Dolutegravir Monotherapy in HIV-infected Patients with Sustained Viral Suppression: A 24-week Pilot Study

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Patients and End-points

- **Elegible participants** were virally suppressed patients without known resistance to INSTI in whom the treating physician switched to DTG 50mg QD for ≥2 of the following reasons:
  - antiretroviral-related adverse effects,
  - comorbidities overlapping antiretroviral toxicity,
  - need for chronic non-ART placing the patient at risk for clinically significant interactions with antiretroviral drugs, or
  - archived resistance compromising antiretroviral efficacy.

- **Primary end-point**
  - Proportion of patients with plasma HIV-1 RNA <37 copies/mL at 24 weeks (ITT non-completer=failure)

- **Secondary end-points** were:
  - CD4 and CD8 cell counts, and CD4/CD8 ratio
  - Lipids, creatinine and CKD-EPI, and high-sensitivity CRP
  - Adverse events
  - Impact on the reasons underlying antiretroviral therapy switch
  - HIV resistance mutations in plasma (Trugene, Siemens) and PBMCs (454 GS-Junior platform, Roche) in case of viral failure.
Reasons for switch *

- Underlying (prior or current) reasons were:
  - Comorbidities n=32 (97%)
  - Risk for interactions n=28 (85%)
  - ART-related adverse effects n=25 (76%)
  - Resistance mutations n=16 (48%)

- Immediate (current) reasons were:
  - Interactions n=13 (39%)
  - GI symptoms n=11 (33%)
  - Dyslipidemia n=9 (27%)
  - Osteoporosis n=6 (18%)
  - High CV risk (Framingham ≥20%) or CV disease n=4 (12%)
  - Progression of chronic kidney disease n=1 (3%)

* According to treating physician
Baseline characteristics

- **Age**: 56 (50-62)
- **Women**: 18 (55%)
- **Years since HIV diagnosis**: 19 (17-23)
- **AIDS-defining events**: 13 (39%)
- **Years with VL below detection threshold**: 8 (4-13)
- **CD4 cells (/mm$^3$)**: 596 (420-843)
- **CD8 cells (/mm$^3$)**: 990 (624-1288)
- **CD4/CD8 ratio**: 0.64 (0.46-1.01)
- **ART regimens withdrawn:**
  - PI/r-based: 22 (67%)
  - NNRTI-based: 9 (27%)
  - INSTI-based: 2 (6%)

Data are median (interquartile range) unless otherwise expressed.
Virological and immunological response

- At 24 weeks, the therapeutic efficacy of dolutegravir monotherapy was 97% (95% CI 83%-100%) (ITT non-completer=failure). One patient had low-level virological failure after 4 weeks. 118R was detected in PBMC integrated-DNA at 24 weeks.
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<tr>
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<th>Baseline</th>
<th>24 weeks</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Glucose (mg/dL)</td>
<td>93 (89-101)</td>
<td>93 (86-104)</td>
<td>0.2501</td>
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<tr>
<td>Triglycerides (mg/dL)</td>
<td>205 (160-303)</td>
<td>112 (95-160)</td>
<td>&lt;0.0001</td>
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<td>High-sensitivity CRP (mg/dL)</td>
<td>0.08 (0.04-0.21)</td>
<td>0.07 (0.04-0.10)</td>
<td>0.0054</td>
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<td>Total cholesterol (mg/dL)</td>
<td>221 (185-255)</td>
<td>185 (171-211)</td>
<td>&lt;0.0001</td>
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<td>LDL cholesterol (mg/dL)</td>
<td>129 (109-161)</td>
<td>119 (100-135)</td>
<td>0.0004</td>
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<td>HDL cholesterol (mg/dL)</td>
<td>46 (37-53)</td>
<td>42 (37-55)</td>
<td>0.5157</td>
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<td>Total-to-HDL ratio</td>
<td>4.62 (4.14-5.79)</td>
<td>3.89 (3.21-5.12)</td>
<td>0.1971</td>
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<td>Creatinine (mg/dL)</td>
<td>0.83 (0.64-0.95)</td>
<td>0.90 (0.73-1.05)</td>
<td>0.0203</td>
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<tr>
<td>CKD-EPI (mL/min/1.73m²)</td>
<td>97 (80-107)</td>
<td>89 (72-98)</td>
<td>&lt;0.0001</td>
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Data are median (interquartile range)
• Patients <50 cp/mL for ≥2 yrs
• Stable triple cART
• No resistance to INSTI and 3TC/FTC
• N=150 per arm

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<th>A. Protocol Information</th>
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<tr>
<td>A.1 Member State Concerned</td>
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<td>A.2 EudraCT number</td>
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<td>A.3 Full title of the trial</td>
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<tr>
<td>A.3.1 Title of the trial for lay people, in easily understood, i.e. non-technical, language</td>
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<tr>
<td>A.3.2 Name or abbreviated title of the trial where available</td>
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Maintain ART (control arm)

Switch to DTG+3TC (bitherapy arm)

Switch to DTG (monotherapy arm)

48 weeks