Update From vCROI 2021

Financial Relationships With Commercial Entities
Dr Lennox has received research support from ViiV Healthcare. (Updated 04/24/21)

Learning Objectives
After attending this presentation, learners will be able to:
- Explain the results of treatment with a maturation and with a capsid inhibitor
- Advise their patients regarding weight gain and bone loss on ART
- Use SARS-CoV-2 mAbs for treatment and prevention
CROI 2021 - Statistics

- Abstracts accepted: 698
- Oral abstracts: 109
  - 17 Late breaker
- Posters: 589
- SARS-COV-2: 161 (23%)

New ARVs

GSK 3640254 – Maturation Inhibitor

- Small Phase IIA dose-ranging study in 6 patients per dose

Primary endpoint: maximum change from Day 1 in plasma HIV-1 RNA during parts 1 and 2
GSK 3640254 – Maturation Inhibitor

- Phase 1: resistance emerged in the high dose, 10-day arm
- Phase 2: No resistance in 7-day arm, good antiviral activity

Lenacapavir – Capsid Inhibitor

- Potent antiviral at the picomolar level against all HIV-1 subtypes
- Active against clinical isolates with resistance to other ART
- Half-life compatible with once weekly dosing
- Single Sub-Q dose produced HIV RNA reduction of ~2 log

Lenacapavir – Drug interaction Study

- Administered with DRV/r (3A4 inhibitor), ATV/r (UGT1A1 + PgP inhibition), Rifampin (3A4/PgP/UGT inducer), Famotidine
- Minimal effect with PI, acid reducer
- Do not use Rifampin with Lenacapavir
Lenacapavir in Treatment Experienced

Key eligibility criteria:
- FV1 > 10% viral suppression
- Resistant to 4-12 drugs
- 2-3 live active agents

Randomized cohort (double blind)

Nonrandomized cohort (open label)

Functional Monotherapy

- SC LEN
- Failing regimen
- OBR

Maintenance

- SC LEN
- QM for 22 weeks
- OBR

Segal-Maurer CROI 2021

Funcional Monotherapy

With OBR

- Injection Site Reactions in 33/72, mostly mild
- 2/72 participants developed LEN resistance

Lenacapavir - Results

MK8507 - NNRTI

- Resistance profile similar to Doravirine
- Plasma 11/2~70 hours suitable for once weekly dosing

MK8507 has potency changes <5-fold against common NNRTI resistance-associated variants (K103N, Y181C, G190A)

Diamond CROI 2021
MK8507 – Single Dose Antiviral Potency

- Plan – Once weekly Islatravir + MK8507 for HIV treatment

ARV Strategies & Complications

DRV/c/FTC/TAF v. DTG/3TC/ABC – SYMTRI

- Randomized, open label, non-Inferiority, Rx naïve, 316 patients, >90% men
- Primary endpoint HIVRNA <50c/ml @ 48 wk, 10% NI
- DRV/c/FTC/TAF not non-inferior to DTG/3TC/ABC
- No difference in weight gain (~3kg)
**DRV/r vs DTG for second line - NADIA**

- Compared DRVr v DTG, and TDF/3TC v AZT/3TC
- Failing NNRTI based therapy, no resistance testing - Similar to WHO TLD plan

**Efficacy outcomes: DTG vs DRV/r**

- 58% TDF resistant and 92% 3TC resistant at switch
- TLD switch for NNRTI failure may result in DTG resistance

**Continued Follow up of DTG/3TC – Week 144**

- Naïve trials of DTG/3TC vs DTG+3TC/TDF
- After week 96 open label
- Week 144 data on ~1250
- During 48 weeks extension DTG/3TC gained 1.3kg more weight than 3 drug arm, no differences by race or sex
Naïve BIC/FTC/TAF – Metabolic Outcomes

- Week 192 open label extension of trials #1489, #1490
- BMD changes maximal at 16 weeks (-0.9% spine, -1.4% hip), no change thereafter

![Weight Changes From Baseline Through Week 192 on B/F/TAF](image-url)

Efficacy BIC/FTC/TAF – Baseline ARV Resistance

- In naïve trials (1489/1490) subjects excluded if baseline RT resistant, not NNRTI resistant
- Retrospective deep sequencing for resistance to INI, RT, NNRTI, PI

<table>
<thead>
<tr>
<th>Baseline Resistance</th>
<th>HIV RNA &lt;50c @ wk 48</th>
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<tbody>
<tr>
<td>BIC/FTC/TAF</td>
<td>DTG+ ABC/3TC or FTC/TAF</td>
</tr>
<tr>
<td>NRTI</td>
<td>21/21 (100)</td>
</tr>
<tr>
<td>NNRTI</td>
<td>81/82 (99)</td>
</tr>
<tr>
<td>PI</td>
<td>18/18 (100)</td>
</tr>
<tr>
<td>INSTI</td>
<td>7/7 (100)</td>
</tr>
</tbody>
</table>

Effect of HIV status on CVD Risk

- Population: Kaiser N. California
- 8285 HIV+, 179,517 HIV-
- CVD events and treated risk factors analyzed 2013-17

![Effect of HIV status on CVD Risk](image-url)

Treated HIV increased CVD risk, as did well controlled HTN
Preventing Bone Loss Due to ARV-

- Ofotokun showed that bone loss was prevented with one-time long-acting injectable bisphosphonate given at ART initiation
- APART study compared oral Alendronate 70mg weekly for 14 weeks vs placebo in ART naive
- Analysis stratified by gender and ART type. ART was primarily TDF and INSTI based

Alendronate to Prevent Bone Loss

COVID-19
Convalescent Plasma for Severe COVID-19
- 14 sites in the Netherlands performed a Randomized trial of CP
- SARS-CoV-2 within 96 hours, not on Mechanical Ventilation > 96 hrs
- Plasma selected to have high titer antibody
- Trial Stopped for Futility
  - No difference in mortality
  - No difference in time to discharge

BLAZE 2 – Bamlanivimab Prophylaxis
- Nursing homes with COVID+ residents
- Bam 4200mg IV vs. placebo, 1:1 as prevention
- 1 outcome: Prevention of symptomatic COVID-19 + no disease progression
- 2 outcome: Prevention of all COVID-19
- 1,175 persons enrolled (residents and employees). 29% > 65 years (78% of residents).
- 4 deaths in the Placebo arm, no deaths in the BAM arm
- NP Viral load was lower in those in the BAM arm who became infected
Casirivimab + Imdevimab – Prophylaxis

- Interim analysis in household contacts of COVID-19 randomized SubQ injection 1.2g Combo mAb v. PLA
- Mean age 45, 78% White, 53% female

- Symptomatic COVID-19
  - 4.0 (95% CI: 0.05, 0.40)
  - 0.9 (95% CI: 0.10, 0.37)

- Asymptomatic COVID-19
  - 0.8 (95% CI: 0.30, 1.12)

O’Brien CROI 2021

Bamlanivimab + Etesevimab Treatment

- Phase 3 follow up to Phase 2 study (JAMA)
- Mild–Moderate COVID diagnosed within 72 hours and ≥1 risk factor for progression to severe disease
- Randomized to BAM + ETS (both 2800mg) IV v. PLA
- 1035 enrolled, >90 White, 52% female, 31% ≥ age 65, Mean BMI 32

- COVID-19 related hospitalization or all-cause death by Day 29

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>Events</th>
<th>Rate (%)</th>
</tr>
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<tbody>
<tr>
<td>Placebo</td>
<td>533</td>
<td>45</td>
<td>7.5%</td>
</tr>
<tr>
<td>Bamlanivimab 2000 mg + Etesevimab 2000 mg</td>
<td>500</td>
<td>11</td>
<td>2.2%</td>
</tr>
</tbody>
</table>

- All 10 Deaths occurred in the placebo arm

Bamlanivimab + Etesevimab Results

- Initial v. day 7
  - Day 1: 0.02, 0.01
  - Day 2: 0.01, 0.01
  - Day 3: 0.005, 0.005
  - Day 4: 0.005, 0.005
  - Day 5: 0.005, 0.005
  - Day 14: 0.005, 0.005

Dougan CROI 2021
Question-and-Answer Session