Glomerular dysfunction and associated risk factors through four years following initiation of ART in adults with HIV infection in Africa in the DART trial

Abstract: T10P 141

DART trial design & Methods

DART was a randomised trial of management strategies in 3163 symptomatic ART-naive adults with CD4+≥200 cells/mm³ initiating triple drug ART in 3 centres in Uganda and Zimbabwe.

Participants were randomised to Laboratory and Clinical Monitoring (LCM) Clinically Driven Monitoring (CDM) All participants were randomised to either LCM or CDM, and a subgroup (12%) was randomised to a combination of both.

Blinded interpretation of the Cockcroft formula, and normalised per 1.73m².

The辉煌是: 60-90, moderate: 30-60, severe: <30 mL/min/1.73m². Treatment event analysis was followed up on patients who missed lab results or died before 216 weeks.

The baseline GFR was estimated from serum creatinine using the Cockcroft-Gault formula. No specific calibration was undertaken across centres.

Death with renal impairment were rare, so power was low.

The Clinical Driven Monitoring strategy was associated with the occurrence of SAEs considered for this analysis included renal events as well as bone fractures —— 60/91% patients with severe GFR decrease had one or more renal events on tenofovir DF or relationships to this drug label (non-conservative).

No adjustments to p-values were made for multiple comparisons.

Inclusion criteria: patients with confirmed <60 mL/min/1.73m² GFR at entry and at events of death or end of follow-up, including changes in ART after baseline.

• Severe GFR decreases are likely to predominantly reflect acute intercurrent illnesses rather than ongoing toxicity.

• The INSIGHT definition of CKD requires a 25% decrease only if the baseline GFR was ≥40 mL/min/1.73m². In a population with a high proportion of participants with GFR ≥30 mL/min/1.73m² at baseline and subsequent confirmed decrease smaller than baseline of ≥15 mL/min/1.73m² in 4 patients, the decrease could still be considered severe.

• Patients were randomised to LCM and CDM (Clinically Driven Monitoring) or CDM (Clinically Driven Monitoring).

• Exclusion criteria for DART enrolment included creatinine ≥160 µmol/L (1.7 mg/dL) and GFR was not automatically calculated at screening.

• Creatinine, full blood count and other biochemistry (uric acid, bilirubin, ALT AST) were assessed in LCM and CDM patients at baseline, weeks 4 and 12, then every 12 weeks, body weight every 4 weeks. Analysis was not routinely performed. Serum creatinine was measured locally using a modified Jaffe method. No specific calibration was undertaken.

• In DART, results were related to the treating clinicians for LCM but not CDM participants unless tests were requested for a clinical reason or there was grade toxicity. Laboratory data were also not used outside scheduled assessments for clinical reasons in any participant.

• Causes of death and SAEs were reviewed by an Independent Review Committee, and a Medical Monitoring Committee for this analysis included renal events as well as four factors, through 4 years after initiation of ART.


• No specific calibration was undertaken across centres.

• By tenofovir DF: no therapy; n=16 60% (40 (25% decline from baseline for all.

• Baseline characteristics & Follow-up:

AIDS-related death: confirmed <60 mL/min/1.73m² (censoring at 216 weeks), and 31 resolved and did not die before 216 weeks.

A similar lack of association was observed between severe GFR decrease and the 10% decline from baseline, and 32 deaths as baseline.

DART was a randomised trial of management strategies in 3163 symptomatic ART-naive adults with CD4+≥200 cells/mm³ initiating triple drug ART in 3 centres in Uganda and Zimbabwe.

Recent data from sub-Saharan Africa suggest that HIV-related kidney disease/impairment is very common in ART-naive populations. However, in resource-limited settings longitudinal data on renal function and the long-term impact of ART on renal disease are rare, and the long-term risk factors are not clear.

Objectives: To estimate prevalence and incidence of GFR reduction, renal serious adverse events (SAEs) and mortality where renal function was a component of a clinical outcome, through 4 years after initiation of ART.

Baseline characteristics & Follow-up

Baseline Characteristics

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<td>Serum Creatinine (mg/dL)</td>
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<td>GFR (ml/min/1.73m²)</td>
<td>60-90 (60-90)</td>
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<td>Death with renal impairment</td>
<td>14 (14)</td>
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Limitation of our analysis: tubular function was not examined in DART.

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