Poster # TuPe5.2P01

Atazanavir Use in Pregnancy

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Background

- In the United States, most HAART regimens used during pregnancy include a protease inhibitor in order to meet two goals:
  1. Optimal treatment for the health of the woman and
  2. To prevent perinatal HIV transmission
- Data are available in the published literature on nelfinavir and several other PIs, however, no data exist on some of the newer agents.
- Atazanavir has a pregnancy category B label. While unconjugated hyperbilirubinemia is commonly noted with atazanavir use in non-pregnant adults, it is not known if the administration of this drug during pregnancy is safe in mothers or will exacerbate physiological hyperbilirubinemia in neonates. At this time, there are no published studies evaluating atazanavir in pregnant women. Prospective trials employing various HAART regimens during pregnancy are underway, however, additional observational data are needed to inform the field until these trials are complete.

Methods

- This is a retrospective, observational study of all pregnant women treated with atazanavir in one clinical practice through June 2005.
- Institutional review board approval was obtained.
- Data were abstracted from charts on maternal CD4 cells, viral loads, bilirubins, and jaundice.
- Infant weights, heights, the presence or absence of hyperbilirubinemia, and infant HIV infection status were recorded.
- Adverse effects were also recorded in mothers and infants.

Results

- To date nine women have been treated with atazanavir during pregnancy. Six of nine were on boosted atazanavir.
- ZDV/3TC was used in six women; tenofovir in the other three.
- At the onset of pregnancy, the mean viral load of women not on ART (n=7) was 31,133 copies/mL. The two women on ART at the time of conception had undetectable viral loads < 50 copies/mL.
- At delivery, all had HIV-1 RNA levels <100 copies/mL, with 7/9 having <50 copies/mL.
- The mean CD4 count increased from 366 to 450 cells/mm^3 during the course of pregnancy.
- Maternal total bilirubin at time of delivery ranged from 0.3-3.5 mg/dL.
- No hepatic, renal, or pancreatic abnormalities were seen in the mothers during pregnancy.
- The regimens were well tolerated in all women.
- All pregnancies were full term. There were 8 singleton and one twin pregnancies for a total of 10 infants.
- The highest infant bilirubin was 11.5 mg/dL; three infants were treated briefly with phototherapy.
- Mean birth weight and height were 3091.2 grams and 50.17 cm, respectively.
- The PCRs on 8 infants are negative at ≥ 4 months. The initial PCRs of the twins at one week of age are negative.

Demographics

	n
Age, years [range]	**29 [20-35]**
Ethnicity	
Hispanic	5
White	2
Black	2
Mode of HIV acquisition	
Heterosexual	6
Vertical	2
Injection drug use (past)	1
CDC class	
A	5
C, < 200 CD4 cells/mm^3	4

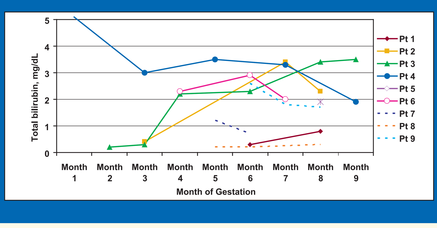
Nucleoside/Nucleotide Backbones

Number of women	Regimens
6	ZDV/3TC
2	ddI/TDF
1	TDF/3TC

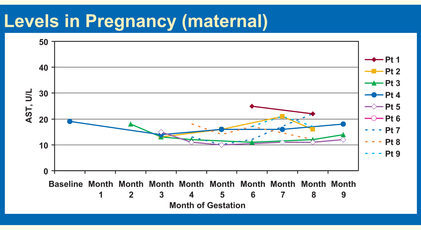
Prior Antiretroviral Regimens

Number of women	Regimens
4	No prior ART
1	ZDV,3TC
2	ZDV,3TC,NFV
1	ZDV,3TC, ddI, d4T, EFV, NFV, IDV, RTV
1	ZDV,3TC, ddI, d4T, EFV,LPV

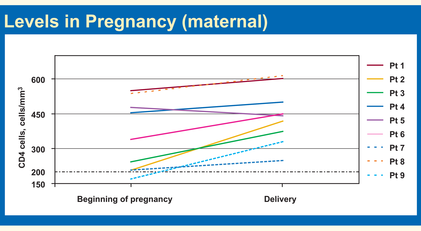
Total Bilirubin Levels In Pregnancy (maternal)



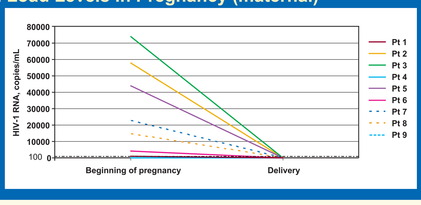
AST Levels in Pregnancy (maternal)



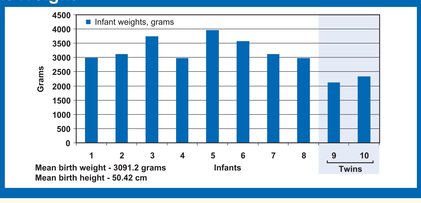
CD4 Levels in Pregnancy (maternal)



Viral Load Levels in Pregnancy (maternal)



Infant Weight



Discussion

- The immunologic and virologic response to atazanavir based regimens during pregnancy in this cohort has been excellent and is comparable to reports of other PI based regimens in pregnancy. Women tolerated the medications well and no adverse clinical or laboratory events were noted.
- In the first eight pregnancies, no transmission has occurred. The twins delivered to the ninth woman are also HIV negative thus far, however, they are too young for these results to be definitive.
- Neonatal hyperbilirubinemia, defined as total serum hyperbilirubin of ≥5 mg/dL, occurs frequently in the general population with up to 60% of infants experiencing clinical jaundice. This jaundice typically results from deposition of unconjugated bilirubin in the skin & mucus membranes. Common causes include fetal-maternal blood group incompatibility, prematurity, previously affected sibling, bruising / trauma from instrumented delivery, breastfeeding, and medications, including oxytocin (Pitocin®). The incidence of hyperbilirubinemia in this cohort is within the range of reported rates in the general population.
- Phototherapy is typically instituted when an infant's total serum bilirubin is ≥15 mg/dL. In a healthy full-term infant without hemolysis, the provider should be concerned for potential neurologic consequences (kernicterus) when the total serum bilirubin is >25 mg/dL. The highest total serum bilirubin in this cohort of infants was 11.5 mg/dL.

Conclusion

- Atazanavir based regimens in this cohort of pregnant women were very well tolerated in both the mothers and infants.
- To date all have had good responses immunologically and virologically and no infant has been infected.
- Infants' serology will continue to be followed 1 year post delivery to confirm HIV status.
- Until prospective data are available, this series helps to inform the field.

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