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# Elevated leukocyte adhesion marker VCAM-1 in HIV-1 infected in women during pregnancy

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# Background

- Elevated preterm delivery (PTD <37 wks) in HIV infected women pre ART era (16%<sup>1</sup> vs 8%<sup>2</sup> general population)
- Associated with specific classes of therapy
  - Mma Bana RCT<sup>3</sup>: 2 fold risk with PI-based ART vs ABC/3TC/ZDV
- Importance of timing
  - St Mary's Hospital<sup>4</sup>: 22% new cART vs 10% preconception cART vs ZDV 6%
  - 36% new PI cART (eligible for ZDV)
- **Hypothesis: underlying inflammation fetal-placental unit**

# Inflammation

- Cytokine environment in pregnancy (IL10)<sup>1,2</sup>
- Leukocyte adhesion proteins VCAM-1 and ICAM-1, have been associated with chorioamnionitis and PTD<sup>3,4</sup>
- Elevated ICAM-1 in placentas of HIV-infected vs uninfected women<sup>5</sup>
- Elevated ICAM-1 in placentas of women initiating cART before 36 weeks vs post 36 weeks<sup>5</sup>
- Role in HIV associated PTD unknown

# Objective

- To characterize maternal plasma leukocyte adhesion markers throughout gestation in HIV-infected and uninfected pregnancies
- To compare by antiretroviral therapy class and timing of initiation
- To correlate with gestational age at delivery

# Methods

HIV-1 + and - pregnant women recruited  
St Mary's and St Thomas' Hospitals,  
London  
2007 and 2011

•Whole blood  
at 12, 20, 28, 34 and  
38 weeks

Therapy classified:  
cART (PI/NNRTI based) or  
NRTI-only (ZDV/m or  
ZDV/3TC/ABC)

Routine CD4 cell and HIV plasma  
RNA quantification

•Plasma fraction separated from  
unstimulated PBMCs and stored at -80°C.  
•VCAM-1, ICAM-1, SSA and CRP  
concentrations measured using multiplex  
immunoassays  
(Human vascular injury panel II, MSD)

•Maternal demographics, expected delivery date and pregnancy outcome

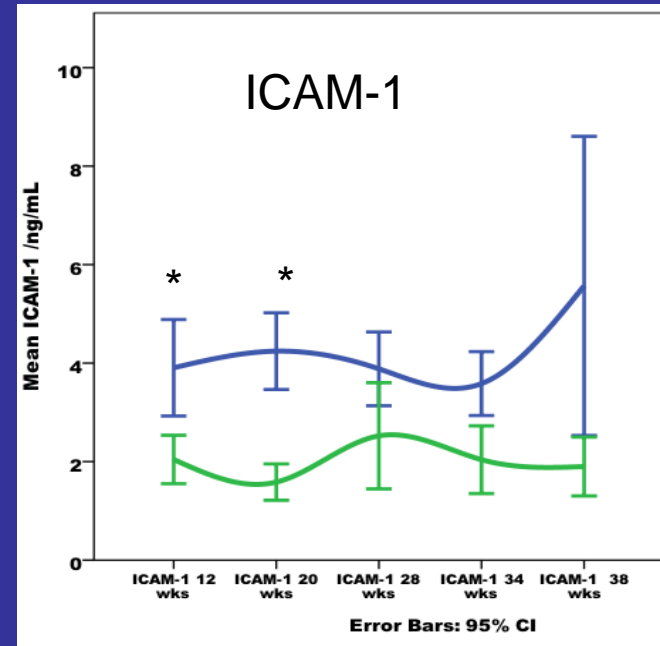
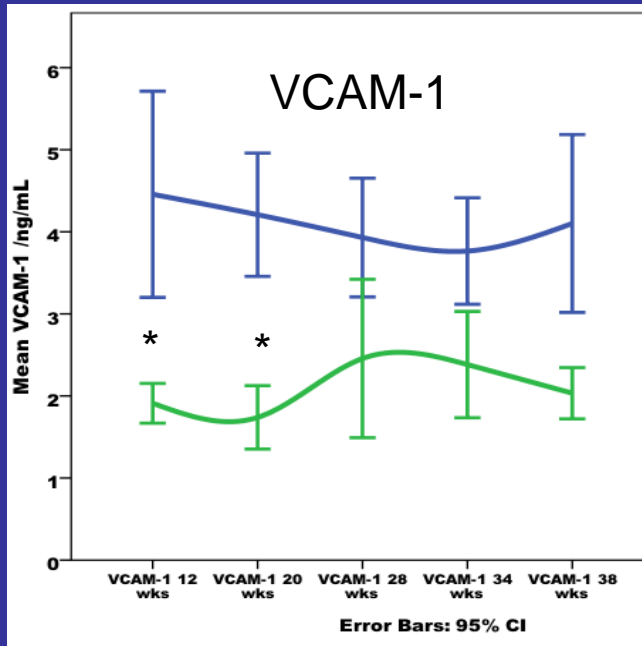
**Analyses:** : Mean biomarker concentrations, linear regression, mixed ANOVA to compare by HIV status, ART, ART timing & PTD

# Results

Treatment group	PI/NNRTI cART (n=39)	NRTI only (n=12)	HIV uninfected (n=12)	p value
Mean age /years (SD)	30 (7)	29 (6)	33 (5)	0.42
PI based cART (%)	22 (56)		-	
Conceived on cART (%)	22 (56)			
Conceived on PI cART (%)	10 (25)			
Median gestation at ART initiation /weeks (range)	0 (0-28)	26 (19-28)	-	
Median CD4 at entry cells/mm <sup>3</sup> (range)	390 (170-1520)	492 (260-810)	-	0.18
Median gestational age at delivery /weeks (range)	39 (32-41)	38 (38-42)	40 (37-44)	0.20
PTD <37 weeks (%)	6 (15)*	0 (0)	1 (8)	0.49

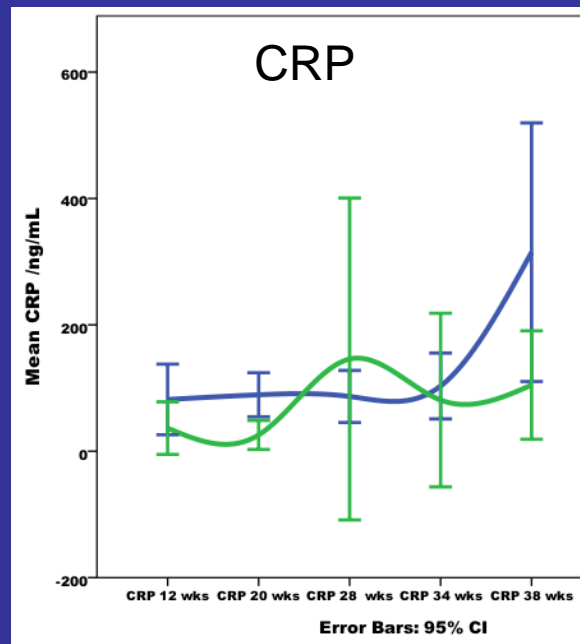
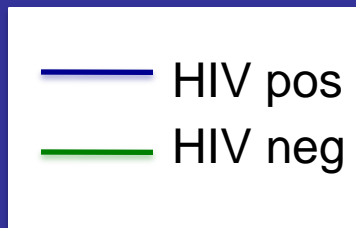
\* 4 PI/ 2 NNRTI

# Mean maternal plasma vascular marker concentrations across gestation by HIV status



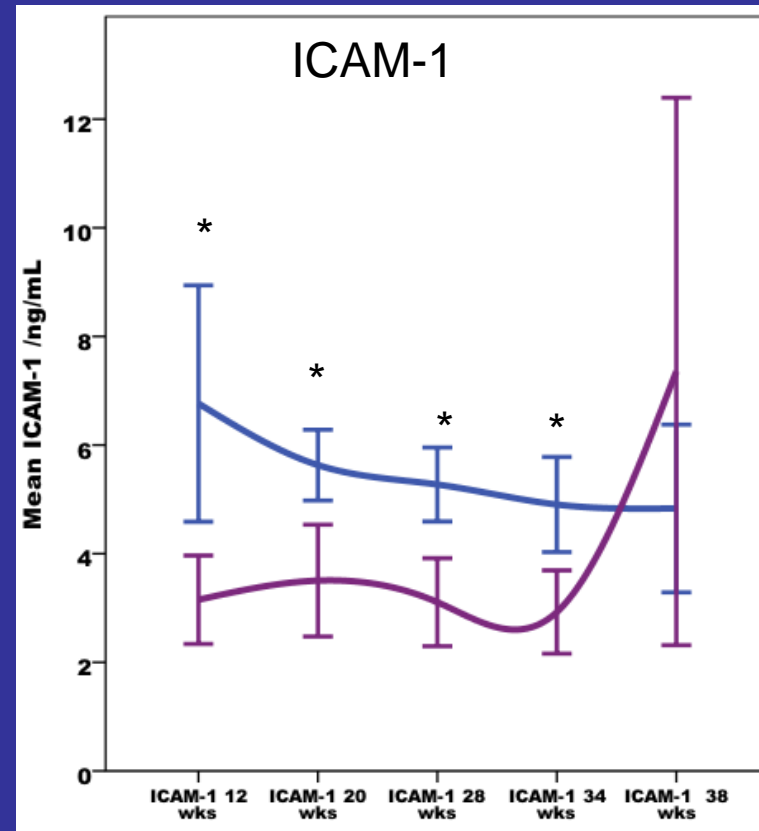
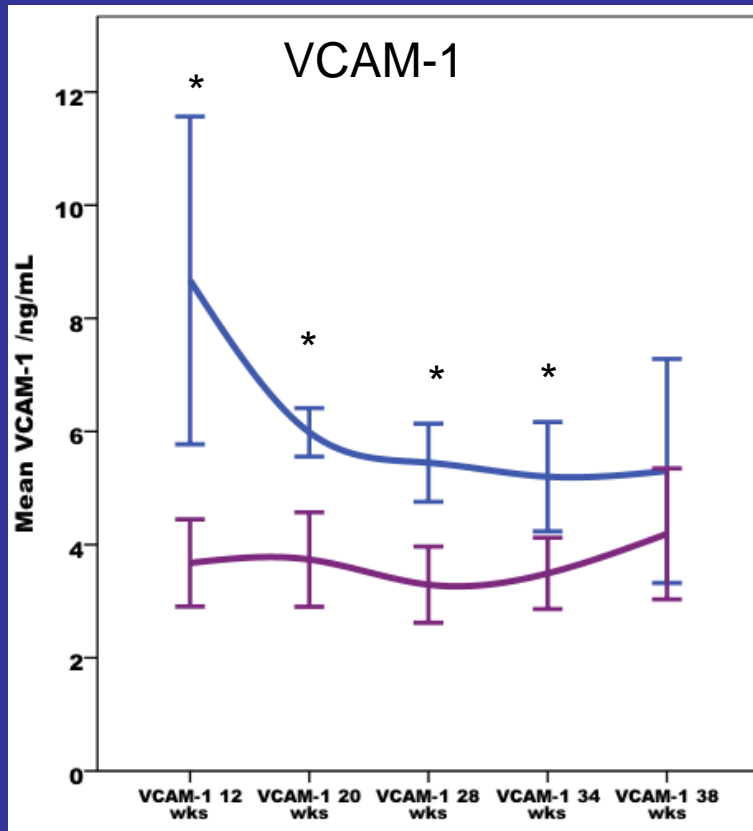
VCAM-1 & ICAM-1 2-3 fold higher at week 12, 20

\*  $p < 0.002$





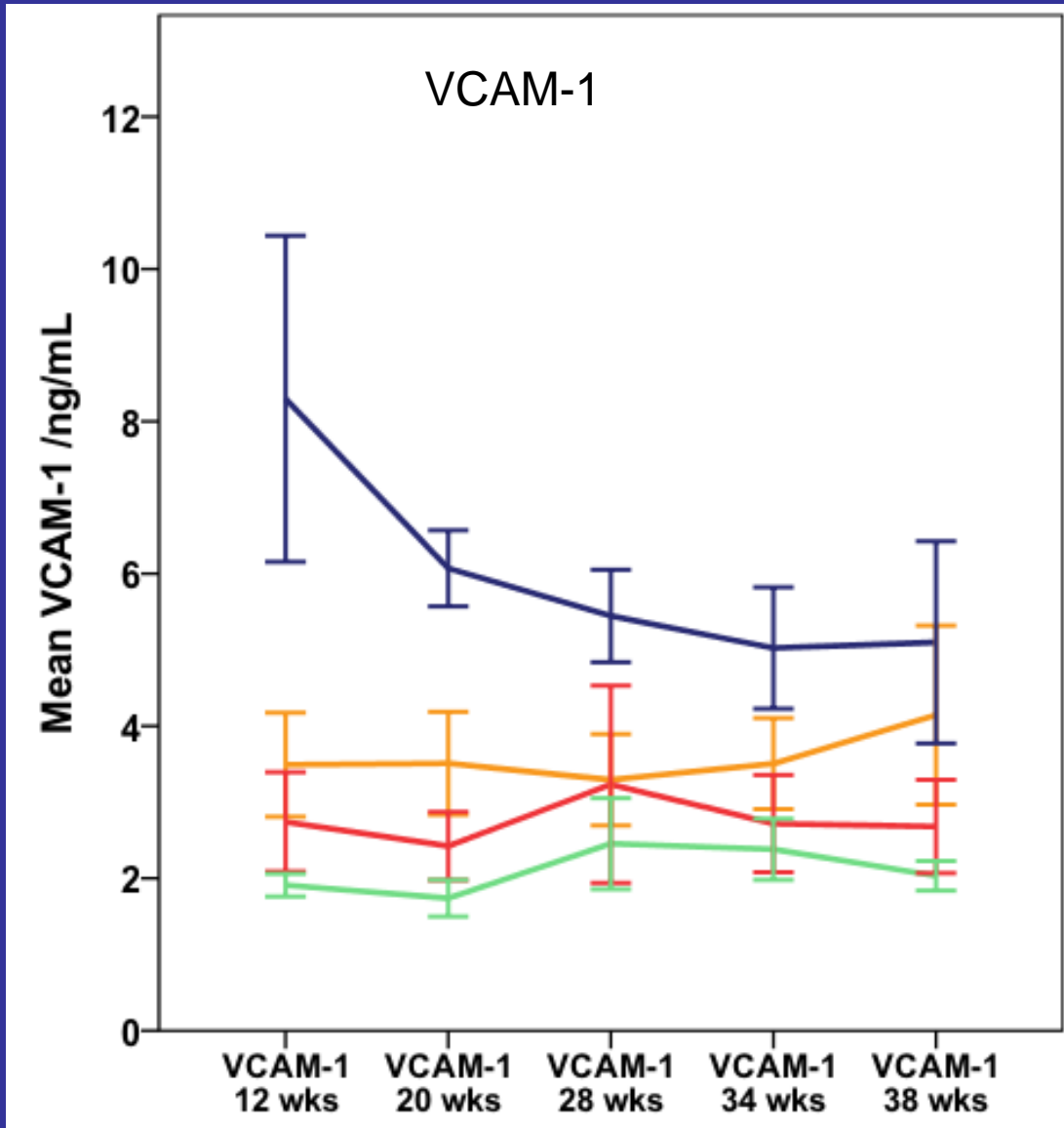
Mean maternal plasma vascular marker concentrations across gestation comparing HIV-1 women initiating PI cART versus women conceiving on PI cART



2 fold higher at weeks 12-34 \* = p < 0.01

— New PI  
— Preconception PI

# Mean maternal plasma vascular marker concentrations across gestation comparing HIV-1 women in HIV infected women by treatment and in HIV uninfected women

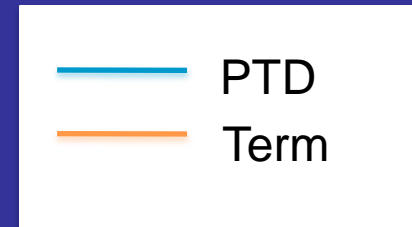
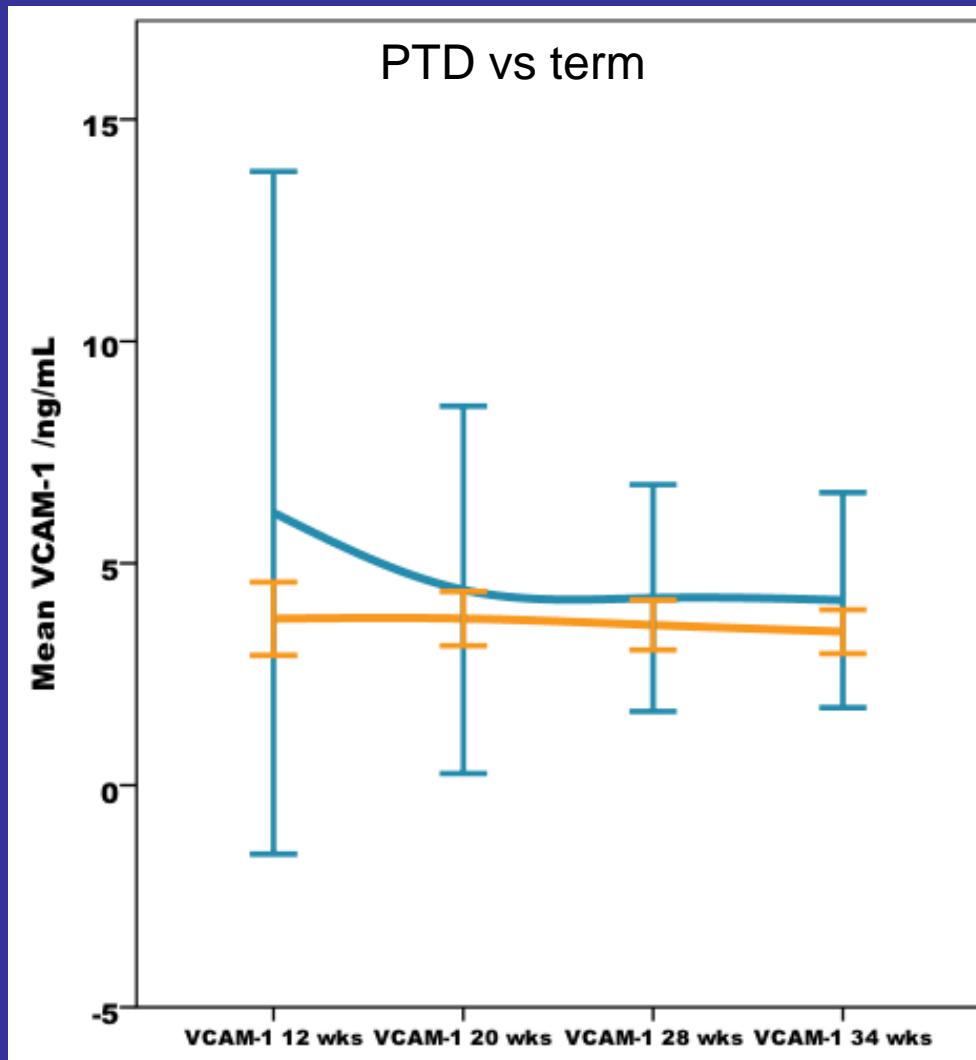


- New PI
- Preconception PI
- NRTI only
- HIV neg

# Associations with VCAM-1

- No correlation with:
  - Log HIV VL  $R= 0.16$   $p=0.862$
  - CD4 count  $R=0.10$   $p=0.606$
  - Gestational age at sampling  $R= -0.07$   $p=0.690$

# Mean maternal plasma VCAM-1 concentrations across gestation comparing women experiencing PTD versus term deliveries



# Limitations


- Potential confounders: different pt groups, other PTD risk factors
- Small numbers not powered to associate with delivery outcome or type of PTD (PROM/SPTB/PET)

# Summary

- Significantly higher leukocyte adhesion molecules in women initiating PI cART vs preconception PI cART, NRTI-only and uninfected women
- VCAM-1 was higher in women delivering preterm (not statistically significant)
- No association with CD4 cell count or viral load
- High VCAM-1 predated treatment initiation, declined through gestation suggestive of confounding

# Acknowledgments

- NIHR, Imperial BRC, BHIVA, Save the Baby Fund, Abbvie
- St Thomas' hospital, LHPRG



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British HIV Association  
**BHIVA**

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**19th Annual Conference of the  
British HIV Association (BHIVA)**

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