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

**Induction Phase**
- 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

**Maintenance Phase**
- *Randomized 1:1
- IM CAB + IM RPV every 4 weeks (n = 283)
- Continue DTG-ABC-3TC (n = 283)

*Randomized if HIV RNA <50 copies/mL at week 16

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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>IM CAB + IM RPV (n = 283)</th>
<th>DTG-ABC-3TC (n = 283)</th>
<th>Overall (n = 566)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median</td>
<td>34</td>
<td>34</td>
<td>34</td>
</tr>
<tr>
<td>Female, n, %</td>
<td>63 (22)</td>
<td>64 (23)</td>
<td>127 (22)</td>
</tr>
<tr>
<td>White, n, %</td>
<td>216 (76)</td>
<td>201 (71)</td>
<td>417 (74)</td>
</tr>
<tr>
<td>Black, n, %</td>
<td>47 (17)</td>
<td>56 (20)</td>
<td>103 (18)</td>
</tr>
<tr>
<td>Median body-mass index</td>
<td>24</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>CD4 count &lt;200 cells/mm³, n, %</td>
<td>16 (6)</td>
<td>23 (8)</td>
<td>39 (7)</td>
</tr>
<tr>
<td>CD4 count ≥500 cells/mm³, n, %</td>
<td>108 (38)</td>
<td>108 (38)</td>
<td>216 (38)</td>
</tr>
<tr>
<td>HIV RNA ≥200k copies/mL, n, %</td>
<td>26 (9)</td>
<td>23 (8)</td>
<td>39 (7)</td>
</tr>
<tr>
<td>HIV RNA 10k-50k copies/mL, n, %</td>
<td>95 (34)</td>
<td>113 (40)</td>
<td>208 (37)</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Country; HIV-1 Subtype</th>
<th>At Baseline</th>
<th>At Virologic Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV RNA</td>
<td>INSTI RAMs</td>
</tr>
<tr>
<td>Russia; A1</td>
<td>54,000 copies/mL</td>
<td>L74I</td>
</tr>
<tr>
<td>Russia; A1</td>
<td>23,000 copies/mL</td>
<td>L74I</td>
</tr>
<tr>
<td>Russia; A1</td>
<td>20,000 copies/mL</td>
<td>L74I</td>
</tr>
</tbody>
</table>

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

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

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

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.

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.”
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)

- **IM CAB + IM RPV**
  - 245/283
  - 87

- **Oral DTG-ABC-3TC**
  - 253/283
  - 89

*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)

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

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

<table>
<thead>
<tr>
<th>Drug-Related Adverse Event (AE)</th>
<th>IM CAB + IM RPV (n = 283)</th>
<th>DTG-ABC-3TC (n = 283)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE, n (%)</td>
<td>246 (87)</td>
<td>33 (12)</td>
</tr>
<tr>
<td>Any AE, excluding ISR, n (%)</td>
<td>95 (34)</td>
<td>33 (12)</td>
</tr>
<tr>
<td>Grade 3 or 4 AE, n (%)</td>
<td>16 (6)</td>
<td>0</td>
</tr>
<tr>
<td>Serious AE, n (%)</td>
<td>1 (&lt;1)</td>
<td>0</td>
</tr>
<tr>
<td>AE leading to withdrawal, n (%)</td>
<td>3 (1)</td>
<td>4 (1)</td>
</tr>
</tbody>
</table>

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

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.”

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

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

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.”

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