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Inflammatory plasma proteins are differentially expressed in pregnant women on ART and can predict adverse pregnancy outcomes.

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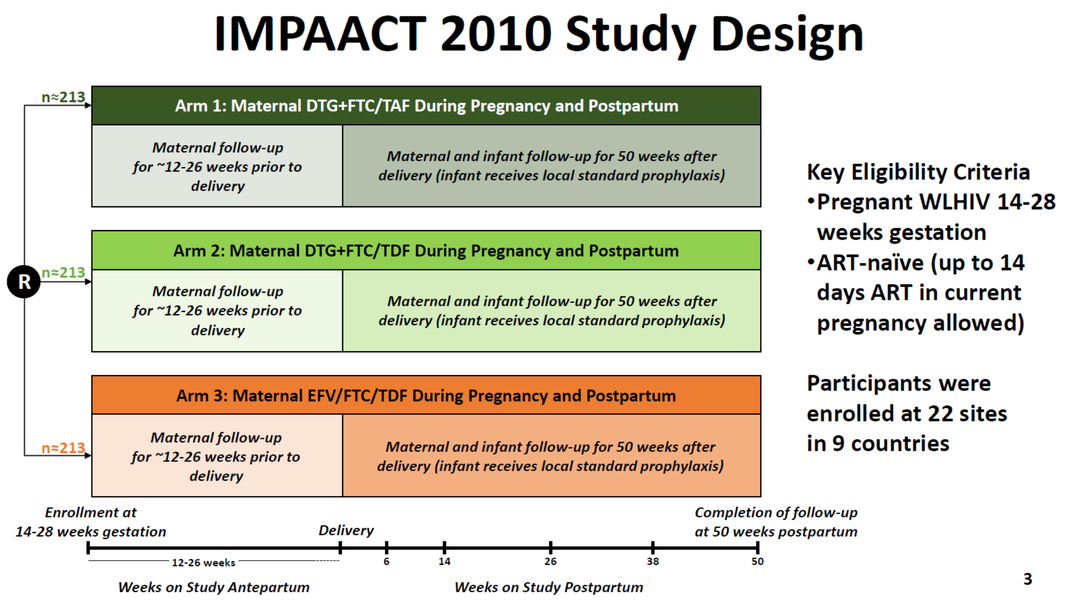
BACKGROUND

- ART is recommended for all women living with HIV during pregnancy.
- Some ART regimens have been associated with adverse pregnancy outcomes (APOs), but underlying biological mechanisms are not fully understood.
- In an exploratory analysis, we assessed inflammatory protein profiles in pregnant women randomized to initiate efavirenz (EFV)-based or dolutegravir (DTG)-based ART, and the predictive value of these inflammatory proteins for APOs

Inflammatory proteins in plasma differ between individuals on DTG and EFV-based ART regimens, with higher levels expressed in the EFV group. These proteins may serve as early predictive biomarkers for adverse pregnancy outcomes.

METHODS

- We tested plasma samples collected at enrolment (which occurred 14-28 weeks of gestation) and 8 weeks post-entry in women with HIV who enrolled into the IMPAACT 2010 trial in Zimbabwe.
- The APO measures included spontaneous abortion, stillbirth, preterm delivery, or being small for gestational age.
- We measured 92 plasma inflammatory proteins using a normalized, relative quantification assay (Olink Bioscience, Massachusetts).
- Applying a constrained longitudinal data analysis model, we fixed the baseline means to be equal across groups and compared how protein levels changed over time between randomized DTG-ART vs EFV-ART arms. Elastic net models were employed to identify proteins predictive of APO.



RESULTS

A total of 244 participants with plasma samples at baseline (n=242) and/or week 8 (n=233) were included. At baseline, median age was 27 years, gestational age 26 weeks, median CD4 count 458 cells/mm³ and HIV log10 viral load of 3 copies/mL. Seventy-nine (32%) women experienced at least one APO event. EFV-based ART was associated with higher mean expression of CCL25, CCL23, CX3CL1, IL-10, FGF21, VEGFA, KITLG, IL18R1, FLT3LG, DNER and CSF1 at week 8, while DTG-based ART showed higher mean IL-2 and AXIN1 expression (**Figure 1**). Elastic net models identified 17 proteins predictive of APOs, yielding AUCs of 0.7-0.8, depending on the cross-validation split, indicating moderate predictive accuracy. Biological pathway-level differences were observed between treatments (**Figure 2**).

Figure 1:Volcano Plot Highlighting Differential Protein Expression: DTG Compared to EFV (Week 8)

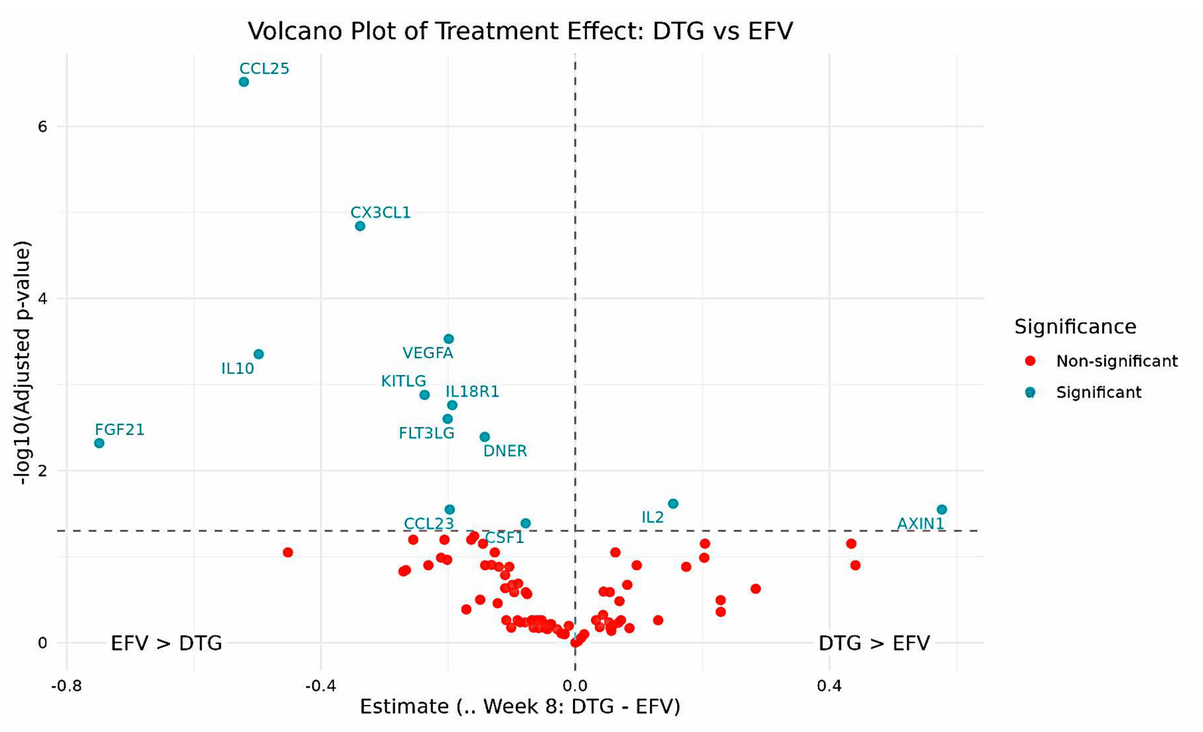
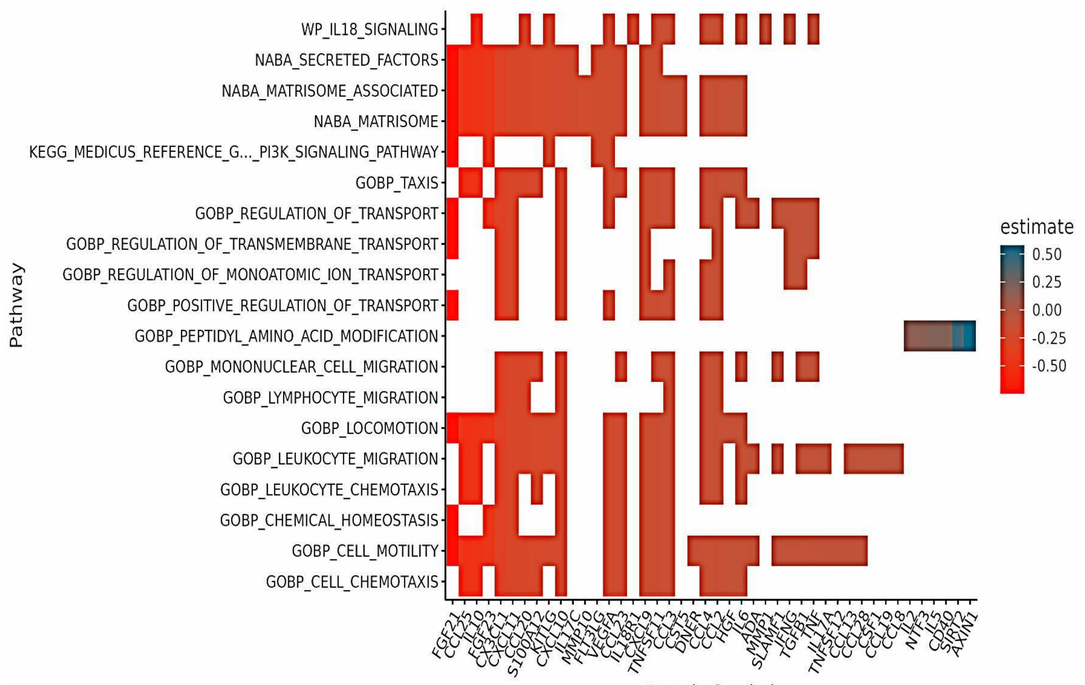


Figure 2: Gene set enrichment analysis showing overly represented biological pathways



CONCLUSIONS

- Inflammatory proteins in plasma are expressed differently in individuals using DTG-based versus EFV-based ART regimens, with the latter group exhibiting higher levels.
- The inflammatory proteins that are differentially expressed provide moderate accuracy and serve as predictive biomarkers for adverse pregnancy outcomes.
- Further research is needed on these identified biomarkers to evaluate their predictive potential for single APO events with extended periods of ART use.

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