Poster 50
Abstract 0249

Darunavir in Pregnancy
A Multicentre Retrospective Analysis

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1.Imperial College Healthcare NHS Trust 2.Guys and St Thomas' NHS Trust 3.Barts Health NHS Trust 4.Royal Sussex County Hospital NHS Trust 5.Lewisham and Greenwich NHS Trust 6.London North West Healthcare NHS Trust 7.Royal Free London NHS Foundation Trust 8.Mortimer Market Centre, Central and North West London NHS Foundation Trust

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Background

Protease inhibitors in pregnancy:

- No increase in teratogenicity observed[1]
- Transplacental passage is low[2]
- Plasma concentrations reduced particularly in 3rd trimester[3]
- Reports of increased pre-term delivery[4]

Darunavir in pregnancy:

- No increased risk of birth defects reported by APR in >200 T1 exposures[1]
- Reduced plasma concentrations in second and third trimesters[5]
- Concerns regarding 800/100mg once daily dosing[6]
- Recommended as an alternative to Atazanavir or Lopinavir[7]
- Limited experience in pregnancy: tolerability, safety and efficacy data are scant.

Aim

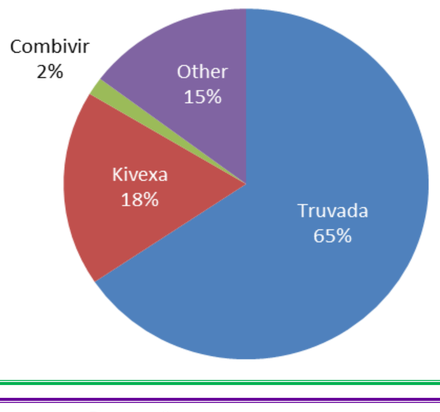
To describe current use, efficacy and tolerability of Darunavir in pregnancy in UK.

Methods

Case notes from HIV-1 infected women prescribed Darunavir/Ritonavir during pregnancy between October 2007 and October 2014 reviewed across 8 sites in London and Brighton. Demographics, history of and risk factors for preterm delivery (PTD), antiretroviral therapy (ART) including dosing, treatment switches and discontinuations, virological response, gestational age (GA) at delivery, maternal and infant outcomes were collected. Categorial variables assessed by Chi Square Test.

Results

- 55 women
- 59 pregnancies
- 3 multiple pregnancies (2 twins, 1 triplets)
- 2 pending live births
- 65% Truvada backbone



Demographics	
Median age	34 (IQR 23-47)
Ethnicity	46 Black African (83.6%)
Heterosexual transmission	55 (100%)
Hepatitis B co-infected	3 (5.4%)
Hepatitis C co-infected	0 (0%)
Nadir CD4 (cells/µl)	208 (IQR 10-745)
Median gravida	3 (IQR 0-10)
Median parity	5 (IQR 0-5)
Baseline antenatal characteristics	
History of PTD	6 (10.1%)
GA at booking visit	14 (IQR 4-34)
Baseline CD4 count	374 (IQR 125-1400)
CD4 <200 (cells/µl)	6 (10.1%)
HIV Viral Load <50 copies/ml	27 (49%)

Conclusions

- Our data support the use of Darunavir in pregnancy and reflect its increasing use.
- Our data are novel by including PTD risk factors not routinely collected by APR.
- **Well tolerated**: Increased ALT associated with high plasma Darunavir concentration where measured (1 out of 2 cases)
- **Virologically activity:** Suppression at median 30 days from initiation and no MTCT (including with once daily dosing in those conceiving on Darunavir)
- 93% virologically suppressed at delivery (exceeds 80% suppression rate with other protease inhibitors[8])
- **Safety:** The association of PTD seen with other Protease Inhibitors was also observed in our cohort with Darunavir, but not if commenced pre-conception.
- **Further work:** Analysis of PTD risk with multiple regression analyses needed. Data on timing, initiation of once daily dosing, including long term outcomes for mother and baby needed.

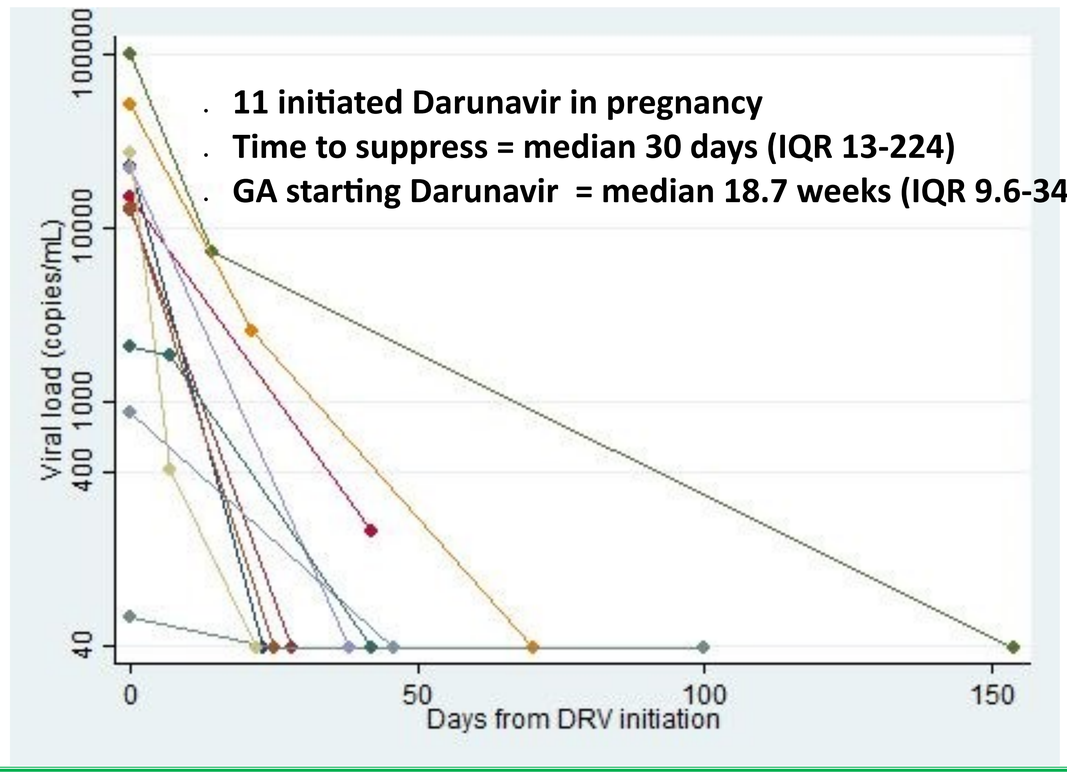
References

1. Antiretroviral Pregnancy Registry Steering Committee, APR International Interim report for 1 Jan 1989 through 31 July 2014. www.APRegistry.com
2. Marzolini C et al, AIDS 2002 Apr 12; 16(6):889-93
3. Colbers et al, Poster #1013, CROI 2012
4. Powis K.M et al, J Infect Dis. 2011 Aug 15; 204(4): 506–514
5. Lambert J et al, Journal of the International AIDS Society 2014, **17** (Suppl.3):19485
6. Colbers A et al, Low Darunavir exposure during pregnancy with 800/100mg Darunavir QD dosing, Poster Abstract 887, CROI 2014
7. BHIVA guidelines for the management of HIV-1 infection in pregnant women, HIV Medicine (2014) **15** (Suppl.4), 1-77
8. Read P.J et al, AIDS 2012, **26**: 1095-1103

Results—Efficacy

- 93% (n=55/59) HIV undetectable at delivery and **no cases of MTCT**

	Pre-Conception	Initiated	Switched
Total pregnancies (%)	39 (66.1)	11 (18.6)	9 (15.2)
Antenatal Baseline CD4 (cells/µl) *Median (IQR)*	407 (125-1400)	332 (127-713)	353 (130-634)
Antenatal Baseline HIV VL (copies/ml) *Median (IQR)* Number undetectable (%)	<50 (<50 – 22,217) 26 (66.6)	15,000 (<50 – 99,032) 0 (0)	1500 (<50- 28,000) 2 (22.2)
Baseline Darunavir dose 600mg bd 800mg od	7 32	4 7	3 6
PTD risk factor (%)	7 (11.8)	3 (5.1)	2 (3.3)



- **11 initiated Darunavir in pregnancy**
- **Time to suppress = median 30 days (IQR 13-224)**
- **GA starting Darunavir = median 18.7 weeks (IQR 9.6-34.3)**

Results—Safety

- 7/59 (11.8%) PTDs in cohort
- PTD risk factors most commonly found in pregnancies conceived on Darunavir
- PTD occurred most commonly in pregnancies switched to Darunavir (4/9)
- Commencing Darunavir after conception was associated with PTD (p<0.05) and low birth weight (p<0.05)
- This association persisted after excluding multiple pregnancies.

	Pre-Conception	Initiated	Switched
Live births (%)	35 (89.7)	10 (90.9%)	9 (100)
Twins Triplets	1 0	0 0	1 1
Late miscarriages & Intrauterine Death	3	0	0
Not yet delivered	1	1	0
VL >50 copies/ml at delivery (%)	1/35 (2.8)	3/10 (30)	0/9 (0)
PTD <37/40 (%)	1/35 (2.8)	2/10 (20)	4/9 (44.4)
Median GA at delivery (weeks) *Median (IQR)*	39 (35-43.3)	38.4 (33.9-41.3)	38 (28-40)
Birth weight (g) *Median (IQR)*	3280 (2270-4208)	2880 (1580-3870)	2300 (1150-3850)
Low birth weight <2500g (%)	1/35 (2.8)	3/10 (30)	6/9 (66.6)

Results— Tolerability

- 2 discontinuations due to elevated LFTs
  - Both patients initiated 800/100mg OD at 31.1 and 19.9 weeks GA
  - Both switched to Raltegravir at 35 and 21 weeks GA
- 1 dose reduction from 800/100mg OD to 600/100mg OD due to elevated LFTs and high drug levels (Therapeutic Drug Monitoring level 1399ng/ml)
- 3 dose adjustments from 800/100 OD to 600/100 BD