# Cabotegravir plus Rilpivirine (*Cabenuva*)

## *Extended Release Injectable Suspension*

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# Cabotegravir and Rilpivirine (*Cabenuva*) *Indication*

- Replace antiretroviral regimen in persons with HIV RNA <50 copies/mL
- On stable antiretroviral regimen
- No history of treatment failure
- No known or suspected resistance to cabotegravir or rilpivirine

**Source: Cabenuva Prescribing Information**

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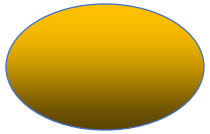
# Cabotegravir and Rilpivirine
## *Oral and Injectable Preparations*

### Oral: Lead-In for 1 Month




Cabotegravir 30 mg → INSTI

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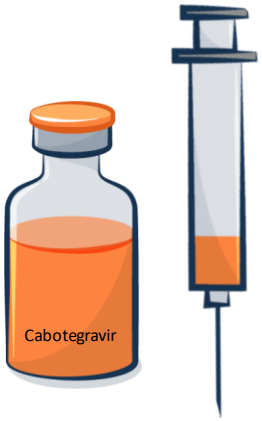
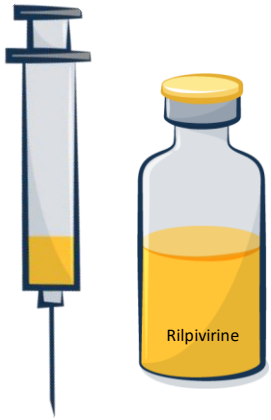
Rilpivirine 25 mg → NNRTI

### Injection: Loading Dose & Monthly




Cabotegravir 200 mg/mL → INSTI

\+

Rilpivirine 300 mg/mL → NNRTI

**Source: Cabenuva Prescribing Information**

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# Cabotegravir and Rilpivirine (*Cabenuva*) *Dosing Schedule*

**Oral Lead-In x 1 month (≥28 days)**

Cabotegravir 30 mg daily +
Rilpivirine 25 mg daily

***Initiation Injections (x 1)**

Cabotegravir (600 mg): 3 mL IM +
Rilpivirine (900 mg): 3 mL IM

***Continuation Injections (Monthly)**

Cabotegravir (400 mg): 2 mL IM +
Rilpivirine (600 mg): 2 mL IM

*Administer injections at opposite gluteal sites (or at least 2 cm apart) and give both during the same visit.

**Source: Cabenuva Prescribing Information**

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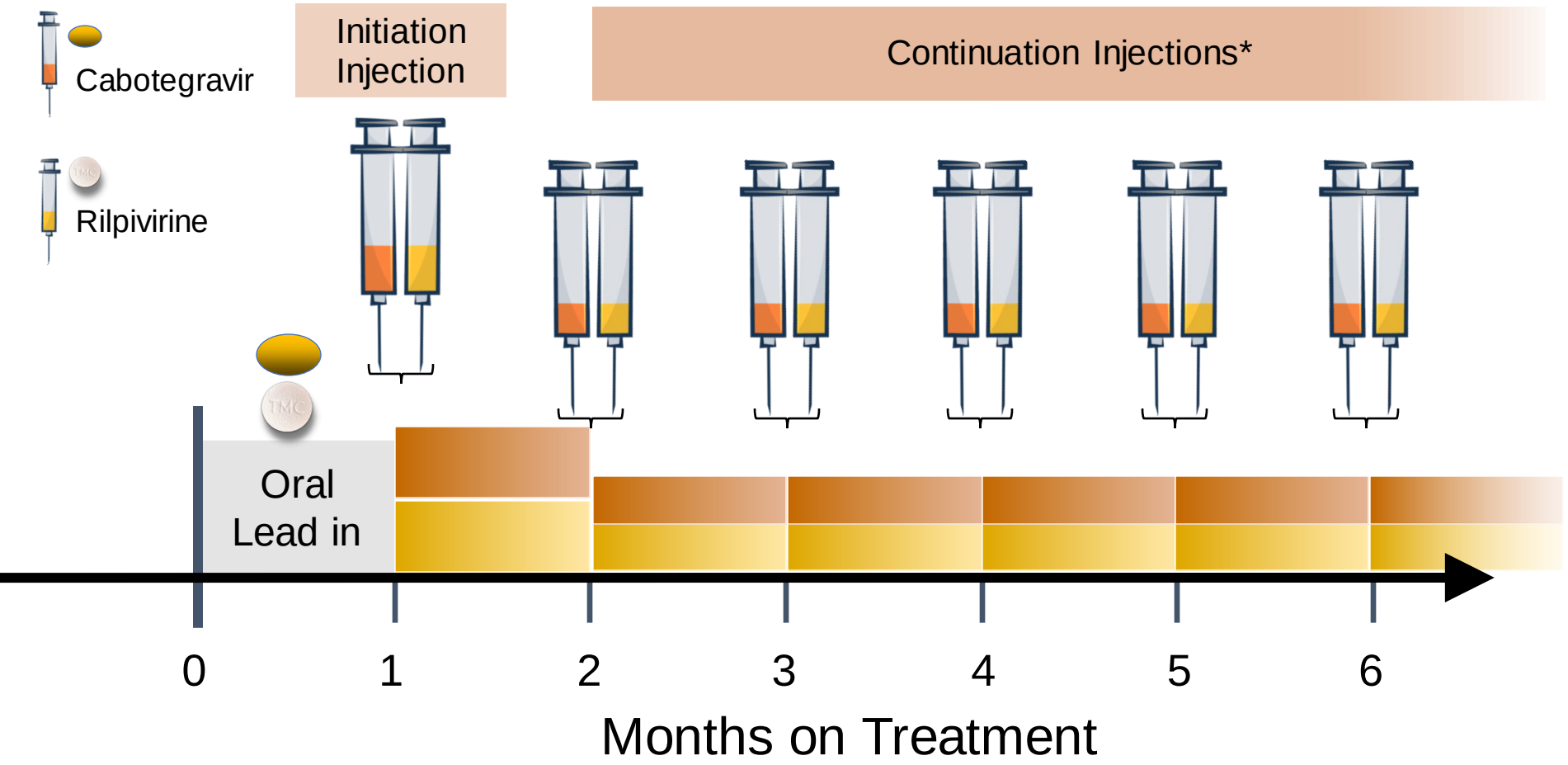
# Cabotegravir and Rilpivirine Extended-Release Injectable Suspension

## *Dosing Schedule*




*Patients may receive cabotegravir and rilpivirine up to 7 days before or after the date of the scheduled monthly injection dosing visit.

**Source: Cabenuva Prescribing Information**

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# Summary of Key Phase 3 Studies
# Cabotegravir and Rilpivirine Long-Acting Injectable

- Phase 3 Trials in Treatment Experienced
  - ATLAS: Switch to monthly IM CAB-RPV or stay on 3-drug ART
  - ATLAS-2M: switch to IM CAB-RPV every 4 or 8 weeks
- Phase 3 Trials in Treatment Naïve
  - FLAIR: IM CAB-RPV every month versus oral DTG-ABC-3TC

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Long-Acting Cabotegravir and Rilpivirine for HIV Maintenance

# ATLAS Study

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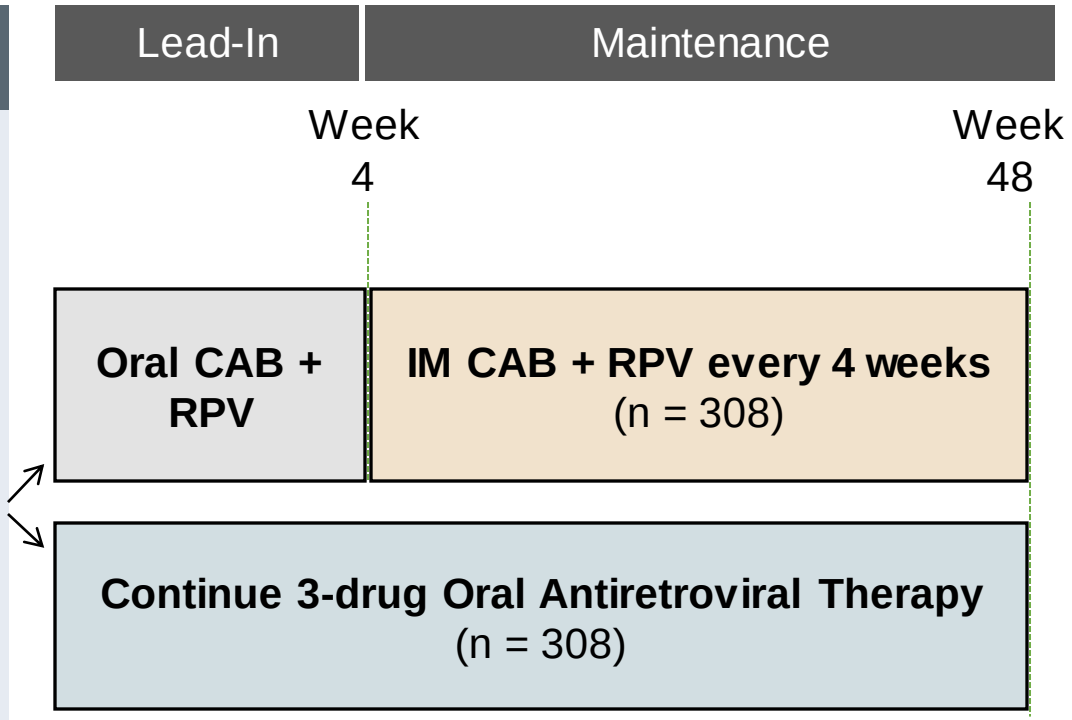
# Long-Acting IM Cabotegravir and Rilpivirine for HIV Maintenance
# ATLAS Study: Design

**Study Design:**

- **Background**: Phase 3, randomized, open-label trial assessing IM cabotegravir plus IM rilpivirine after oral induction for adults taking a 3-drug oral antiretroviral therapy regimen
- **Inclusion Criteria**
  - Age ≥18 years
  - Taking 2NRTI + INSTI, NNRTI, or PI
  - Stable ARV regimen ≥6 months
  - HIV RNA <50 copies/mL ≥6 months
  - No history of virologic failure
  - No INSTI or NNRTI resistance (K103N allowed)
  - No chronic hepatitis B




Abbreviations: CAB = cabotegravir; RPV = rilpivirine

Source: Swindells S, et al. N Engl J Med. 2020;382:1112-23.

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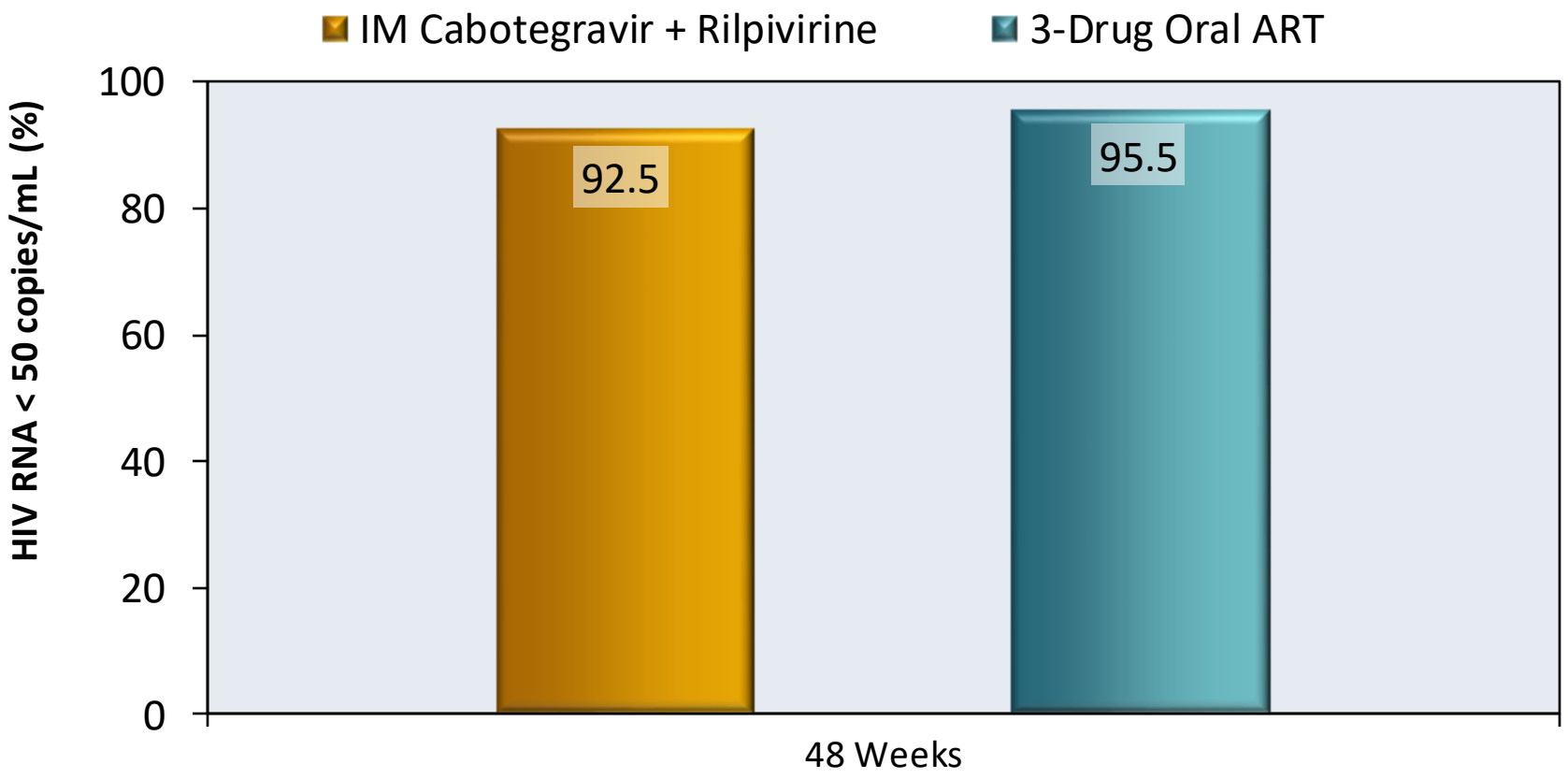
# Long-Acting IM Cabotegravir and Rilpivirine for HIV Maintenance ATLAS Study: Results

## Weeks 48: Virologic Response by FDA Snapshot Analysis




HIV RNA ≥50 copies/mL at 48 weeks: 1.6% CAB + RPV, 1.0% 3-drug oral ART

**Source: Swindells S, et al. N Engl J Med. 2020;382:1112-23.**

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Cabotegravir and Rilpivirine Every 2 Months for HIV Maintenance

# ATLAS-2M

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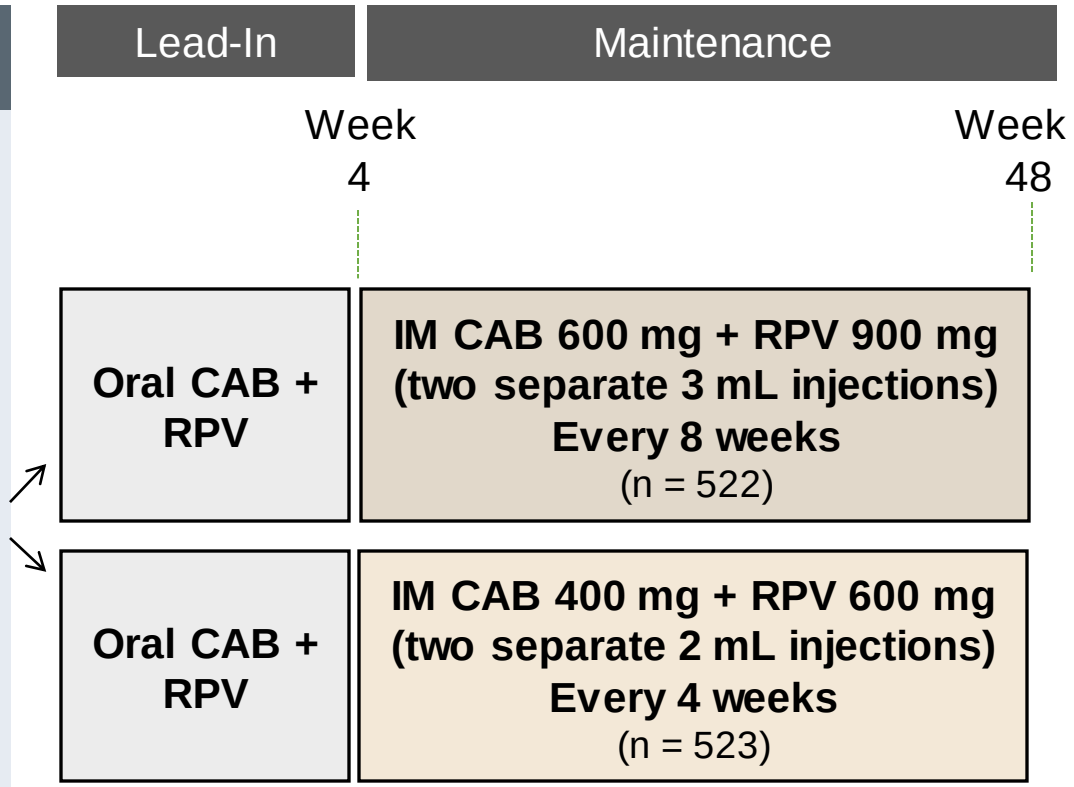
# Cabotegravir and Rilpivirine Every 2 Months for HIV Maintenance
# ATLAS-2M Study: Design

**Study Design:**

- **Background**: Phase 3, randomized, open-label trial assessing IM CAB-RPV maintenance ART administered every 8 weeks versus every 4 weeks
- **Inclusion Criteria***
  - Age ≥18 years
  - Taking an uninterrupted first or second oral standard of care ART regimen for ≥6 months
  - HIV RNA <50 copies/mL ≥6 months at screening and >2x in prior year
  - No history of virologic failure
  - No INSTI or NNRTI resistance (K103N allowed)




*Some individuals enrolled after participating in the ATLAS trial; individuals already receiving IM CAB + RPV through ATLAS did not require oral lead-in for ATLAS-2M

Source: Overton ET, et al. Lancet. 2020:396:1994-2005.

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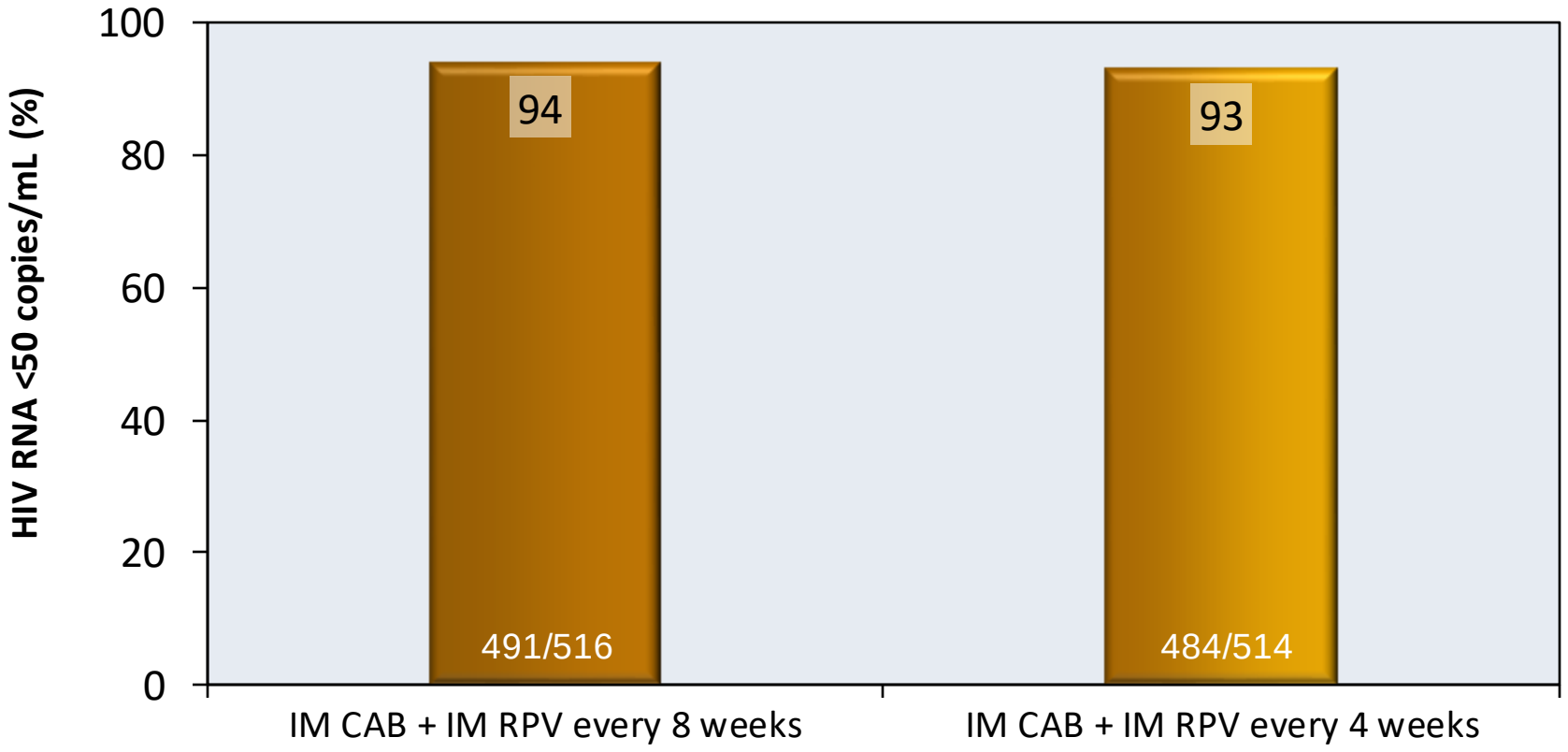
# Cabotegravir and Rilpivirine Every 2 Months for HIV Maintenance ATLAS-2M Study: Results

## Weeks 48: Virologic Response by FDA Snapshot Analysis




HIV RNA ≥50 copies/mL at 48 weeks: 9/522 (2%) in q8-week arm, 5/523 (1%) in q4-week arm

**Source: Overton ET, et al. Lancet. 2020:396:1994-2005.**

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Long-Acting Cabotegravir and Rilpivirine after Oral Induction

# FLAIR Study

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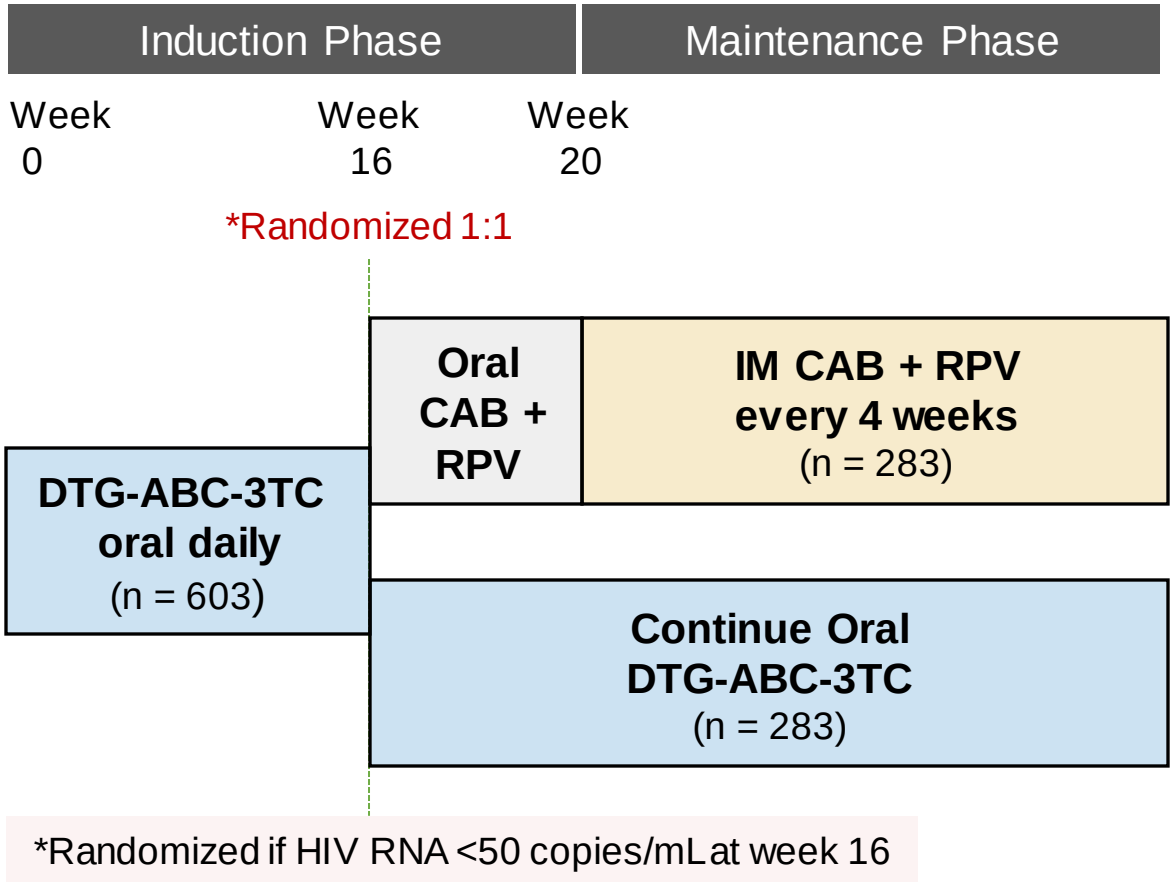
# Long-Acting IM Cabotegravir and Rilpivirine after Oral Induction FLAIR Study: Design

## Study 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.**

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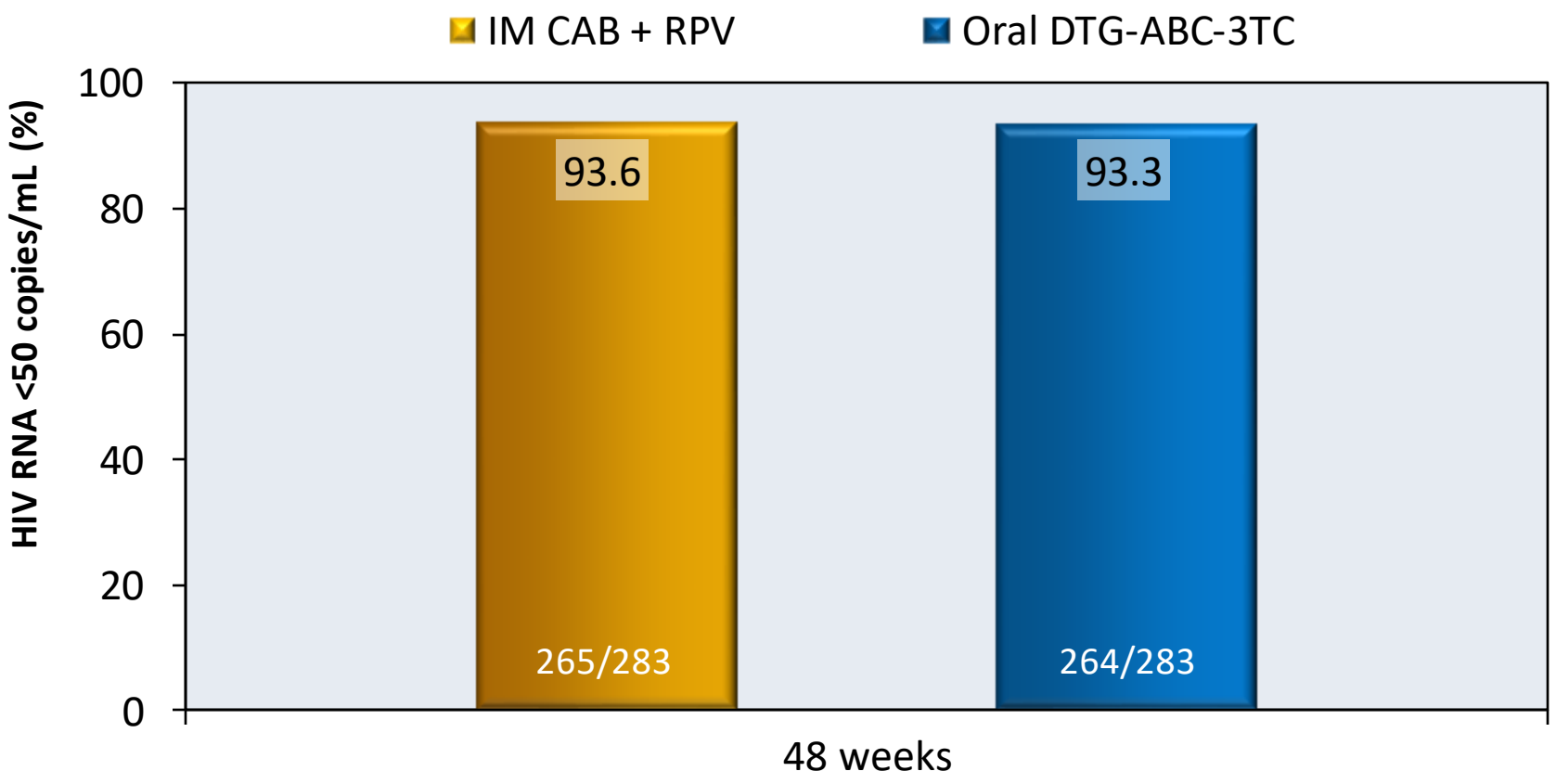
# Long-Acting IM Cabotegravir and Rilpivirine after Oral Induction FLAIR Study: Results

## 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.**

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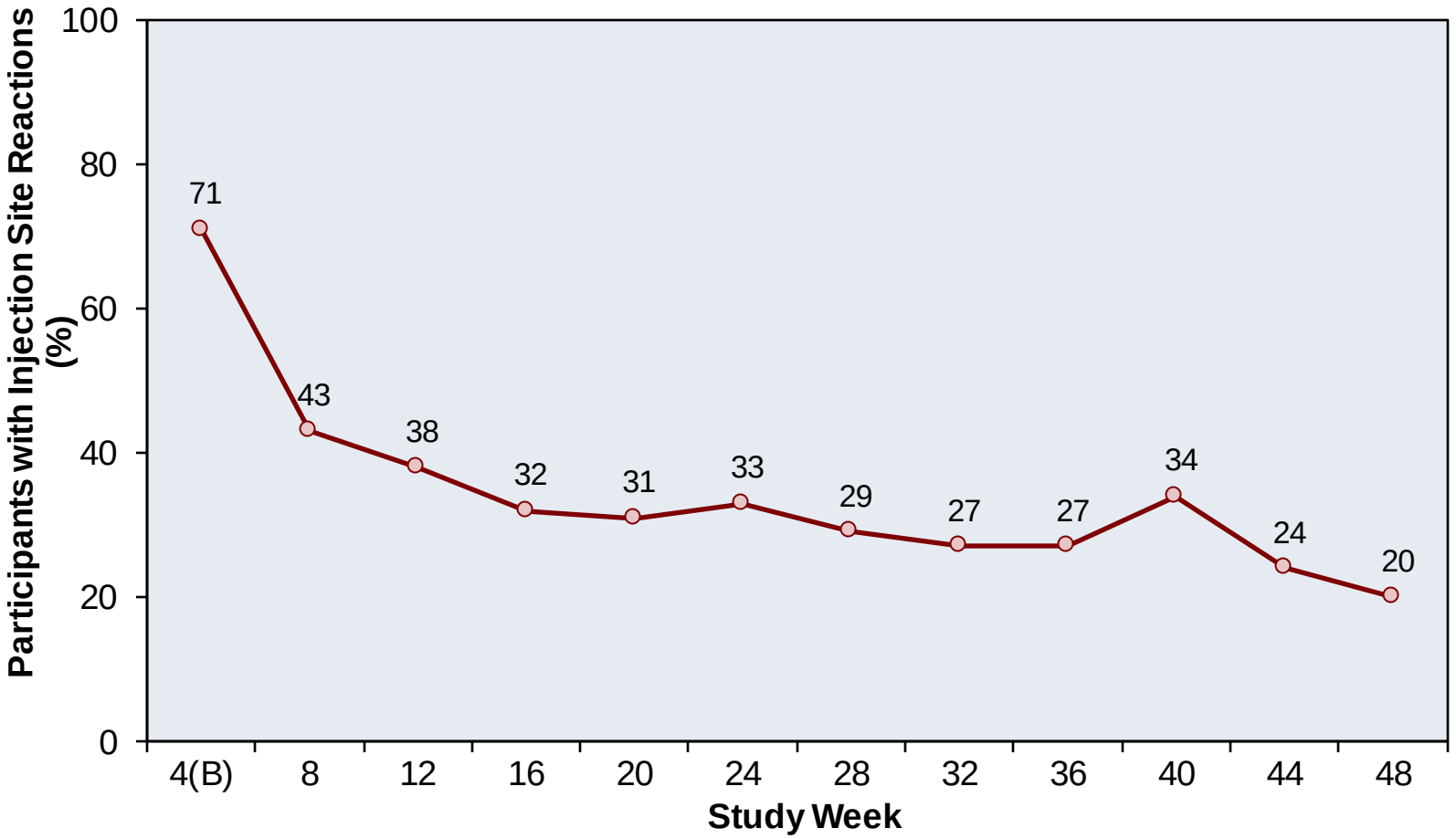
# Adverse Effects

# Long-Acting IM Cabotegravir and Rilpivirine after Oral Induction FLAIR Study: Injection Site Reactions

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

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# Resistance

# Emergence of Drug Resistance on Cabotegravir + Rilpivirine
# Pooled analysis from FLAIR, ATLAS, ATLAS-2M

- 7/591 (1.2%) with virologic failure (HIV RNA ≥200 copies/mL)
- 5 of 7 had baseline HIV-1 subtype A1 and L74I polymorphic accessory mutation
- 2 of 7 had baseline HIV-1 subtype AG and without L74I mutation
- 6 of 7 from Russia (prevalence of HIV-1 subtypes A, A1, AG high in Russia)*
- HIV-1 subtypes A, A1, AG are uncommon in U.S. (B subtype dominant)
- 2 of 7 developed Q148R mutation
- 1 of 7 developed N155H

*HIV-1 subtypes A, A1, AG are uncommon in United States (HIV-1 B subtype dominant)

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# Special Dosing Considerations

# Timing Flexibility of Cabotegravir and Rilpivirine Injections

What if they arrive 3 days early for their injection?

What if they are 5 days late for their injection?

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# Timing Flexibility of Cabotegravir and Rilpivirine Injections

What if they arrive 3 days early for their injection?

What if they are 5 days late for their injection?

Patients may receive cabotegravir and rilpivirine up to 7 days before or after the date of the scheduled monthly injection dosing visit.

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# Planned Missed Cabotegravir and Rilpivirine Injections (Time from last injections is greater than 1 month + 7 days)

What if they they are traveling out of country and are planning to miss at least 1 injection?

*Oral therapy = cabotegravir 50 mg plus rilpivirine 25 mg, both taken once daily with food

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# Planned Missed Cabotegravir and Rilpivirine Injections (Time from last injections is greater than 1 month + 7 days)

## What if they they are traveling out of country and are planning to miss at least 1 injection?

- Take daily oral therapy to replace up to 2 consecutive monthly injection visits.
- Start oral therapy* approximately 1 month after the last injection doses.
- Continue oral therapy* until the day injection dosing is restarted.

*Oral therapy = cabotegravir 50 mg plus rilpivirine 25 mg, both taken once daily with food

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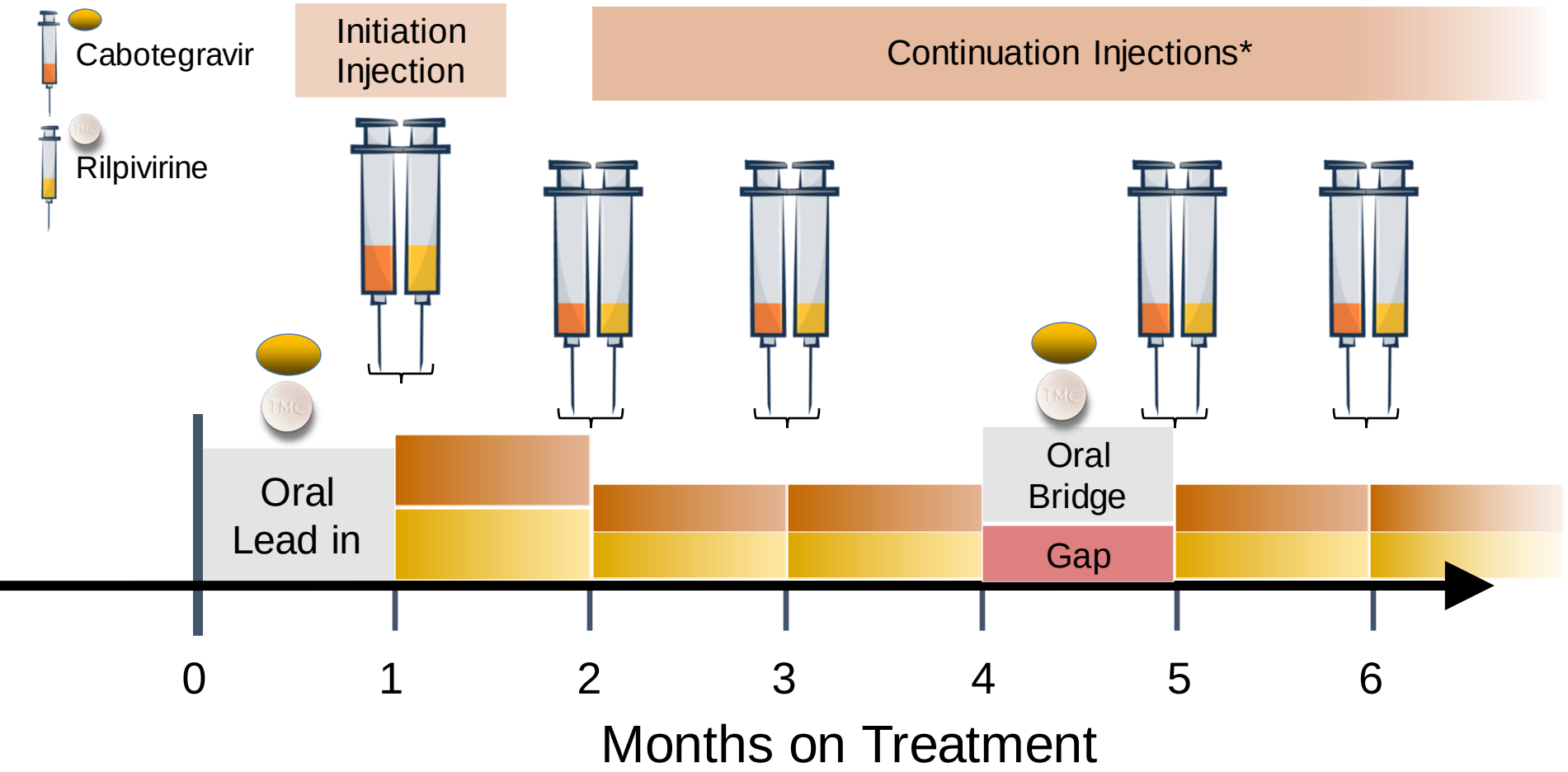
# Cabotegravir and Rilpivirine
## *Dosing Schedule with Oral Bridge (up to 2 months)*




*Patients may receive cabotegravir and rilpivirine up to 7 days before or after the date of the scheduled monthly injection dosing visit.

**Source: Cabenuva Prescribing Information**

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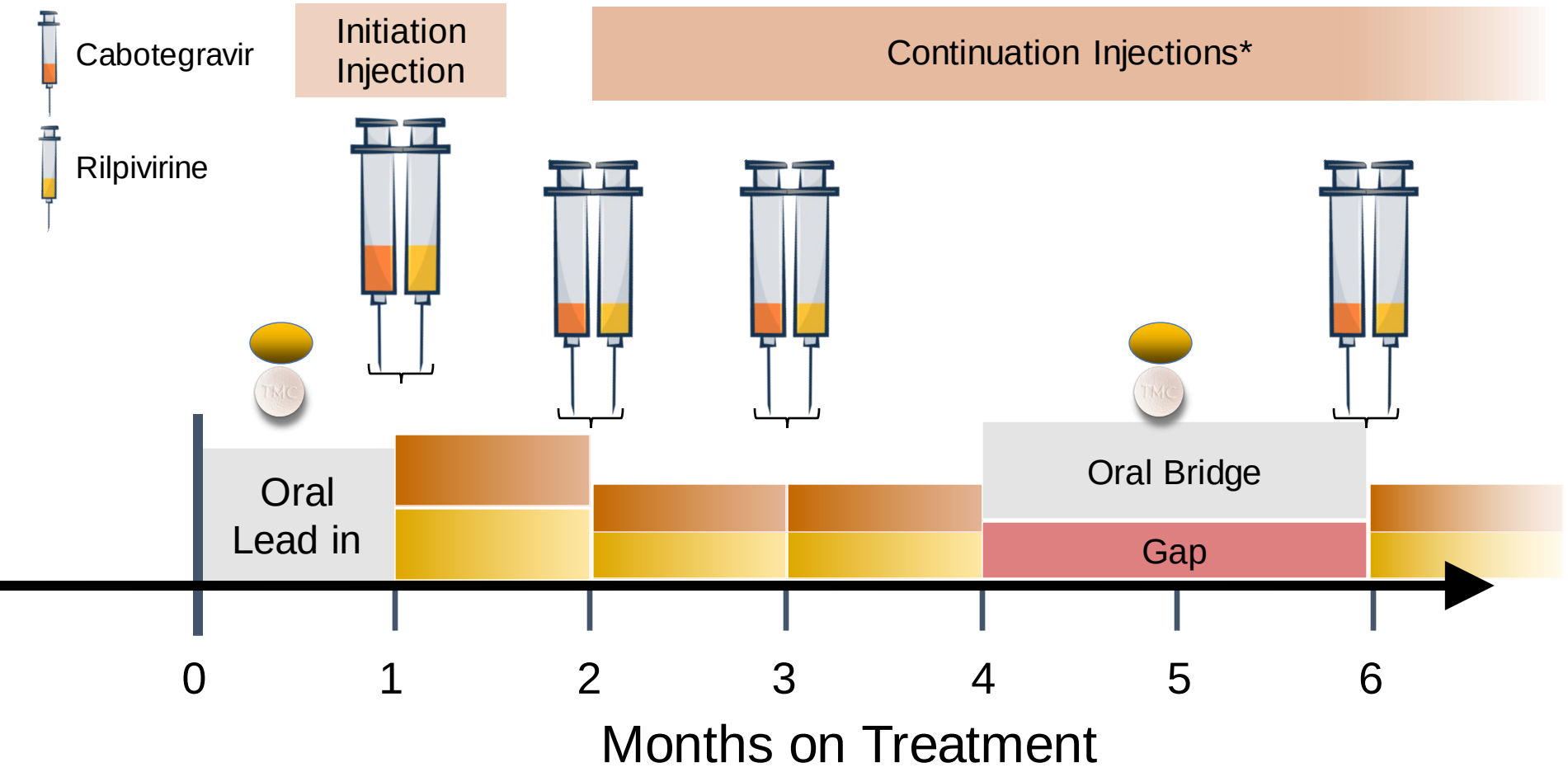
# Cabotegravir and Rilpivirine
## *Dosing Schedule with Oral Bridge (up to 2 months)*




*Patients may receive cabotegravir and rilpivirine up to 7 days before or after the date of the scheduled monthly injection dosing visit.

**Source: Cabenuva Prescribing Information**

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# Timing Flexibility of Cabotegravir and Rilpivirine Injections

What if they temporarily drop out of care and miss >1 injections?

# Recommendation for Resumption of Injections After Missed Injections (>1 month + 7 days)

- If oral therapy has not been taken…
  - Reassess to ensure resumption of injections is appropriate
- Time Since last injection ≤2 months
  - Resume with 2 mL standard monthly dosing
- Time Since last injection >2 months
  - Resume with 3 mL x 1 initiation dose, followed by 2 mL monthly dose

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AETC AIDS Education & Training Center Program Mountain West