Poster
P002

Use of integrase inhibitors in HIV-positive pregnant women- Data from the Frankfurt HIV Cohort

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Background: Integrase inhibitors (INSTI) are highly recommended for the treatment of HIV-positive adults including women of reproductive age. However there are concerns about the use of INSTI in pregnant women. Decreased drug levels of elvitegravir/cobicistat in late pregnancy can potentially result in virologic failure and increase the risk of HIV-mother-to-child-transmission (MTCT). For dolutegravir (DTG) a so called „Red Hand Letter" has just been sent out in June 2018. Neural tube defects occured in a small number of neonates whose mothers had been treated with DTG in early pregnancy. In this retrospective study we analysed the maternal and infant outcome of INSTI versus non-INSTI containing ART during pregnancy in the Frankfurt HIV Cohort.

Method: All women of the Frankfurt HIV Cohort who gave birth between January 2008 and June 2018 were included in this retrospective analysis. Primary objective: virologic response defined as viral load (VL) <50 copies/mL at the time of delivery. Secondary objectives: rate of HIV-mother-to-child-transmissions and the rate of malformations in the ART exposed children. For all parameters we performed a subanalysis of INSTI- and non-INSTI containing regimen. Table 1 shows characteristics of the INSTI and the non-INSTI group.

Baseline characteristics		(n= 274)	(n= 222)	(n= 52) INSTI Regime
Age (years; mean ± SD)		32,0 ± 5,6	32,1 ± 5,4	31,2 ± 6,3
range (years)		19 - 47	19 - 47	20 - 45
Origin (%)	Sub-Sahara Africa	49,6	48,6	53,8
	Western Europe	27	28,8	19,2
	Asia	5,5	5,9	3,8
	Eastern Europe	11,3	10,8	13,5
	Latin America	3,3	2,7	5,8
	South Europe	1,5	1,4	1,9
	North Afrika	0,4	0,5	/
	Unknown	1,5	1,4	1,9
ART Start (%)	Before pregnancy	62,8	63,5	59,6
	1. Trimester	6,6	6,8	5,8
	2. Trimester	17,2	17,1	17,3
	3. Trimester	8	7,2	11,5
	Unknown	5,4	5,4	5,8
CD4 abs./µl (mean ± SD)		492,5 ± 262,8	475,5 ± 241,2	564,1 ± 332,6
range		0 - 1385	19 - 1325	0 - 1385
Viral load <50 cop./ml (%)		50,4	50,5	50
Viral load >50 copies/ml (mean ± SD)		46702,1 ± 139528,6	38488,17 ± 77532,2	79215,8 ± 271902,6
range (copies/ml)		50 - 1290000	50 - 434027	53 - 1290000

Table 1: Baseline characteristics

Results: We observed 274 pregnancies resulting in 281 children (5 twins + 1 triplet). INSTI based regimen were used in 52 pregnancies (19%), predominantly raltegravir (n=48); DTG (n=4). 3 of the 4 DTG-based regimen were switched to RAL during pregnancy (pregnancy week 4, 15 and 18). There were 21 conceptions (40%) on INSTI containing ART. Table 2 shows the last lab results before delivery and the number of mother-to-child transmissions.

Outcome (last values before childbirth)	(n= 274)	(n= 222)	(n= 52) INSTI Regime
CD4 abs./µl (mean ± SD)	525,3 ± 257,1	519,4 ± 252,3	550,7 ± 277,8
range	0 - 1617	0 - 1617	90 - 1202
Viral load <50 cop./ml (%)	81,4	81,1	82,7
Viral load >50 copies/ml (mean ± SD)	41544,6 ± 262722,2	50371,8 ± 289708,5	1822,1 ± 2875
range (copies/ml)	50 - 1764000	50 - 1764000	66 - 9252
MTCT	1	1	0

Table 3: CD4-cell count and VL close to delivery and vertical transmissions

The three most common maternal adverse events in the INSTI group were nausea/vomiting (7,7%), elevation of liver enzymes (5,8%) and cystitis (1,9%). In the non-INSTI group nausea/vomiting (8,1%), cystitis (4,5%) and gestational diabetes (2,7%). In the non-INSTI arm 81,1% of patients had a viral load <50 cop./mL at the time of delivery, in the INSTI arm 82,7%. The predominant mode of delivery was a cesarean section in 63% of all pregnant women and there was no difference between the INSTI and non-INSTI arm. In utero ART exposure was 226 days in the non-INSTI and 155 days in the INSTI group (p= 0.002). There was one malformation in the INSTI exposed neonates, a laryngomalacia. Malformations in the non-INSTI group were: One defect of the abdominal wall, one dextrocardia, one epicanthus, one case of syndactile of fingers/toes and one ventricular septal defect. The vertical transmission in the non-INSTI group was caused by maternal non-adherence. Chart 1 shows the overall rate of late presenters (ART start > 24th week of pregnancy) and the rate of INSTI vs. non-INSTI containing ART.

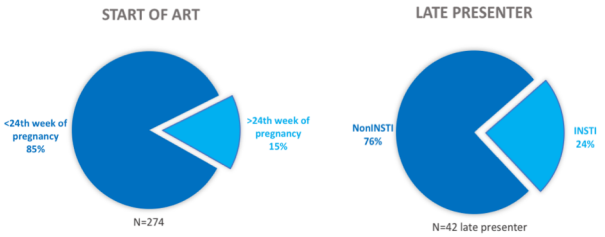
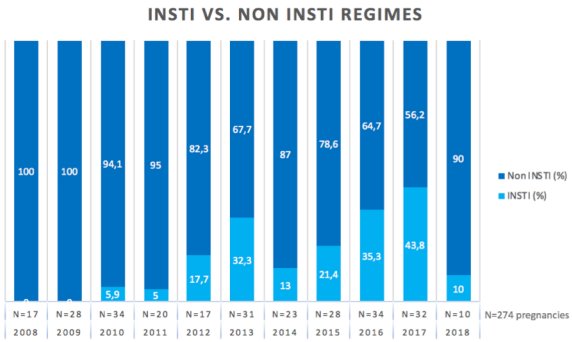


Chart 1: Start of ART (week of pregnancy) and late presenters (>pregnancy week 24)



Conclusions: We observed 274 pregnancies of HIV positive women, resulting in 281 children. 52 (19%) of the pregnant women received INSTI based ART; 48 raltegravir and 4 dolutegravir. Despite the significant shorter in-utero-exposure to ART in the INSTI arm - due to a higher rate of late presenters in this group - there were no differences between the INSTI and non-INSTI group in terms of virologic response, vertical HIV transmission and the rate of congentital malformations in the exposed neonates.

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