17TH ANNUAL CONFERENCE OF THE BRITISH HIV ASSOCIATION (BHIVA)

British HIV Association BHIVA

Dr Tristan Barber

Chelsea and Westminster Hospital, London

6-8 April 2011, Bournemouth International Centre

UK HIV Drug Resistance Database

Protease inhibitor (PI) resistance mutations in patients receiving lopinavir boosted with low dose ritonavir (LPV/r) as the first PI

Dr Tristan J Barber

on behalf of the UK HIV Drug Resistance Database

and the UK CHIC Study

Background

- Lopinavir co-formulated with ritonavir (LPV/r) has been an extensively used protease inhibitor (PI) against HIV
- Development of PI resistance reduces sequencing options
- Identifying predictors of PI resistance might better our ability to sequence therapy
- Many studies report few resistance mutations under lopinavir drug pressure (in virological) failure
  - can be difficult to identify LPV associated resistance pathways

Aims

- Evaluate patients in the UK failing LPV/r as their first PI
- Quantify the prevalence of PI resistance in this group
- Explore the patterns of PI mutations
- Identify possible factors contributing to the development of PI resistance

Methods

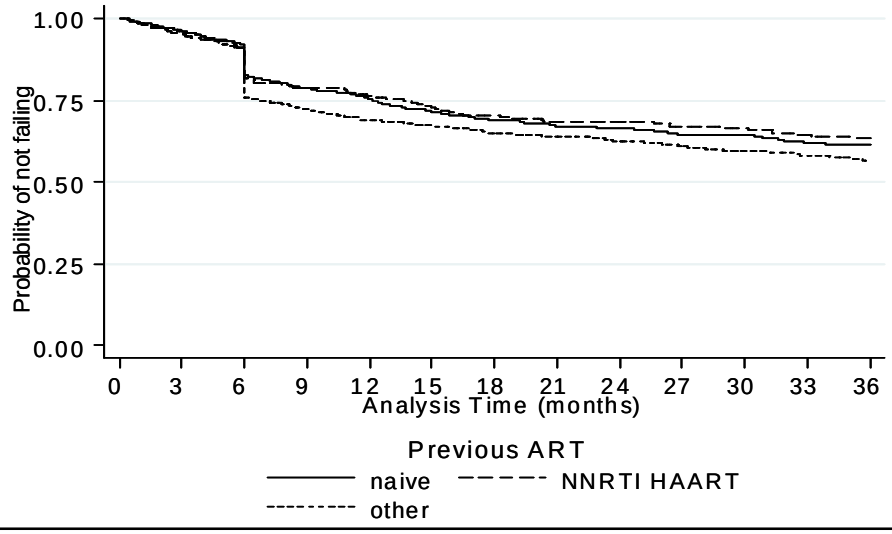
- *Pol* gene sequences retrieved from the UK HIV Drug Resistance Database
- Demographic and clinical data were obtained via linkage to UK CHIC
- Eligible patients were receiving LPV/r as their first PI
  - ART naïve
  - having previously received non-PI based regimen
- Virological failure defined at 6 months as:
  - >400 c/ml after previous suppression to <400 c/ml
  - >400 c/ml for the first 6 months

Methods

- Resistance tests were included if performed on patients with virological failure
  - whilst on LPV/r
  - within 30 days of stopping
- All PI mutations were scrutinised
  - both major and minor according to IAS-USA 2008
  - we looked at 18,791 ART-naïve patients and excluded PI mutations/polymorphisms with prevalence >1%
- Final mutations analysed:

L24I	D30N	V32I	L33F	E34Q	E35G	K43T
M46IL	I47VA	G48V	I50V	F53LY	I54LVAMTS	
Q58E	G73CSTA	T74P	L76V	V82AFTSL		
N83D	I84V	I85V	N88DS	L89V	L90M	

Time from initiation of LPV/r to virological failure



Results

- Data from a large clinical cohort suggests prior (NNRTI based) ART failure does not compromise subsequent LPV/r response
- RAMs at positions 32 **46** 47 **54** 76 82 were associated with LPV/r failure
  - 3056 patients included
  - 811 (27%) failures
  - 291 resistance tests
  - 32 showed resistance (4% of failures but 11% of those failing with a test)
  - No demographic factors found to be associated with risk of LPV/r failure

Results

- We also looked at length of LPV exposure to detectable viraemia by looking at viral area under the curve (AUC)
- Increasing mutation risk in failures with high AUC suggests that maintaining LPV in a failing regimen may have significant genotypic resistance costs
  - although those with resistance had predicted sensitivity (Stanford) to other PIs – TPV (81%) – DRV (84%)

Thanks

- David Dunn
- Deenan Pillay
- Linda Harrison
- UK CHIC Steering Committee
- UK Collaborative Group on HIV Drug Resistance Steering Committee
- Daniella Chilton
- Avneet Chowdhury
- Anna Maria Geretti
- Richard Gilson
- Nicola Mackie
- Andrew Phillips
- Ian Williams
- Mortimer Market and Archway Centres
  - Erica Allason-Jones
  - Eva Jungmann
  - Patrick French