ABSTRACT (updated)

Although access to ART is increasing in developing countries, there are few data on the CD4 RESPONSE at 24 WEEKS. We have not been able to identify important predictors of immunological response in previously untreated adults in such settings.

Methods: CD4 at randomisation was not significantly associated with short-term CD4 response, defined as an increase of 100 cells/mm³ or more at 24 weeks.

CD4 at randomisation was lower in patients who were male (by, on average, 18 cells/mm³ [95% CI 12-24; p=0.001]), who had WHO stage 3 or 4 disease (by, on average, 18 and 24 cells/mm³ [95% CI 25-42 and 10-25] respectively compared to WHO stage 2; p=0.001), who were younger (by, on average, 5 cells/mm³ for every 10 years younger [95% CI 13-10; p=0.001]), and who had lower total lymphocytes (by, on average, 38 cells/mm³ for every 1 x10⁹/l lower [95% CI 34-41; p=0.001]). This probably represents a complex relationship between duration of infection and survival to ART enrolment.

Overall CD4 increases in DART

<table>
<thead>
<tr>
<th>OVERALL CD4 INCREASES in DART</th>
<th>Median CD4 increase at 12 and 24 weeks was 70 cells/mm³ (95% CI 29 to 124) (4/12 to 14) respectively (Figure 2)</th>
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<tr>
<td>mean increase was 6.7 cells/mm³ per week to week 12, then 1.1 cells/mm³ per week from week 12 to week 24</td>
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<td>CD4 increases in these 2 periods differed significantly (&lt;0.001)</td>
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<td>402/1157 (35%) had achieved a CD4 count of 200 cells/mm³ or higher at 12 weeks; and 192/474 (41%) at 24 weeks (Figure 2)</td>
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Figure 1: CD4 counts through 24 weeks in DART (baplot)

CD4 RESPONSE at 24 WEEKS

- CD4 at randomisation was not significantly associated with short-term CD4 response, defined as an increase of 100 cells/mm³ or more at 24 weeks.
- OR=1.12 per 30 cells/mm³ higher baseline CD4 (95% CI 0.96-1.31), (P=0.10) (Figure 4)
- Therefore, by week 24 most patients appear to be able to achieve similar CD4 increases regardless of baseline.
- CD4 at randomisation was strongly associated with achieving threshold levels at 24 weeks, because smaller CD4 increases are needed to achieve these thresholds for patient with 150-199 cells/mm³ at randomisation, compared with patients with 0-49 cells/mm³ at randomisation.

Figure 2: Proportion of patients reaching CD4 cell count levels at 24 weeks

- Note: this increase to the 200 cells/mm³ level is an increase of less than 30 cells for a patient randomised with a CD4 below 100 cells/mm³ for a patient randomised in the 0-4 group.
- CD4 count at ART initiation. This was a global analysis, not broken down by randomised group.
- Remaining 1000 patients are enrolled and followed up in DART is planned to continue until the end of 2007.
- We will continue to monitor short-term response, as the remaining 1000 patients are enrolled and followed up in DART is planned to continue until the end of 2007.

Figure 3: Proportion of patients with absolute CD4 increases from randomisation to 24 weeks

- OR=0.87 per 1mg/dl higher baseline HDL (95% CI 0.79-0.97; p=0.01)
- There was no additional effect of CD4 (p=0.2), or any other factor, after adjusting for baseline haemoglobin.
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