Abstract Preview - Step 3/4

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Topic: B23 Clinical trials - phase III/post-licensing

Title: Impact of routine laboratory monitoring over 5 years after antiretroviral therapy (ART) initiation on clinical disease progression of HIV-infected African adults: the DART Trial final results

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Text: **Background:** ART is often managed without routine laboratory monitoring in low-income countries; the clinical outcome of this strategy is unknown.

Methods: 3316 ART-naive adults (median(IQR) CD4 86(31-139)cells/mm^3; WHO stage 2/3/4 20%/56%/23%) initiating ART in Uganda/Zimbabwe were randomised to Laboratory and Clinical Monitoring (LCM) versus Clinically Driven Monitoring (CDM) and followed for median 4.9 years. Participants initiated zidovudine/lamivudine plus tenofovirDF(74%), abacavir(9%) or nevirapine(16%) and switched to second-line after new/recurrent WHO stage 3/4 events or (LCM only) CD4< 100cells/mm^3. Routine 3-monthly haematology and biochemistry (for toxicity) and CD4 results from participants in LCM were returned to clinicians; in CDM, only grade 4 toxicity results were returned, but tests (not CD4) could be requested if clinically indicated.

Results: 459 (28%) CDM versus 356 (22%) LCM participants had a new WHO Stage 4 event or died (event rate 6.94 versus 5.24 per 100 person-years (PY); absolute difference +1.70/100 PY (95%CI +0.87 to +2.54/100 PY); HR 1.31 [1.14-1.51],log-rank p=0.0001). Death rates per 100PY were 2.94 in CDM versus 2.18 in LCM (difference +0.77/100PY[0.25-1.28], p=0.004; 130 PY of laboratory monitoring to prevent one death). Differences between strategies occurred from the third year on ART whereas lower rates of switching to second-line ART occurred in CDM from the second year. There were no differences between strategies in time to first serious adverse event (HR=1.12[0.94-1.31];p=0.20), grade 4 toxicity (HR=1.08[0.97-1.20];p=0.18) or ART-modifying toxicity (HR=1.01[0.88-1.16];p=0.85).

Conclusions: Overall survival at 5 years (CDM:87%;LCM:90%) was excellent, strongly reinforcing WHO guidelines that ART should never be withheld due to lack of laboratory monitoring. The differences in WHO 4 event-free survival were small but suggest a role for targeted CD4 monitoring to guide switching from the second year on ART; moreover, first-line regimens used in DART can be given without need for routine toxicity laboratory monitoring, even in advanced disease. Cost-effectiveness analysis will further inform ART programme policy.

Country of research: Uganda, Zimbabwe

Ethical Research Declaration: Yes

Conference: 5th IAS Conference on HIV Pathogenesis Treatment and Prevention · Abstract: A-155-0080-03807 · **Status: Draft**

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