Lower exposure to bictegravir in third trimester in pregnant women living with HIV

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Introduction

- Antiretroviral treatment in pregnant women living with HIV serves to reduce the risk of mother to child transmission of the virus, but also to guarantee maternal health.
- Due to physiological changes during pregnancy, drug concentrations may be altered, whereby drug efficacy might be hampered.

Objective

To compare the pharmacokinetic profile of bictegravir – an integrase inhibitor which is increasingly being used in the treatment of HIV - during the third trimester of pregnancy and in a non-pregnant state

Methods

In this multicentre, open-label, non-randomized trial (www.PANNAstudy.com) pregnant women living with HIV and using a bictegravir containing regimen were included.
Pharmacokinetic sampling (t = 0, 0.5, 1, 2, 3, 4, 6, 8, 12, and 24 hours) was performed in the third trimester and 4-6 weeks postpartum.
Plasma concentrations were determined with the use of LC-MSMS.

Results

Demographics Plasma concentrations of 9 women were obtained. Median (IQR) was 35 (33-34) year. All women had a suppressed viral load at delivery. Median (IQR) time post partum was 5 (4.5 - 8) weeks.

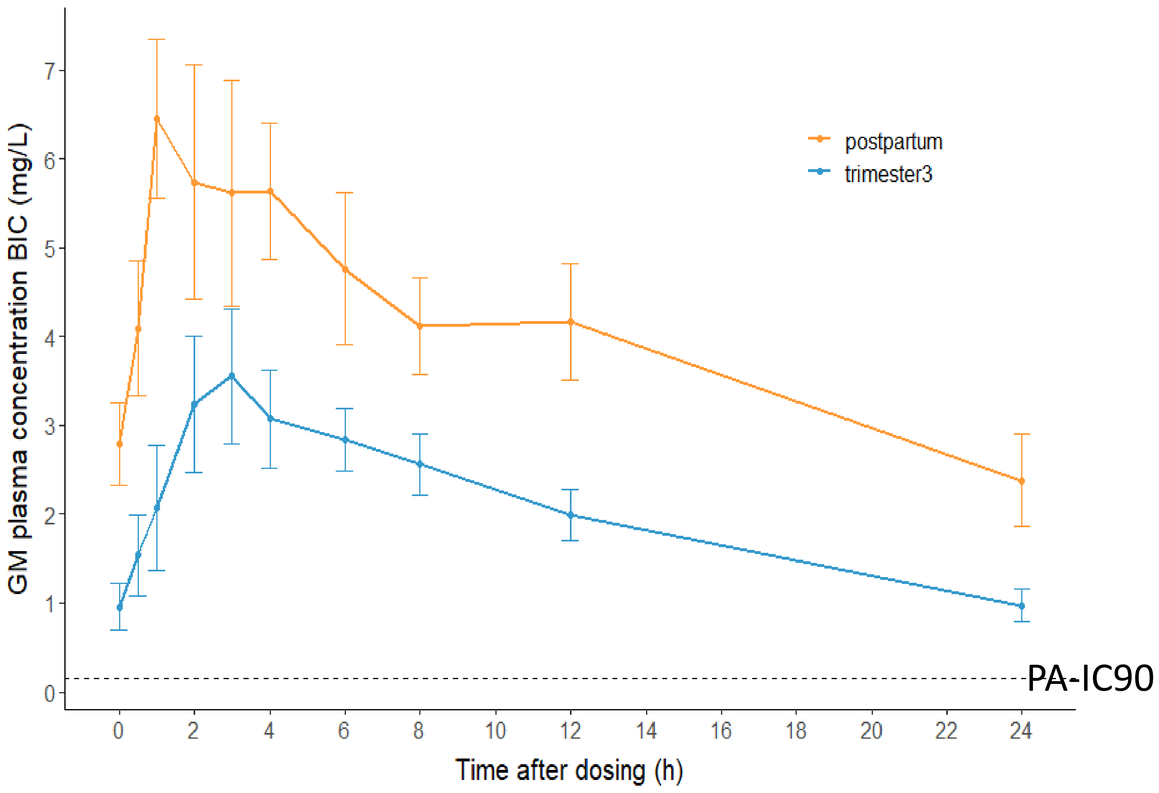

Figure 1: Geometric mean and CV% of plasma concentrations of bictegravir in 3rd trimester and post partum

	3rd trimester (n =8)	Postpartum (n =7)	GMR (CI90%)
$AUC_{0-24,}$ mg*h/L (CV%)	47.3 (21.5)	94.2 (28.2)	0.50 (0.40- 0.62)
C_{max}, mg/L (CV%)	3.9 (17.0)	6.8 (21.3)	0.59 (0.48 – 0.73)
$C_{trough,}$ mg/L (CV%)	0.9 (38.4)	2.4 (46.3)	0.38 (0.28 – 0.51)
$T_{1/2}$, h (CV%)	12.2 (38.7)	15.8 (33.1)	0.70 (0.53 – 0.91)

Table 1: PK parameters in 3rd trimester and postpartum.
1 subject was excluded from noncompartmental analysis of 3rd trimester values, because too many missing values.
2 women did not return for post partum assessment.

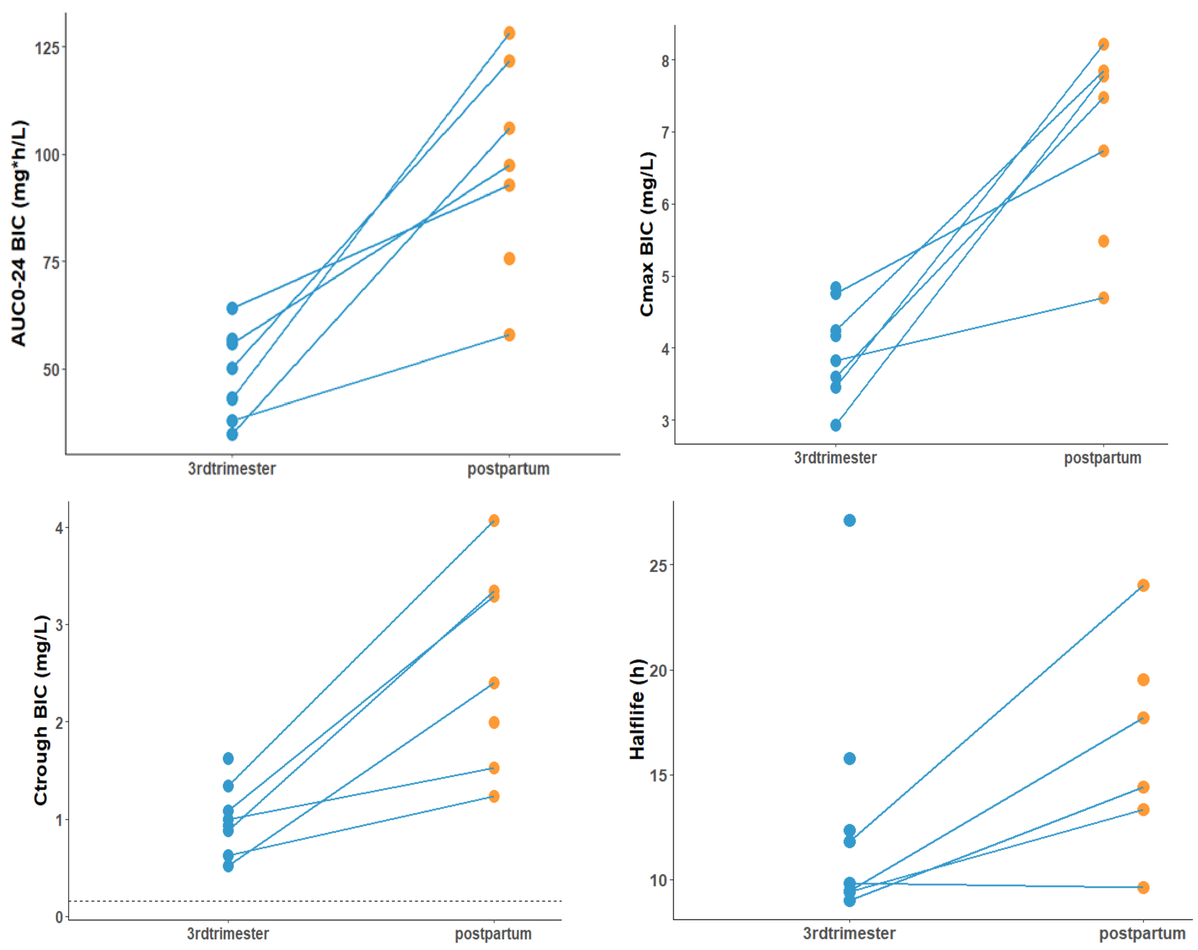

Figure 2-4 AUC_{0-24}, C_{max} C_{trough} (dotted line is PA-IC90 0.16mg/) and $T_{1/2}$ of individual patients

Safety
No mother to child transmission or congenital abnormalities were observed.
Cordblood was obtained from 3 neonates and the maternal plasma cord blood ratios were 0.65, 1.42 and 1.49 respectively.

Conclusion

- **Bictegravir-exposure is lower in third trimester compared to postpartum, but C_{trough} remained above the PA-IC95**
- **This effect can probably be attributed to increased hepatic clearance trough CYP3A4 and UGT1A1.**
- **More data are needed to confirm our findings.**

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