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HIV genotype and drug resistance profile in vertically infected children

Francesca Compagno*[1], Klaudia Naegele[2], Christian Kahlert[3], Irene Hoesli[4], Karoline Aebi-Popp[5], Begona Martinez de Tejada[6], Paolo Paioni[7], Sabine Yerly[8], Juerg Boeni[9], Manuel Battegay[10], Christoph Rudin[11], Hans H. Hirsch[1]

[1]*Universität Basel; Division of Infection Diagnostics, Transplantation and Clinical Virology; Department of Biomedicine*

[2]*Universität Basel; Department of Biomedicine; Departement Biomedizin, Abt. Infektionsdiagnostik*

[3]*University Hopsital St Gallen*

[4]*University Women Hospital*

[5]*Department of Infectious Disease - University Hospital*

[6]*University Hospital of Geneva*

[7]*University Children's Hospital*

[8]*University Hospitals of Geneva*

[9]*Institute of Medical Virology - University of Zuerich*

[10]*University Hospital Basel; Division of Infectious Diseases & Hospital Epidemiology*

[11]*University Children's Hospital, Basel, Switzerland*

Background: The availability and timely administration of effective combined anti-retroviral therapy (cART) not only reduced the rate of mother-to-child transmission (MTCT), but also improved the prognosis of HIV-infected newborns. With respect to cART efficacy, one of the main concerns in HIV-

infected children is drug resistance (DR). While DR-HIV strains may result from suboptimal adherence and dosing in the HIV-infected child, defined as selected DR (sDR), they may also originate from MTCT, defined as transmitted DR (tDR). The aim of this study is to evaluate the frequency of tDR in HIV infected children.

Material/methods: We performed a retrospective analysis of prospectively entered data of HIV transmission in mother-child (MC) pairs of the MoCHiV cohort. Genotype and DR profile of each MC-pair were determined around the time of or shortly after birth to identify tDR. Children were then tested at all available follow-up visits to define the genetic evolution of HIV and to investigate the emergence of newly sDR. Sanger sequencing was performed from both viral load and proviral samples. Data regarding viral load, CD4+ T-cell count, cART, adherence and clinical information completed our results.

Results: The study population comprised 22 MC pairs. Almost all mothers (95,5%) were treatment-naïve before pregnancy and only 50% received antiretroviral therapy (intrapartum zidovudine and/or cART) during pregnancy or at birth. Children were followed approximately around 15 years (median, range). The most prevalent subtype was B, found in 59% (13/22), with accordance in all pairs. Considering only major DR, sDR emerged in 16 children of 22 (72%), while we identified one case of tDR (4,5%). CD4+ T-cell counts were significantly lower in the sDR group, whereas no association was found with VL. However, presence of tDR were associated with earlier emergence of sDR (0.83 vs 3.5 years). The number of ART changes during paediatric lifetime was greater in those with sDR (6.4 vs 4 times), but early cART (<10 months of age) seemed to be protective (sDR 68% vs. 100%).

Conclusions: The rate of tDR was lower than in other studies but still within the previously described range. tDR was associated with a higher risk to develop further sDR mutations. Children who were managed by early ART were more prone to develop sDR and therefore underwent more ART changes. Since some children presented sDR without being exposed to any previous treatment, adherence, TDM, and the possibility of undetected tDR mutations that may have escaped detection by standard diagnostic tools could play a role in the development of MC DR. These finding strengthen the notion that sensitive baseline resistance profile with specific attention to minority variants in NGS may be important for successful HIV management in MC pairs.