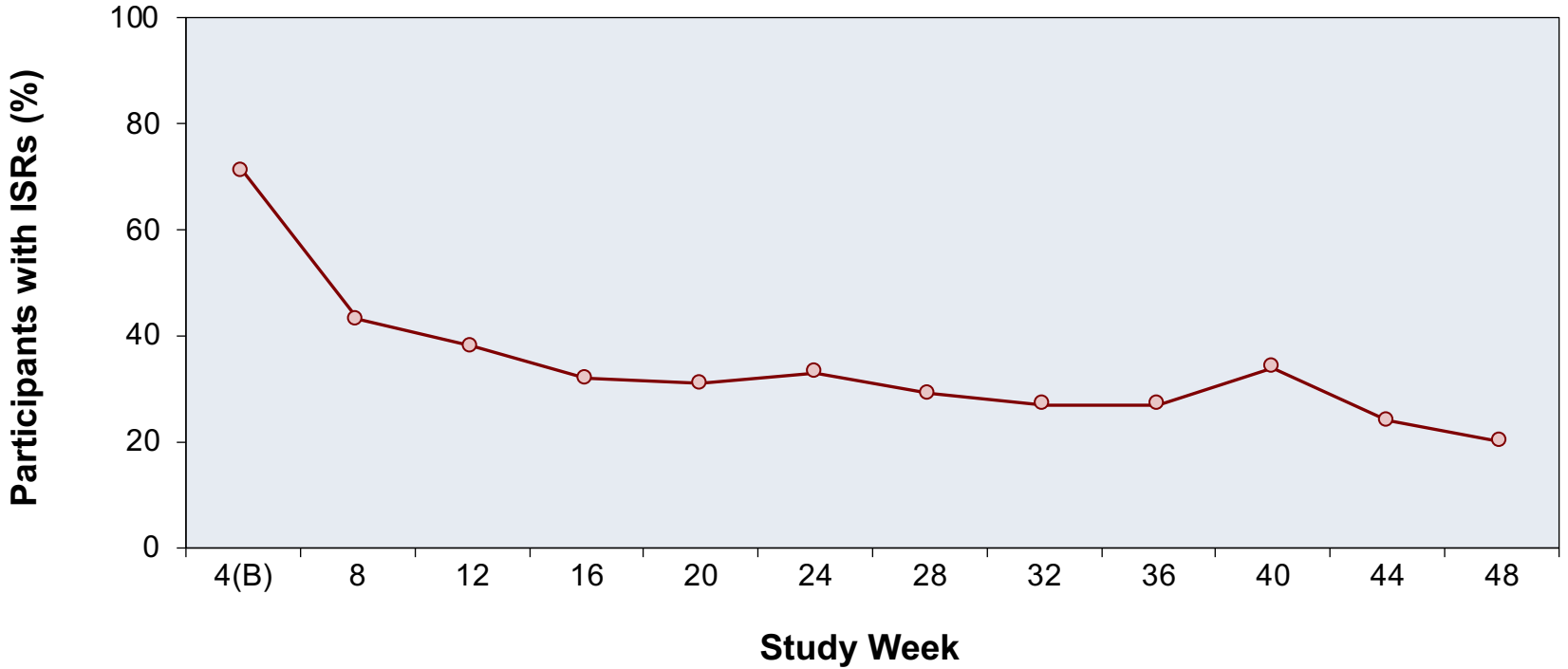
Source: Orkin C, et al. N Engl J Med. 2020;382:1124-35.

Long-Acting IM Cabotegravir and IM Rilpivirine after Oral Induction FLAIR Study (48-Week Data): Adverse Events

Drug-Related Adverse Events and Injection Site Reactions (ISR)		
Drug-Related Adverse Event (AE) All reported as: n (%)	**IM CAB + IM RPV** (n = 283)	**DTG-ABC-3TC** (n = 283)
Any AE	236 (83)	28 (10)
Any AE, excluding ISR	79 (28)	28 (10)
Grade 3 or 4 AE	14 (5)	0
Grade 3 or 4 AE, excluding ISR	4 (1)	0
Any injection site pain	227 (80)	NA
Grade 3 or 4 injection site pain	11 (4)	NA

Source: Orkin C, et al. N Engl J Med. 2020;382:1124-35.

Long-Acting IM Cabotegravir and IM Rilpivirine after Oral Induction FLAIR Study (48-Week Data): Injection Site Reactions (ISRs)



99% of ISRs mild to moderate in severity. Median duration 3 days. 4 participants withdrew due to ISR.

Source: Orkin C, et al. N Engl J Med. 2020;382:1124-35.

Long-Acting IM Cabotegravir and IM Rilpivirine after Oral Induction FLAIR Study (48-Week Data): Conclusions

Conclusions: “Therapy with long-acting cabotegravir plus rilpivirine was noninferior to oral therapy with dolutegravir–abacavir–lamivudine with regard to maintaining HIV-1 suppression. Injection-site reactions were common.”

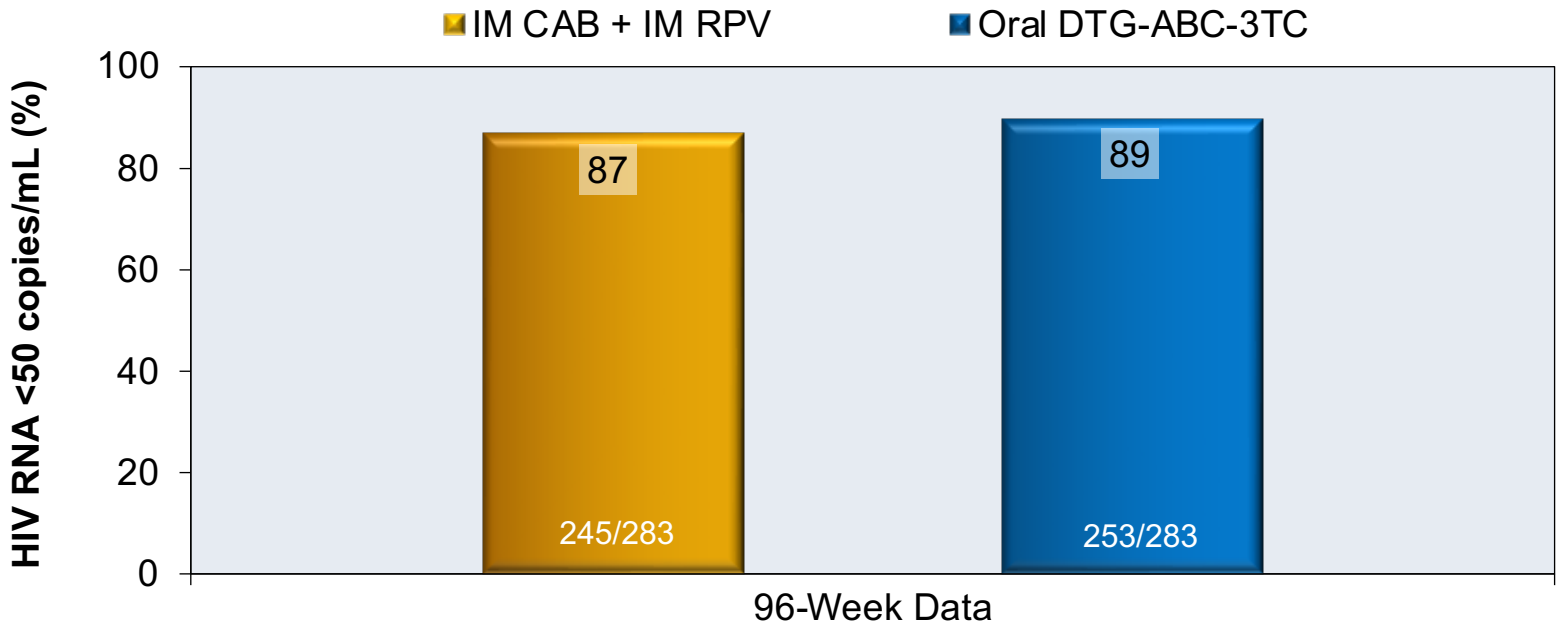
Source: Orkin C, et al. N Engl J Med. 2020;382:1124-35.

Long-Acting IM Cabotegravir and IM Rilpivirine after Oral Induction

FLAIR Study: 96-Week Data

Long-Acting IM Cabotegravir and IM Rilpivirine after Oral Induction FLAIR Study (96-Week Data): Results

Week 96: Virologic Response by Snapshot Outcomes (Intention-to-Treat Population)

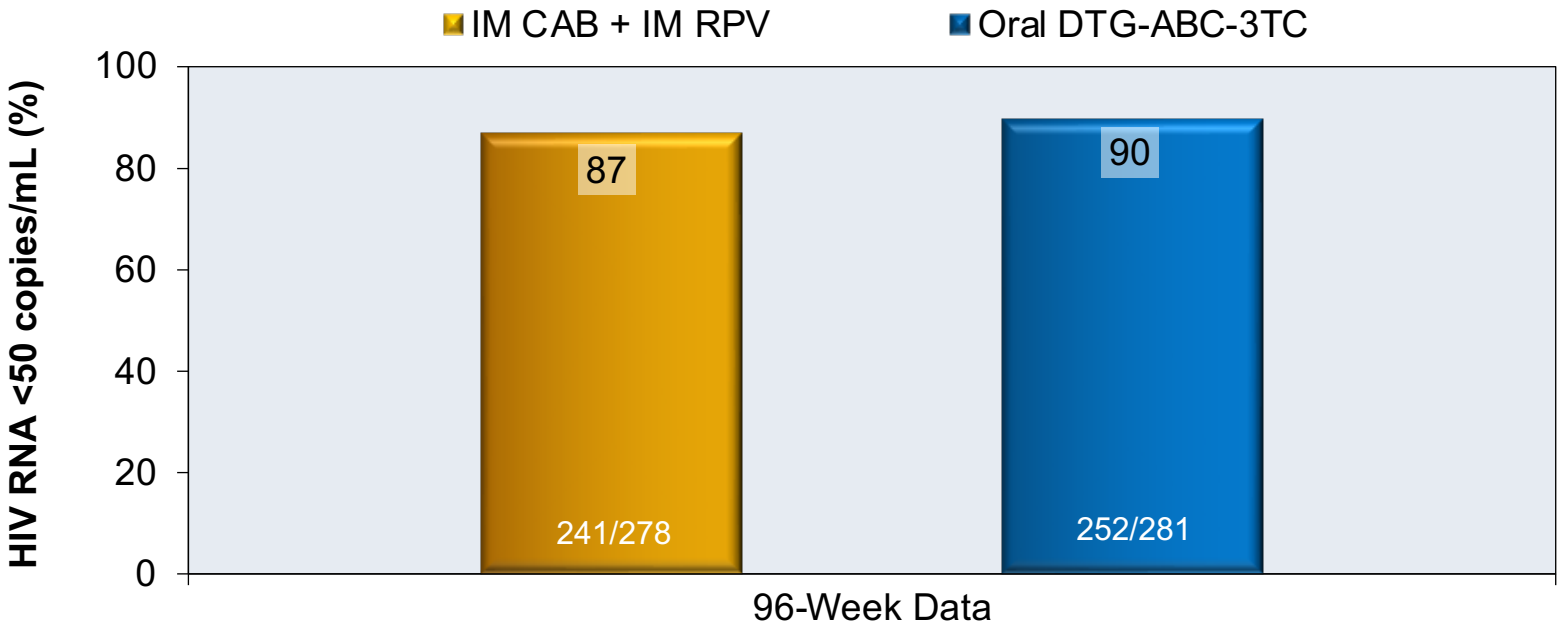


*HIV RNA ≥50 copies/mL at 96 weeks: n = 9 (3%) CAB-RPV, n = 9 (3%) DTG-ABC-3TC
*Only 1 virologic failure occurred between weeks 48 and 96 (in the DTG-ABC-3TC group)

Source: Orkin C, et al. Lancet HIV. 2021;8:e185-e196.

Long-Acting IM Cabotegravir and IM Rilpivirine after Oral Induction FLAIR Study (96-Week Data): Results

Week 96: Virologic Response by Snapshot Outcomes (Per Protocol Population)



*HIV RNA ≥50 copies/mL at 96 weeks: n = 9 (3%) CAB-RPV, n = 9 (3%) DTG-ABC-3TC

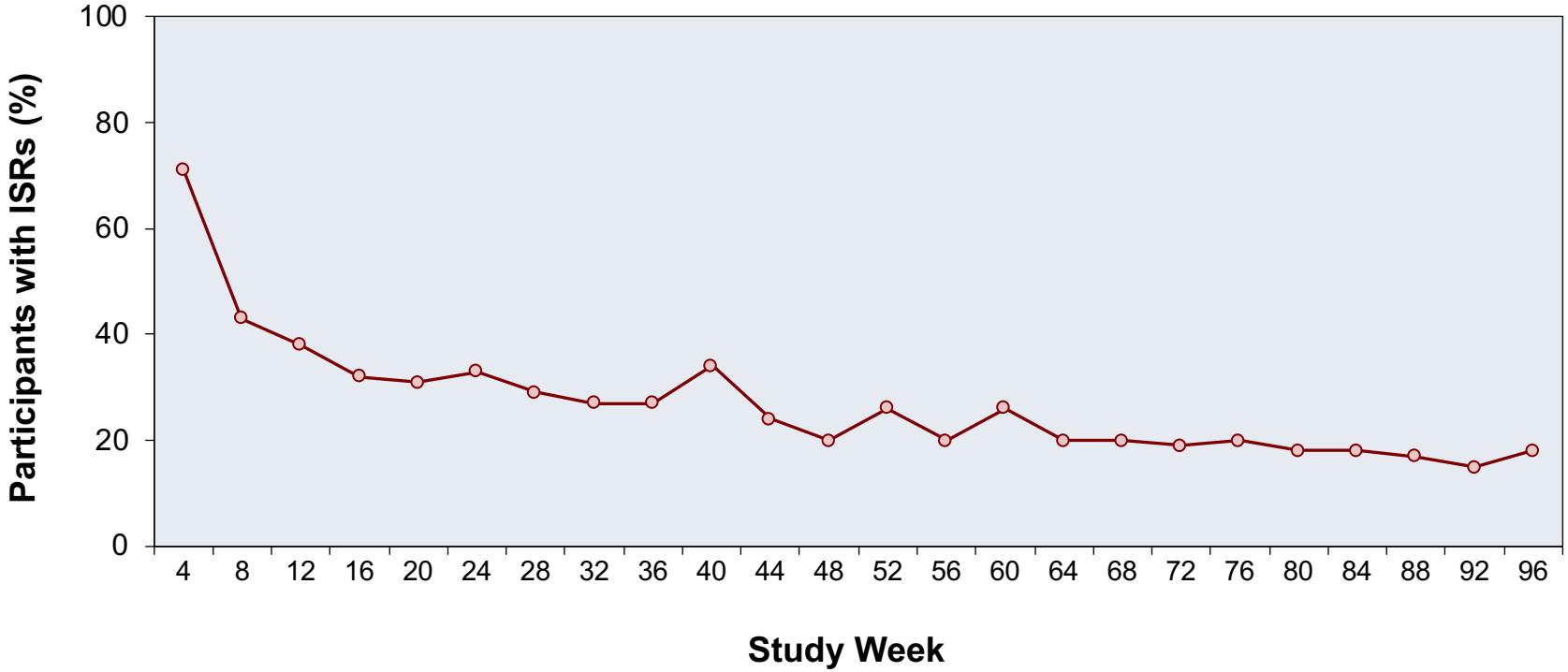
Source: Orkin C, et al. Lancet HIV. 2021;8:e185-e196.

Long-Acting IM Cabotegravir and IM Rilpivirine after Oral Induction FLAIR Study (96-Week Data): Adverse Events

Drug-Related Adverse Events and Injection Site Reactions (ISR)		
Drug-Related Adverse Event (AE)	**IM CAB + IM RPV** (n = 283)	**DTG-ABC-3TC** (n = 283)
Any AE, n (%)	246 (87)	33 (12)
Any AE, excluding ISR, n (%)	95 (34)	33 (12)
Grade 3 or 4 AE, n (%)	16 (6)	0
Serious AE, n (%)	1 (<1)	0
AE leading to withdrawal, n (%)	3 (1)	4 (1)

Source: Orkin C, et al. Lancet HIV. 2021;8:e185-e196.

Long-Acting IM Cabotegravir and IM Rilpivirine after Oral Induction FLAIR Study (96-Week Data): Injection Site Reactions (ISRs)



Source: Orkin C, et al. Lancet HIV. 2021;8:e185-e196.

Long-Acting IM Cabotegravir and IM Rilpivirine after Oral Induction FLAIR Study (96-Week Data): Conclusions

Interpretation: “The 96-week results reaffirm the 48-week results, showing long-acting cabotegravir and rilpivirine continued to be non-inferior compared with continuing a standard care regimen in adults with HIV-1 for the maintenance of viral suppression. These results support the durability of long-acting cabotegravir and rilpivirine, over an almost 2-year-long period, as a therapeutic option for virally suppressed adults with HIV-1.”

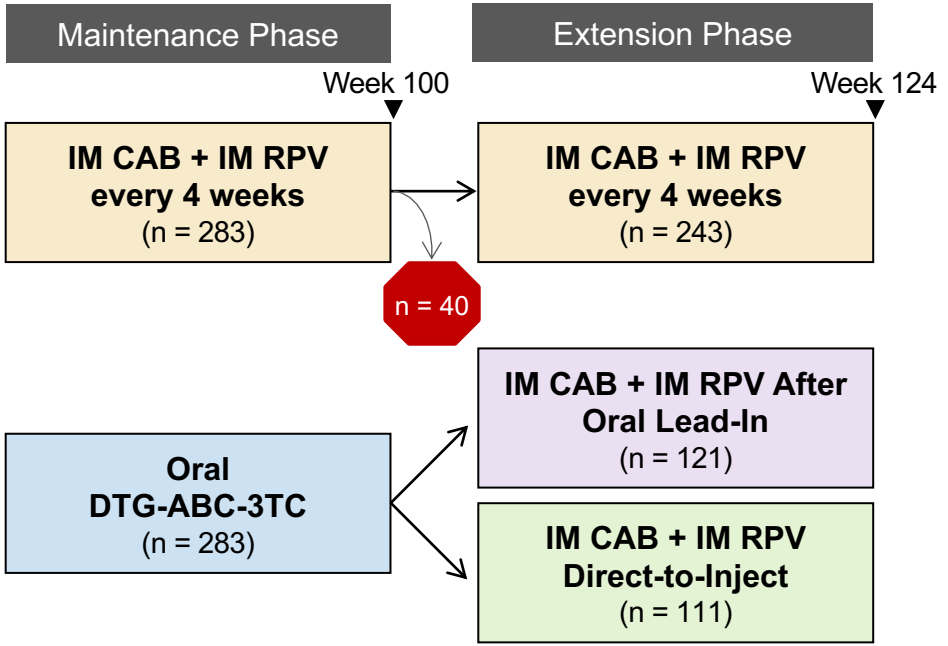
Source: Orkin C, et al. Lancet HIV. 2021;8:e185-e196.

Long-Acting Cabotegravir and Rilpivirine with Oral Lead In versus Direct-to-Inject

FLAIR Study: Week 124 Extension Phase

Long-Acting IM CAB and IM RPV With or Without Oral Lead In FLAIR Study (124-Week Extension): Design

- **Background**: Extension of phase 3, randomized, open-label trial assessing IM CAB + IM RPV compared to DTG-ABC-3TC for treatment-naïve adults
- **Inclusion Criteria**: After 100-week maintenance phase, participants receiving IM CAB + IM RPV every 4 weeks could choose to continue (*Continuation Group*) or withdraw; those assigned to oral ART could choose to transition (*Switch Group*) to IM CAB + IM RPV after oral lead in or without oral lead in ("direct to inject")

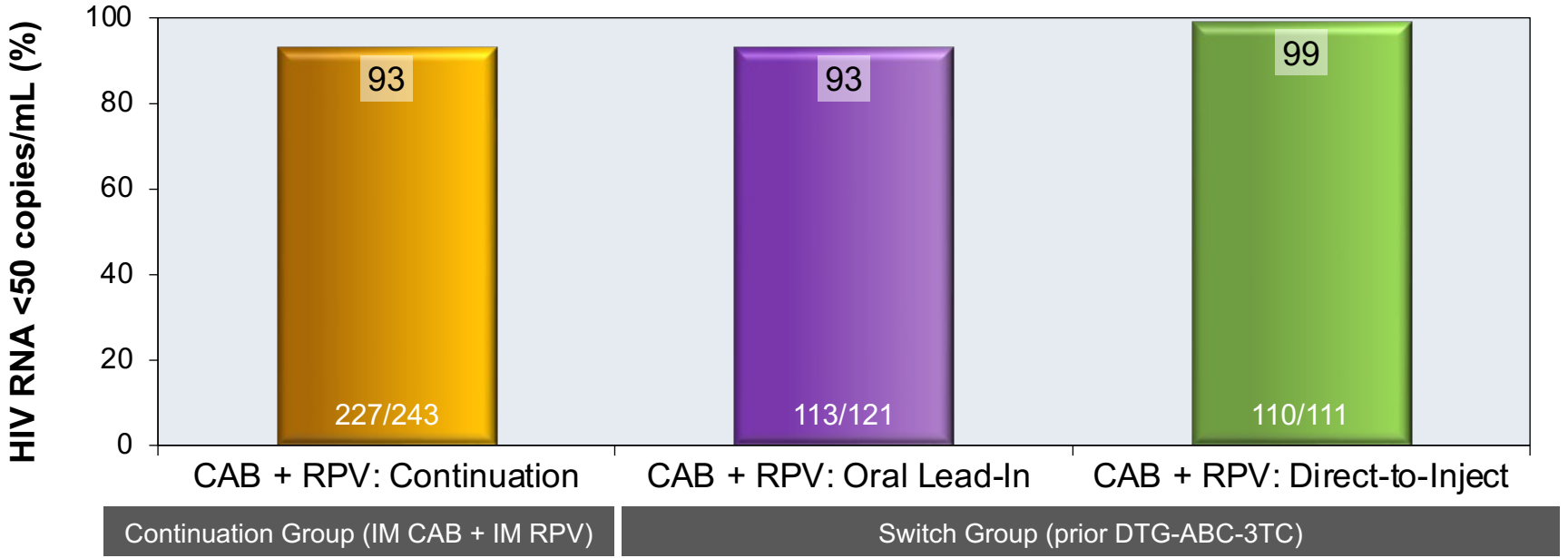


Oral lead in dosing: cabotegravir 30 mg daily and rilpivirine 25 mg daily x 4 weeks
Loading injections: cabotegravir 600 mg IM and 900 mg rilpivirine IM x 1
Maintenance injections: cabotegravir 400 mg IM and 600 mg rilpivirine IM monthly

Source: Orkin C, et al. Lancet HIV. 2021;8:e185-e196.

Long-Acting IM CAB and RPV With or Without Oral Lead In FLAIR Study (124-Week Extension): Results in Extension Phase

Virologic Responses During 24-Week Extension Phase



Continuation group: randomized to IM CAB + IM RPV at baseline and at week 100 opted to continue IM CAB + IM RPV until week 124.
Switch group: randomized to DTG-ABC-3TC and at week 100 switched to IM CAB + IM RPV with either oral lead in or direct-to-inject strategy

Source: Orkin C, et al. Lancet HIV. 2021;8:e185-e196.

Long-Acting IM CAB and RPV With or Without Oral Lead In FLAIR Study (124-Week Extension): Conclusion

Interpretation: “After 24 weeks of follow-up, switching to long-acting treatment with or without an oral lead-in phase had similar safety, tolerability, and efficacy, supporting future evaluation of the simpler direct-to-injection approach. The week 124 results for participants randomly assigned originally to the long-acting therapy show long-acting cabotegravir plus rilpivirine remains a durable maintenance therapy with a favourable safety profile.”

Source: Orkin C, et al. Lancet HIV. 2021;8:e185-e196.

Acknowledgments

The **National HIV Curriculum** is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of a financial assistance award totaling $1,021,448 with 0% financed with non-governmental sources. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government. For more information, please visit HRSA.gov. This project is led by the University of Washington's Infectious Diseases Education and Assessment (IDEA) Program.

AETC AIDS Education & Training Center Program

National HIV Curriculum

IDEA INFECTIOUS DISEASES EDUCATION & ASSESSMENT