**PENTA 15: Plasma pharmacokinetic study of once versus twice daily abacavir and lamivudine as part of combination antiretroviral therapy in HIV-1 infected children aged 3 to 36 months**

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**Objectives**

To compare plasma PK parameters of once daily vs twice daily dosing of ABC and 3TC.

To compare age related differences in the PK parameters of once vs twice daily dosing of ABC and 3TC in children in 3 age groups (3-12, 12-24 and 24-36 months).

To describe child and family acceptance of and adherence to once compared to twice daily dosing.

**Baseline characteristics**

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<th>Table 1: Baseline characteristics</th>
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<tr>
<td>Age (months): 3-12/12-24/24-36</td>
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<td>Route of infection: vertical</td>
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<td>Median age range: 12 months</td>
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<td>Yearly GMR, mean (90% CI)</td>
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<td>Number of drugs ever received: mean (SD)</td>
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<td>ABC and once vs twice</td>
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<td>3TC and once vs twice</td>
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**Safety and efficacy**

Maintenance of virological control: at screening, 4, 8, 12 and 24 weeks 89%, 93%, 93%, 94% and 100% of children had HIV RNA <400 copies/ml and the proportion <50 copies/ml remained stable over time.

Maintenance of CD4 and CD4%: No resistance seen in children with HIV RNA >100 copies/ml.

2 non-ART related SAEs (1 croup, 1 scalp laceration).

No new CDC B and C Events.

No children discontinued once daily before week 12 (1 child discontinued at week 16.3 due to fluctuating HIV RNA and adherence concerns).

No increase in toxicity.

**Age comparison**

For ABC, in the oldest age group the AUC0-24 on twice daily was lower than for younger children (p=0.03). On once daily the middle and oldest age groups tended to have a lower AUC0-24 than the youngest (p=0.06). These observations are likely to be due to the small sample size per age group, and there were no linear trends with age (p=0.8 for both). There was no difference in AUC0-24 between age groups for 3TC.

For ABC, on both twice and once daily dosing, there was no difference (P>0.05) among age groups for the AUC0-24 of ABC or 3TC.

**Adherence and acceptability**

Adherence reported by carers (visual analogue scale) was 70-100%.

71% (week 6), 80% (week 4) and 56% (week 12) reported 100% adherence.

3 children were enrolled in PENTA 13.

To compare ABC and once daily 3TC.

4 children were evaluated for ABC and 17 (94%) for 3TC.

A GMR with a 90% CI including 1.0 and falling entirely within (95% CI) was considered as bioequivalence for ABC and 3TC.

**Conclusion**

In HIV-infected children aged 3 to 36 months, the AUC0-24 for once daily dosing of both ABC and 3TC was bioequivalent to twice daily. At expected, AUC0-24 was approximately two times higher on once compared to twice daily therapy. There was no evidence of loss of efficacy or increased toxicity on once daily therapy. Follow-up continues to week 48.

**Acknowledgements**

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