Induction-Maintenance ARV Therapy: Why, Who, When and How?

Pedro Cahn
Disclosures

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

• To improve adherence
• 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
- HCV treatment
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

Caution: Proceed carefully.
‘How’ is not just a question.

how™

IS THE ANSWER.
How? Make sure that you know ....

- **Potency:** Is the new regimen at least as potent as the current one?
- What is the genetic barrier of the new regimen?
- Tolerability is improved or at least maintained
- No toxicity concerns
- Treatment history is carefully considered
- No resistance history
- Patient acknowledges that new side effects might develop
- Patient agrees and takes ownership of the change
A menu of switches....

Modifying NRTIs:
• Replace d4T and/or ddI (do it now!!!)
• Replace ZDV (Proceed shortly)
• Replace TDF (renal issues)
• Replace ABC (lipids, cardiovascular risk?)

Modifying NNRTIs:
• Replace Efavirenz (CNS side effects, lipids)
• Replace Nevirapine (BID dosing)

Modifying PIs: (Tolerability, lipids, DDIs)
• Delete Ritonavir (only with Atazanavir)
• Switch from BID to QD
• Switch to NNRTIs or InSTIs
• Switch to PI monotherapy
• Switch to PI + 3TC
• Switch to INSTi monotherapy
**Design**

311 HIV+ adults
On ABC/3TC + PI/r ≥ 3 months
HIV-1 RNA < 200 c/mL ≥ 3 months
No prior resistance to study drugs

* Stratification by PI: 32% LPV/r vs 68% non-LPV/r

**PI/r at baseline**

<table>
<thead>
<tr>
<th></th>
<th>LPV/r</th>
<th>ATV/r</th>
<th>FPV + RTV 100 mg</th>
<th>FPV + RTV 200 mg</th>
<th>DRV/r</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF/FTC</td>
<td>48/311 (15%)</td>
<td>62/311 (20%)</td>
<td>22/311 (7%)</td>
<td>12/311 (4%)</td>
<td>9/311 (3%)</td>
</tr>
<tr>
<td>ABC/3TC</td>
<td>53/311 (17%)</td>
<td>60/311 (19%)</td>
<td>12/311 (4%)</td>
<td>19/311 (6%)</td>
<td>11/311 (4%)</td>
</tr>
</tbody>
</table>

Primary endpoint: proportion of patients with HIV-1 RNA < 200 c/mL through W48 (TLOVR failure = virologic failure [confirmed RNA ≥ 200 c/mL or last value ≥ 200 c/mL], premature discontinuation, ARV modification); lower limit of the 95% CI for the difference = -12%

HIV RNA < 200 c/mL at W48, ITT-TLOVR

Virologic failure

The percentage of subjects who discontinued study drug due to an AE was higher in the FTC/TDF group (4.5% (n = 7/155), compared to the 3TC/ABC 1.9% (n = 3/156))

95% CI of the difference: - 5.1 ; 11.2

Confirmed HIV RNA ≥ 200 c/mL or last value ≥ 200 c/mL

Fasting Lipids: median change from baseline to W48, mg/dL [mmol/L]

- **Total chol**
  - TDF/FTC: -21 [-0.54] mg/dL
  - ABC/3TC: -20 [-0.54] mg/dL
  - *Wilcoxon rank-sum test: p=0.26*

- **LDL-c**
  - TDF/FTC: -7 [-0.18] mg/dL
  - ABC/3TC: -6 [-0.17] mg/dL
  - *Wilcoxon rank-sum test: p=0.007*

- **HDL-c**
  - TDF/FTC: 2 [0.05] mg/dL
  - ABC/3TC: -1 [-0.03] mg/dL
  - *Wilcoxon rank-sum test: p<0.001*

- **TG**
  - TDF/FTC: -18 [-0.20] mg/dL
  - ABC/3TC: -9 [-0.10] mg/dL
  - *Wilcoxon rank-sum test: p=0.074*

No significant difference between groups in total cholesterol/HDL-c ratio at W48

* Wilcoxon rank-sum test

Switching to FTC/TDF from 3TC/ABC maintained virologic suppression, had fewer VFs, more AE-related discontinuations, improved lipid parameters and Framingham scores, while slight declines in eGFR were observed.
Conclusions
In conclusion, a significant improvement of the serum creatinine, eGFR and UACR was observed in 286 HIV-positive patients who were switched to ABC after receiving a TDF-based ART regimen for at least six months. Of note, after the switch, the plasma HIV RNA remained suppressed and the CD4 cell count increased in the majority of patients. Similar trends were observed regardless of whether or not the third drug in the regimen was atazanavir. These findings highlight that it is safe and effective to switch from TDF to ABC if there are concerns regarding serum creatinine and eGFR, as long as the HLA-B*5701 test is negative and the patient’s HIV RNA viral load is suppressed. Finally, the continued use of atazanavir did not appear to have a significant effect on the recovery of the renal function parameters.
**Virologic outcome at W48 and W96 (ITT, snapshot)**

- **E/C/F/TAF (N = 959)**
  - HIV RNA < 50 c/mL: 97.2%
  - Virologic failure: 1%
  - No virologic data: 5%

- **TDF-based regimens (N = 477)**
  - HIV RNA < 50 c/mL: 93.1%
  - Virologic failure: 1.3%
  - No virologic data: 9%

**Difference (95% CI)**

- Week 48: 4.1% (1.6 to 6.7)
- Week 96: 3.7% (0.4 to 7.0)

**Superiority of E/C/F/TAF**

- Superiority at Week 48: 3.7% (0.4 to 7.0)
- Superiority at Week 96: 3.7% (0.4 to 7.0)

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*One patient in the TAF group with virologic failure (W8) had genotypic resistance: M184I/M. The patient resuppressed 4 weeks later without a change of regimen.*

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Efavirenz to Etravirine switch in patients with CNS adverse events

### Design

- **Randomisation**: 1:1
- **Endpoints**
  - **Primary**: change in the proportion of patients experiencing grade 2-4 CNS toxicity at week 12
  - **Secondary**: change in CNS score, median number of grade 2-4 CNS adverse events, viral suppression, CD4 change, fasting lipids, safety

**HIV+ adults**
- On 2 NRTI + EFV ≥ 12 weeks
- HIV-1 RNA < 50 c/mL
- CD4 > 50/mm³
- Ongoing CNS symptoms

**N = 20**
- **Blinded Phase W0-W12**: 2 NRTI + ETR 400 mg QD + EFV placebo
- **Open-label Phase W12-W24**: 2 NRTI + ETR 400 mg QD

**N = 18**
- **Blinded Phase W0-W12**: 2 NRTI + ETR 400 mg QD + EFV placebo
- **Open-label Phase W12-W24**: 2 NRTI + ETR 400 mg QD

### Endpoints

- Primary: change in the proportion of patients experiencing grade 2-4 CNS toxicity at week 12
- Secondary: change in CNS score, median number of grade 2-4 CNS adverse events, viral suppression, CD4 change, fasting lipids, safety
Efavirenz to Etravirine switch in patients with CNS adverse events

- Combined analysis, at W12 of ETR in both arms
  - Grade 2-4 CNS AE
    - **Significant reductions** (baseline; W12) in overall AE (89%; 60%; p=0.009), insomnia (63%; 37%; p=0.016), abnormal dreams (57%; 20%; p=0.001) and nervousness (29%; 9%; p=0.046)
    - HIV-1 RNA < 50 c/mL at all visits, median CD4 rise: +43/mm³
  - Fasting lipids
    - Reductions in total cholesterol (-0.64 mmol/L, p<0.001) and LDL-cholesterol (-0.58 mmol/L, p=0.021)
    - No rash or hepatotoxicity

**Conclusion**

Switching EFV to ETR led to a significant reduction in some but not all grade 2-4 CNS adverse events. Once-daily ETR is an efficacious, tolerable and lipid-friendly alternative to EFV in patients with persistent CNS toxicity.
SPIRIT Study: Switch PI/r to TDF/FTC/RPV

**Design**

- **Randomisation**
  - 2:1
  - Open-label

- **Population**
  - 476 HIV+ adults
  - Stable 2 NRTI* + PI/r** for ≥ 6 months
  - HIV RNA < 50 c/mL ≥ 6 months
  - No known genotypic resistance to study drugs
  - NNRTI naive

**Endpoints**

- **Primary:** non inferiority in the proportion of patients with HIV-1 RNA < 50 c/mL at W24 (FDA snapshot analysis), lower limit of the 95% CI for the difference = - 12%

- **Secondary:** fasting lipids, safety and tolerability, CD4

* NRTI = TDF/FTC: 81% ; ABC/3TC: 13.2%
** PI/r = ATV/r: 37.0% ; LPV/r: 32.6% ; DRV/r: 20.2% ; FPV/r: 7.8%
SPIRIT Study: Switch PI/r to TDF/FTC/RPV

HIV-1 RNA < 50 c/mL at W24 (snapshot, ITT)

≠ (95 % CI) TDF/FTC/RPV - PI/r
3.8 (- 1.6 ; 9.1): non inferiority

CV < 50 c/mL, ITT, M = Excluded
RPV = 99.7% vs PI/r = 94.7%

Non inferiority

Historical baseline pretreatment HIV RNA
(23 patients on TDF/FTC/RPV and 14 on PI/r excluded because data not available)

Palella F AIDS. 2014 Jan 28;28(3):335-44
Through Week 48, 88.3% of subjects switching to FTC/RPV/TDF at baseline maintained virologic suppression (HIV-1 RNAB50 copies/mL by FDA snapshot analysis), while improving total cholesterol, LDL, and triglycerides.

All 17 patients with baseline K103N who switched to TDF/FTC/RPV maintained virologic suppression.

Discontinuation for AE by W24 - TDF/FTC/RPV, N = 6 [renaltubulopathy, N = 1, CNS, N = 4] - 2 NRTI + PI/r, N = 0

Decrease in eGFR (Cockroft-Gault) significantly higher for RPV.

<table>
<thead>
<tr>
<th></th>
<th>RPV</th>
<th>PI/r</th>
</tr>
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<tbody>
<tr>
<td>Grade 3-4 AE</td>
<td>5%</td>
<td>6.9%</td>
</tr>
<tr>
<td>Grade 3-4 lab. abnormalities</td>
<td>6.3%</td>
<td>11.3%</td>
</tr>
</tbody>
</table>

Fasting lipids: mean change at W24

<table>
<thead>
<tr>
<th></th>
<th>TDF/FTC/RPV</th>
<th>2 NRTI + PI/r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total chol. (mg/dL)</td>
<td>-1</td>
<td>-16</td>
</tr>
<tr>
<td>LDL-c (mg/dL)</td>
<td>-53</td>
<td>-4</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL-c (mg/dL)</td>
<td>-4</td>
<td>-1</td>
</tr>
<tr>
<td>TC: HDL ratio</td>
<td>0.08</td>
<td>-0.27</td>
</tr>
</tbody>
</table>

p < 0.001 for all comparisons

Significant reduction in 10-yr Framingham score (p=0.001) at W24 among TDF/FTC/RPV

Palella F AIDS. 2014 Jan 28;28(3):335-44
Switch from unboosted protease inhibitor to a single-tablet regimen containing rilpivirine improves cholesterol and triglycerides

Antonio Di Biagio a, Niccolò Riccardi a,x, Lucia Taramasso a, Amedeo Capetti b, Giovanni Cenderello c, Alessio Signori d, Paola Vitiello e, Michele Guerra f, Giuseppe Vittorio de Socio g, Giovanni Cassola c, Tiziano Quirino e, Claudio Viscoli a

Fig. 1. Change in plasma levels of cholesterol, triglycerides (TG) and bilirubin from baseline though to Week 12.

Switching to RPV/FTC/TDF from an unboosted PI in virologically suppressed HIV-infected patients is safe and is associated with a reduction in triglycerides, cholesterol and cART-related costs.

**Design**

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

293 HIV+ adults
On 2 NRTIs + (PI or NNRTI)
Darunavir-naïve
No history of prior virologic failure
HIV-1 RNA < 50 c/mL > 6 months

N = 129
DRV/r 800/100 mg qd
+ 2 NRTIs (optimisation at D0**)

N = 127
DRV/r 800/100 mg qd

* Randomisation was stratified on the use of PI or NNRTI
  (57% patients on PI, 43% on NNRTI)
** NRTI used at baseline: TDF + FTC = 46%; ABC + 3TC: 31%;
  ZDV + 3TC = 10%; TDF + 3TC = 7%; other combinations: 6%

**Objective**

- Non inferiority in the proportion of patients with HIV-1 RNA < 50 c/mL at W48 (per-protocol analysis, switch= failure, TLOVR algorithm); lower limit of the 95% CI for the difference= -12%, 80% power

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* MONET Study: Switch PI or NNRTI to DRV/r QD monotherapy

**MONET**

Arribas J, AIDS 2010;24:223-230
HIV-1 RNA < 50 c/mL at W144 (ITT-TLOVR)

Switch* = failure Switch* included

Lower margin of the 95% CI of the ≠
- 16.9 % - 8.7 %

2 consecutive HIV-1 RNA > 50 c/mL:
- DRV/r monotherapy, N = 21
- DRV/r + 2 NRTI, N = 13
- 18/21 and 10/13 had HIV-1 RNA < 50 c/mL at W144

Level of HIV-1 RNA at baseline and HCV co-infection were significantly associated with transient viremia during the 144 weeks (p < 0.05)

Resistance emergence to PI (IAS-USA): 1 in each arm, both before W24

Non inferiority of DRV/r monotherapy only in the « switch-included » analysis

* Change in ARV

Monotherapy with darunavir/ritonavir or lopinavir/ritonavir versus standard antiretroviral therapy: a randomized clinical trial (2pm Study).

Nicola Gianotti 1*, Laura Galli 1, Renato Maserati 2, Laura Sighinolfi 3, Diego Ripamonti 4, Loredana Palvarini 5, Sergio Lo Caputo 6, Emanuele Focà 7, Benedetto Maurizio Celesia 8, Franco Baldelli 9, Gaetana Sterrantino 10, Adriano Lazzarin 1,11

In conclusion, in this randomized clinical trial of DRV/r-MT or LPV/r-MT versus continuing ongoing cART, virological failure was observed in only one patient receiving LPV/r-MT, suggesting that a strategy of PI/r-MT can be suitable for patients suffering from NRTI toxicity.
Protease inhibitor monotherapy for long-term management of HIV infection: a randomised, controlled, open-label, non-inferiority trial

Nicholas I Paton, Wolfgang Stühr, Alejandro Arenas-Pinto, Martin Fisher, Ian Williams, Margaret Johnson, Chloe Orkin, Fabian Chen, Vincent Lee, Alan Winston, Mark Gompels, Julie Fox, Karen Scott, David T Dunn, for the Protease Inhibitor Monotherapy Versus Ongoing Triple Therapy (PIVOT) Trial Team

www.thelancet.com/hiv Vol 2 October 2015

N: 587

MT: > Viral rebound
Resuppression achieved
Non-inferiority shown

Interpretation
Protease inhibitor monotherapy, with regular viral load monitoring and prompt reintroduction of combination treatment for rebound, preserved future treatment options and did not change overall clinical outcomes or frequency of toxic effects. Protease inhibitor monotherapy is an acceptable alternative for long-term clinical management of HIV infection.
Conclusions

The potential benefits of dual therapy regimens include reduced toxicity, improved tolerability and adherence, and reduced cost. Although the data reviewed here provide valuable insights into the effectiveness and tolerability of dual therapy regimens, it remains unclear whether these potential benefits can be maintained long-term. Appropriately powered studies with longer follow-up periods are needed to more definitively assess potential toxicity reduction advantages with dual therapy.
OLE: Study design

- 48-week multicenter, prospective, randomized, open-label, non-inferiority trial (n:250)

- Eligibility criteria

  HIV-infected patients with plasma HIV-1 RNA < 50 copies/ml
  for ≥ 6 months on TT with LPV/r + 3TC/FTC + NRTI and
  no resistance to LPV/r or 3TC/FTC

- Primary endpoint:

  - Proportion of patients free of therapeutic failure at 48 weeks, in the m-ITT population
    defined as two consecutive viral load measurements >= 50 copies/ml, death, progression to new AIDS defining disease, loss to follow-up or change or

OLE: Main endpoints

Virological suppression (< 50 copies/ml) at 48 weeks

- Protocol defined VF
  - DT (LPV/r+3TC): 97.3%
  - TT: 97.3%

- Any blip
  - DT (LPV/r+3TC): 89.8%
  - TT: 90.1%

- Protocol defined VF or any blip
  - DT (LPV/r+3TC): 87.3%
  - TT: 87.6%

**Difference (95% CI)**

- Protocol defined VF: 0.05% (-5.3% to +5.1%)
- Any blip: -0.25% (-8.2% to +7.6%)
- Protocol defined VF or any blip: 0.3% (-8.5% to +8.3%)

**Protocol defined VF:** 2 consecutive VL >= 50 copies/ml; **VF or any blip:** any detectable VL >= 50 copies/ml
Switching regimens in virologically suppressed HIV-1-infected patients: evidence base and rationale for integrase strand transfer inhibitor (INSTI)-containing regimens

F Raffi,1 S Esser,2 G Nunnari,3 I Pérez-Valero4 and L Waters5

HIV Medicine (2016), 17 (Suppl. 5), 3–16

- SWITCHMRK [30]
- SPIRAL [31–35]
- STRATEGY-PI [40,45,46]
- STRATEGY-NNRTI [39,42,43]
- STRIIVING (unpublished at the time of submission) [36,37]
- GS-US-292-0109 (GS Study 109) [38,47]
Design: 2 parallel trials, SWITCHMRK 1 and 2

- Randomisation: 1:1 Double-blind
- HIV+ ≥ 18 years
- On LPV/r + ≥ 2 NRTIs
- HIV RNA < 50 c/mL (PCR) or < 75 c/mL (bDNA) > 3 months

**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

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

### SWITCHMRK Study: Good for lipids

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

<table>
<thead>
<tr>
<th></th>
<th>Total cholesterol</th>
<th>Non-HDL-C</th>
<th>Triglycerides*</th>
<th>LDL-C</th>
<th>HDL-C</th>
<th>Total cholesterol</th>
<th>Non-HDL-C</th>
<th>Triglycerides*</th>
<th>LDL-C</th>
<th>HDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SWITCHMRK 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>SWITCHMRK 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>5.6 5.3</td>
<td>4.3 4.1</td>
<td>2.1 1.8</td>
<td>3</td>
<td>2.7</td>
<td>5.6 5.5</td>
<td>4.3 4.2</td>
<td>2.4 2.5</td>
<td>2.7</td>
<td>2.7</td>
</tr>
<tr>
<td>W12</td>
<td>4.8 5.3</td>
<td>3.6 4.1</td>
<td>1.3 1.9</td>
<td>2.8</td>
<td>2.7</td>
<td>4.7 5.5</td>
<td>3.6 4.3</td>
<td>1.4 2.7</td>
<td>2.7</td>
<td>2.7</td>
</tr>
</tbody>
</table>

* median changes for triglycerides
** not tested

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

A case of success: The SPIRAL Study:

### Design

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

- **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 ;
  - Secondary: virologic failure (confirmed HIV-1 RNA > 50 c/mL), CD4, fasting lipids, adverse events

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

### Endpoints

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+ ≥ 18 years</td>
<td>On 2 ARV + PI/r</td>
</tr>
<tr>
<td>HIV RNA &lt; 50 c/mL &gt; 6 months**</td>
<td>Raltegravir-naïve</td>
</tr>
</tbody>
</table>

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

Martinez E, AIDS 2010;24:1697-1707
SPIRAL Study: Switch PI/r to RAL: Good for lipids

- 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

<table>
<thead>
<tr>
<th></th>
<th>RAL</th>
<th>PI/r</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>89.2</td>
<td>86.6</td>
</tr>
<tr>
<td>Prior virologic failure or suboptimal therapy</td>
<td>88.6</td>
<td>83.1</td>
</tr>
<tr>
<td>Yes</td>
<td>90</td>
<td>89.9</td>
</tr>
<tr>
<td>No</td>
<td>96.9</td>
<td>95.1</td>
</tr>
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</table>

Absence of virologic failure

<table>
<thead>
<tr>
<th></th>
<th>RAL</th>
<th>PI/r</th>
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<tbody>
<tr>
<td>All patients</td>
<td>97.2</td>
<td>93.1</td>
</tr>
<tr>
<td>Prior virologic failure or suboptimal therapy</td>
<td>96.4</td>
<td>96.9</td>
</tr>
<tr>
<td>Yes</td>
<td>96.4</td>
<td>96.9</td>
</tr>
<tr>
<td>No</td>
<td>96.4</td>
<td>96.9</td>
</tr>
</tbody>
</table>

95% CI for the ≠

- Yes: -5.2; 10.6
- No: -5.9; 17.6

Martinez E, AIDS 2010;24:1697-1707
STRATEGY – PI: randomised, open-label study in virologically suppressed patients = PI/r + FTC/TDF continuation (n=140) vs switch to EVG/c/FTC/TDF (n=293)

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

- **Virologic Success W48**: 94% (E/C/F/TDF, n=290) vs 87% (PI + RTV + FTC/TDF, n=139)
- **Virologic Failure W48**: <1% vs 1%
- **No Virologic Data W48**: 6% vs 12%

4 patients excluded from analysis:
- 3 in EVG/c arm
- 1 in PI/r arm

95% CI for Difference:
- **favours PI/r + FTC/TDF**: -12% to 6.7%
- **favours E/C/F/TDF**: 0.4% to 13.7%

Pre-specified sequential testing
Statistical superiority (p=0.025)

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

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

STRATEGY-NNRTI: randomised, open-label study in virologically suppressed patients
= NNRTI + FTC/TDF continuation (n=143) vs switch to EVG/c/FTC/TDF (n = 290)

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

- Improvement in reported outcome for patients who switched from EFV
  - lower rates of neuropsychiatric symptoms compared to baseline
  - Higher treatment satisfaction scores
- DC for AE: 2%
- 1 case of proximal renal tubulopathy

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

Pozniak A, Lancet Infect Dis 2014; 14:590-9
STRIIVING: Switch from suppressive ART to fixed-dose DTG/ABC/3TC

- Multicenter, randomized, open-label phase IIIb study
  - Conducted in US, Canada, and Puerto Rico
  - Primary endpoint: HIV-1 RNA < 50 copies/mL at Wk 24

Pts with HIV-1 RNA < 50 copies/mL on stable ART ≥ 6 mos, no previous virologic failure, HLA-B*5701 negative (N = 553)

Baseline ART* (n = 278)  DTG/ABC/3TC (n = 244)

*Containing 2 NRTIs plus NNRTI, PI, or INSTI.

STRIIVING study: week 48 results

LATTE-2: CABOTEGRAVIR IM + RILPIVIRINE IM FOR LONG-ACTING MAINTENANCE ART

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

**Induction Phase**

- **Wk 16:** RPV 25 mg PO QD added

**Maintenance Phase**

- **Wk 32**
  - CAB 400 mg + RPV 600 mg IM Q4W (n = 115)

- **Wk 48**
  - CAB 600 mg + RPV 900 mg IM Q8W (n = 115)
  - CAB 30 mg + ABC/3TC 600/300 mg PO QD (n = 56)

**ART-naive** HIV-infected pts younger than 18 yrs of age with CD4+ cell count > 200 cells/mm³ (N = 309)

*Pts with HIV-1 RNA < 50 copies/mL from Wk 16-20 continued to maintenance phase.
†Pts eligible for Q4W or Q8W LA extension past Wk 96.

Virologic Outcomes

- **HIV-1 RNA <50 c/mL, %**
  - **Virological success:**
    - Q8W (n=115): 92%
    - Q4W (n=115): 91%
    - CAB 744 (n=56): 89%
  - **Virological non-response:**
    - Q8W (n=115): 7%
    - Q4W (n=115): 2%
    - CAB 744 (n=56): <1%
  - **No virologic data:**
    - Q8W (n=115): <1%
    - Q4W (n=115): 8%
    - CAB 744 (n=56): 9%

Both Q8W and Q4W comparable to Oral CAB at Week 48

### Treatment Differences (95% CI)

- **Q8W IM:**
  - Oral: -12.4 - 11.6
  - Q8W IM: 2.9 - 12.4
  - Q4W IM: 2.0 - 7.6

Margolis D, et al. AIDS 2016; Durban, South Africa; July 18-22, 2016; Abst. THAB0206LB
## LATTE-2: WK 48 PT SATISFACTION WITH IM AND PO REGIMENS

Pt satisfaction assessed using 0 to 6 scoring (0 = very dissatisfied, 6 = very satisfied)

<table>
<thead>
<tr>
<th>Wk 48 Patient-Reported Outcomes, %</th>
<th>IM CAB + RPV Q4W (n = 103)</th>
<th>IM CAB + RPV Q8W (n = 109)</th>
<th>PO CAB + ABC/3TC (n = 49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>How satisfied are you with your current treatment?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>79</td>
<td>83</td>
<td>67</td>
</tr>
<tr>
<td>5</td>
<td>20</td>
<td>14</td>
<td>29</td>
</tr>
<tr>
<td>&lt; 5</td>
<td>1</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>How satisfied would you be to continue with your present form of treatment?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>85</td>
<td>88</td>
<td>55</td>
</tr>
<tr>
<td>5</td>
<td>13</td>
<td>11</td>
<td>33</td>
</tr>
<tr>
<td>&lt; 5</td>
<td>2</td>
<td>1</td>
<td>12</td>
</tr>
</tbody>
</table>

DTG Monotherapy?

Moreira JAC 2016;71:2675-6

DoluMono cohort retrospective study:
29/31 (94%) remained undetectable at 24 weeks.
But 1 patient developed confirmed virologic failure (538 copies/mL) with new INSTI mutations (Q148H/G140S)

Oldenbuettel JAIDS 2016 (epub)
Quality of life of HIV-infected patients who switch antiretroviral medication due to side effects or other reasons

Eric M. Maiese⁹, Phaedra T. Johnson⁸, Tim Bancroft⁹, Alyssa Goolsby Hunter⁹ and Albert W. Wu³

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.
And more results are around the corner...
Switch studies
Glasgow 2016

<table>
<thead>
<tr>
<th>Study</th>
<th>Regimen</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATLAS-M</td>
<td>Atazanavir/3TC</td>
<td>Gagliardini</td>
</tr>
<tr>
<td>ANRS 1286/MOBIDIP</td>
<td>PIs + 3TC</td>
<td>Ciaffi</td>
</tr>
<tr>
<td></td>
<td>TAF + Darunavir/Cobi</td>
<td>Gallebaut</td>
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<tr>
<td></td>
<td>TAF + Rilpivirine</td>
<td>Orkin</td>
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<tr>
<td></td>
<td>TAF 96 weeks</td>
<td>Raffi</td>
</tr>
<tr>
<td>DOMONO</td>
<td>Dolutegravir Monotherapy</td>
<td>Rijnders</td>
</tr>
<tr>
<td>DUAL</td>
<td>Darunavir/r + 3TC</td>
<td>Arribas</td>
</tr>
</tbody>
</table>
Regional Considerations

- General principles of switching apply everywhere
- Local availability and cost/reimbursement of ART medications need to be taken into account
- Historically, most switching studies were investigator-driven or academic studies in Europe
- More recently, switching studies were performed in other parts of the world (eg, the SWITCHMRK studies\textsuperscript{[a]})
- Switching studies have become registration trials
- CAVEAT: done in very clean and adherent patients, not necessarily reflecting clinical practice reality

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!
Acknowledgements

- Jose Arribas
- José Gatell
- Francois Raffi
- Anton Pozniak
- Trip Gulick
- HIV-trials.com
- Medscape

Thank you for your attention