Unexpected High Failure rate of Lopinavir (LPV/r) Monotherapy

F. Zenger [1], A. Cusini [2], C. Fux [3], M. Opravil [2], HJ. Furrer [3], L- Decosterd [4], S.Yerly [5], P. Vernazza [1] and the Swiss HIV Cohort study (SHCS)

[1] Cantonal Hospital St.Gallen, [2] University Hospital Zürich, [3] University Hospital Bern, [4] University Hospital Lausanne, [5] University Hospital Geneva

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Introduction:

- Previous PI- monotherapy studies demonstrated full viral load (VL) suppression over more than one year
- Concerns remain regarding the activity in compartments
- The ongoing MOST study evaluates antiviral activity of LPV/r –monotherapy in the genital tract and the central nervous system

Methods:

- Patients on successful treatment are randomised to either continued standard therapy or LPV/r monotherapy for 48 wk
- At baseline and w48, VL in CSF and genital secretions is measured in all patients
- We present preliminary findings on blood VL failure while the study is ongoing

Results:

- 58 patients have currently been randomised
- Median study duration is 8 months
- 23 or 26 patients on monotherapy have a follow up of at least 6 or 12 weeks, respectively
- At baseline, all patients had undetectable plasma VL
- One patient had a CSF VL of 82 cp/ml (randomized to continued HAART)
- Five patients (all mono-arm) failed therapy (>400cp/ ml, confirmed) in blood (table)
- Lumbar puncture was performed in four failing patients
- In these four VL in CSF was significantly higher than in blood
- All patients confirmed optimal adherence, but drug levels were extremely low in two of five
- Thee failing patients had neurological symptoms at failure (headeache, dizziness, visual disturbance, deficit in concentration, atactic gait
- All blood and CSF samples were wildtype on genotyping at the time of failure

Tab. 1: Evaluation of the 5 failing patients at the time of virological failure in blood

Week	Symptom	VL Blood (log_{10} cp/ml)	VL CSF (log_{10} cp/ml)	CD4 (abs) cell/µl	CD4 (%)	LPV plasma level (ng/ml percentile)
12	Yes	4.3	5.1	680	52	87 (<1)
24	Yes	3.0	4.2	130	14	6438 (50th)
6	No	5.0	n.d.	250	18	4661 (25th)
24	Yes	3.0	3.7	710	37	Undetectable
15	No	4.1	4.9	380	36	6388 (25-50th)

Conclusion:

- Failure rates during LPV/r monotherapy may be higher than expected from previous studies (Ref 1-2) and may involve the central nervous system
- The use of monotherapy in the treatment of HIV-infectino should be restricted to clinical studies (3)

References and Acknowdedgement:

References

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