Integrase inhibitors mutational viral load in HIV infected pregnant women in Argentina

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This study was funded by MSD Argentina

Background
• Integrase inhibitors (INSTI): raltegravir (RAL) and dolutegravir, constitute preferred options for antiretroviral therapy (ART) in HIV-infected pregnant women (HPW) and RAL is recommended as part of neonatal prophylaxis in high-risk newborns (1, 2).
• In HPW population, Argentina has reported moderate to high levels of transmitted drug resistance to non-integrase drug classes, with high frequency of mutational viral loads (ML) >1000 copies/mL (threshold for highest risk for mother-to-child transmission, formal indication of cesarean section for non-nucleoside reverse transcriptase inhibitors (3, 4).
• We aim to describe the ML for integrase resistance major and accessory mutations among INSTI-unexposed HPW of an historical cohort (2008-2014).

Material and Methods
• ML was estimated considering baseline viral load value and the obtained frequency of each INSTI resistance mutations by Ultra Deep sequencing (UDS) using a Public Health Agency of Canada genotyping protocol on Miseq sequencing (Illumina) and HyDNA web.
• Stored baseline samples of 56 INSTI-naive HPW were included (38 ART naïve; 18 exposed to other drug classes) for this analysis.

Results (see also Tables 1 & 2)
• Median (interquartile range, IQR) viral load of the cohort was 15545 (5228-47688) c/mL.
• Prevalence of viral subtypes B and B/F were 21.4 and 78.5%, respectively.

• Major INSTI-mutations were detected at <5% cut-off sensitivity threshold:
  o Overall prevalence of 8.6% (5/56).
  o Median (range) ML (c/mL) was: 355 (50.2-11705); only 1 case >1000 c/mL (1/56; 1.7%), at expenses of a high baseline maternal viral load (487732 c/mL).
  o ML for Y143C, Y143S, E629K, L74I, and T97A were detected, respectively (and 1/13; 7.7%, respectively (tables 1 and 2).

• Accessory mutations were detected mostly with 20% sensitivity threshold:
  o Overall prevalence 23.2% (13/56).
  o Median (IQR) ML (c/mL) was: 23929 (4009-63158); all cases >1000 c/mL.

• The following accessory mutations were described: T97A (2/13), ML: 23149 and 17447, respectively.
  o G163K (5/13), median (range) ML: 23929 (3327-62922) and G163R (6/13), median (range) ML: 28614 (1317-154697).
  o A description of ML in each individual sample is shown in tables 1 and 2.

Conclusion
• In a cohort of INSTI-naive HPW, major integrase resistance associated mutations rarely exceed highest perinatal transmission risk threshold of 1000 copies/mL, as not predominant within viral quasispecies.
• Conversely, accessory mutations exceed this threshold with potential risk of transmission of mutations to the newborn. Clinical impact on maternal ART and neonatal prophylaxis remains to be determined.

References

Disclosure
This study was funded by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Whitehouse, NJ, USA.