

Infertility Treatment and HIV

Infertility Treatment by IVF Or Intra-cytoplasmic Sperm Injections (ICSC) In Chronic HIV-1 Sero- discordant Couples (Poster 670)

- Retrospective study of outcome of IVF or ICSC in 80 HIV-1 sero discordant infertile couples and 82 HIV -ve control couples attending La Pitié Salpêtrière, Paris
- In HIV SC couples; 27/28 men and 47/52 women on ARVs
- 92.5.% HIV VL <50. Median CD4 level was 562/ μ l (163-1340)
- Overall take home baby rate of 25% in HIV discordant couples

	Control group Men HIV- Women HIV-	Women HIV+ (Men HIV-) Group A
Number of couples	82	52
Mean female age (years)	35	35
Infertility ethiology (%)		
▪ Female pathology	67	59.6
▪ Male factor	33	40.4
Number of Transfer (ET)	88	85
Clinical pregnancies /OR (%)	12.9	15.8
Clinical pregnancies (%)	13.9	17.6
Take Home Baby Rate :%	13 (15.9)	14 (26.9)
	p = 0.8 ns	

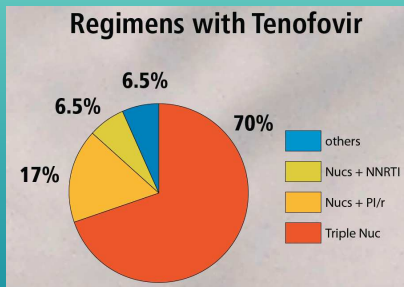
Small numbers, but no difference in outcomes of infertility treatment by gender of HIV +ve or infertile partner or compared to HIV -ve couples.

Pregnancy and ARVs

Safety and efficacy of TDF in pregnancy (poster 627a)

- 76 pregnant women Frankfurt HIV cohort received TDF containing regimens for mean of 12 weeks (range 1-38)

All 78 delivered by LSCS
 No HIV transmission
 No TDF-related infant toxicity



n = 78 (36 female; 42 male)	
Mode of delivery: Caesarean section (n)	78
Mean Week of Pregnancy at Delivery (01 - 40)	37
Birthweight (mean in g) (1,523 - 4,270)	2,880
Length at birth (mean in cm) (07 - 54)	49
Circumference of head (mean in cm) (08 - 43)	34
Intrauterine TDF-exposure (mean in weeks) (-1 - 38)	12
Vertical HIV-transmission (n)	0

Conclusions

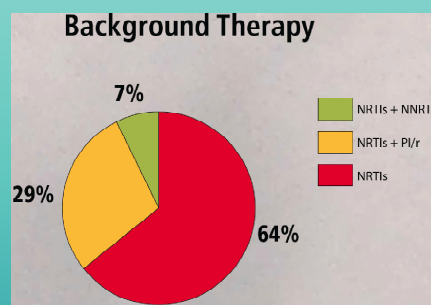
- TDF was effective and safe
- All 78 exposed children were HIV–ve and had no signs of TDF-related toxicity.
- None of the observed birth malformations was associated with TDF.

Malformations	
n = 78	
Malformations (n)	<ul style="list-style-type: none"> • Polydactily (3)* • Diaphragm hernia (1)* • Renal cyst (1)* • Cardial malformation in 1 child with Down Syndrome
* Diagnosed before onset of TDF	

TDF should be considered for mother-to-child-transmission prophylaxis

Use of Enfuvirtide in HIV + pregnant women (poster 627b)

- ENF used in 14 pregnant women in Frankfurt cohort. All ENF naïve.
- Reasons for use:
 - viral load not suppressed (n=7)
 - late presenters >32 weeks (n=4)
 - premature labour (n=3)



ENF was combined with at least 3 other antiretroviral drugs.

Use of Enfuvirtide in HIV + pregnant women - continued

- Mean duration ENF = 17 days before delivery (range, 1 to 57).
- No ENF-related adverse events observed in mothers and children
- Rapid drop in HIV VL

Change in Viral Load

n = 14	
Mean viral load at onset of enfuvirtide (copies/ml)	Mean antenatal viral load (copies/ml)
75120 (40 – 1000000)	218 (<40 – 1780)

Outcome of Newborns

n = 14 (5 female; 9 male)	
Mode of delivery C-section (n)	14
Mean week of pregnancy at delivery	37 (31 – 41)
Mean enfuvirtide-exposure (days)	15 (1 – 57)
Mean birthweight (g)	2716 (1580 – 4270)
Vertical HIV-Transmission (n)	0

Conclusion

ENF in combination with other antiretroviral drugs was successful and safe MTCT prophylaxis in late pregnancy

The use of Enfuvirtide in pregnant women is a useful option, particularly for late presenters, multi-drug-resistant virus and premature delivery.

Pregnancy ART PK studies

Pregnancy ART PK studies

Abstract	n	Drugs	Trim	Results
Poster 624	21	ATV/r 300/100	3rd	AUC 40% and C _{min} 20% lower than controls. Dose increase to ATV/r 400/100 to be evaluated
Poster 625	9	ATV/r 300/100	1-3rd	ATV related hyper-bilirubinaemia not increased in pregnant HIV+. Placental transfer of bilirubin in neonates was above normal range, but not associated with AE
Poster 626	35	TDF/FTC (2 tabs) during labour and 1 tab o.d for 7/7 post partum	3rd	TDF and FTC have good placental transfer. TDF neonatal plasma half life was just over 8 hours.
Poster 629	21	LPV/r 400/100 and 600/150	2-3rd	With LPV/r 400/100, 2nd trim AUC ↓50% cf postpartum. 600/150 dose should be used in 3rd trim and in 2nd trim if PI experienced. LPV/r dose can be reduced in the early postpartum.

Maternal to Child Transmission (MTCT)

Very Low Risk of MCT in UK and Ireland in
Women who Achieve Viral Suppression (2000-
2006). Poster 653

National Study of HIV in Pregnancy & Childhood (NSHPC)

- National surveillance scheme for paediatric and obstetric HIV in the UK and Ireland.
- Carried out through confidential, active reporting schemes; information sought on all pregnancies in diagnosed HIV-infected women.
- Children followed up to establish infection status:
Uninfected = negative PCR after one month of age,
or negative antibody test after 18 months of age

	MTCT rate	95% CI	n infected	total
Overall	1.2	(0.9 - 1.5)	61	5151
2000 - 2002	1.6	(1.0 - 2.4)	23	1456
2003 - 2006	1.0	(0.7 - 1.4)	38	3695
At least 14 days of ART	0.8	(0.6 - 1.1)	40	4864
ART and mode of delivery				
HAART + elective CS	0.7	(0.4 - 1.2)	17	2337
HAART + planned vaginal	0.7	(0.2 - 1.8)	4	565
HAART + emergency CS	1.7	(1.0 - 2.8)	15	877
ZDV mono + elective CS	0.0	(0.0 - 0.8)	0	467
HAART	1.0	(0.7 - 1.3)	40	4120
HAART from conception	0.1	(0.0 - 0.6)	1	928
HAART + VL<50 copies/ml	0.1	(0.0 - 0.4)	3	2117

Transmission rates were lower in 2003-2006 than in 2000-2002 ($p=0.069$).

In women on HAART there was no difference in MTCT rates between VD and LSCS ($p=1.00$).

3/2117 infants infected despite maternal HAART and viral load <50 copies/ml. 2/3 had positive PCR tests at 72 hours suggesting *in utero* transmission

Infection status was available for 86.8% (5151/5930) of infants; 1.2% were infected.

Rates were particularly low in women who had at least 14 days of ART, were on HAART when they became pregnant, or had viral loads < 50 copies/ml

Conclusions

- There was no difference in MTCT rates according to the management strategies outlined in the BHIVA guidelines:
 - HAART with elective caesarean section,
 - HAART with planned vaginal delivery, and
 - ZDV monotherapy with elective caesarean section.
- There were only three transmissions (0.1%) from women with viral load <50 copies/ml; two probably occurred *in utero*.
- The risk of MTCT in appropriately managed pregnancies in the UK and Ireland is very low

Amniocentesis and MTCT: The French ANRS EPF Cohort CO1/11 (Poster 654)

- The proportion of pregnancies where amniocentesis was performed increased from 1.0% (58 of 5831) before 2001, to 2.7% (67 of 2441) in 2001 to 2006
- In mothers not on ARVs there was NS trend to higher MTCT rate with amniocentesis (25.0% [3/12] vs 16.3% [343/2104]; $p = 0.43$),
- In mothers on HAART (at least 3 drugs), there was no difference in MTCT rate (0.0% [0/38] vs 1.4% [23/1613] $p = 1.0$).

Results suggest that amniocentesis does not increase the risk of MTCT of HIV if the mother is treated with an effective ART

Preventing Mother to Child Transmission (PMTCT)

TEmAA ANRS 12109 (Tenofovir-FTC for PMTCT in Africa and Asia) Oral 45b

Methods

- Phase II open-label clinical trial, enrolled 38 HIV-infected women - Ivory Coast, Cambodia, and South Africa.
- Median age 27, median CD4 450 cells/mm³, median HIV-1 RNA was 4.1 log₁₀ copies/mL.
- ZDV from enrolment (~28 to 38 weeks) until labour.
- In labour given sd-NVP and 2 tabs TDF/FTC (Truvada).
- Following delivery, TDF/FTC one tablet od for 1/52.
- Infants given sd-NVP syrup on day 1 and ZDV syrup for 1/52

Results

- Grades 3/4 adverse events in 24% (9/38) inc anaemia and leucopenia.
- 39 live births
- 9/39 (23%) suffered AE; n=4 died (meningitis, gastroenteritis, intestinal obstruction, and severe idiopathic encephalopathy).
- Maternal VL ↓ one log at day 2 postpartum
- HIV-1 RNA was detected in 2/39 infants at 3 days and was confirmed at 4 weeks. Both infections occurred in utero

Conclusions

- There were no findings of genotypic viral resistance to ZDV, NVP, FTC, or TDF in mothers or infants.
- No intrapartum HIV transmission was reported.

The investigators concluded that this combination is well-tolerated and that 7 days of postpartum therapy appeared to avoid NVP-resistance mutations in mothers and infants

PMTCT among HIV-infected
breastfeeding mothers using
ARVs

PMTCT among HIV-infected breastfeeding mothers using ARV

Abstract	n	ARV Regime	Results
Oral 42LB (Malawi)	3016	BF infants randomised to 1. Control regimen (CR) of sd NVP + 1 wk AZT, or 2. CR + NVP to 14 wks or 3. CR + NVP/AZT to 14wks	NVP or NVP/AZT for 14 wks reduced HIV transmission in infants at 9/12 age from 90% in controls to 30%. NVP/AZT not superior to NVP alone
Oral 43 (Ethiopia Uganda India)	1807	BF infants randomised to 1. sd NVP, or 2. sd NVP + NVP 5mg/kg day 8 to day 42	Infants on ext NVP had 20% lower risk of HIV transmission than sd NVP (6.9% vs 9.0%)
Oral 45aLB (Kenya)	497	Mothers: AZT/3TC/NVP from 34 weeks gestation to 6/12 Postpartum. Infants: sd NVP At birth. Exclusive BF and wean 6/12	Low 12-month infant HIV transmission rates (5.9%) achieved using maternal HAART from late pregnancy through 6 months BF

PMTCT among HIV-infected breastfeeding mothers using ARV

These studies may lead to new strategies for PMCT where BF is necessary due to lack of access to formula or clean water, strong cultural traditions of breastfeeding or fear of stigmatisation for not breastfeeding.

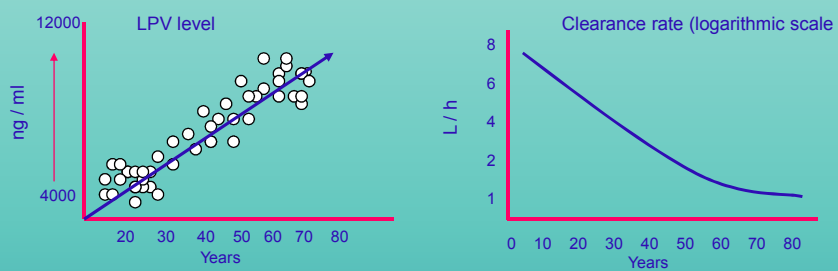
Changes in Bone Mineral Density

Changes in Bone Mineral Density

Abstract	n	ARV Regime	Results
Poster 969 Cross-sectional study	299	NNRTI/NRTI and PI based	On DEXA scan 54% had osteopenia and 13% osteoporosis Associations with ↓BMD: age, BMI, ethnicity, and current CD4 count and in men - ↓physical activity and ↑alcohol intake TDF, but not PIs or total ART exposure associated with ↓BMD
Poster 966 RCT	155	ART naïve subjects randomised to EFV/ZDV/3TC or LPVr/ZDV/3TC.	At 96 weeks F/U, RF for >5% decrease BMD from baseline - low baseline CD4, non black race. No association with ARV regime used.
Poster 967 Observational Cohort	71	36 on NNRTI/PI, 19 on PI/2NRTI, and 16 on NNRTI/2NRTI	BMD impaired in 31% of patients pre ARV suggesting causative role of HIV. At 1 year, ↓ in lumbar spine BMD from baseline more pronounced in either PI-containing regimens compared to NNRTI/2NRTI.

PK and Age

Ageing: Pharmacology ACTG 5015



35% reduction in clearance of drugs from age 25 to 80 years
Effect on P-450 increases with advancing of age
Less effect on phase 2 metabolism
Missing of dose more common in young age (< 45 years Vs. >45 years, 10% Vs. 2.5%)
No association with sex and ethnicity

Flexner C, Oral:106



**BHIVA 'BEST OF CROI'
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February 2008