Pregnancy is a key period in the course of a woman's life and its outcome may be influenced by several factors linked to her viral status regarding HIV and hepatitis viruses. It is debated whether co-infection with HCV alters the course of pregnancy in HIV-infected mothers, whereas it is quite well established that the risk of HCV transmission to the newborn is impacted by the level of HCV replication and may be enhanced when HIV is uncontrolled. Where the use of peg-interferon and ribavirin was formally contra-indicated in pregnant women due to the therathogenic nature of ribavirin, direct antiviral agents may be prescribed if it is considered that the benefit outweighs the risk. However, the conditions of prescription are not well established to date. In this session, a concrete case will be presented and issues arising from HCV management in pregnant women will be discussed, from the natural course of HCV infection to its treatment during pregnancy.

O34 – Late Breakers/Hot Topics

O341

New ARV drugs and strategies

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Introduction: Thirty years after the commercialisation of the first ARV drug, more than 20 million individuals worldwide receive combination therapy. While current ARVs are capable of meeting the third "90" of the "90-90-90" UNAIDS target (i.e. viral suppression), new approaches are needed to ensure that this capability is realised.
Discussion: Durable viral suppression can only be achieved if the patient's safety and quality of life are assessed, reported and ensured. Observational cohort studies are invaluable tools for evaluating such outcomes and identifying new or unexpected safety concerns, but current clinical trials are often limited in their duration and demographic scope. Indeed, new drug formulations are not readily tested in the paediatric population and more work is needed to assess simplified maintenance regimens or dual therapies in both treatment-naïve and -experienced patients. Patient-centric trials on drug effectiveness are also missing. For instance, ample evidence supports the use of dolutegravir (DTG) as a preferred first-line regimen in naïve patients, as well as a second-line therapy and post-exposure prophylaxis. However, the drug's reputation has been tarnished by teratogenic safety concerns during the preconception period. A patient-centred approach to provide adequate information and choice concerning contraception and ARV options will be critical to appropriately assess the place of DTG in future ARV regimens.
Conclusion: There are strong arguments to challenge the classic sequence of triple-based first, second and salvage regimens. New drugs and (paediatric-adapted) formulations are theoretically capable of providing durable viral suppression, but this can only be achieved through long-term academic-led research focused on providing quality care to minorities and vulnerable populations, particularly in low-income settings.

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Dolutegravir- versus an efavirenz 400 mg-based regimen for the initial treatment of HIV-infected patients in Cameroon: 48-week efficacy results of the NAMSAL ANRS 12313 trial

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Background: The updated World Health Organization 2018 guidelines for ARV treatment recommend a dolutegravir (DTG)-based regimen as the preferred first-line regimen (with the notable exception of women seeking to become pregnant) and efavirenz (EFV) 400 mg as an alternative option. If the superiority of DTG versus EFV-600 has been described, there is no head-to-head comparison of DTG versus EFV-400. We assessed the efficacy and safety of DTG and EFV-400 in Cameroon, a country known for its high HIV-1 genetic diversity, where an increasing rate of NRTI- and NNRTI-transmitted resistance has been observed.
Materials and methods: We conducted a Phase III randomised, open label, multicentre trial in three hospitals in Yaoundé. HIV-1 infected ARV-naive adults with HIV-RNA viral load (VL) >1000 copies/mL were randomised (1:1) to DTG or EFV-400, both with tenofovir (TDF)/lamivudine (3TC). Randomisation was stratified by screening VL and by site. The primary endpoint was the proportion of patients with VL <50 copies/mL at Week 48 (FDA Snapshot algorithm). The treatment difference adjusted for the baseline VL was calculated and non-inferiority was tested with a 10% margin. A superiority test was planned if non-inferiority was demonstrated.
Results: Eight hundred and twenty participants were assessed for eligibility. Among these, 616 were randomised and 613 (310, DTG; 303, EFV-400) received at least one dose of study medication (modified intention-to-treat [ITT] population). Baseline characteristics were balanced between arms. Overall, 66% were women. Median age was 37 years (29 to 44), median CD4 counts, 281 (154 to 444), median VL, 5.3 (4.8 to 5.8) $\log_{10}$ copies/mL; 66% of patients had a high VL (>100,000 copies/mL). In the ITT analysis snapshot, the proportion of patients with HIV RNA <50 copies/mL was 74.5% (231/310) in the DTG arm and 69.0% (209/303) in the EFV-400 arm (difference, 5.5%; 95% CI -1.6 to 12.7; *p*-value for the superiority test, 0.13). For patients with a baseline VL <100,000 copies/mL, the proportion was 91.3% (94/103) and 83.5% (86/100), respectively (difference, 7.8%; 95% CI -1.2 to 16.8). For patients with a VL >100,000 copies at baseline, the proportion was 66.2% (137/207) and 61.5% (123/200), respectively (difference, 4.7%; 95% CI -4.6 to 14.0). In ITT analysis for VL <200 copies/mL the proportion was 89% (276/310) for the DTG arm and 83.5% (253/303) in the EFA-400 arm (difference, 5.5%; 95% CI +0.1 to 11.0), *p*-value superiority test 0.046.
Conclusion: The overall viral suppression at Week 48 was 71.8%. DTG-based regimen was non-inferior to the EFV-400-based, but superiority was not demonstrated when considering a threshold of 50 copies. For patients with a VL >100,000 copies, suboptimal VL suppression at the threshold of 50 copies was observed, but with no statistical differences between the two arms. Particular attention has to be given to patients with persistent low level viraemia, and it is essential to ensure a long-term follow-up.

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Efficacy of MK-8591 against diverse HIV-1 subtypes and NRTI-resistant clinical isolates

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