Three year follow-up of the PENTA 5 Trial
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Abstract (updated)

PENTA 5 was a 48 week prospective randomised controlled trial comparing 3 dual NRTI combinations with or without NFV in ART-naive therapy. We describe the long term response to 160 weeks.

Methods

128 children were randomised to ZDV+3TC (n=36), ZDV+ABC or 3TC+ABC. Asymptomatic children (n=78) were also randomly randomized to NFV or placebo; all other children received NFV/placebo. 1 child was lost to follow-up before 48 weeks. Data on the remaining 126 children are presented. Changes in ART were treated as censored.

Results: Median follow-up was 160 weeks (Q160=160, Q250=160). Two children had new AIDS events after 48 weeks (one after 60 weeks, and at week 160). One child died without AIDS (week 160). Although 2 children had died at 160 weeks (at 164 weeks, following relapse of Hodgkin’s lymphoma); at week 160, 56%, 55% and 59% were still on randomised NRTI combination as randomised (Figure 1). At 160 weeks, 56% children had not changed from allocated therapy at 160 weeks. Clinical evidence of lipodystrophy was reported in only 2 (2%) children.

Follow-up & clinical events

- All 126 children with follow-up at 160 weeks were followed up for 160 weeks (36 ZDV+3TC, 44 ZDV+ABC, 46 3TC+ABC). Median follow-up to 31 December 2002 was 180 weeks (Q92-204, range 97-245 weeks).
- 2 children had new AIDS events after 48 weeks (one after 60 weeks, and at week 160).
- 1 child died without AIDS at week 164 (following Hodgkin’s lymphoma).

HIV-1 RNA at and to 160 weeks

- The decline in HIV-1 RNA at 48 weeks was sustained to week 160 (Figure 2(a)), but the difference between the NRTI groups was smaller (Figure 2(b)).

- More children in the ZDV+3TC group had switched to second line therapies for lack of virological response or virological failure.

Overall results at 160 weeks were continued to support superiority of 3TC+ABC.

Results at 160 weeks continued to support superiority of 3TC+ABC. Although similar proportions had HIV-1 RNA <400 copies/ml at weeks 48 (66%) and 160 (58%), at week 160 fewer children had <50 copies/ml (38%) than week 24 (48%).

However, some tests at 160 weeks were <400 copies/ml on standard assays and are conservatively considered NOT <50 copies/ml (2 ZDV+3TC, 4 ZDV+ABC, 4 3TC+ABC).

Conclusions: By 160 weeks, 44% children had made at least 1 change to randomised regimen for virological, virological failure, compliance or other reasons. However, improved efficacy (in terms of HIV-1 RNA suppression and growth changes) and lower rates of switching with detectable HIV-1 RNA at 160 weeks compared with 48 weeks clinical evidence of lipodystrophy was reported only in 2 (2%) children.

Background & Objectives

PENTA 5 was a 48 week randomised controlled trial comparing 3 dual nucleoside analogues reverse transcriptase inhibitor (NRTI) combinations with or without NFV (NFV+, ZDV, ABC) in ART-naive children. To investigate longer term response with these NRTI combinations, we analysed changes in CD4+ cell counts, viral load and proportions with HIV-1 RNA below 400 copies/ml in the 3 NRTI groups respectively. One aim was to identify a treatment combination which was not superior to any other and which would allow the minimum of ART changes.

Follow-up at 160 weeks shows only 2 children in the ZDV+3TC group had switched to a second line therapy or NFV plus NFV placebo (2 ZDV+3TC). No other children had switched ART or had stopped taking NFV as allocated (Table 1).

Table 1: ART at 160 weeks

<table>
<thead>
<tr>
<th>Randomised NRTI combination</th>
<th>ZDV+3TC</th>
<th>ZDV+ABC</th>
<th>3TC+ABC</th>
</tr>
</thead>
<tbody>
<tr>
<td>NFV/placebo</td>
<td>20 (58%)</td>
<td>24 (55%)</td>
<td>27 (59%)</td>
</tr>
<tr>
<td>NFV+NFV</td>
<td>20 (58%)</td>
<td>24 (55%)</td>
<td>27 (59%)</td>
</tr>
</tbody>
</table>

ART to 160 weeks

- At 160 weeks, 56% children were still taking their randomised NRTI combination including NFV NFV as randomised (Table 1).
- A further 13% children had not switched from their NRTI combination (all had added NFV or switched NFV to NFV or the other NRTI).

Therefore logrank (p=0.13) (Table 1)

CD4, height and weight at 160 weeks

Changes in CD4%, absolute CD4, age-adjusted CD2 score, height-for-age and weight-for-age at 160 weeks broadly mirrored the changes observed at 48 weeks (Figure 2 and 3).

In spite of differences in HIV-1 RNA response, increased in CD4% were similar in all 3 groups and had plateaued between 48 and 96 weeks.

At 160 weeks increases in CD4% were 35% on average.

Height-for-age continued to increase significantly between 48 and 160 weeks.

Significant differences in height-for-age at both 48 weeks and 160 weeks reflected reduced HIV-1 RNA across the NRTI groups at these timepoints.

Conclusions: Despite the smaller difference in HIV-1 RNA and lipodystrophy between ZDV+3TC and ZDV+ABC at week 160, the benefits of 3TC+ABC were sustained at 160 weeks.

References