Retrovirology

Poster presentation

Oral administration of a mixture of PR, RT and INT inhibitors to rhesus macaques that were persistently infected with SHIV-pr

Eiji Ido*, Misa Ishimatsu, Tetsuko Tada, Shizuka Iwamoto and Aya Umehara

Address: Institute for Virus Research, Kyoto University, Kyoto 606-8507, Japan
* Corresponding author

from Frontiers of Retrovirology: Complex retroviruses, retroelements and their hosts
Montpellier, France. 21-23 September 2009

Published: 24 September 2009

Retrovirology 2009, **6**(Suppl 2):P42 doi:10.1186/1742-4690-6-S2-P42

This abstract is available from: http://www.retrovirology.com/content/6/S2/P42

Background

Although the current anti-retroviral therapy (ART) is truly effective to prolong the patient's life, the long-term uptake of drugs also appears to be raising issues such as troublesome side effects. Recently integrase (INT) inhibitors have been added in a list of the medicines in addition to protease (PR) and reverse transcriptase (RT) inhibitors. Emergence of multi-drug-resistant virus will be soon a serious concern. We should present recommendations of the regime(s) including INT inhibitors as early as possible ideally by pre-clinical experiments. However, no good animal model to test efficacies of anti-HIV-1 drugs especially by oral administration is available so far. Thus we attempted to establish a new animal ART model in which a combination of three groups of drugs can be tested using monkeys.

Materials and methods

Two rhesus macaques infected with SHIV-pr that possesses the PR gene of HIV-1 [1] were used in this study. When the monkeys were persistently infected, a mixture of three drugs (nelfinavir, didanosine, and raltegravir) contained in a solid diet was orally administered to them twice a day for 4 weeks. Doses were determined by body weight according to those for human use. Plasma viral loads and CD4 cells were monitored during the whole period of ART. Drug concentrations of raltegravir in plasma were also measured by LC-MS.

Results

Plasma viral loads of two monkeys reached to 10^5-10^6 copies/ml before medication. The viral load of one monkey was suppressed below the detection limit by the 4th week of ART, but quickly rebounded to the initial level after the cease of medication. The trough of raltegravir was sufficiently beyond the effective value. The load of another monkey decreased one order of magnitude by the 2nd week of ART, but this animal gradually lost appetite during ART and died of pneumonia thereafter.

Conclusion

The fact that one monkey died showing AIDS-like symptoms indicates that our SHIV-pr was not only replication-competent but potentially pathogenic in monkeys. Overall, the present data suggest that this new animal ART model was fairly good to evaluate efficacies of various combinations of anti-HIV-1 drugs in vivo.

References

1. Ishimatsu M, Suzuki H, Akiyama H, Miura T, Hayami M, Ido E: **Construction of a novel SHIV having an HIV-1-derived protease gene and its infection to rhesus macaques: a useful tool for in vivo efficacy tests of protease inhibitors.** *Microbes Infection* 2007, **9:**475-482.