“State of the art” of ART

Medical Management of AIDS
December 8, 2016

Monica Gandhi MD, MPH
Professor of Medicine, Division of HIV, Infectious Diseases and Global Medicine, UCSF
Medical director, "Ward 86", San Francisco General Hospital

Outline

- State of ART coverage globally
- The viral lifecycle
- Ascent of the integrase inhibitor (descent of ATV and EFV)
- Single pill combinations
- TAF vs TDF
- 2-drug therapy (monotherapy not so much)
- New drugs

Adults and children estimated to be living with HIV | 2015

- Total: 36.7 million [34.0 million – 39.8 million]

People with HIV on antiretroviral therapy | 2010-2015

- Total: 17 million (46%)

Fast-Track Targets

- by 2020
  - 90-90-90
    - HIV treatment
  - 500 000
    - New HIV infections or fewer
  - ZERO
    - Discrimination

- by 2030
  - 95-95-95
    - HIV treatment
  - 200 000
    - New HIV infections or fewer
  - ZERO
    - Discrimination
HIV viral lifecycle

1) Virus Entry
   - Attachment
   - Entry (CD4, CCR5)

2) Reverse transcriptase
   - DNA to RNA
   - RNA to DNA

3) Integration
   - RT, Protease
   - Integrase

4) Transcription
   - Viral RNA to DNA
   - DNA to mRNA

5) Translation
   - mRNA to polypeptide

6) Cleavage
   - Cleavage

7) Packaging
   - Viral components

8) Maturation
   - Assembly
   - Glycoproteins

9) Re-infection
   - Virus entry

Antiretroviral Drugs and Combinations

Viral combination agents

- Nucleos(t)ide RTIs
  - Zidovudine, AZT (Retrovir)
  - Abacavir, ABC (Ziagen)
  - Lamivudine, 3TC (Epivir)
  - Didanosine, ddI (Videx)
  - stavudine, d4T (Zerit)
  - Tenofovir, TDF (Viread)
  - Emtricitabine, FTC (Emtriva)
  - Tenofovir Alafenamide

- NNRTIs:
  - Delavirdine (D Nevirapine, NVP (Viramune)
  - Efavirenz, EFV (Sustiva)
  - Etravirine (Intelence)
  - Rilpivirine (Edurant)

- Protease inhibitors:
  - Indinavir, IDV (Crixivan)
  - Saquinavir, SQV (Invirocept)
  - Nelfinavir, NVP (Viracept)
  - Amprenavir, APV (Agenerase)
  - Atazanavir, ATV (Reyataz)
  - fosamprenavir, FPV (Lexiva)
  - Lopinavir/ritonavir (Kaletra)
  - Tipranavir (Aptivus)
  - Darunavir (Prezista)

- CCR5 receptor blockers
  - Maraviroc (Selzentry)

- Integrase inhibitors
  -Raltegravir (Isentress)
  •  Elvitegravir (EVG)
  •  Dolutegravir (Tivicay)

- NNRTIs:
  •  Delavirdine (Dolavirdine)
  •  Nevirapine, NVP (Viramune)
  •  Efavirenz, EFV (Sustiva)
  •  Ettravine (Intelence)
  •  Rilpivirine (Edurant)

- Fusion inhibitors:
  - Enfuvirtide
  - T20 (Fuzeon)

- Protease inhibitors:
  - Indinavir, IDV (Crixivan)
  - Saquinavir, SQV (Invirocept)
  - Nelfinavir, NVP (Viracept)
  - Amprenavir, APV (Agenerase)
  - Atazanavir, ATV (Reyataz)
  - fosamprenavir, FPV (Lexiva)
  - Lopinavir/ritonavir (Kaletra)
  - Tipranavir (Aptivus)
  - Darunavir (Prezista)

- Single Tablet Regimens
  •  EFV/FTC/TDF (Atripla)
  •  RPV/FTC/TDF (Complera)
  •  RPV/FTC/TAF (Odefsey)
  •  EVG/coibi/FTC/TDF (Stribild)
  •  EVG/coibi/FTC/TAF (Genvoya)
  •  DTG/ABC/3TC (Triumeq)

The history of ARV approvals- let’s talk about the ascent of the integrase inhibitor and the descent of EFV/Atazanavir

Cumulative problems for EFV (CNS side effects) - EFV as Initial Therapy: Increased Risk for Suicidal Ideation

- Review of 4 ACTG studies in ART-naive patients
- Compared 3241 patients starting EFV vs 2091 patients starting non-EFV-based ART
- Median duration f/u 96 weeks
- First suicidal ideation OR attempted OR completed suicide in each group
  - 8.08 events per 1000 PY in EFV group vs 3.66 events per 1000 PY in EFV-free group
  - (HR: 2.28; 95% CI, 1.27-4.0; P=.006)

**ARS: What is the mean increase of Cr seen with Cobicistat in Gilead 102, 103 trials?**

1. Mean creatinine increases of 0.05 mg/dL
2. Creatinine increases of 0.08 mg/dL
3. Creatinine increases of 0.14 mg/dL
4. Creatinine increases of 0.25 mg/dL
5. Creatinine increases of 0.5 mg/dL

**PROS**

- Well tolerated
- Fewest drug-drug interactions
- OK in hepatic and renal failure
- No food requirements
- Can use RAL with cations except Al and Mg (do not co-administer)

**CONS**

- Low genetic barrier to resistance
- BID dosing (but emerging data for higher dose once daily)
- No single pill combination
- CK elevations; rhabdomyolysis

**PROS**

- Two single pill combinations
- Gilead 102, 103 showed similar efficacy compared to EFV or ATV/r, respectively

**CONS**

- Low genetic barrier and cross resistance with RAL
- Cobicistat increases Cr (0.1-0.4 mg/dL [mean 0.14])
- Most drug-drug interactions due to cobicistat (statins, rifamycins, anticonvulsants...)
- Food requirements (373 kcal)
- Stribild- GFR > 70 mL/min
- Space all cations out by 2 hours
ONCEMRK STUDY

- 802 pts randomized (2:1)
  - RAL 1200 mg QD + TDF/FTC
  - RAL 400 mg BID + TDF/FTC
- RAL QD non-inferior to RAL BID
  - VL <40: 88.9% vs. 88.3%
- RAL QD (600 x 2) likely available next year

Wk 48 VL<40 (Snapshot)

Cahn P et al. IAS, 18-22 July 2016, Durban, South Africa. Abstract FRAB0103LB

Pivotal phase III/IIb trials of dolutegravir – TREATMENT NAIVE

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient population</th>
<th>Main outcome</th>
<th>Dose</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>SINGLE</td>
<td>Treatment naive (ABC/3TC + DTG vs TDF/FTC/EFV)</td>
<td>DTG regimen superior to EFV, driven mainly by more discontinuations with EFV</td>
<td>50mg once daily</td>
<td>Walmsley S. NEJM 2013</td>
</tr>
<tr>
<td>SPRING-2</td>
<td>Treatment-naive (TDF/FTC or ABC/3TC with either DTG or RAL)</td>
<td>DTG regimen non-inferior to RAL-based regimens</td>
<td>50mg once daily</td>
<td>Raffi F. Lancet 2013 (48 wks) and Lancet ID (96)</td>
</tr>
<tr>
<td>FLAMINGO</td>
<td>Treatment naive (TDF/FTC or ABC/3TC with either DTG or DRV/r)</td>
<td>DTG regimen superior to DRV/r, driven by more d/c with DRV/r and more virologic response with DTG with vl &gt;100,000 copies/mL</td>
<td>50mg once daily</td>
<td>Cahn P. Lancet 2013 (48 wks) 32</td>
</tr>
</tbody>
</table>

SAILING
- ART-experienced, INSTI-naive patients with at least 2-class resistance: DTG vs RAL with OBR
- DTG regimen superior to RAL, driven by more d/c, virologic failures and treatment-emergent resistance with RAL
- 50mg once daily
- Cahn P. Lancet 2013 (48 wks)

VIKING-3, 4
- Patients with resistance to 2 or more ART classes, including INSTI. DTG vs optimized
- DTG regimen superior to optimized regimen with failures most prominent (78%) in patients with the Q148HR +2 other mutations
- 50mg po twice daily
- Eron JJ. JID 2013 33 and Nichols G. JID 2014; Castagna JID 2014

Bottom line with DTG resistance

- Higher barrier to resistance to DTG than RAL/EVG
- Major pathways INSTI resistance: N155, Q148, Y143, E92 (EVG)
- Baseline INSTI mutation of Q148H (especially + G140S) reduces DTG susceptibility (e.g. don’t use)
- Treatment emergent resistance can occur in highly-experienced patients (Hardy AAC 2015)

ARS: What is the mean increase of dolutegravir AUC seen with a moderate-fat meal?

1. 0% increase
2. 33% increase
3. 41% increase
4. 66% increase
5. 100% increase

Low-fat (300 kcal, 7% fat), moderate-fat (600 kcal, 30% fat), or high-fat (870 kcal, 53% fat) meal
ARS: What is the mean change in dolutegravir AUC with renal insufficiency (CrCl <30 ml/min)?

1. 0%
2. 10% increase in AUC
3. 10% decrease in AUC
4. 40% increase in AUC
5. 40% decrease in AUC

Dolutegravir not appreciably removed by hemodialysis (Bollen AIDS 2016; Molto AAC 2016)

Pros and cons of dolutegravir

**PROS**
- Potent and high genetic barrier
- Available in single pill combination with ABC/3TC
- Well tolerated (though insomnia, psychiatric effects real-world populations, esp. women, older pts)
- No food requirements (although 33%, 41%, 66% increase in AUC with low, moderate, high-fat meal, respectively)
- Can use DTG with cations of Ca and Fe if administer with meal

**CONS**
- Inhibits creatinine secretion (mean rise Cr 0.11mg/dL)
- Abacavir in SPC needs HLA-B5701 testing
- Separate from Mg, Al containing antacids by 2 hours
- Increase dose with concomitant rifampin, EFV, CBZ; don't give with etravirine unless boosted PIs present; no dose adjustments with RPV
- Increases metformin levels
- Largest pill size of SPCs
- Not coformulated with tenofovir
- Decreased AUC with CrCl <30


Outline

- State of ART coverage globally
- The viral lifecycle
- History of ART and ascent of the integrase inhibitor (descent of ATV and EFV)
- Single pill combinations
- TAF vs TDF
- 2-drug therapy (monotherapy not so much)
- New drugs, long-acting ART

Single pill combinations may aid in adherence

“Drugs don’t work in patients who don’t take them”

C. Everett Koop

ARS: How many single pill combinations do we have for the treatment of HIV in 2016?

1. 3
2. 4
3. 5
4. 6
5. 7

Currently available SPCs

<table>
<thead>
<tr>
<th>Picture of SPC</th>
<th>Drugs in SPC</th>
<th>Approval date</th>
<th>Food effects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TDF/FTC/efavirenz (Atripla®)</td>
<td>2006</td>
<td>Food ↑ levels</td>
</tr>
<tr>
<td></td>
<td>TDF/FTC/rlpivirine (Complera®)</td>
<td>2011</td>
<td>Take with solid meal (390kcal)</td>
</tr>
<tr>
<td></td>
<td>TDF/FTC/elvitegravir/ cobicistat (Stribild®)</td>
<td>2012</td>
<td>Take with food (373kcal)</td>
</tr>
<tr>
<td></td>
<td>ABC/3TC/dolutegravir (Triumeq®)</td>
<td>2014</td>
<td>Food ↑ levels</td>
</tr>
<tr>
<td></td>
<td>TAF/FTC/elvitegravir/ cobicistat (Genvoya®)</td>
<td>2015</td>
<td>Take with food (373kcal)</td>
</tr>
<tr>
<td></td>
<td>TAF/FTC/rlpivirine (Odefsey®)</td>
<td>2016</td>
<td>Take with solid meal (390kcal)</td>
</tr>
</tbody>
</table>

ARS: In your practice, are you switching everyone on TDF to TAF?

1. Yes, switching all patients from TDF to TAF
2. No, I am evaluating on a case-by-case basis

Tenofovir alafenamide

- TAF is prodrug of tenofovir (as is TDF). Both require conversion to TFV-DP for activity
- Plasma levels of TFV 4-7x lower with TAF (25mg daily) than with TDF (300mg daily). TFV-DP levels much higher (4-7x) within lymphocytes with TAF
**Only one phase 3 trial of TAF head to head with TDF; rest bioequivalence or switch studies**

<table>
<thead>
<tr>
<th>Type of study</th>
<th>ARVs</th>
<th>Dose of TAF</th>
<th>Numbers / Reference</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial therapy</td>
<td>TDF/FTC/ELV/cobi VS</td>
<td>10mg</td>
<td>Noninferior (Gilead 104, 111)</td>
<td></td>
</tr>
<tr>
<td>Switch study</td>
<td>TDF/FTC-containing</td>
<td>10mg</td>
<td>1443 pts, 96 wks</td>
<td>• Maintained virologic suppression</td>
</tr>
<tr>
<td></td>
<td>regimens TO</td>
<td></td>
<td></td>
<td>• Improved eGFR, proteinuria</td>
</tr>
<tr>
<td></td>
<td>TAF/FTC/EFV/cobi</td>
<td></td>
<td></td>
<td>• Improved bone mineral density</td>
</tr>
<tr>
<td>Switch study</td>
<td>TDF/FTC TO TAF/FTC</td>
<td>10 or 25mg</td>
<td>663 pts, 48 wks</td>
<td>• Increased lipids</td>
</tr>
<tr>
<td></td>
<td>with 3rd agent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Switch study</td>
<td>TDF/FTC/EFV TO</td>
<td>25mg</td>
<td>630 pts, 48 wks</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TAF/FTC/RPV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAF/FTC/EFV/RPV</td>
<td>25mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial therapy</td>
<td>DRV/Cobi/TDF/FTC VS</td>
<td>10mg</td>
<td>153 pts, 48 weeks</td>
<td></td>
</tr>
<tr>
<td>(phase 2, safety)</td>
<td>DRV/Cobi/TAF/FTC</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


**TAF vs. TDF in Treatment-Naïve Pts (104, 111)**

- 1733 treatment naive adults (eGFR >50): 866 E/C/F/TAF vs 866 E/C/F/TDF
- TAF associated with:
  - Smaller decrease in eGFR (-6.4 vs. -11 mL/min)
  - Less proteinuria
  - Smaller decrease in bone mineral density (BMD)
  - But greater increase in cholesterol, LDL, HDL, TGs
    - Δ TC: +29 mg/dL
    - Δ LDL: + 14 mg/dL
    - Δ TC, HDL: same

- EVG/c/FTC/TAF approved for patients with CrCl down to 30
- 144 week date presented Sept 2016
- 84% TAF vs 80% TDF, 12 renal events with TDF

---

**Lingering questions on TAF**

- What are long-term clinical implications of the changes in renal and bone markers?
- Is lack of systemic exposure good?
  - What is impact of lack of exposure in extrapyramidal tissues and genital mucosa for prevention and cure?
- Reduced dose of TAF: Concern with concomitant human cellular metabolic enzymes or efflux transporters e.g. rifampin (induces p-gp)
- Will 25mg of TAF give too high of intracellular TFV-DP with boosted PIs (which inhibit p-gp)?
- FDA only approved 25mg/200mg TAF/FTC tablet
Should TAF replace TDF?

**Reasons to choose TAF**
- TAF is virologically as effective as TDF.
- Compared with TDF, TAF has more favorable effects on renal and bone markers.
  - Don’t have enough evidence on whether to use with existing enal or bone disease, but maybe those with high risk of these complications.
- Cost of TAF- and TDF-regimens currently similar.

**Reasons to choose TDF**
- Compared with TAF, more and longer-term data with TDF, particularly in treatment naïve.
- More favorable lipid effects.
- Renal and bone marker advantages of TAF not yet known to translate into better clinical outcomes.
- TDF-regimens likely to be cheaper than TAF when TDF goes generic
  - Patient on rifamycins (TB)
  - For PrEP
  - No data in pregnant women
  - With boosted PIs (no data on 25mg TAF and boosted PIs)

ARS: What do you think about TAF/FTC for PrEP?

a. They should be roughly equivalent and I am using TAF/FTC for PrEP
b. Don’t know implications of plasma and intracellular concentration discrepancies between TDF and TAF on prevention efficacy
c. TAF may give lower TFV-DP concentrations in cervicovaginal and rectal tissues than TDF
d. Under study but in men/TGW only
e. b, c and d

Need more data for TAF/FTC and PrEP

- TFV-DP was undetectable in 75% of female genital tissues with TAF 25mg (25% undetectable with TDF)
- TFV-DP was undetectable in 63% of rectal tissues with TAF 25mg (0% undetectable with TDF), but FTC same
- Discover trial (TAF/FTC vs TDF/FTC for PrEP) only enrolling men/TG women

Outline

- State of ART coverage globally
- The viral lifecycle
- History of ART and ascent of the integrase inhibitor (descent of ATV and EFV)
- Single pill combinations
- TAF vs TDF
- 2-drug therapy (monotherapy not so much)
- New drugs
**Why dual therapy as opposed to 3-drug?**

- NRTI intolerance (HLA-B5701 and renal failure) or NRTI mutations
- Minimize pill burden
- Minimize toxicities
- Minimize cost
- Preserve treatment options for future
- INSTIs (e.g. dolutegravir, cabotegravir) potent and high genetic barrier to resistance – will this allow the possibility?
- Allow for long-acting therapy (just 2 available right now)

**Monotherapy**

- Some evidence for PI/r monotherapy, but inferior to 3-drug therapy
- Dolutegravir monotherapy of interest (no treatment emergent resistance in naive trials)
  - “Meta-analysis” of 4 tiny studies (one 5 patients), 87 patients
    - 6% virologic failure rate overall (4 out of 5 who failed had INSTI experience)
    - 4 who failed developed INSTI RAMs on DTG monotherapy
    - Unacceptable rate of INSTI resistance – this is not ready for prime time, 9 pts in Italy

**ARS: Many NRTI-sparing trials failed. For which combo below do we have some evidence of success?**

1. ATV/r + RAL (HARNESS)
2. MVC + DRV/r (MODERN)
3. LPV/r + EFV (AS142)
4. DRV/r + RAL (NEAT)
5. DRV/r + TDF (NOT-1)
6. DTG + TDF (NOT-2)

**Dual therapy as initial therapy – emerging evidence for mainly 3 oral combinations**

<table>
<thead>
<tr>
<th>Dual combination</th>
<th>Particular ARVs, Study name</th>
<th>Results</th>
</tr>
</thead>
</table>
| 1) Boosted PI + 3TC | LPV/r + 3TC GARDEL | • Noninferior to LPV/r + 2NRTIs (n=426)  
• High pill burden, toxicities |
| 2) Boosted PI + INSTI | DRV/r + RAL NEAT-001, PROGRESS | • Overall noninferior (n=805)  
• Didn’t do as well as DRV/r + TDF/FTC if CD4 <200 or vlt >100K  
• More failures with DRV/r + RAL and more resistance (5 INSTI RAMs, gulp)  
• PROGRESS (206) vs LPV/2N, 2 M184Vss |
| 3) INSTI + 3TC | DTG + 3TC (PADDLE), AS353 etc. | • Open-label single-arm, naïve patients  
• n=20 only  
• All maintained suppression at 24 wks |

EFV/LPV/r* in AS142 had more NRTI resistance

Two-drug therapy regimens that work AFTER virologic suppression (maintenance)

**COMPLETED**
- LPV/r + 3TC vs 2N (OLE, n=250)\(^1\)
- ATV/r + 3TC vs 2N (SALT, n=286)\(^1\)
- DRV/r + RPV vs standard cART (PROBE, n=60)\(^1\)
- CAB + RPV po vs EFV/2N (LATTE-1, n=243)\(^1\)
**UNDER STUDY**
- DRV/r + 3TC (DUAL)
- DRV/r + DTG (DUALIS)
- DTG + 3TC (ASPIRE, AS353, LAMADOL, GEMINI 1 and 2-Viiv)
- IM Cabotegravir + IM RPV (LATTE-2, n=309)\(^4\) – Going to 96 wks


**LATTE-2: Cabotegravir IM + Rilpivirine IM for Long-Acting Maintenance ART**

- Multicenter, open-label phase IIb study
- Primary endpoints: HIV-1 RNA < 50 c/mL by FDA snapshot, PDVF, and safety at maintenance Wk 32

**Induction Phase**
- CAB 400 mg IM + RPV 600 mg IM Q4W (n = 115)
- CAB 600 mg IM + RPV 900 mg IM Q8W (n = 115)

**Maintenance Phase**
- ART-naive HIV-infected pts with CD4+ cell count > 200 cells/mm\(^3\) (N = 309)

**LATTE-2: Maintenance Wk 32 Virologic Efficacy (ITT-Maintenance Exposed)**

- Virologic efficacy of Q4W and QBW IM regimens similar to oral regimen
- 1 patient in q8 wk arm and 1 pt in oral arm met protocol defined VF
- No INSTI, NNRTI, or NRTI resistance mutations detected

**LATTE-2: Safety data through wk 32**

- Most frequent ISRs were pain (67%), swelling (7%), and nodules (6%)
  - ISR events/injection: 0.33
  - 99% of ISRs grade 1-2; none grade 4
  - Proportion of pts reporting ISRs decreased with time from 86% on Day 1 to 33% at Wk 32; 1% of pts withdrew for ISRs
- Patient satisfaction with LA regimen high

**AEs, %**

<table>
<thead>
<tr>
<th>Drug-related grade 3/4</th>
<th>Pooled CAB + RPV IM</th>
<th>Oral CAB + ABC/3TC</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEs (excluding ISRs)</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Serious AEs</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>AEs leading to withdrawal</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

Margolis DA et al, CROI 2016, Abstract 31LB
Switching to DTG + RPV in Heavily pre-Treated Patients Who are Virologically Suppressed

- Open label cohort study (n=38), 19 yrs multidrug tx experience all virologically suppressed, previous history of virologic failure
- Regimen at time of switch to DTG + RPV (median 4.3 drugs):
  - NRTI + NNRTI + PI + INSTI: 53% (rest NRTI + NNRTI + PI)
- Pre-existing resistance mutations: NRTI: 65%; NNRTI 37%; PI 32%; INSTI: NA
- Virologic suppression in 35 of 38 (92%) at wk 48
- No VF: 1 patient stopped b/o GI toxicity, 1 b/o drug interactions, 1 b/o physician decision
- 132 pts in clinic in Italy\(^1\) and 14 pts in Newark similar results\(^3\)
- Phase III SWORD trials (DTG/RPV) still ongoing


ARS: Which novel anti-HIV drug in development seems most exciting to you?

1. Bictegravir, an INSTI
2. VRC01, broadly neutralizing antibody
3. Doravirine, an NNRTI
4. Fostemsavir, an attachment inhibitor
5. BMS-663068, a maturation inhibitor
6. EFDa, an NRTI inhibitor
7. None, too many vir names to remember!

New anti-HIV drugs

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Name of drug</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRTI</td>
<td>EFDa (4’-ethynyl-2-fluoro-2’-deoxyadenosine)</td>
<td>Phase I data; animal data; weekly oral and may be formulated to ONCE YEARLY</td>
</tr>
<tr>
<td>NNRTI</td>
<td>Doravirine</td>
<td>Phase III in progress; being studied as SPC with 3TC/TDF; can use against RPV-resistant virus</td>
</tr>
<tr>
<td>INSTI</td>
<td>GS-9883 or Bictegravir</td>
<td>Phase III in progress with SPC as bictegravir/TAFT/FTC; high genetic barrier to resistance</td>
</tr>
<tr>
<td>Attachment inhibitor</td>
<td>BMS-663068 or fostemsavir</td>
<td>Looks good in phase Ib; now in Phase III; novel class</td>
</tr>
<tr>
<td>Maturation inhibitor</td>
<td>BMS-955176</td>
<td>Promising in phase I; now in Phase II</td>
</tr>
<tr>
<td>Broadly neutralizing Ab</td>
<td>VRC01, for prevention or treatment</td>
<td>Early in development; Bar et al. NEJM Nov 9, 2016 – delays viral rebound but resistance</td>
</tr>
</tbody>
</table>

stop aids. make the promise

Thank you to Drs. Diane Havlir, Raj Gandhi, Meg Newman, Vivek Jain, Gabe Chamie, Harry Lampiris, Annie Luetkemeyer