Journal of the International AIDS Society

Oral presentation

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O222 Treatment interruption in children with chronic HIV-infection: the results of the paediatric European network for treatment of AIDS (PENTA) 11 trial

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from Ninth International Congress on Drug Therapy in HIV Infection
Glasgow, UK. 9–13 November 2008

Published: 10 November 2008

Journal of the International AIDS Society 2008, **11**(Suppl 1):O21 doi:10.1186/1758-2652-11-S1-O21

This abstract is available from: http://www.jiasociety.org/content/11/S1/O21

Background

Compared to adults, children are likely to spend longer on antiretroviral treatment (ART), particularly if ART is started in infancy, and may respond differently to PTIs due to higher thymic activity.

Methods

PENTA 11 was a Phase II randomised trial to compare CD4-guided PTI with continuous therapy (CT) in children with confirmed viral load (VL) <50 c/ml, and CD4% ≥30% (ages 2–6 years) or CD4% ≥25% and CD4 ≥500 cells/mm3 (7–15 years). In the PTI arm, ART was restarted if confirmed CD4% <20% (<7 years) or CD4% <20% or CD4 <350 cells/mm3 (≥7 years). Additional precautions were subsequently added; duration of a PTI should not exceed 48 weeks and further PTIs undertaken only in children who spent >10 weeks off ART during 1st PTI and had been back on ART for 24 weeks. The primary end-point was CD4% <15% (and CD4 <200 cells/mm3 ≥7 years), or CDC C event or death. Children were followed until the last randomised child completed 72 weeks follow-up. All comparisons were intention-to-treat.

Summary of results

From 2004 to 2006, 109 children from nine countries were randomised to CT (53) or PTI (56): 45% male, median age 9 (range 2–16) years; 35% white, 31% black; 26% CDC stage C, median time on ART 6 years. Median baseline CD4% was 37% (IQR: 33,41), CD4 966 (793,1258) cells/mm3; prior to ART nadir CD4% 18% (10,27) and CD4 627 (320,1050) cells/mm3. After median 130 (80,144) weeks follow-up (one child lost), 4% of time was spent off ART in CT vs. 48% in PTI. On 1st PTI 21 (38%) children restarted ART before 48 weeks (14 protocol, seven other reasons); 32 (57%) restarted at 48 weeks and three remained off ART. 16 children had a 2nd PTI. No child died or had a CDC C event; 1 CT vs. 4 PTI children had a CD4 end-point (p = 0.4); 98.4% vs. 95.9% of time was spent with CD4 ≥350 cells/mm3. Mean CD4 change from 0–72 weeks was -106 vs. -240 cells/mm3 in CT vs. PTI (difference -134 cells/mm3, 95% CI -237, -31, p = 0.01; six children were off ART in PTI). However, mean CD4 change 0–72 weeks was -124 cells/mm3 in 27 children in the PTI arm who had been back on ART for ≥24 weeks. In the PTI arm CD4 recovery adjusted for age

appeared better in younger children (CD4 z-score change from 0–24 weeks after restarting -0.1, -0.9, -1.3 for ages 2–6, 7–10 and 11+ years, respectively, p = 0.02). At 72 weeks, 94%/85% vs. 81%/58% children had VL <400/<50 c/ml in CT vs PTI (p = 0.04/0.002). Of the 28 PTI children back on ART for ≥24 weeks, 89%/68% had VL <400/<50 c/ml.

Conclusion

In summary, PENTA 11 was the first randomised trial of planned treatment interruptions (PTIs) in children with chronic HIV infection. In this pilot study we observed no deaths or serious clinical events. Overall, fewer PTI children were suppressed <50 c/ml at 72 weeks (analysis of resistance results is ongoing) and CD4 recovery after PTI appeared better in younger children. However, longer-term assessment of all children after restarting ART will be required to fully assess risks and benefits of PTI in this population.