British HIV Association
BHIVA
20th Annual Conference

BASHH
12th Annual Conference

Third Joint Conference

of the
British HIV Association (BHIVA)
with the
British Association for Sexual Health and HIV (BASHH)

1–4 April 2014

Arena and Convention Centre · Liverpool

Dr Margaret Kingston

Manchester Royal Infirmary

Central Manchester University Hospitals NHS
NHS Foundation Trust
The Manchester Centre for Sexual Health
at The Hathersage Centre
280 Upper Brook Street Manchester M13 0FH

The Clinical Utility of Therapeutic Drug Level Monitoring of Atazanavir and Darunavir in Pregnancy

Amabel Dessain, Margaret Kingston & Orla McQuillan

Manchester Centre for Sexual Health


World Tuberculosis Day
"ON THE MOVE AGAINST TUBERCULOSIS
Innovate to accelerate action"
March 24th,
MINISTRY OF HEALTH
equal health for all
NOTICE

TDM in pregnancy: Benefits

- Optimal HIV control (VL undetectable) minimises the risk of:
  - HIV transmission to baby
  - Requirement for
    - CS delivery
    - Neonatal triple therapy
- There are concerns about maintaining therapeutic drug levels for protease inhibitors (PIs) during the third trimester of pregnancy
- We can (hope to) achieve optimal PI concentrations by TDM & dose modification

TDM in pregnancy: Drawbacks

- Changing treatment in pregnancy is bad:
  - Increasing pill burden
  - Increasing toxicity
  - Increasing dosage frequency
- TDM is pragmatically difficult:
  - More visits at less flexible times
  - Time delay for results
  - Are we doing
    - The right test?
    - At the right time?

Our regional guidelines

- Concerns re: BHIVA 2012 guidelines
- Introduction of TDM for patients taking PIs towards end 2nd trimester, analysis of results:
  - Does routine TDM improve outcomes?
  - Was TDM clinically useful?
    - *reduction in number of CS deliveries required*
    - *babies requiring triple therapy*

Previous work by us: Kaletra TDM vs VL for dosage modification in pregnancy

Review of 23 women taking Kaletra during pregnancy: 17 had TDM

- 15 TDM indicated therapeutic levels of Kaletra – BUT 6 had low level vireamia
  - Dose of Kaletra increased to 3 tablets BD in all & all VL< 40 at delivery
- 2 low levels of Kaletra were identified by TDM - both compliance issues
  - One woman changed her regime completely & VL<40 by delivery
  - Other ongoing viraemia due to adherence problems

Conclusions:

- **HIV VL is a better indication than TDM of the need to increase the dose of Kaletra in pregnancy**
- **Increasing the dose of Kaletra as required from 2 to 3 tablets BD even when TDM indicates adequate levels can achieve HIV VL<40 at delivery**

CS Babu, S Bennett, O McQuillan, V Lee, M Kingston; 2008 BHIVA 14th annual conference, Belfast, P59

Information needed now is for Atazanavir & Darunavir

Retrospective case note review of pregnancies in women taking Atazanavir & Darunavir between 2008 until April 2013

- Did the introduction of routine TDM in pregnancy influence outcomes?
  - HIV VL at delivery and consequently requirement for:
    - PLCS
    - Neonatal triple therapy

Methods

Retrospective case note review of our patients from the HIV antenatal clinic:

- Babies born 1.7.2008 to 28.5.2013
- Mother prescribed Atazanavir and/or Darunavir for at least 6 weeks during the pregnancy
- Gestation of at least 25 weeks achieved

Methods

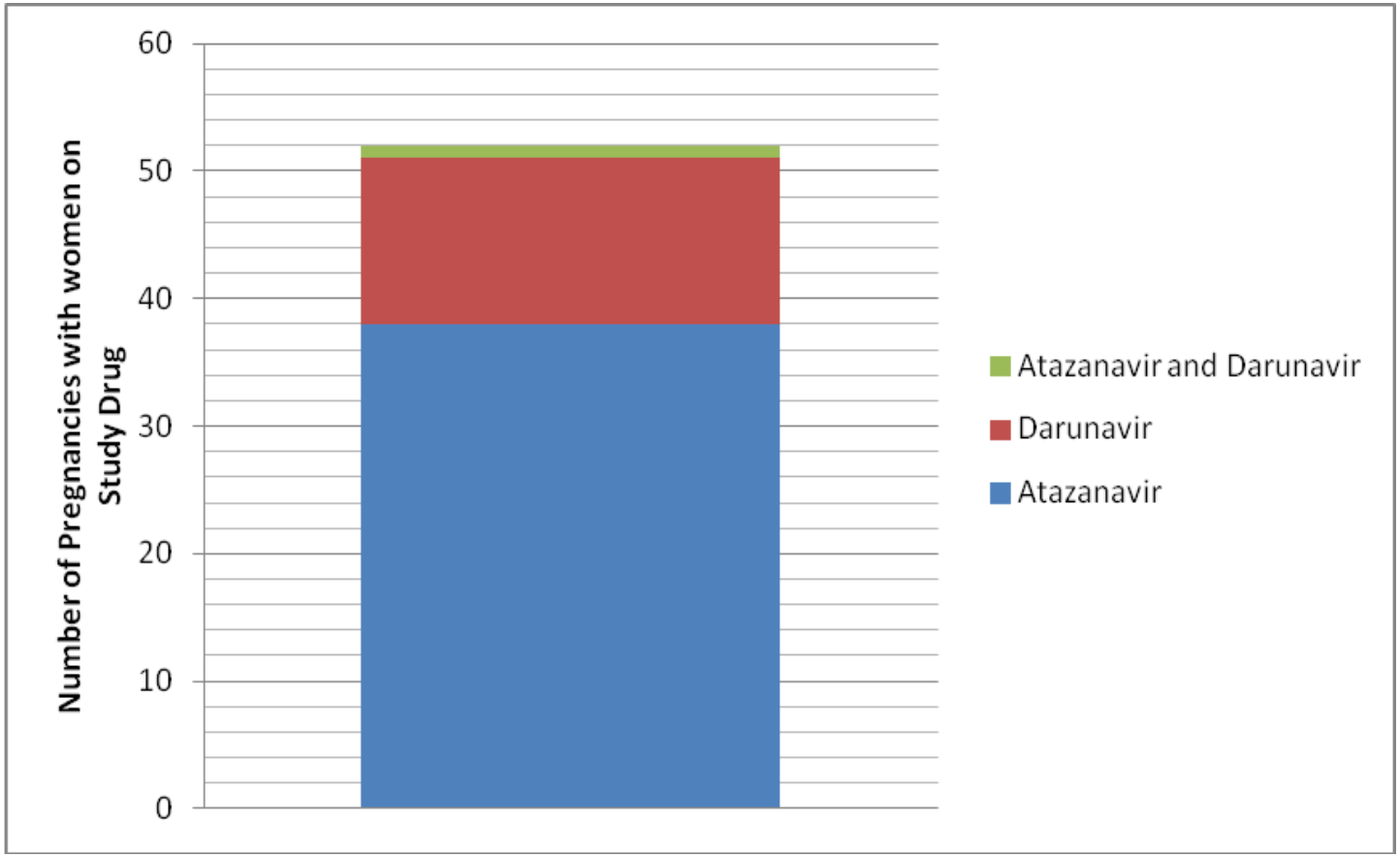
Data collected included:

1. Maternal demographics
2. HIV drugs and parameters
3. Details of TDM performed and results
4. Obstetric details
5. Infant details and HIV status

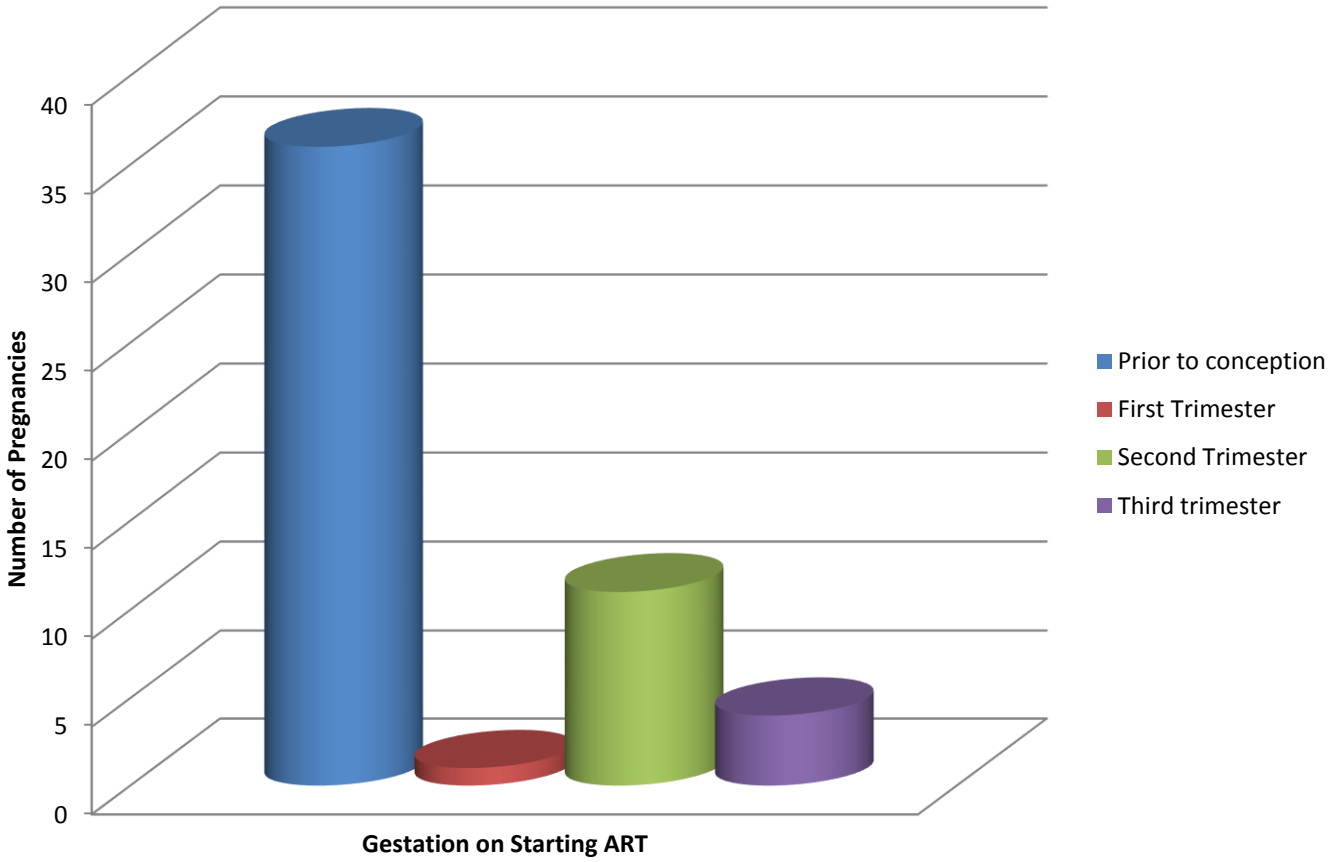
Data analysis:

1. Excel spreadsheet of results
2. Timelines for pregnancies on different drugs constructed
3. Fisher's exact test performed for the difference in HIV VL<40 between TDM yes/no groups

Results: PI taken during pregnancy



Results: When HAART was started



Results: Viral load of TDM and non TDM patients on Atazanavir or Darunavir at delivery

Atazanavir & Darunavir	pregnancies with HIV VL <40	pregnancies with HIV VL >40
NO TDM performed	26 (93%)	2 (7%)
TDM performed	22(92%)	2 (8%)
Fishers Exact Test	P>0.9999 CI 95%	

Results: Points of Interest

- All those on Darunavir OD & 69 % on Atazanavir 300mg dose had TDM of therapeutic levels; all had HIV VLs <40
- In those on Atazanavir, NRTI backbone did not appear to be relevant
- 13 % more in the no-TDM arm had a NVD
- No HIV transmission at all

Discussion

The patients who received TDM did not have better outcomes than the patients who did not have TDM performed

- Are we measuring the wrong thing?

"Total drug concentrations are decreased during pregnancy whereas the unbound concentrations (pharmacologically active) tend to remain stable"

Conclusions

The patients who received TDM did not have better outcomes than the patients who did not have TDM performed

- All patients in whom TDM detected a sub-therapeutic drug level had undetectable viral loads at the time of TDM and at delivery
- In all patients who had a detectable viral load at delivery, and had TDM, therapeutic drug levels were detected
- TDM requires more patients visits, staff time and may increase ARV toxicity and disrupt an established & effective HIV regime
- Close HIV VL monitoring is more helpful than TDM when deciding on treatment changes in pregnancy – as in our Kaletra work before - but treatment strategies have changed, and we would now intensify - *"Reach for the Raltegravir"*

Recommendations

- TDM should be not be routinely performed in pregnant women on an effective ARV regimen….
  - ✓ ….but it should performed in the same circumstances as when indicated in non pregnant women
- Monitor the HIV VL closely in pregnancy, support patients & optimise compliance

Questions?

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