#17

Elvitegravir pharmacokinetics during Pregnancy and Postpartum

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Disclosures - partners PANNA

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BMS

MSD

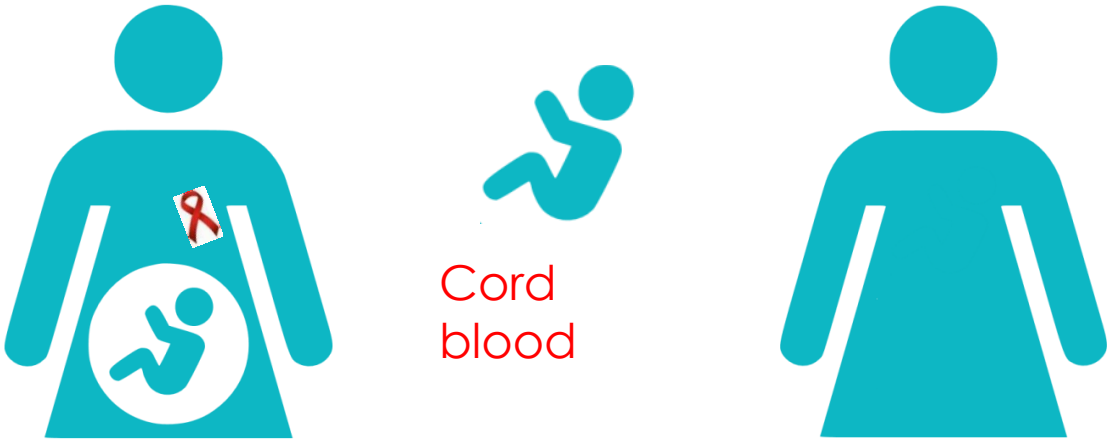
ViiV Health Care

Janssen Pharmaceuticals N.V.

Gilead Sciences.

A European clinical pharmacology network to investigate the Pharmacokinetics of newly developed ANtiretroviral agents in HIV-infected pregNAnt women

Objective: To evaluate elvitegravir/cobicistat concentrations in pregnant HIV-positive women the 3rd trimester and post-partum



Week 33 pregnancy

4-6 weeks postpartum

Blood samples: predose, 0.5, 1, 2, 3, 4, 6, 8, 12 and 24h after dosing

Results

General (n=7)	
Age at start pregnancy (years)	32 (25-40)
Black; white [n (%)]	5 (72%); 2 (28%)
Conception on elvitegravir [n (%)]	7 (100%)
Concomitant ARVs [n (%)]: NRTI	6 (86%) TDF+FTC; 1 (14%) TAF+FTC
HIV RNA undetectable <50 cps/mL [n (%)]	6 (86%); one 6363 copies/mL
Pregnancy outcomes (n=7)	
Gestational age (weeks)	39 (36-40)
Infant birth weight (grams)	3140 (2240-4480)
Infant HIV negative [n(%)]	7 (100%)

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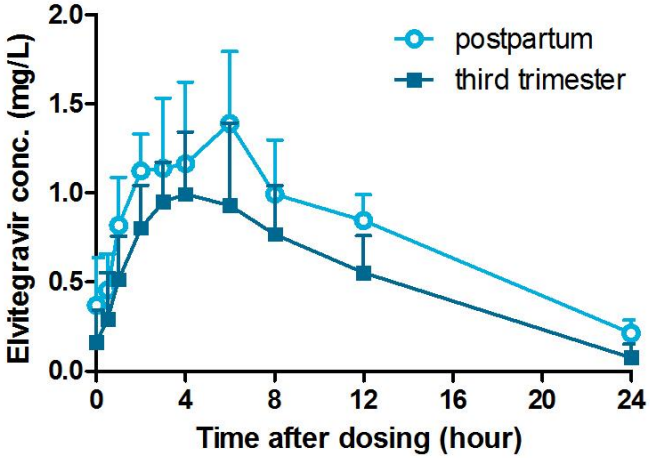

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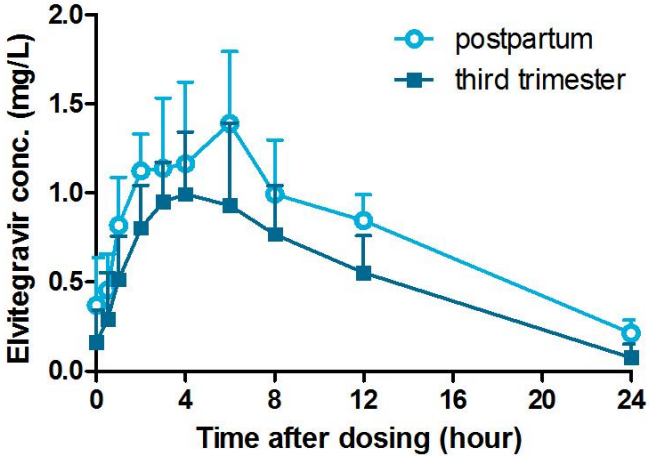

	PANNA GMR (90% CI) Third Trimester / Postpartum	IMPAACT GMR (90% CI) Third Trimester / Postpartum
Elvitegravir	**n=6**	**n=15**
$AUC_{0\text{-}24h}$ (h*mg/L)	0.67 (0.47-0.96)	0.58 (0.48-0.69)
C_{max} (mg/L)	0.79 (0.61-1.02)	0.74 (0.60-0.91)
T_{half} (h)	0.76 (0.48-1.22)	0.39 (0.33-0.46)
C_{trough} (mg/L)	0.35 (0.0.16-0.76)	0.13 (0.07-0.17)
C_{trough} below 0.13mg/L % 3rd vs PP	71% versus 17%	85% versus 19%
Cobicistat		
$AUC_{0\text{-}24h}$ (h*mg/L)	0.44 (0.30-0.67)	0.43 (0.34-0.55)
C_{max} (mg/L)	0.74 (0.62-0.88)	0.64 (0.50-0.82)
T_{half} (h)	0.48 (0.24-0.97)	0.64 (0.56-0.73)

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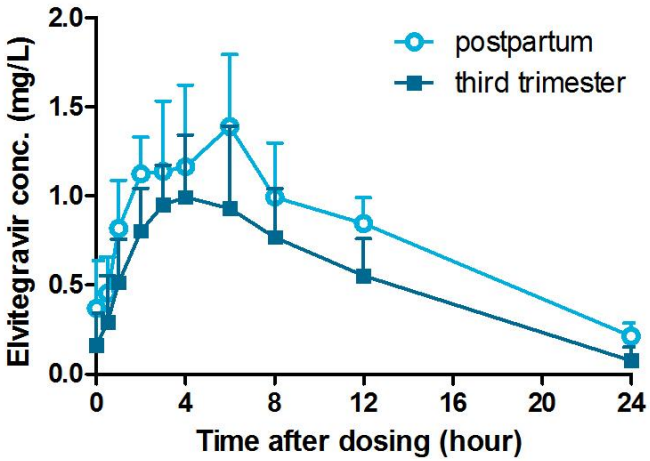

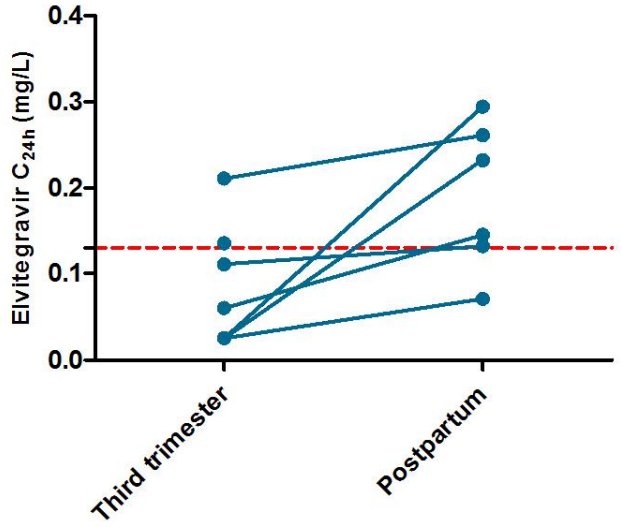

Median (range) ratios of elvitegravir cord/maternal (n=4)
0.87 (0.3-1.2)

Discussion

- PANNA results are in line with IMPAACT results (Best, 2017), and these results led to adaptation of DHHS perinatal guideline: Not Recommended for Initial Use in Pregnancy
- Cobicistat exposure was 56 % lower during pregnancy, this might have led to less boosting and increased elvitegravir clearance (and lower exposure)
- One patient with virological failure and multidrug resistance, low but not lowest levels, adherence problems could not be ruled out

Conclusion

In this small population (n=7) exposure to elvitegravir seems lower during pregnancy (third trimester) than postpartum.

During pregnancy 71% of the patients showed sub-therapeutic C_{trough} versus 17% postpartum. One patient had a detectable viral load prior to delivery.

The CB:MB elvitegravir plasma concentration ratio indicates substantial fetal exposure around delivery.

These data need to be confirmed in a larger group of patients, but support the recommendations in perinatal guidelines.

Acknowledgements

- Participants PANNA study
- Doctors and (research)nurses PANNA network
- Laboratory technicians dept. of pharmacy Radboudumc
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- Prof. Dr. David Burger (Principal Investigator PANNA)