Difficulties in achieving suppression of viral replication in vertically infected HIV-1 infants early treated with d4T+ddI+NFV: The PENTA 7 Study

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Background

Many authors recommend starting early antiretroviral therapy for all infants aged less than 12 months as soon as is confirmed diagnosis is established, regardless of clinical or immunologic status or viral load. The rationale for early antiretroviral therapy in vertically infected infants <3 months of age is supported by the presence of high viral load and the risk of rapid disease progression. However, only few data concerning the approach are available.

The purpose of this study was to assess the efficacy and pharmacokinetics of triple therapy with d4T/ddI/NFV in infants.

Methods

PENTA 7 is a multicentre, phase II, open-label, non-comparative study. 20 vertically HIV-1 infected infants aged less than 3 months were enrolled since 1 year and treated with d4T+ddI+NFV. Nelfinavir (NFV) was introduced to all children over 2 months of age. NFV was introduced at a dose of 400mg/day in the first 4 infants. Resistance testing at entry was required if the infant had documented resistance to d4T/ddI

Results

Within PENTA 7, the median age (range) of study entry was 39 days (22-48). Triplet therapy was started within 4 weeks of a virologic follow-up in all children. No severe adverse events related to the treatment occurred. However longer follow-up will be needed to determine long-term safety.

Discussion

Despite good short-term tolerance and clinical and immunological stability, more than half of the infants had detectable viral load (1-9 fold) and only 30% had evidence of genetic resistance.

In accordance with other studies, we showed that tolerance of multi-therapy in infants was good and no severe adverse events related to the treatment occurred. However, longer follow-up will be required to determine long-term safety. Despite the lack of evidence of resistance in these infants, we did not observe major virologic progression, in particular the unexplained virologic failures in infants and in one child. We are aware that this is of concern when patients have been treated in the past with a single drug regimen, but the fact that the patient had stable virologic response in the past and still under treatment with NFV is important. Overall, we believe that NFV is a safe alternative in the first months of life when d4T or ddI are not tolerated.