

# Mr Timothy Rawson

Imperial College London

# Factors associated with cerebrospinal fluid HIV RNA in HIV infected subjects undergoing lumbar puncture examination in a clinical setting

Timothy Rawson<sup>1</sup>, David Muir<sup>2</sup>, Nicola E Mackie<sup>1, 2</sup>, Lucy J Garvey<sup>1, 2</sup>,  
Alex Everitt<sup>2</sup> and Alan Winston<sup>1, 2</sup>

<sup>1</sup>Imperial College London

<sup>2</sup>St Marys Hospital, Imperial College Healthcare Trust

# Background

- Since the introduction of cART a changing phenotype of HIV associated CNS disease has been observed
  - Decreasing prevalence of HIV associated dementia (HAD)
  - Reports of ongoing NC (neurocognitive) impairment in effectively treated HIV infected patients
- CSF HIV RNA may be a useful tool in the management of CNS disease in HIV infected subjects
- Quantification of CSF HIV RNA in clinical practice remains poorly described:
  - Limited data regarding the prevalence of detectable CSF HIV RNA in the cART era
  - Factors associated with CSF HIV RNA not well described
- The literature currently describes discordance between plasma & CSF HIV RNA in:
  - 10% subjects on cART <sup>1</sup>
  - 3 to 10% of subjects with a suppressed plasma HIV RNA (<50 copies/mL) <sup>1, 2</sup>

1. Eden, A., Fuchs, D., Hagberg, L. *et al.* (2010). *HIV-1 viral escape in cerebrospinal fluid of subjects on suppressive antiretroviral treatment. J Infect Dis* 202, 1819-1825.

2. Canestri, A., Lescure, F. X., Jaureguiberry, S. *et al.* (2010). *Discordance between cerebral spinal fluid and plasma HIV replication in patients with neurological symptoms who are receiving suppressive antiretroviral therapy. Clin Infect Dis* 50, 773-778.

# Study Aims

To investigate a large HIV infected cohort undergoing lumbar puncture examination, which included assessment of CSF HIV RNA in the recent cART era, to:

1. Quantify CSF HIV RNA
2. Investigate factors associated with CSF HIV RNA

# Method - Subjects

## Inclusion Criteria

- All HIV infected individuals who underwent LP examination which included quantification of CSF HIV RNA
  - Between January 2008 & October 2010
  - St. Mary's, London, UK

## Data Collected

- A prospective electronic patient database was used to collect patient information & laboratory parameters from time of LP
  - HIV disease parameters such as:
    - Current and nadir CD4+ lymphocyte count
    - Plasma HIV RNA
    - ARV history
    - HCV
    - Syphilis data
  - We also calculated the CNS penetration effectiveness score<sup>3, 4</sup>

# Method – Reason for LP

Patient Identifier	Date of LP	Clinical reason for LP
Mxxxxx	15.02.08	<i>HIV Encephalopathy</i>
Mxxxxx	02.08.08	<i>PML</i>
Mxxxxx	13.08.08	<i>Query NCI</i>
Mxxxxx	18.02.09	<i>MAI Infection</i>
Mxxxxx	20.09.09	<i>Syphilis</i>

- Reason for LP determined by treating physician:
  - Investigation of presumed HIV encephalopathy (IxHE)
  - Investigation of other CNS AIDS defining illness
  - Investigation of early syphilis
  - Investigation of acute illness where CNS disease may not be directly related to HIV

# Methods - Statistics

- Assessed number of subjects with CSF viral escape defined as follows:
  - CSF HIV RNA  $\geq 0.5 \log_{10}$  copies/mL greater than plasma HIV RNA
  - **And** if plasma HIV RNA was undetectable CSF HIV RNA > 200 copies/mL
- Used stepwise multivariate regression model to assess factors associated with detectable CSF HIV RNA (>50 copies/mL)
  - P-values <0.05 considered significant

# Baseline Results

Parameter	Description	Value
Number		142
Age	<i>Years (mean, range)</i>	45 (24 -83)
CSF HIV RNA	<i>Number Detectable (%)</i>	77 (54)
Plasma HIV RNA	<i>Number Detectable (%)</i>	68 (48)
On cART	<i>Number (%)</i>	99 (70)
Current cART Duration	<i>&gt; 6 months</i>	70
CPE Score	<i>Median Score (Range)</i>	1.5 (0 – 3.5)
IxHE (%)		57 (48)
CNS AIDS Illness (%)		39 (28)
Syphilis (%)		20 (14)
Not HIV Related (%)		26 (18)



# Results – CSF Viral Escape

- Currently in the literature suggests CSF viral escape is observed in:
  - 10% subjects on cART <sup>1</sup>
  - 3 to 10% of subjects with a suppressed plasma HIV RNA(<50 copies/mL) <sup>1, 2</sup>

## Results for CSF Viral Escape

Group	N=	Number (%) with CSF HIV RNA > Plasma HIV RNA	Number (%) with CSF Viral Escape*
Overall	142	37 (26%)	30 (21%)
On cART	99	27 (27%)	21 (21%)
On cART & plasma HIV RNA undetectable	69	16 (23%)	9 (13%)

\* CSF Viral Escape defined as CSF HIV RNA  $\geq 0.5 \log_{10}$  copies/ml greater than plasmas HIV RNA and if plasma HIV RNA was undetectable CSF HIV RNA > 200 copies/mL

# Results – Multivariate Analysis

## Overall cohort (n=142)

- Only plasma HIV RNA was significantly associated with detectable CSF HIV RNA in our entire cohort ( $p < 0.001$ )

## Undetectable plasma HIV RNA (n=69)

- In those subjects with undetectable plasma HIV RNA, a significant association is observed between lower CPE scores and detectable CSF HIV RNA ( $p = 0.044$ )

## Multivariate results for subjects with plasma HIV RNA <50 copies/mL

Parameter		P-Value	Coefficient	Lower CI (95%)	Upper CI (95%)
HCV RNA Positive		0.135	-0.244	-0.567	0.078
Previous History of Syphilis		0.135	-0.244	-0.567	0.078
CPE Score		<b>0.044</b>	-0.217	-0.429	-0.006
ART Duration		0.118	0.195	-0.051	-0.441

# Results – Multivariate Analysis

## Analysis of individual clinical scenarios separately

- All clinical scenarios showed similar results as previously described (except IxHE)
- Only in patients under investigation for HIV encephalopathy do we observe both plasma HIV RNA and CPE score independently associated with CSF HIV RNA

## Multivariate results for subjects undergoing Investigation of HIV encephalopathy

Parameter		P-Value	Coefficient	Lower CI (95%)	Upper CI (95%)
Plasma HIV RNA		<b>0.019</b>	0.438	0.075	0.800
Age		0.170	-0.095	-0.233	0.043
CPE Score		<b>0.003</b>	-0.511	-0.842	-0.179

# Summary

- High rates of detectable CSF HIV RNA are observed within clinical settings
  - Given this high yield, routine quantification of CSF HIV RNA may be justified in similar patient populations
  - We are currently investigating whether clinical decisions are influenced by these results
- Factors associated with CSF HIV RNA:
  - Overall**
    - Plasma HIV RNA is associated with CSF HIV RNA
    - Once plasma HIV RNA becomes suppressed lower CPE scores are associated with detectable CSF HIV RNA
  - An unexpected finding:**
    - In subjects undergoing investigation for HIV encephalopathy, both plasma HIV RNA & CPE scores are independently associated with CSF HIV RNA. This differs from the other clinical scenarios we defined


# Future Work

- More detailed assessment of CSF HIV RNA
  - CSF HIV resistance testing now also implemented in the department
- Different factors associated with CSF HIV RNA in different clinical scenarios
  - In order to assist in pre-determining which patient groups may best benefit from quantification of CSF HIV RNA

# Acknowledgments

- All patients involved
- HIV Clinical Trials Unit, Imperial College, London UK
- Staff from the HIV Department, St Mary's Hospital, London UK
- NIHR Biomedical Research Centre funding scheme at Imperial College Healthcare NHS Trust, London, UK for infrastructure funding support.

**Imperial College**  
**London**

Imperial College Healthcare   
NHS Trust

