Dolutegravir as Maintenance Monotherapy

First Experiences in 5 HIV-1 Infected Patients

and

The Foundation of a Randomized Clinical Trial

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Monotherapy – Boosted Protease Inhibitors

- RCTs on monotherapy boosted PIs.
  - Lopinavir/ritonavir:
    - Experienced: OK$^1$, OK04$^2$, KAIMO$^3$
    - Naive: MONARK$^4$
  - Darunavir/ritonavir: MONO-ANRS 136$^5$, MONET$^6$, PROTEA$^7$.
  - Atazanavir/ritonavir: MODAT$^8$

- Meta-analysis on DRV/r monotherapy$^9$
  - CD4 nadir <200 cells/mm$^3$ + prior NNRTI exposure ∞ failure.

References:
1 JAIDS 2005 Arribas et al.
2 AIDS 2008 Pulido et al.
3 Hiv Clin Trials 2009 Nunes et al.
4 AIDS 2008 Delfraissy et al.
5 AIDS 2010 Katlama et al.
6 AIDS 2010 Arribas et al.
7 J Int AIDS 2014 Soc Antinori et al.
8 AIDS 2014 Castagna et al.
9 CROI 2015 Ripamonti et al.
Dolutegravir monotherapy?

The feasibility of dolutegravir maintenance monotherapy is currently unknown.
Methods

- Series of 5 consecutive HIV-1 patients off-label switch to DTG mono.
  - All were on single-tablet regimens (STR) cART or preferred STR.
  - Contra-indications to current/alternative cART.

- Patients were:
  - INI naive, HIV-RNA <50 copies/mL.
  - No previous virological failure or known resistance mutations.

- Informed consent.
  - Return to original regimen upon failure.
DOMONO trial design
clinicaltrials.gov: NCT02401828

Central Question:
- Can HIV-1 suppression (OT) be maintained by DTG monotherapy in HIV-1 infected, virologically suppressed patients on cART?

**Phase IV randomised open label controlled trial DTG monotherapy vs cART**

- HIV-1 adults, ≥18 years
- No previous virological failure
- HIV-1 RNA <50 c/mL for >24 weeks
- CD4 nadir >200 cells/mm³
- HIVRNA pre-cART <100,000

**Screening Visit**

**Randomisation Day 1**

**Interim analysis Week 12**

**Primary Endpoint Week 24**

**Group A: End of study week 48**

**Group B: End of study week 48**

**Screening period**

**Randomised phase**

Primary endpoint: proportion of subjects with HIV-1 RNA <200 c/mL at week 24 (OT)
Methods

- Power 80% to show non-inferiority if the lower bound of 95% CI difference in proportion does not exceed -12%.

- Exploratory secondary endpoints:
  - HIV-RNA <200/<50 at w24/w48 on DTG mono (ITT/OT).
  - CD4 change and CD4 reservoir HIV-DNA.
  - Resistance and AE.
  - Metabolic endpoints.
  - Cost effectiveness.

- October 2015: included >80 HIV-1 patients.
Conclusion

- DTG monotherapy may be a valuable ART maintenance option but evidence should first be established in a RCT.

- The added value of DTG monotherapy could be:
  - Side effects.
  - Elderly.
  - Comedication.
  - Pill burden (adherence?)
  - NRTI related toxicity.
  - Costs.
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<tr>
<th>Session</th>
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<td>PS4/2</td>
<td>Dolugetravir Monotherapy in HIV-infected Patients with Sustained Viral Suppression: A 24-week Pilot Study</td>
<td>15:15 - 15:30</td>
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<td>PS4/4</td>
<td>Dolugetravir Monotherapy in HIV-infected Patients with Suppressed HIV Viremia</td>
<td>15:30 - 15:45</td>
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Final comments

- Virology Education

This study would not be possible without the help of:
- Bart J.A. Rijnders
- Carolina A.M. Schurink
- Charles A.B. Boucher

Our 5 patients thank you for the ongoing enthusiasm to participate in studies and help the HIV research field further