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Dolutegravir Plasma Protein Binding and Unbound Concentrations During Pregnancy and Postpartum

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Abstract

Background: Clinical interpretation of the reduced dolutegravir (DTG) plasma concentrations reported during pregnancy is complicated by its high plasma protein binding. Plasma proteins significantly decrease during pregnancy and understanding changes in DTG protein binding and its therapeutically active unbound concentrations are necessary to evaluate the impact of pregnancy changes on DTG pharmacokinetics.

Methods: Retrospective assessment of plasma samples from pregnant women living with HIV enrolled in the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network P1026s study receiving 50 mg DTG film-coated tablets once daily as part of clinical care. Unbound and total DTG concentrations were determined pre-dose (C_0) and at maximum (C_{max}) concentrations during the second trimester (2T), third trimester (3T) and postpartum (PP). Percentage unbound was calculated as the ratio of ultrafiltrate unbound DTG concentration to total DTG concentration.

Results: Twenty-nine mothers were included for protein binding evaluations, 15, 27 and 23 from the 2T, 3T, and PP, respectively. DTG %unbound for C_0 and C_{max} were significantly different by stage of pregnancy, with 3T significantly higher compared to PP; 1.02% vs. 0.69% (p=0.0067) for C_0 and 0.76% vs. 0.46% for Cmax (p=0.0056). Median (IQR) unbound concentrations for C_0 were

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6.3 (4.7–18.4) for the 2T, 8.0 (5.6–16.9) for the 3T, and 13.3 (8.4–22.7) ng/mL PP, significantly different between 2T and PP (p=0.0039), but not different between 3T and PP (p=0.46).

Conclusion: Lower total DTG plasma concentrations during pregnancy coincide with temporal decreases in DTG protein binding, resulting in comparable unbound DTG concentrations during the 3T and PP.

INTRODUCTION

Antiretroviral treatment (ART) is essential for all pregnant and breastfeeding women living with HIV for their own health and to prevent mother-to-child transmission (PMTCT) of HIV[1]. Among the 1.3 million pregnant women with HIV globally in 2021, 81% received ART for PMTCT[2]. The selection and dosing of antiretroviral (ARV) drugs to treat HIV during pregnancy is complex. In addition to the primary concerns regarding safety of the mother and fetus, standard adult doses of ARVs may not be appropriate for pregnant women[3]. Physiological, anatomical, and biochemical changes associated with pregnancy can have a significant impact on drug disposition[4]. Subtherapeutic ARV concentrations during pregnancy may lead to maternal viremia, selection of resistant viruses, and consequently an increased risk of vertical HIV transmission. The potential impact of pregnancy on ARV pharmacokinetics was evident with recent data demonstrating lower drug exposure of cobicistat-boosted ARVs during pregnancy[5,6], leading the U.S. Food and Drug Administration (FDA) to recommend against their use during pregnancy.

Dolutegravir (DTG) is an integrase strand transfer inhibitor (INSTI) approved for use in combination with other ARVs for the treatment of adults and children with HIV[7,8]. Due to its high potency, favorable tolerability and safety profiles, and high barrier to resistance, DTG is recommended as one of the preferred ARVs in the U.S. and WHO treatment guidelines[1]. Dolutegravir is widely used as part of the generic TLD fixed-dose combination [dolutegravir (50 mg), tenofovir disoproxil (300 mg), and lamivudine (300 mg)]. Over 18 million people living with HIV receive TLD or DTG for 1st and 2nd-line treatment in low- and middle-income countries (LMICs), representing ~80% of adults on ART in these settings[9]. Although pregnant women were excluded from trials conducted as part of the DTG drug development program, several post-licensing studies have assessed DTG use during pregnancy and lactation. Our team (IMPAACT P1026s) was the first to describe the pharmacokinetics and safety of DTG in pregnant women living with HIV and found that total plasma DTG drug exposures were on average 29% lower during the third trimester compared to postpartum[10]. Clinical interpretation of lower total DTG drug exposures is complicated due to high plasma protein binding (>99%) in nonpregnant adults, with <1% of DTG unbound (or ‘free’) to exert therapeutic effect. The concentrations of plasma proteins, principally albumin and alpha-1 acid glycoprotein (AAG), significantly decrease during pregnancy due to plasma volume expansion and increased urinary protein excretion[11]. Increased competition for protein binding sites from steroids and placental hormones can also decrease drug binding to plasma proteins during pregnancy. These changes in protein binding during pregnancy can lead to higher free drug concentrations and increased drug clearance. Therefore, understanding pregnancy-related changes in DTG protein binding and unbound concentrations is critical to interpreting the decrease in total DTG exposure[12].

In this context, using available samples from pregnant women who received DTG as part of clinical care and had pharmacokinetic sampling through the IMPAACT P1026s study, our objectives were to assess the degree of plasma protein binding of DTG, and quantify unbound DTG concentrations during pregnancy (2nd and 3rd trimesters) and post-partum.

METHODS

The International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network P1026s study was an open-label, parallel-group, multi-center, phase IV pharmacokinetic and safety study of ARVs and related drugs during and after pregnancy (NCT00042289). P1026s used an opportunistic design, enrolling pregnant women living with HIV who were already receiving ART as part of clinical care. The current analysis includes women prescribed 50 mg DTG film-coated tablets orally once daily. Informed consent was obtained from all participants. The study was approved by the institutional review boards of participating sites and performed in accordance with the ethical standard of the 1964 Declaration of Helsinki.

Steady-state 24-hour intensive blood sampling for pharmacokinetic assessments were performed during the 2nd trimester (2T, optional), 3rd trimester (3T), and 6–12 weeks postpartum (PP). Blood samples were drawn pre-dose and at 1, 2, 4, 6, 8, 12 and 24 hours post-dose. Albumin levels were measured at each visit. The primary results describing the pharmacokinetics of total plasma DTG concentrations have been previously reported[10]. In this analysis, unbound DTG concentrations and percentage unbound were determined for the pre-dose (C_0) and maximum (C_{max}) concentration in the intensive pharmacokinetic profile for each participant at each visit. Drug measurements were performed at the IMPAACT Pediatric Clinical Pharmacology Laboratory at the University of California, San Diego, USA, which participates in the DAIDS supported external pharmacology quality control program. The unbound DTG fraction was obtained by ultrafiltration. Both total and unbound concentrations were determined by liquid chromatography tandem mass spectrometry assay and was validated over the concentration range of 3.91–2,000 ng/mL for total DTG concentrations and 1.56–100 ng/mL for unbound DTG concentrations (in 10 KDa ultrafiltrate). The accuracy and precision were <+/− 10% and 5%, for total and unbound DTG, respectively. The %unbound was calculated as the ratio of unbound DTG concentration to total DTG concentration x 100. Unbound concentration below the lower limit of quantification of the assay (LLOQ) were assigned a value of half of the LLOQ (0.78 ng/mL) for the analysis.

Ninety percent confidence limits (90%CI) of the geometric mean ratio for albumin level, DTG %unbound, and DTG unbound concentrations in antepartum versus postpartum conditions (2T vs. PP, and 3T vs. PP) were calculated. Within-subject comparisons between antepartum and postpartum were also compared using a Wilcoxon signed-rank test, with $p<0.10$ considered statistically significant. Data points with protein binding <98% were considered outliers and excluded. Linear regression was utilized to compare albumin levels with DTG %unbound and unbound concentrations for C_0 and C_{max} separately. All statistical comparisons were completed using SAS v.9.4. Target thresholds for total DTG plasma concentrations include the 90% effective concentration (EC_{90}) of 320 ng/mL and the *in-vitro*

90% protein-adjusted minimal inhibitory concentration (IC_{90}) of 64 ng/mL[13]. A minimal threshold for unbound DTG concentrations was the proposed IC_{90} of 0.85 ng/mL[14].

RESULTS

Twenty-nine mothers enrolled in P1026s with a total of 132 protein binding evaluations (matched unbound and total for C_0 and Cmax) were available. Eight outlier (6%) samples were excluded and four C_0 unbound DTG concentrations were below the LLOQ of the assay. Of these 29 participants, data from 15, 27 and 23 during the 2T, 3T, and PP, respectively, were analyzed for protein binding evaluations. Demographics and selected laboratory values are summarized in Table 1. Albumin levels were 13% lower in the 2T (n=7, p=0.078, GMR=0.87, 90%CI 0.78–0.98) and 18% lower in the 3T (n=13, p=0.0017, GMR= 0.82, 90%CI 0.76–0.89) compared to PP. A significant relationship between %unbound and albumin concentrations for C_0 (p=0.004, R^2=0.25) and C_{max} (p=0.015, R^2=0.12) was observed.

The DTG %unbound for C_0 and C_{max} 2T, 3T and PP are presented in Figure 1 (a-b). The median (interquartile rage, IQR) %unbound for C_0 was 0.85% (0.76–0.98%), 1.02% (0.78–1.14%), and 0.69% (0.49–0.88%); and for C_{max} was 0.69% (0.50–0.84%), 0.76% (0.60–1.01%), and 0.46% (0.34–0.70%) for 2T, 3T and PP, respectively. For 2T vs. PP, DTG C_0 %unbound was not significantly different (n=10, p=0.38, GMR=1.41, 90%CI 0.91–2.20); while DTG Cmax %unbound was significantly higher (n=12, P=0.09, GMR=1.71, 90%CI 1.18–2.49). For 3T vs. PP, DTG C_0 %unbound (n=17, p=0.0067, GMR=1.49, 90% CI 1.13–1.96) and Cmax %unbound (n=20, P=0.0056, GMR= 1.50, 90% CI 1.27–1.77) were approximately 50% higher in the 3T compared to PP.

Dolutegravir unbound (‘free’) concentrations for C_0 and C_{max} samples 2T, 3T and PP are shown in Figure 1 (c-d). Median (IQR) unbound concentrations for C_0 were 6.3 (4.7–18.4), 8.0 (5.6–16.9), and 13.3 (8.4–22.7) ng/mL; and C_{max} were 24.4 (14.9–32.0), 25.8 (20.9–33.3), and 24.6 (16.0–36.3) ng/mL for 2T, 3T, and PP, respectively. Unbound DTG C_0 was significantly (61%) lower in 2T (n=10, p=0.0039, GMR=0.39, 90%CI 0.19–0.82) compared to PP; while unbound DTG C_{max} was not significantly different (n=12, p=0.52, GMR=1.03, 90%CI 0.69–1.55). Both unbound DTG C_0 (n=17, p=0.46, GMR=0.77, 90%CI 0.51–1.17) and C_{max} (n=20, p=0.38, GMR= 1.13, 90%CI 0.96–1.32) during the 3T were not significantly different compared to PP.

Among sixty DTG C_0 samples, 55 (92%) total plasma concentrations were above the 320 ng/mL EC_{90} target (with only 1 of these sample below the lower 64 ng/mL IC_{90} target); while for unbound plasma DTG C_0 samples, 56 (93%) - 3 during pregnancy and 1 postpartum - were above the IC_{90} target of 0.85 ng/mL [note: LLOQ was 1.56 ng/mL; 4 samples below LLOQ].

DISCUSSION

Initial PK data on the standard adult dose of DTG (50 mg daily) during pregnancy demonstrated significantly decreased total plasma exposures. For example, median DTG exposures ($AUC_{0–24}$) and 24-hour post-dose concentrations (C_{24}) were reduced by 29–51%

relative to postpartum in the IMPAACT 1026s study[10] and 14–29% in the PANNA study[14]. The recommendation to use standard dosing during pregnancy was based on the observation that the majority of women achieved minimum levels above *in-vitro* derived inhibitory concentrations, coupled with virologic data available in these PK studies and larger studies in pregnant women[15,16]. However, to fully elucidate the pharmacological impact of the observed reduced 'total' plasma drug concentrations of DTG during pregnancy it is essential to consider the temporal changes in DTG plasma protein binding during pregnancy and the associated effect on unbound, i.e., therapeutically active, drug concentrations.

Dolutegravir is highly protein bound in non-pregnant patients (>99%), so that minor changes in binding during pregnancy can have a large impact on concentrations of unbound drug. As a low hepatic extraction ratio drug[17], DTG elimination is expected to be largely independent of hepatic blood flow but contingent on hepatic intrinsic clearance and fraction unbound (*fu*). Generally, for highly protein bound drugs with a low extraction ratio, a decrease in protein binding is expected to increase clearance. The DTG %unbound in our study for C_{max} was significantly higher during the third trimester (0.77%) compared to postpartum (0.46%), consistent with the lower albumin concentrations observed during pregnancy. An increase in DTG %unbound for C_{max} was also reported in the PANNA study between the 3rd trimester and postpartum (0.40 vs. 0.34%)[13]. Interestingly, while the trend in DTG %unbound was similar, the size of the difference and percentages were somewhat different from our study. The DTG %unbound has been assessed in different non-pregnant populations and found to be between 0.38%−0.55% in adults living with HIV on ART[18], 0.4%−0.5% in subjects with moderate hepatic impairment, 0.84%−1.01% in subjects with severe renal impairment, and 0.23%−1.1% in healthy volunteers[17]. Methodologies to quantify unbound drug concentrations are non-standardized, and ultracentrifugation, ultrafiltration, or equilibrium dialysis of plasma may be used. Methodological differences for ultrafiltration can also contribute to variability[19]. These factors may explain some of the observed differences in reported DTG %unbound.

A key finding of the current study is that unbound DTG concentrations were comparable between the 3rd trimester and postpartum, a critical timepoint at which significant decreases in total plasma concentrations have been observed. Of note, unbound DTG C0, but not Cmax, was significantly lower 2T vs. PP but it is unclear if was driven by the fewer number of women or the slightly lower total drug exposure reported[10]. Moreover, the unbound DTG C_0 and C_{max} values observed were in the range previously reported in non-pregnant populations with HIV on ART[17,20]. This provides reassurance that the physiological changes during pregnancy do not reduce the therapeutically active drug available that can cross cell membranes and reach the infected cellular reservoir of HIV. This finding is also consistent with the high virologic efficacy of DTG reported during pregnancy despite a reduction in total plasma concentrations, highlighting the importance of including assessments of unbound drug concentrations for highly plasma protein bound drugs during pregnnacy[12].

An added value of the protein binding data generated during pregnancy is their utility to strengthen the framework of physiologically based pharmacokinetic (PBPK) models to predict drug disposition in pregnancy. It is anticipated that the development of robust PBPK models that can accurately predict maternal-fetal/neonatal pharmacokinetics could

help accelerate studying new ARVs (and non-ARVs) in pregnancy, including long-acting (LA)-ARVs for HIV prevention and treatment. Indeed, DTG shares similar pharmacologic properties to cabotegravir (CAB) and bictegravir (BIC) – including high protein binding (>99%) – and extrapolating protein binding changes for DTG to CAB and BIC within PBPK models may help guide initial dosing with these drugs, in particular the long-acting CAB formulation, in this complex population. Robust assessment of the temporal changes of common metabolic drug pathways of ARVs during pregnancy would also help improve these PBPK models.

The current study has limitations. Predose (C0) values were used for the minimum concentrations rather than C24 (post-dose) values. As PK sampling was performed at steady-state it is expect that these values are similar; however, C0 samples were not obtained after observed doses, so this could have affected the observed concentrations. A statistically significant relationship between % unbound and albumin concentrations was observed but the relatively low R2 values indicates the linkage is relatively weak and the relationship may be less clinically relevant. We also excluded samples that were less 98% protein bound from the analysis; however, these outliers may have represented real values rather than assay error and could potentially have affect the analysis.

In conclusion, the reduction in total (bound plus unbound) DTG concentrations during late pregnancy occurs alongside decreased plasma protein binding so that unbound DTG concentrations are comparable to postpartum. These results further support the standard DTG dose recommendation for pregnant women.

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References

1. World Health Organization. CONSOLIDATED GUIDELINES ON HIV PREVENTION, TESTING, TREATMENT, SERVICE DELIVERY AND MONITORING: RECOMMENDATIONS FOR A PUBLIC HEALTH APPROACH 2021;
2. Organization WH. https://www.who.int/data/gho/data/indicators/indicator-details/GHO/estimated-percentage-of-pregnant-women-living-with-hiv-who-received-antiretrovirals-for-preventing-mother-to-child-transmission. 2022;
3. Buckoreelall K, Cressey TR, King JR. Pharmacokinetic optimization of antiretroviral therapy in pregnancy. Clin Pharmacokinet Oct 1 2012;51(10):639–59. doi:10.1007/s40262-012-0002-0 [PubMed: 23018528]
4. Koren G, Pariente G. Pregnancy- Associated Changes in Pharmacokinetics and their Clinical Implications. Pharm Res Feb 12 2018;35(3):61. doi:10.1007/s11095-018-2352-2 [PubMed: 29435666]

5. Momper JD, Best BM, Wang J, et al. Elvitegravir/cobicistat pharmacokinetics in pregnant and postpartum women with HIV. AIDS Nov 13 2018;32(17):2507–2516. doi:10.1097/QAD.0000000000001992 [PubMed: 30134297]
6. Momper JD, Wang J, Stek A, et al. Pharmacokinetics of darunavir and cobicistat in pregnant and postpartum women with HIV. AIDS Jul 1 2021;35(8):1191–1199. doi:10.1097/QAD.0000000000002857 [PubMed: 34076612]
7. TIVICAY (dolutegravir) tablets, for oral use. Package Insert. ViiV Healthcare group of companies Revised: June 2016.
8. Cottrell ML, Hadzic T, Kashuba AD. Clinical pharmacokinetic, pharmacodynamic and drug-interaction profile of the integrase inhibitor dolutegravir. Clin Pharmacokinet Nov 2013;52(11):981–94. doi:10.1007/s40262-013-0093-2 [PubMed: 23824675]
9. Organization WH. Update on The Transition To Dolutegravir-Based Antiretroviral Therapy: Report of a WHO Meeting file:///C:/Users/Tim%20Cressey/Desktop/9789240053335-eng.pdf. 2022.
10. Mulligan N, Best BM, Wang J, et al. Dolutegravir pharmacokinetics in pregnant and postpartum women living with HIV. AIDS Mar 27 2018;32(6):729–737. doi:10.1097/QAD.0000000000001755 [PubMed: 29369162]
11. Zhao S, Gockenbach M, Grimstein M, et al. Characterization of Plasma Protein Alterations in Pregnant and Postpartum Individuals Living With HIV to Support Physiologically-Based Pharmacokinetic Model Development. Front Pediatr 2021;9:721059. doi:10.3389/fped.2021.721059 [PubMed: 34722417]
12. Schalkwijk S, Greupink R, Burger D. Free dug concentrations in pregnancy: Bound to measure unbound? Br J Clin Pharmacol Dec 2017;83(12):2595–2598. doi:10.1111/bcp.13432 [PubMed: 28983934]
13. Bollen PDJ, Moore CL, Mujuru HA, et al. Simplified dolutegravir dosing for children with HIV weighing 20 kg or more: pharmacokinetic and safety substudies of the multicentre, randomised ODYSSEY trial. Lancet HIV Aug 2020;7(8):e533–e544. doi:10.1016/S2352-3018(20)30189-2 [PubMed: 32763217]
14. Bollen P, Freriksen J, Konopnicki D, et al. The Effect of Pregnancy on the Pharmacokinetics of Total and Unbound Dolutegravir and Its Main Metabolite in Women Living With Human Immunodeficiency Virus. Clin Infect Dis Jan 23 2021;72(1):121–127. doi:10.1093/cid/ciaa006 [PubMed: 32103260]
15. Waitt C, Orrell C, Walimbwa S, et al. Safety and pharmacokinetics of dolutegravir in pregnant mothers with HIV infection and their neonates: A randomised trial (DolPHIN-1 study). PLoS medicine Sep 2019;16(9):e1002895. doi:10.1371/journal.pmed.1002895 [PubMed: 31539371]
16. Kintu K, Malaba TR, Nakibuka J, et al. Dolutegravir versus efavirenz in women starting HIV therapy in late pregnancy (DolPHIN-2): an open-label, randomised controlled trial. Lancet HIV May 2020;7(5):e332–e339. doi:10.1016/S2352-3018(20)30050-3 [PubMed: 32386721]
17. Dolutegravir, GSK1349572 (TIVICAY) Clinical Pharmacology Review US-FDA Reference ID: 3310563 https://www.fda.gov/files/drugs/published/N204-790-Dolutegravir-Clinpharm-PREA.pdf. 2012;
18. Metsu D, Lanot T, Fraissinet F, et al. Determination of dolutegravir's unbound fraction in human plasma using validated equilibrium dialysis and LC-MS/MS methods. Clin Chim Acta Apr 2018;479:56–65. doi:10.1016/j.cca.2017.12.034 [PubMed: 29277535]
19. Metsu D, Lanot T, Fraissinet F, et al. Comparing ultrafiltration and equilibrium dialysis to measure unbound plasma dolutegravir concentrations based on a design of experiment approach. Sci Rep Jul 23 2020;10(1):12265. doi:10.1038/s41598-020-69102-y [PubMed: 32703975]
20. Letendre SL, Mills AM, Tashima KT, et al. ING116070: a study of the pharmacokinetics and antiviral activity of dolutegravir in cerebrospinal fluid in HIV-1-infected, antiretroviral therapy-naive subjects. Clin Infect Dis Oct 2014;59(7):1032–7. doi:10.1093/cid/ciu477 [PubMed: 24944232]

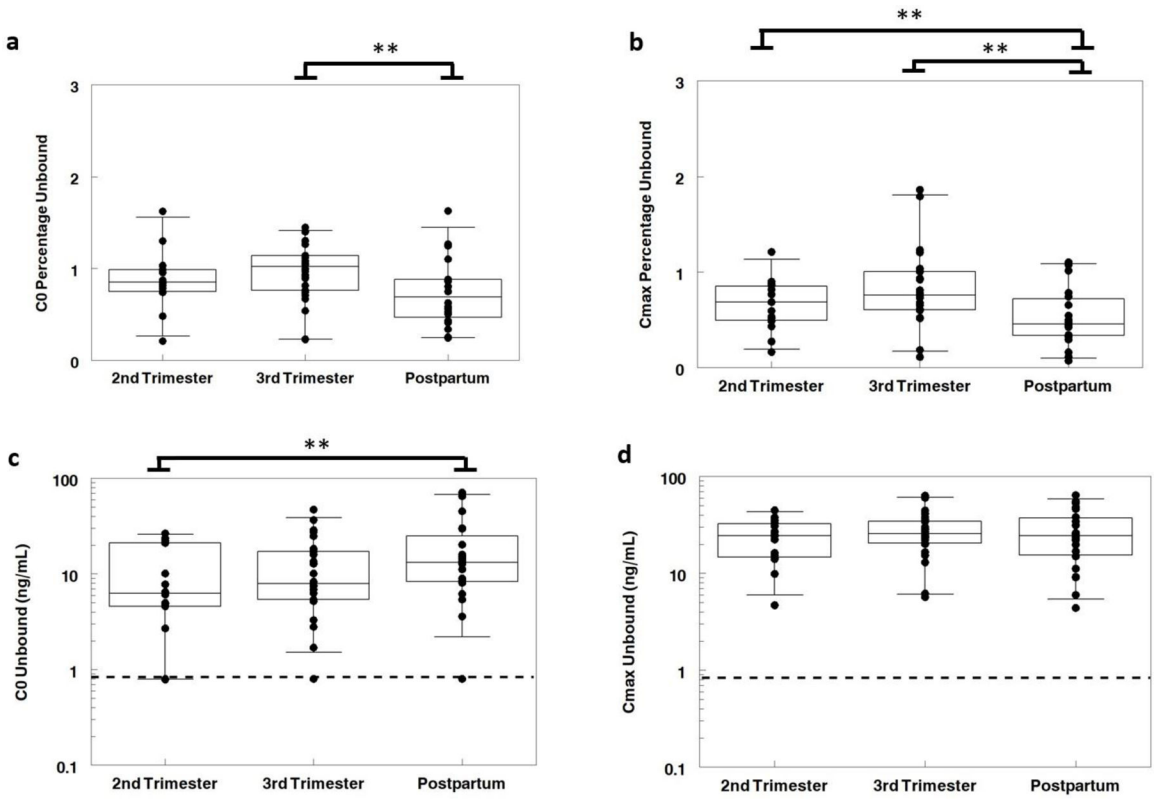

Figure 1:

(a) Pre-dose (C_0) dolutegravir (DTG) percentage unbound antepartum and postpartum (b) DTG maximum concentration (C_{max}) percentage unbound antepartum and postpartum (c) DTG C_0 unbound antepartum and postpartum concentrations (ng/mL) (d) DTG C_{max} unbound concentrations (ng/mL) antepartum and postpartum. Dashed line represents the proposed minimal threshold of 0.85 ng/mL [IC_{90}] for unbound DTG concentrations. ** represent p-value less than 0.1 by Wilcoxon signed-rank test.

Table 1:

Participant Characteristics

Demographic[#]	**Second Trimester (n=15)**	**Third Trimester (N=27)**	**Postpartum (N=23)**
Gestational Age (weeks)	24 (20 – 25)	33 (30 – 37)	48 (44 – 62)
Age (years)	31 (21 −42)	31 (21 −42)	32 (21 – 42)
Weight (kg)	81.8 (46.8 −138.5)	84.7 (51.4 −141.1)	79.2 (45.9 −137.9)
Albumin (g/dL)[*]	3.5 (3.2 −3.8)	3.4 (2.8 −4.0)	4.2 (3.0 −4.6)
Ethnicity	Black (80%) Other (20%)	Black (74%) Other (26%)	Black (74%) Other (26%)

[#]Values: median (range);

[*]N=13, 18, 14, respectively; postpartum albumin concentrations were significantly higher than values during pregnancy