Switching antiretroviral therapy to safer strategies based on integrase inhibitors

Pedro Cahn
Disclosures

Research Grants: Abbvie-Merck-Richmond-ViiV
Advisory boards: Merck-Sandoz-ViiV
Switching in Virologically Suppressed Patients: Why would you do that?

- To improve adherence
- To maintain viral suppression and to avoid resistance
- To reduce pill burden and dosing frequency
- To reduce tolerability and toxicity
- To avoid food or fluid requirements
- To reduce drug-drug interactions
- To adapt regimen to pregnancy
- To adapt regimen to ageing patients
- To reduce costs
Switching in Virologically Suppressed Patients: Why would you do that?

Also...
- Concerning laboratory values
- Long term toxicity
- Simplification
- To adapt regimen to comorbidities
- To adapt to coinfections (HBV, HCV, TB, etc)
Who? A word of caution.....

• How long has been your patient suppressed?
• Has the patient failed former ARV regimens?
• Who is asking for a switch?
  ✓ Patient initiated switch
  ✓ Care provider initiated switch:
  ✓ Urgent need or strategic switch (e.g. chemotherapy)
# Principles of Regimen Switching in Virologically Suppressed Pts

<table>
<thead>
<tr>
<th><strong>Drug Resistance:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Review ART history for possible VF</td>
</tr>
<tr>
<td>▪ Review all available resistance test results</td>
</tr>
<tr>
<td>▪ If prior resistance uncertain: only consider switch if new regimen likely to maintain suppression of resistant virus</td>
</tr>
<tr>
<td>▪ Caution when switching from boosted PI to another class if full treatment/resistance history not known</td>
</tr>
<tr>
<td>▪ Consult an expert when switching if resistance to ≥ 1 class</td>
</tr>
<tr>
<td>▪ Within class switches usually maintain virologic suppression if no resistance to drugs in that class are present</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Safety:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Review ART history for intolerance</td>
</tr>
<tr>
<td>▪ Must be HLA-B*5701 negative if considering ABC</td>
</tr>
<tr>
<td>▪ Drug–drug interactions with comedications</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Comorbidity:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ HBV coinfection</td>
</tr>
<tr>
<td>▪ Cardiovascular disease or risk</td>
</tr>
<tr>
<td>▪ Renal function</td>
</tr>
<tr>
<td>▪ Bone mineral density</td>
</tr>
<tr>
<td>▪ Other coinfections</td>
</tr>
</tbody>
</table>

*DHHS ART Guidelines. May 2018.*
Quality of life of HIV-infected patients who switch antiretroviral medication due to side effects or other reasons

Eric M. Maiese\textsuperscript{a}, Phaedra T. Johnson\textsuperscript{b}, Tim Bancroft\textsuperscript{b}, Alyssa Goolsby Hunter\textsuperscript{b} and Albert W. Wu\textsuperscript{c}

Results: Patients who switched their ART regimen due to treatment-related side effects ($n = 50$) had statistically significant improvements ($p < .05$, baseline to follow-up) in mean Physical and Mental Health Summary scores (MOS-HIV scale) and in all three HIVTSQ summary scores. Patients who switched for other reasons ($n = 44$) did not experience statistically significant improvements in these same measures.
A case of failure: The SWITCHMRK Study:

- **Design:** 2 parallel trials, SWITCHMRK 1 and 2

  - **Randomisation**: 1:1 Double-blind
  - **N = 350**: Switch to RAL 400 mg bid + placebo LPV/r bid + continue other ARVs
  - **N = 352**: LPV/r bid + placebo RAL bid + continue other ARVs

  - *Randomisation was stratified on LPV/r use before entry (≤ 1 year vs > 1 year)*

- **Primary endpoints**
  - Mean percentage changes in fasting lipid concentrations from baseline to week 12
  - Proportion of patients with HIV-1 RNA < 50 c/mL at week 24
  - Frequency of adverse events up to week 24

SWITCHMRK Study: Good for lipids

Mean* % changes in fasting lipid concentrations from baseline to W12

### SWITCHMRK 1

- **Total cholesterol**: Baseline 5.6, W12 4.8
- **Non-HDL-C**: Baseline 4.3, W12 3.6
- **Triglycerides**: Baseline 4.1, W12 4.1
- **LDL-C**: Baseline 2.1, W12 1.3
- **HDL-C**: Baseline 1.8, W12 1.9

**Mean changes (%)**:
- Total cholesterol: -12.8% (p < 0.0001)
- Non-HDL-C: -15.2% (p < 0.0001)
- Triglycerides: -41.5% (p < 0.0001)
- LDL-C: -2.4% (p = 0.7)
- HDL-C: -2.1% (p = 0.7)
- **NT**

### SWITCHMRK 2

- **Total cholesterol**: Baseline 5.6, W12 4.7
- **Non-HDL-C**: Baseline 4.3, W12 3.6
- **Triglycerides**: Baseline 4.1, W12 4.3
- **LDL-C**: Baseline 2.1, W12 1.3
- **HDL-C**: Baseline 1.8, W12 1.9

**Mean changes (%)**:
- Total cholesterol: -12.4% (p < 0.0001)
- Non-HDL-C: -14.8% (p < 0.0001)
- Triglycerides: -42.8% (p < 0.0001)
- LDL-C: -0.6% (p = 0.2)
- HDL-C: -2.5% (p = 0.2)
- **NT**

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**Notes**:
- * median changes for triglycerides
- ** not tested

**Eron JJ, Lancet 2010;375:396-407**
SWITCHMRK Study:
Not so good for viral suppression

Proportion of patients with HIV-1 RNA < 50 c/mL

SWITCHMRK 1

SWITCHMRK 2

RAL + ARV
LPV/r + ARV

RAL + ARV
174 166 169 173 172
LPV/r + ARV
174 171 171 171 174

Δ(95% CI) : -6.6 (-14.4 ; 1.2)

Δ(95% CI) : -5.8 (-12.2 ; 0.2)

Weeks

A case of success: The SPIRAL Study:

### Design

- **Randomisation***
  - 1 : 1
  - *Open-label*

- **HIV+ ≥ 18 years**
- **On 2 ARV + PI/r**
- **HIV RNA < 50 c/mL > 6 months**
- **Raltegravir-naïve**

- **N = 142**
  - Switch to RAL 400 mg bid + continue other ARVs
- **N = 140**
  - Continue PI/r + other ARVs

* Randomisation was stratified by current use of lipid-lowering therapy
** Median time with virologic suppression was > 6 years

### Endpoints

- **Primary:** non inferiority in the proportion of patients with treatment failure at W48* (non completer = failure, intent-to-treat analysis), lower limit of the 95% CI for the difference = -12.5%, 80% power
  * events occurring in the 2 weeks after W48 were included in the analysis
- **Secondary:** virologic failure (confirmed HIV-1 RNA > 50 c/mL), CD4, fasting lipids, adverse events

Martinez E, AIDS 2010;24:1697-1707
At entry, median total cholesterol (TC) was 198 mg/dL, 15% of the patients had TC > 240 mg/dL, 12% LDL-cholesterol > 160 mg/dL, 40% triglycerides > 200 mg/dL.

Percentage changes in fasting lipid concentrations from baseline to W48:

Martinez E, AIDS 2010;24:1697-1707
SPIRAL Study: Switch PI/r to RAL:
Also good for viral suppression

Results: Efficacy analyses

- Absence of treatment failure
  - All patients: 89.2% (RAL) vs 86.6% (PI/r)
  - Prior virologic failure or suboptimal therapy:
    - Yes: 88.6% (RAL) vs 83.1% (PI/r)
    - No: 90% (RAL) vs 89.9% (PI/r)

- Absence of virologic failure
  - All patients: 96.9% (RAL) vs 95.1% (PI/r)
  - Prior virologic failure or suboptimal therapy:
    - Yes: 97.2% (RAL) vs 93.1% (PI/r)
    - No: 96.4% (RAL) vs 96.9% (PI/r)

95% CI for the ≠
- All patients: -5.2; 10.6
- Prior virologic failure or suboptimal therapy:
  - Yes: -5.9; 17.6
  - No: -11.2; 10.9
- Prior virologic failure or suboptimal therapy:
  - Yes: -3.9; 13.9
  - No: -9.3; 7.6

Martinez E, AIDS 2010;24:1697-1707
STRATEGY – PI and NNRTI: randomised, open-label studies in virologically suppressed patients

Primary Endpoint: HIV-1 RNA <50 c/mL (ITT, snapshot)

Improvement in patient reported outcome
- diarrhoea, bloating
- Higher treatment satisfaction scores
No case of proximal renal tubulopathy

Improvement in reported outcome from patients who switched from EFV
- lower rates of neuropsychiatric symptoms compared to baseline

ITT analysis set excluded subjects with prohibited mutations on historical genotype and those not on PI at randomisation.

Pozniak A, Lancet Infect Dis 2014; 14:590-9
STRIIVING study: week 48 results

HIV-1 RNA <50 Copies/mL, %

Early Switch

- Virological success: 85%
- Virological non-response: 1%
- No virologic data: <1%

Late Switch

- Virological success: 92%
- Virological non-response: <1%
- No virologic data: 7%

DTG/ABC/3TC, Day 1-Week 24 (n=275)
cART, Day 1-Week 24 (n=278)
DTG/ABC/3TC, Day 1-Week 48 (n=275)

Switch to DTG/ABC/3TC, Week 24-Week 48 (n=244)

- > Satisfaction score
- AE 4% vs 0%
- No PDVF

Dual Therapy: Potential InSTI-Based Regimens for Maintenance Therapy

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTG + 3TC</td>
<td>• ASPIRE (randomized phase III)</td>
</tr>
<tr>
<td>DTG + RPV</td>
<td>• SWORD 1/2* (randomized phase III)</td>
</tr>
<tr>
<td>DTG + DRV/RTV</td>
<td>• DUALIS (randomized phase III)</td>
</tr>
<tr>
<td>DTG + ATV/RTV</td>
<td>• DOLATAV (phase II)</td>
</tr>
<tr>
<td>DTG + MVC</td>
<td>• HP-00056162 (single-arm phase III)</td>
</tr>
<tr>
<td>RAL + ETR</td>
<td>• ETRAL</td>
</tr>
<tr>
<td>RAL + 3TC</td>
<td>• RALAM</td>
</tr>
<tr>
<td>RAL + DRV/r</td>
<td>• Maddeu et al</td>
</tr>
<tr>
<td>RAL + DRV/r</td>
<td>• Calza et al</td>
</tr>
<tr>
<td>RAL + DRV/r</td>
<td>• Casado et al</td>
</tr>
</tbody>
</table>
Dual therapy with RAL & DRV/r

- In Italy, about 40% of raltegravir is used in Dual therapy, mainly with DRV/r.

- G. Maddedu et al:
  DRV/r + RAL is a valuable NRTI-sparing option, especially in female and older patients, with a relatively low risk of VF and good tolerability after 2 years since start in an ART-experienced population (1).

- L Calza. et al.:
  Simplification to a dual therapy containing raltegravir plus darunavir/ritonavir after 48 weeks maintained viral suppression in more than 90% of patients and showed a good tolerability with a favourable effect on proteinuria, ipophosphoreemia, and lipid metabolism (2).

- JL Casado et al: DRV/r + RAL
  A dual treatment with the combination of raltegravir and boosted darunavir is associated with maintenance of virologic suppression, even in severely experienced patients, and is associated with improvements in CD4+ count, CD4/CD8 ratio, and renal and bone toxicity (3).

(1) Efficacy and tolerability of switching to a dual therapy with darunavir/ritonavir plus raltegravir in HIV-infected patients with HIV-1 RNA ≤50 cp/mL. G. Maddedu et al., Infection Springer 2017.
(3) Switching to a dual regimen with the combination of boosted darunavir plus raltegravir in severely experienced patients: a multicentre, retrospective analysis. JL Casado et al., from Abstract accepted for Glasgow 2018.
Dolutegravir Plus Lamivudine for Maintenance of Suppression (ASPIRE)

Virologic Outcomes at Week 48 (FDA Snapshot)

HIV-1 infected adults virologically suppressed on any 3-drug ARV regimen.
CD4 nadir > 200 cells/mm3
No history of virologic failure

<table>
<thead>
<tr>
<th>HIV RNA &lt;50 cpm</th>
<th>HIV RNA &gt;50 cpm</th>
<th>No Virologic Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTG+3TC</td>
<td>Cont ART</td>
<td></td>
</tr>
<tr>
<td>90.9%</td>
<td>2.3%</td>
<td>6.8%</td>
</tr>
<tr>
<td>88.9%</td>
<td>2.2%</td>
<td>8.9%</td>
</tr>
</tbody>
</table>

N
On Study
40 40 1 1 3 4
44 45 44 45 44 45

ETRAL ANRS:
Switch from PI regimen to RAL/ETR

- 160 patients
  - CD4 current/nadir: 700/209
  - ART duration: 16.8 years
  - Duration of VS: 6.9 years
- ART:
  - QD 73%
  - BID 27%
  - 2 NRTIs + PI/r: 65%
  - NNRTI + PI/r: 7%
  - mono PI/r: 21%
- Comorbidities:
  - Dyslipidemia: 27%
  - High Blood Pressure: 25%
  - Diabetes: 8%
  - Cardiovascular event: 3%
- Co-medications med nb: 5

Efficacy maintained up to W96

One Protocol defined virological failure W24 11 607/18472 ETR R RAL S

Katlama C et Al IAS Paris 2017 absT MOPEB0314
ETRAL: switch from PI regimen to RAL/ETR
Evolution of Lipids  Glucose and Renal n = 165

<table>
<thead>
<tr>
<th></th>
<th>D0</th>
<th>W48</th>
<th>∆ W48 – D0</th>
<th>P-value</th>
<th>Mean % change (±sd)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glomerular Filtration Rate (GFR)</strong> (ml/min/1.73 m²); n(%)</td>
<td>90.3 (17.2)</td>
<td>88.2 (17.6)</td>
<td>-2.1 (9.8)</td>
<td>0.0011</td>
<td>-2.0% ±11.5</td>
</tr>
<tr>
<td><strong>Cholesterol</strong> (mmol/L)</td>
<td>5.44 (1.14)</td>
<td>5.19 (1.05)</td>
<td>-0.25 (1.05)</td>
<td>0.0188</td>
<td>-2.8% ±18.1</td>
</tr>
<tr>
<td><strong>HDL-Cholesterol</strong> (mmol/L)</td>
<td>1.38 (0.47)</td>
<td>1.48 (0.49)</td>
<td>0.09 (0.35)</td>
<td>0.0002</td>
<td>+9.4% ±26.3</td>
</tr>
<tr>
<td><strong>LDL-Cholesterol</strong> (mmol/L)</td>
<td>3.30 (0.94)</td>
<td>3.09 (0.98)</td>
<td>-0.21 (0.89)</td>
<td>0.0084</td>
<td>-3.6% ±27.7</td>
</tr>
<tr>
<td><strong>Non-HDL-Cholesterol</strong> (mmol/L)</td>
<td>4.06 (1.10)</td>
<td>3.71 (1.05)</td>
<td>-0.35 (1.00)</td>
<td>&lt;0.0001</td>
<td>-6.0% ±22.7</td>
</tr>
<tr>
<td><strong>Triglycerides</strong> (mmol/L)</td>
<td>1.66 (0.97)</td>
<td>1.34 (0.82)</td>
<td>-0.32 (0.93)</td>
<td>&lt;0.0001</td>
<td>-10.5% ±45.3</td>
</tr>
<tr>
<td><strong>Ratio Triglycerides/HDL</strong></td>
<td>1.45 (1.35)</td>
<td>1.11 (0.96)</td>
<td>-0.30 (1.16)</td>
<td>&lt;0.0001</td>
<td>-12.3% ±53.1</td>
</tr>
<tr>
<td><strong>Glycaemia</strong> (mmol/L)</td>
<td>5.40 (1.22)</td>
<td>5.49 (1.31)</td>
<td>0.09 (0.91)</td>
<td>0.4171</td>
<td>2.5% ±14.7</td>
</tr>
</tbody>
</table>

At D0: 45 / 165 patients with lipid lowering agents
At W48: 47 / 159 patients with lipid lowering agents

*The missing data has been replaced by the last available value (LOCF method)*
RALAM: Methods

### Design
- HIV+ ≥ 18 years
- On cART (at least 2 ARV)
- HIV RNA < 50 c/mL > 12 months
- No VF to RAL and 3TC

Randomisation 2 : 1
Open-label

- N = 50
- N = 25

Switch to FDC RAL/3TC
Continue on same cART

### Endpoints
- Primary end-point: Patients with therapeutic failure (defined as viral failure, change in treatment for any reason, consent withdrawal, loss to follow-up or death) at week 24.

Secondary end-points: Changes in laboratory (glucose, HOMA, lipids, estimated glomerular filtration rate, urine beta-2-microglobulin, plasma vitamin D, blood cells, CD4 and CD8 cells), body composition (DXA scan), sleep quality (Pittsburgh Sleep Quality Index), and adherence (Morisky-Green test), and overall and severe adverse events. Also, ultrasensitive HIV-1 RNA and HIV reservoir not presented here.
### Therapeutic failure at week 24: ITT analysis

<table>
<thead>
<tr>
<th>Final status at 24 weeks ITT</th>
<th>Control (n=25)</th>
<th>RAL/3TC (n=49)</th>
<th>Total (n=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study completed</td>
<td>20 (80%)</td>
<td>47 (96%)</td>
<td>67 (91%)</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>2 (8%)</td>
<td>0 (0%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Medical decision</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Virological failure</td>
<td>1 (4%)</td>
<td>0 (0%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>ART change</td>
<td>2 (8%)</td>
<td>0 (0%)</td>
<td>2 (3%)</td>
</tr>
</tbody>
</table>

**Proportion of therapeutic failures at 24 weeks**

<table>
<thead>
<tr>
<th></th>
<th>Proportion RAL/3TC</th>
<th>Proportion Control</th>
<th>Difference in proportions (95% CI) (RAL/3TC) - Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion RAL/3TC</td>
<td>0.041</td>
<td>0.200</td>
<td>-0.159 (-0.353; -0.012)</td>
</tr>
<tr>
<td>Proportion Control</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

We can claim that RAL/3TC is not inferior to Control since the upper bound of the confidence interval -0.012 for the difference in proportions does not cross over the pre-specified noninferiority margin, $\delta$ (0.26).

As an exploratory *post-hoc* analysis, not planned in the protocol, superiority test is performed:

<table>
<thead>
<tr>
<th>Therapeutic failure</th>
<th>Control (n=25)</th>
<th>RAL/3TC (n=49)</th>
<th>Total (n=74)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>20 (80%)</td>
<td>47 (96%)</td>
<td>67 (91%)</td>
<td>0.0398</td>
</tr>
<tr>
<td>Yes</td>
<td>5 (20%)</td>
<td>2 (4%)</td>
<td>7 (9%)</td>
<td></td>
</tr>
</tbody>
</table>
• Switch study to RAL QD
• Patients with NDVL in a stable regimen
• One arm, open label
• Currently recruiting (n:100)
• Primary results expected by November 2019
• Clinical trials.gov: NCT 03195452
SWORD-1 and SWORD-2 Phase III Study Design

**Inclusion criteria**

- On stable CAR ≥6 months before screening
- 1st or 2nd ART with no change in prior regimen due to VF
- Confirmed HIV-1 RNA <50 c/mL during the 12 months before screening
- HBV negative

**Primary endpoint at 48 weeks**: subjects with VL <50 c/mL (ITT-E snapshot)\(^a\)

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\(^a\)-8% non-inferiority margin for pooled data. -10% non-inferiority margin for individual studies

**Countries**

- Argentina
- Australia
- Belgium
- Canada
- France
- Germany
- Italy
- Netherlands
- Russia
- Spain
- Taiwan
- United Kingdom
- United States
DTG + Rilpivirine is non-inferior to continuing ongoing ART in virologically suppressed patients

Inclusion criteria
- On stable CAR ≥6 months before screening
- 1st or 2nd ART with no change in prior regimen due to VF
- Confirmed HIV-1 RNA <50 c/mL during the 12 months before screening
- HBV negative

One subject on DTG + RPV meeting virologic withdrawal criteria had an NNRTI resistance-associated mutation (K101K/E)
No INI resistance-associated mutations were identified
What about InSTIs monotherapy?

- Only tested with DTG
- Mixed results in regards to efficacy
- High rate of resistance selection in the integrase gene in case of VF
- Resistance mutations selected: 92Q; 97A; 118R; 140S; 148 K, R, H; 155H; 230R; 263K, among others \(^1,2\).
- DTG monotherapy should not be used for initial therapy or as a simplification strategy

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1. Wensing A et al: Topics in Antiviral Medicine (IAS-USA), 2017
2. Blanco JI et al: Curr Opin Infect Dis 2018
SWITCH STRATEGIES FOR FAILING PATIENTS
Randomized studies of INSTI-naive patients with VF, HIV resistant to 3 ARV classes

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EARNEST: Second-line LPV/RTV + RAL in patients with virologic failure

- Randomized, controlled, open-label phase III study of patients with virologic failure after first-line NNRTI-based ART in resource-limited settings (N = 1277)

DAWNING: Second-line DTG vs LPV/RTV + 2 NRTIs in Patients With Virologic Failure. Virologic Response at Wk 48

Virologic Outcomes

- **ITT-E**: 84/312 (261/312) vs 70/312 (219/312)
- **PP**: 87/283 (246/283) vs 74/274 (204/274)

Treatment Difference, % (95% CI)

- **ITT-E**: -12.73 (7.3-20.3) vs -5.88 (12.3-18.7)
- **PP**: -13.73 (13.8-7) vs -12.3 (12.7)

*P < .001 for superiority.

## DHHS Guidelines: What to Use for ART Switch in Pts With Virologic Suppression

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Switch to</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Good Supporting Evidence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Switching within class</td>
<td>--</td>
<td>▪ Typically maintains virologic suppression if no drug resistance to new ARV present</td>
</tr>
<tr>
<td>Switching between classes</td>
<td>--</td>
<td>▪ Generally maintains virologic suppression if no drug resistance to new regimen’s components</td>
</tr>
<tr>
<td>Switching to 2-drug regimens</td>
<td>RTV-boosted PI + 3TC</td>
<td>▪ Reasonable option where ABC, TAF, or TDF contraindicated or undesirable</td>
</tr>
<tr>
<td></td>
<td>DTG/RPV QD</td>
<td>▪ Reasonable option where NRTI use undesirable and if resistance to DTG or RPV not anticipated</td>
</tr>
<tr>
<td><strong>Some Supporting Evidence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Switching to 2-drug regimens</td>
<td>RTV-boosted DRV + RAL</td>
<td>▪ Efficacy only examined in treatment-naive pts</td>
</tr>
</tbody>
</table>

DHHS Guidelines: Switch Strategies NOT Recommended

As a result of unacceptable efficacy and/or tolerability, including risk of VF and drug resistance in some cases, several switch strategies are specifically NOT RECOMMENDED

Do NOT Switch to:
- Boosted PI or INSTI monotherapy
- DTG monotherapy
- RTV-boosted ATV + RAL
- Maraviroc + boosted PI
- Maraviroc + RAL
New strategies in development
Dual therapy with Cabotegravir IM + Rilpivirine IM as *Long-Acting* Maintenance ART: 96-Wk Results (LATTE-2)

- Cabotegravir: InSTIs formulated as PO tablet and for long-acting IM injection
- LATTE-2: phase IIb study in which pts randomized to **CAB 400 mg + RPV 600 mg IM Q4W, CAB 600 mg + RPV 900 mg IM Q8W**, or **CAB 30 mg + ABC/3TC 600/300 mg PO QD** after induction/virologic suppression with oral CAB + ABC/3TC (N = 309)

![Virologic Success and No Virologic Data](image)

*HIV-1 RNA < 50 copies/mL.

Few drug-related AEs. At 96 wks, ~30% pts receiving IM injection experienced ISR 99% of ISRs mild/moderate /

AEs leading to withdrawal: Pooled Q4W/Q8W IM arms, 4%. PO arm, 2%

~88% of pts receiving IM CAB very satisfied to continue present treatment vs 43% receiving PO CAB

![Treatment Differences (95% CI)](image)

Who Wants to Switch? Gauging Interest in Potential New Antiretroviral Therapies

- Convenience sample of 263 HIV-infected patients from clinics at Duke and the University of South Carolina
  - 56% male, 80% racial/ethnic minority, 89% with virologic suppression, median 12 years on ART
  - 67% on INSTI, 20% on PI, 24% on NNRTI-based regimens; 41% on single tablet

Compared with your Current HIV Medicines, How Interested Would You Be in Switching to a New Treatment that Involves…

- A single pill taken once a week: 58% interested, 38% somewhat interested, 14% not at all interested
- Two shots given in clinic every other month: 15% interested, 14% somewhat interested, 4% not at all interested
- Two small plastic implants in the forearm every six months: 66% interested, 58% somewhat interested, 38% not at all interested

Ostermann J, et al. 25th CROI; Boston, MA; March 4-7, 2018. Abst. 503.
Switching in Virologically Suppressed Patients: Reasons for switching and safeguards to do so

- To improve adherence
- To reduce pill burden
- To reduce tolerability and toxicity
- To avoid food requirements
- To reduce drug-drug interactions
- To adapt regimen to pregnancy
- To adapt regimen to ageing patients
- To reduce costs

- Does your patient want to switch or are there medical reasons to offer switching?
  - Is potency preserved?
  - Your patient has no history of previous failure and/or resistance?
  - Has he/she undetectable pVL for at least 6 months?
  - Have you considered potential drug interactions?
  - Is your recommendation cost-effective?

If so, switch!
Thank you for your attention!

Iguazu Falls, Argentina