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A comparative analysis of risk factors associated with efavirenz, atazanavir/r, darunavir/r, lopinavir/r, and renal impairment

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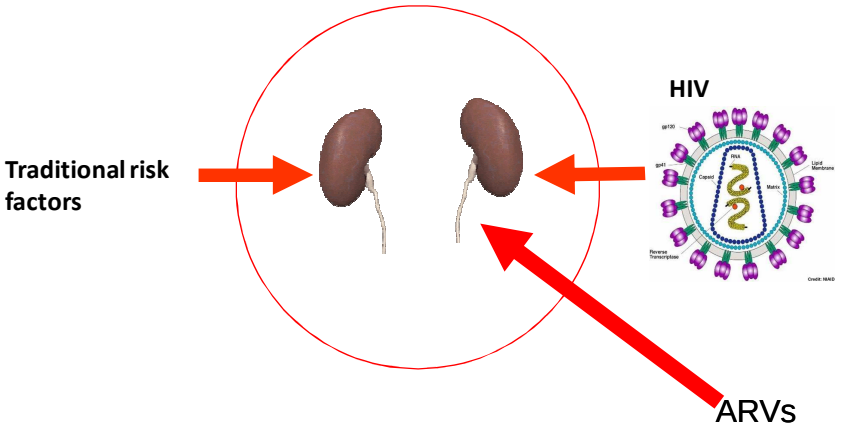
Background (1)

Risk factors for renal disease



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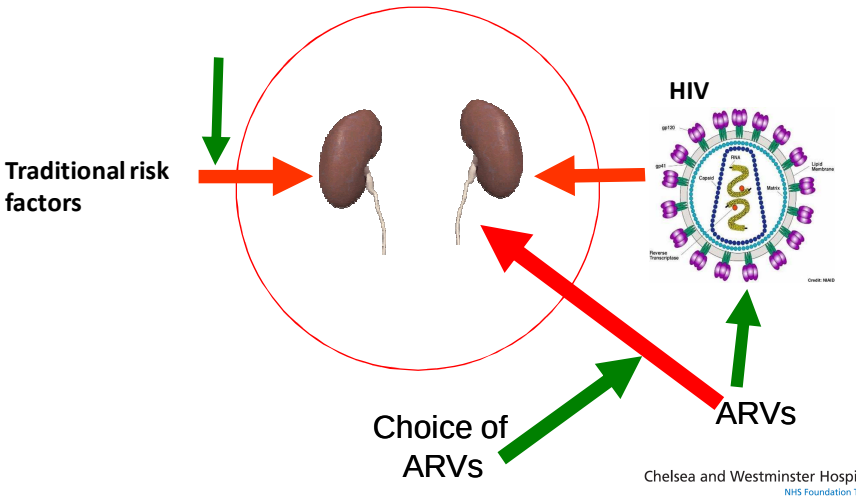
Background (2)

Areas for potential reduction of renal disease



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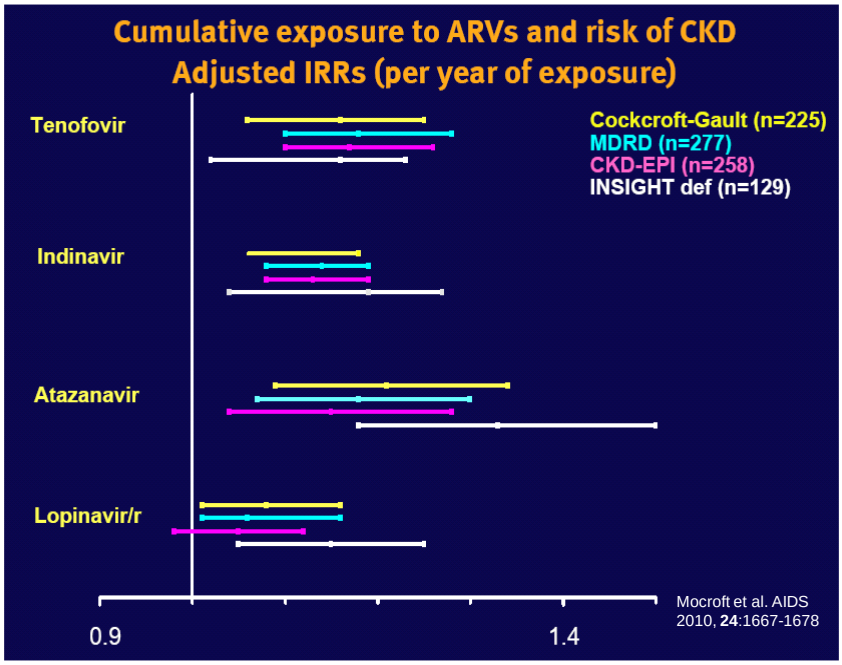

Aims

- To compare the association of EFV, ATZ/r, DRV/r & LPV/r with renal impairment which we defined **as reaching first eGFR<60 ml/min per 1.73m^2** in individuals commencing these therapies with a baseline eGFR above this threshold
- To assess renal recovery over time post first eGFR<60 ml/min per 1.73m^2

*** eGFR: estimated glomerular filtration rate**

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Methods

- Retrospective cohort study: June '06 – Feb '10
- Inclusion criteria:
  - Patients commencing on or switching to HAART containing:
    1. 2NRTI + EFV
    2. 2NRTI+ ATZ/r
    3. 2NRTI + DRV/r
    4. 2NRTI+ LPV/r
  - Available baseline eGFR >60 ml/min per 1.73m^2
- Event was censored at:
  - eGFR<60 ml/min per 1.73m^2
  - stopping study combination
  - death
  - end of study period

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Statistical analysis

- Cox's proportional hazards regression model (univariate and multivariate analysis): to show likelihood of renal impairment (eGFR<60 ml/min per 1.73m$^{2)}$
- Mixed procedure in SAS: estimation of proportion renal recovery with time

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Results (1)

386 (18%) developed renal impairment during study

Baseline demographics	Overall cohort n= 2115
Gender: n (%)	
Male	1842 (87%)
Female	273 (13%)
Ethnicity	
Caucasian	1520 (72%)
Black African	259 (12%)
Other	313 (15%)
Unknown	23 (1%)
Age (yrs) : mean (SD)	43 (9.5)
Median baseline CD4 (cells/mm^3)	383
% with undetectable VL at baseline (<50copies/ml)	60

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Results (2) univariate analysis

Significant associations with eGFR<60 ml/min per 1.73m^2

	Hazard Ratio (95% CI)	P value
Gender		
F	1.5 (1.16-1.96)	**0.002**
M	1	
Baseline age (yrs)		
<35	1	
36-43	1.3 (0.92-1.82)	**<0.001**
43-48	2 (1.5-2.82)	
>48	2.8 (2.03-3.73)	
Baseline eGFR		
<69	12.8 (8.5-19.2)	**<0.001**
69-78	2.4 (1.6-3.8)	
79-84	1.4 (0.8-2.3)	
>84	1	

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Results (3) univariate analysis

Significant associations with eGFR<60 ml/min per 1.73m^2

	Hazard Ratio (95% CI)		P value
Hep S Ag +ve status	1.21	(0.59-1.63)	<0.001
Previous IND exposure	2.03	(1.58-2.62)	<0.001
Previous TFV exposure	1.68	(1.38-2.05)	<0.001
Tot duration TFV exposure	1.09	(1.06-1.12)	<0.001
ATZ/r exposure	1.27	(1.02-1.58)	<0.036
DRV/r exposure	1.53	(1.22-1.92)	<0.001
LPV/r exposure	1.71	(1.38-2.24)	<0.001
EFV exposure	0.6	(0.47-0.73)	<0.001

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Results (4) traditional risk factors

Traditional risk factor	EFV group n=50	PI group n=110	P value
Diabetes n (%)	10 (20)	14 (12.8)	0.34
Hypertension n (%)	16 (32)	22 (20)	0.15
Renal stones n (%)	0 (0)	7 (6.4)	0.16
Cardiovascular disease n (%)	2 (4)	11 (10)	0.33
Peripheral vascular disease n (%)	3 (6)	6 (5.5)	0.82
Nephrotoxic drugs n (%)	22 (44)	45 (40.9)	0.84
Chemotherapy n(%)	1 (2)	14 (12.7)	0.06
Sepsis n (%)	0 (0)	6 (5.45)	0.22

160 patients randomly selected out of 386 who developed renal impairment

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Results (5) multivariate analysis

	¶Hazard Ratio	(95% CI)	P value
LPV/r	1.69	(1.1-2.6)	0.017
ATZ/r	1.52	(1.14-2.03)	0.004
DRV/r	1.31	(0.94-1.81)	0.108
EFV	1		

¶Adjusted for gender, age at start of HAART, baseline eGFR, Hep B SAg , prior exposure to TFV and IND and total duration of TFV exposure

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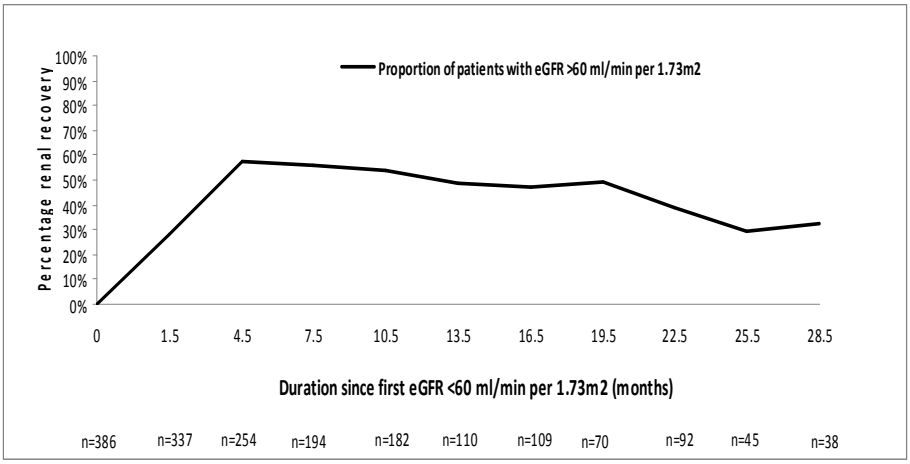
Results (6) renal recovery

% renal recovery with time post first eGFR<60 ml/min per 1.73m²



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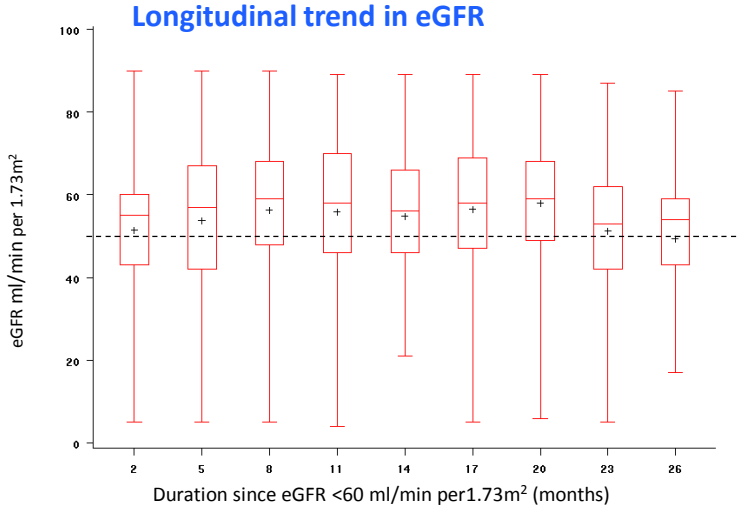
Results (7) renal recovery

Longitudinal trend in eGFR



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Conclusions

- 386 (18%) reached eGFR<60ml/min per1.73m^2 during study
- There was a significant risk of renal impairment with boosted ATZ and LPV
- Post first eGFR<60ml/min per1.73m^2, at 12months, 50% of patients had renal recovery but this decreased with further length of follow up. Also the longitudinal increment in eGFR was not sustained.

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