Oral Abstract Presentations 1

#2 Cost-Utility Analysis of Dolutegravir-Versus Efavirenz 400mg-Based Regimen for the Initial Treatment of HIV-Infected Patients in Cameroon: 96-week Results from the NAMSAL ANRS 12313 Trial

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NAMSAL
ANRS 12313

Context

600mg efavirenz-based regimen (EFV600):

- Preferred first-line regimen for treating HIV in low- and middle-income countries **until 2019**.
- Concerns about adverse neurosensory effects.
- Low genetic barriers, which may result in the accumulation of drug-resistance mutations in the absence of regular viral-load monitoring.

➢ **Updated WHO 2019 guidelines:**

❑ **Preferred first-line regimen: Dolutegravir (DTG) (50mg)**

- Superior to EFV600 in terms of viral suppression and immunological recovery.
- High genetic barrier to resistance.
- Availability in a low-cost fixed-dose combination.
- Concerns about its safety during pre-conception and pregnancy.
- Concerns about its tolerability, because of the associated risk of insomnia and obesity.

❑ **Alternative first-line regimen: low-dose (400mg) efavirenz-based regimen (EFV400)**

- Non-inferior to EFV600 in terms of efficacy, better safety profile.
- Efficient and safe in pregnant women and in patients with tuberculosis.

Evidence before this study

Cost-effectiveness of a DTG-based regimen versus an EFV-based regimen as a first-line antiretroviral therapy (ART) in sub-Saharan Africa: three modelling studies

- **Phillips *et al.* (*Lancet HIV* 2018; 5: e146–54**) -> DTG more effective and cost-effective, with a higher cost-effectiveness in countries where the prevalence of NNRTI pre-treatment drug resistance is greater.

- **Phillips *et al.* (*Lancet HIV* 2019; 6: e116–27)** -> the benefits of transition to a DTG-based regimen for all persons on ART outweighed the risks, including the risk of neural tube defects in infants for women intending to have children in the near future.

- **Phillips *et al.* (*Lancet HIV* 2020; 7: e193–200)** -> accounting for the potential negative effects of weight gain associated with DTG, DTG for women intending pregnancy was cost-effective in 87% of the scenarios.

- No study on PROs or the cost-effectiveness of a DTG-based regimen versus a **low-dose** EFV-based regimen in sub-Saharan African countries.
- No study using individual-level data from a randomized clinical trial.

The NAMSAL (ANRS 12313) trial

- 613 HIV-1 positive, treatment-naïve adults (ie, aged >18 years) enrolled between July 2016 and August 2017 in three HIV day-care centres in Yaoundé, Cameroon.
- Random assignement (1:1) to receive either dolutegravir 50mg (DTG arm) or low-dose (ie, 400mg) efavirenz (EFV400 arm), once daily, combined with tenofovir disoproxil fumarate (TDF) and lamivudine (3TC).
- Clinical visits scheduled at baseline and then quarterly.

➢ **48-Week clinical results** -> **Non-inferiority** of the DTG-based regimen.

Source: NAMSAL ANRS 12313 Study Group. (2019). Dolutegravir-based or low-dose Efavirenz–based regimen for the treatment of HIV-1. *New England Journal of Medicine*, *381*(9), 816-826.

➢ **96-Week clinical results** -> Confirmed **non-inferiority** of DTG, lower proportion of **virological failure** in the DTG arm (8/310 versus 19/303 in the EFV400 arm), with no observed **resistance mutation** to DTG (versus 17 among the 19 EFV400 failure cases).

-> **Weight gain** and incidence of **obesity** was significantly higher in the DTG arm.

Source: Calmy, A., Sanchez, T. T., Kouanfack, C., Mpoudi-Etame, M., Leroy, S., Perrineau, S., ... & Varloteaux, M. (2020). Dolutegravir-based and low-dose efavirenz-based regimen for the initial treatment of HIV-1 infection (NAMSAL): week 96 results from a two-group, multicentre, randomised, open label, phase 3 non-inferiority trial in Cameroon. *The Lancet HIV*, *7*(10), e677-e687.

Added value of this study

- First cost-utility study comparison of DTG versus low-dose EFV in sub-Saharan Africa, using individual-level data from a randomized clinical trial.
- Data on clinical outcomes and medical resource -> collected concurrently in a setting close to real-world health-care delivery in sub-Saharan Africa.
- Data on costs -> collected prospectively and from a health-system perspective (outside the experimental setting).
- Patient's point of view by assessing Patient-Reported Outcomes (including physical and mental health, perceived symptoms, depression, anxiety, and stress) and using QALYs.
- Original method: **cost-effectiveness price threshold analysis** -> determine which regimen should be preferred (ie, have the best economic value), for all price combinations of DTG- and EFV400-based regimens.
- Extrapolation of health benefits and costs over 10 and 15 years.

Main results

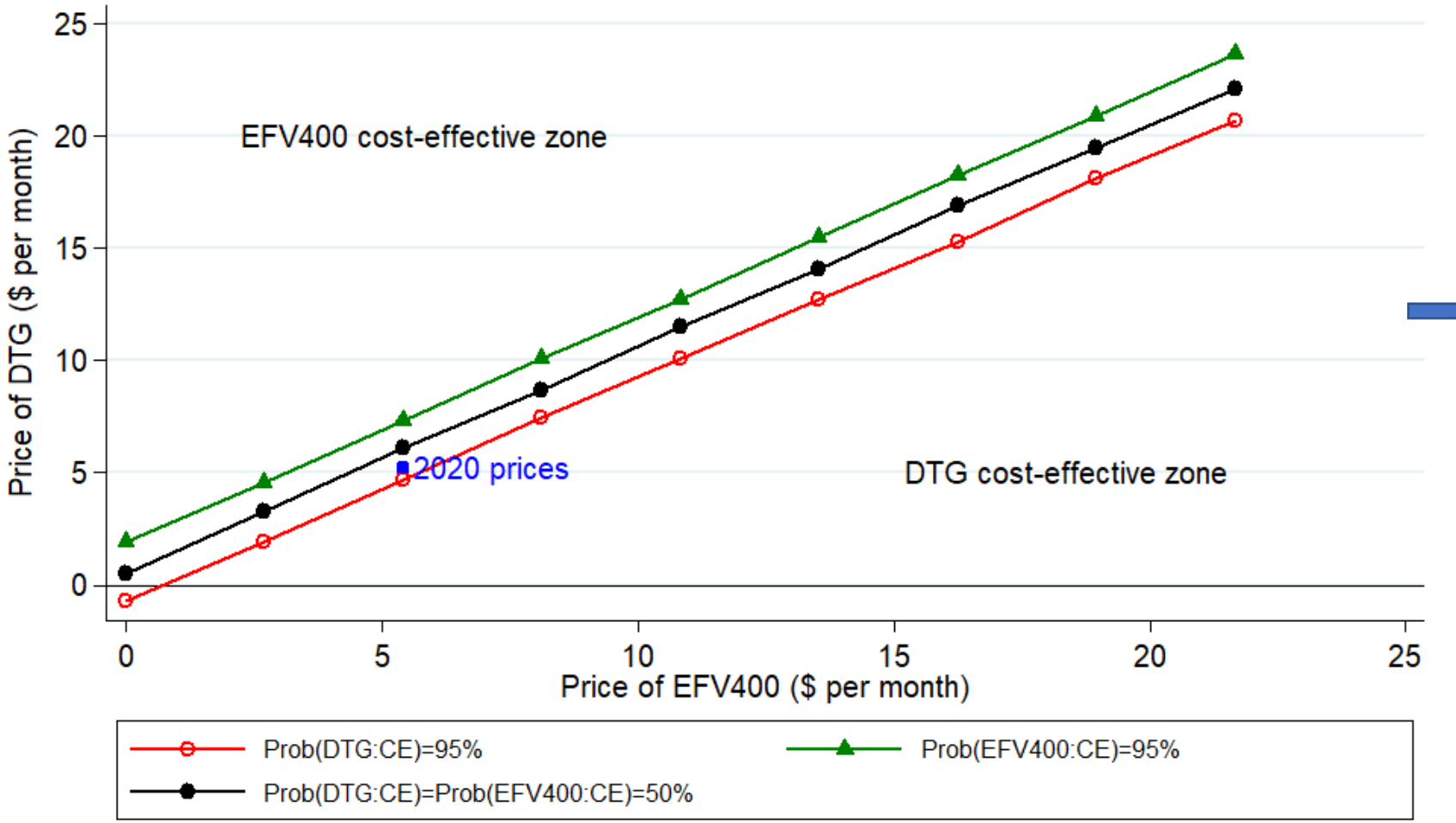
- **Patient-reported outcomes:**

- Improvement between baseline and week 96 in both arms, mainly during the first 48 weeks.
- No significant differences between arms (overall and between gender).
- PROs related to mental health improved less in patients with gained obesity at W96 (a condition with a higher incidence in the DTG arm).

- **Cost-utility analysis:** The DTG-based regimen was **not dominant** over the EFV400-based regimen, but was the **preferred** first-line treatment in the majority of cases:

- **Base-case 96-week analysis**: DTG cost-effective with a **85%** probability (3% discount factor and $500 threshold)
- **Scenario analyses** (discount rate of 0% and 6%, intention-to-treat analysis, subgroup of patients with high baseline viral load): probability of DTG being cost effective between **81% and 85%.**
- **Modelling over 10 and 15 years**: DTG-based regimen had a ≥95% probability of being cost-effective for a large range of cost-effectiveness thresholds.

Main results: cost-effectiveness price threshold analysis



Cost-effective price thresholds for DTG and EFV400 => Which strategy would be preferred at the threshold of $500/QALY and for any price combination of DTG and EFV400 fixed-dose combinations.

Implications of all the available evidence

- Greater economic value of a DTG-based regimen than a low-dose EFV-based regimen in treatment-naive HIV patients in sub-Saharan Africa **at 2020 antiretroviral drug prices**.

- Using a DTG-based regimen as a first-line regimen may be the most efficient use of resources in sub-Saharan Africa
- Results support the choice made by the WHO in its 2019 guidelines.

Thank you for attending this session

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