This presentation is intended for educational use only, and does not in any way constitute medical consultation or advice related to any specific patient.
The majority of HIV+ persons in care in the US do well and achieve viral suppression.
Antiretroviral Therapy Issues

- The majority of HIV+ persons *in care* in the US do well and achieve viral suppression (*but we need this for all!*)

![Graph showing retention in care, ART prescription, and viral suppression rates.](image-url)
LATTE-2: CABOTEGRAVIR + RILPIVIRINE AS LONG-ACTING MAINTENANCE THERAPY: WEEK 32 RESULTS

Abstract 31LB
LATTE-2: Long Acting Cabotegravir + Rilpivirine

• Cabotegravir
  - Novel integrase inhibitor
  - Analogue of dolutegravir
  - 2 formulations:
    • Oral: $T_{1/2}$ 40 hours (previous phase 2 study showed efficacy & safety 30-90 mg/day)
    • LA nanosuspension $T_{1/2}$ 20-40 days (200 mg/mL)

• Rilpivirine
  - FDA approved NNRTI (25 mg/day PO)
  - LA nanosuspension $T_{1/2}$ ~30-90 days (300 mg/mL)

Margolis, D et al. CROI 2016
LATTE-2: Study Design and Participants

• Primary Objectives:
  - Safety & efficacy of LA-cabotegravir + LA-rilpivirine for maintenance ART
  - Select a dose for further study

• Study Design:
  - Multicenter, randomized, open-label, phase 2
  - Oral Induction, then parenteral maintenance phase

• Participants:
  - Age >18 years
  - HIV+
  - Antiretroviral therapy naïve
  - CD4 >200
  - No active hepatitis B

Margolis, D et al. CROI 2016
LATTE-2: Participants and Study Overview

309 pts: 91% male, 15% AA, VL 4.3 log₁₀, 18% >100K, CD4 489

- CAB 30 mg + ABC/3TC PO for 20 wks
- 400 mg CAB + 600 mg RPV IM q4 wks (N=115)*
- 600 mg CAB + 900 mg RPV IM q8 wks (N=115)**
- CAB + ABC/3TC PO q day (N=56)

Induction Phase (24 wks)

- VL<50 on PO
- +PO RPV 4 wks

Maintenance Phase (96 wks)

- 289 entered maintenance
- 2 injections of 2 or 3 mL at a time
- 1° endpoint: VL %< 50 by FDA snapshot analysis
- 32 wk results

* Loading dose of CAB at day 1
** Loading doses of CAB at day 1 & wk 4

Margolis, D et al. CROI 2016
LATTE-2 Week 32 Primary Virologic Results

% with HIV RNA <50 c/mL

Margolis D, et al. CROI 2016
Latte-2: Injection Site Reactions (ISRs)

- 2282/4286 (53%)
- Resulted in 2 pts. D/C in q8w (1%)
- Characteristics
  - Pain 67%
  - Swelling 7%
  - Nodules 6%
- Median duration 3 days
- No differences in rates, grades, duration between arms
- Rates decreased over time (86% day 1 to 33% wk 32)
- Participant questionnaire:
  - Satisfaction/willingness to continue current arm: 98% in both IM arms vs 71% PO arm

<table>
<thead>
<tr>
<th>ISR Grade</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>82%</td>
</tr>
<tr>
<td>2</td>
<td>17%</td>
</tr>
<tr>
<td>3</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>

Margolis D et al, CROI 2016
# Latte-2: Viral Failure and Toxicity Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Q 4 wk N=115</th>
<th>Q 8 wk N=115</th>
<th>PO N=56</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virologic Failure</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>No resistance</td>
</tr>
<tr>
<td><strong>Toxicities:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grades 3-4</td>
<td>10%</td>
<td>9%</td>
<td>2%</td>
<td>Without ISRs</td>
</tr>
<tr>
<td>SAEs</td>
<td>5%</td>
<td>6%</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>AEs leading to D/C</td>
<td>5%</td>
<td>2%</td>
<td>2%</td>
<td></td>
</tr>
<tr>
<td><strong>New Grade 3-4 in</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Maintenance Phase</strong></td>
<td>17%</td>
<td>15%</td>
<td>14%</td>
<td></td>
</tr>
</tbody>
</table>

Most common non-ISR toxicities overall: fever, fatigue, flu-like symptoms in 2-4% each group

Day 1: nausea, headache fatigue
LATTE-2: Conclusions

- High success rate in both dosing groups (as maintenance ART)
- Patients reported high satisfaction
- PK:
  - CAB concentrations similar to 10 & 30 mg oral doses in prior study
  - Lower RPV levels during the initial few weeks than PO
- Potential for novel intermittent parenteral dosing regimen (but many challenges)
- Dose to go forward not yet chosen – looking to 48 week results
SWITCHING TENOFOVIR DF TO TENOFOVIR ALAFENAMIDE IN VIROLOGICALLY SUPPRESSED ADULTS

GS311-1089 WEEK 48 RESULTS

Abstract 29
Tenofovir-DF (TDF) and Tenofovir Alafenamide (TAF)

- **TDF**: 1st line N(t)RTI recommended in U.S & globally
- **TAF** is a novel tenofovir prodrug
  - 91% lower plasma levels than TDF
  - Similar intracellular tenofovir levels
  - FDA-approved doses of TAF in FDCs of
    - EVG/COBI/FTC/TAF (Stribild) (10 mg)
    - RPV/FTC/TAF (Odefsey) (25 mg)
- **FTC/TAF under FDA review (anticipated approval April ’16)**
- 2 prior double-blind phase 3 studies of EVG/COBI/FTC with TDF or TAF showed efficacy & smaller declines in BMD & greater improvements in renal biomarkers with TAF

Gallant J et al. CROI 2016
Tenofovir Alafenamide (TAF) vs Tenofovir-DF (TDF)

- **Primary Objectives:**
  - Compare efficacy, safety of switch from FTC/TDF to FTC/TAF vs continuing FTC/TDF in pts with virologic suppression on a 3-drug regimen

- **Study Design:**
  - Multicenter, randomized, double-blind, phase 3 non-inferiority switch study: 48 week data

- **Participants:**
  - Adults
  - HIV+
  - On 3-drug regimen including TDF/FTC
  - VL< 50 copies/mL
  - eGFR > 50 mL/min

Gallant J et al. CROI 2016
F/TAF vs F/TDF with 3\textsuperscript{rd} Drug: Participants and Overview

663 pts: 84% male, 75% W, 20% H, VL<50, CD4 663, eGFR~99

- FTC/TDF + 3\textsuperscript{rd} agent
  - 46% boosted PI
  - 54% unboosted

- F/TAF* + same 3\textsuperscript{rd} agent + placebo (N=333)
- F/TDF + same 3\textsuperscript{rd} agent + placebo (N=330)
- Maintenance Phase (96 wks)

Characteristics balanced between arms

1\textsuperscript{o} endpoint: % VL < 50 by FDA snapshot

48 wk results

*Dose of TAF depended on 3\textsuperscript{rd} agent
10 mg if boosted with ritonavir or COBI
25 mg if unboosted 3\textsuperscript{rd} agent
F/TAF vs F/TDF with 3rd drug: 48 week Virologic Results

<table>
<thead>
<tr>
<th></th>
<th>F/TAF N=333</th>
<th>F/TDF N=330</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early Discontinuation</td>
<td>21 (6%)</td>
<td>21 (6%)</td>
</tr>
<tr>
<td>VL&lt;50 copies at 48 wk</td>
<td>94%</td>
<td>93%</td>
</tr>
</tbody>
</table>

No differences in virologic outcomes by age, race, sex, type of 3rd agent

Switching to F/TAF arm was non-inferior to continuing F/TDF

Gallant J et al, CROI 2016
TDF vs TAF Safety Outcomes

<table>
<thead>
<tr>
<th></th>
<th>F/TAF N=333</th>
<th>F/TDF N=330</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early D/C</td>
<td>21 (6%)</td>
<td>21 (6%)</td>
<td>No predominant reason</td>
</tr>
<tr>
<td>AEs leading to D/C</td>
<td>7 (2%)</td>
<td>3 (1%)</td>
<td>10 different reasons</td>
</tr>
<tr>
<td>Increased Cre</td>
<td>---</td>
<td>1 person</td>
<td>Prior hypertension</td>
</tr>
<tr>
<td>Grade 3/4 lab</td>
<td>71 (21%)</td>
<td>62 (19%)</td>
<td></td>
</tr>
<tr>
<td>abnormalities</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- No predominant toxicities
- No *major* differences in types, frequency, grade of toxicities (lipids trended to be better with F/TDF)
- Most common signs/symptoms: URIs, diarrhea, H/A

Gallant J et al, CROI 2016
F/TAF vs F/TDF + 3rd Drug: Renal and Bone Outcomes

Small, statistically significant improvements with F/TAF in urine biomarkers protein to Cre ratios (protein, albumin, retinol binding protein, beta-2-microglobulin) occurred vs slight worsening with F/TDF.
F/TAF vs F/TDF + 3rd Drug: Conclusions

- Switch from F/TDF to F/TAF with continuation of 3rd drug was virologically non-inferior to continued F/TDF
- Effect similar across all subgroups & regardless of type of 3rd drug
- Adverse events & grade 3/4 lab abnormalities generally similar in both groups
- F/TAF switch associated with small but significant improvements in eGFR, renal biomarkers, and bone mineral at hip and spine; but increases in lipids

Gallant J et al, CROI 2016
F/TAF: Upcoming Formulations

- Dual drug F/TAF under regulatory review & approval anticipated spring 2016
- Triple drug FDCs under development:
  - Darunavir/cobi/F/TAF
  - GS-9883/F/TAF (investigational integrase inhibitor that doesn’t require “boosting”)
PROJECT HOPE: A PATIENT NAVIGATION/CONTINGENCY MANAGEMENT RCT FOR HOSPITALIZED HIV+ SUBSTANCE USERS: STUDY CTN0049

Abstract 27
Challenges for Substance Users with HIV

• ~50% of persons with HIV have a concurrent substance use disorder
• Associated with decreased rates of viral suppression & faster disease progression
• Up to 50% HIV+ individuals hospitalized for HIV-associated conditions have substance use disorder
• Need for new strategies to improve outcomes for this group

Metsch L et al. CROI 2016
HOPE: Randomized Behavioral Interventions

• Primary Objective: Test effect of structured patient navigation intervention +/- contingency management on virologic suppression rates

• Study Design
  - Multicenter, randomized, open-label, study of 2 behavioral interventions

• Participants:
  - HIV+
  - Active substance users (opioids, stimulants, heavy ETOH)
  - Recently hospitalized
  - VL >200
  - CD4 <500
  - Karnofsky >60

Metsch L et al, CROI 2016
HOPE: Randomized Controlled Behavioral Study

- Conducted by the NIDA Clinical Trials Network at 11 hospitals (Atlanta, Baltimore, Birmingham, Boston, Chicago, Dallas, LA, Miami, NY, Philadelphia, Pittsburgh)

- **Structured Patient Navigator (PN) Intervention:**
  - Up to 11 sessions
  - Included motivational interviewing
  - Linkage to HIV care, ART, drug treatment, other services
  - Included emphasis on substance use treatment

- **Contingency management (CM):**
  - Graded financial incentives for specific outcomes (e.g. PN visits, clinic visits, ART pick-up, blood draws, drug-free specimens, viral suppression, drug treatment)
  - Maximum $1160

Metsch L et al. CROI 2016
HOPE Study: Participants and Study Overview

801 pts: 32% female, 78% AA, 11% H, VL 56K, CD4 110, 38% unstable housing, 78% past jail, 89% income <$20K

Structured Patient Navigators (N=266)

Structured Patient Navigators + Contingency Management (N=271)

Usual Care (N=264)

HIV+ Active Substance Users N=2291 screened

1° endpoint: VL<200 vs detectable VL or death

End Intervention 6 mos Outcome for 95%

1° endpoint 12 mos For 92%
## HOPE: Study Outcomes

<table>
<thead>
<tr>
<th></th>
<th>PN (N=266)</th>
<th>PN + CM (N=271)</th>
<th>U. Care (N=264)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1 PN visit</td>
<td>97%</td>
<td>98%</td>
<td>---</td>
</tr>
<tr>
<td>≥ 6 PN visits</td>
<td>74%</td>
<td>90%</td>
<td>---</td>
</tr>
<tr>
<td>Earned incentive</td>
<td>---</td>
<td>99%</td>
<td>---</td>
</tr>
<tr>
<td>Median incentive</td>
<td>---</td>
<td>$722</td>
<td>---</td>
</tr>
<tr>
<td>Incentive for drug/ETOH free</td>
<td>---</td>
<td>87%</td>
<td>---</td>
</tr>
<tr>
<td>Hospitalized, mean #</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Deaths</td>
<td>No difference</td>
<td>90 (11%)</td>
<td></td>
</tr>
<tr>
<td>Visit to HIV provider, 6 mos</td>
<td>70%</td>
<td>82%</td>
<td>58%</td>
</tr>
<tr>
<td>Visit to HIV provider, 12 mos</td>
<td>66%</td>
<td>75%</td>
<td>59%</td>
</tr>
</tbody>
</table>
### HOPE: Study Outcomes

<table>
<thead>
<tr>
<th></th>
<th>PN (N=266)</th>
<th>PN + CM (N=271)</th>
<th>U. Care (N=264)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virologic suppression, 6 mos</td>
<td>39%</td>
<td>46%</td>
<td>34%</td>
<td>.04</td>
</tr>
<tr>
<td>Virologic suppression, 12 mos</td>
<td>36%</td>
<td>39%</td>
<td>34%</td>
<td>NS</td>
</tr>
<tr>
<td>Substance Use Treatment, 6 mos</td>
<td>26%</td>
<td>31%</td>
<td>18%</td>
<td>&lt;.02</td>
</tr>
<tr>
<td>Substance Use Treatment, 12 mos</td>
<td>21%</td>
<td>21%</td>
<td>20%</td>
<td>NS</td>
</tr>
</tbody>
</table>

- No differences in viral suppression by sex, Hispanic ethnicity
- Less viral suppression in: Stimulant users, Blacks, Sites in the south
HOPE: Conclusions and Implications

- Intensive interventions can increase linkage to HIV care and rates of viral suppression
- Effect of these interventions didn’t persist at 6 mos after the intervention ends
- No evidence for adverse effects of CM
- Very low rates of drug treatment
  - Does this reflect lack of options in these communities?
  - Would hospital-based drug treatment improve this outcome?
- Long-way to go to have this population achieve national goals
Take Home Points

• Viral suppression rates in the US are good for the majority of those prescribed ART
• Novel strategies are in development
• TAF, a novel way to deliver tenofovir, is non-inferior virologically and may have less negative renal and bone effects
• Strategies including contingency management may help substances users link to HIV care, take ART (while intervention ongoing)

Lots more work to do to help all HIV+ persons have success with ART
Thank you

http://www.croiconference.org/