48 week virologic response to a triple nucleoside/nucleotide analogue regimen in adults with HIV infection in Africa during the DART trial

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ABSTRACT

**OBJECTIVES**

- To determine response to ZDV+3TC+TDF up to 48 weeks
- To describe the distribution of resistance mutations in those with HIV-1 RNA >1000 c/ml at 24 weeks

**METHODS**

- 331 patients received triple drug ART
- Virology monitoring not performed in all patients
- 2486 (74%) have received zidovudine/lamivudine (as combivir) plus tenofovir DF (ZDV+3TC+TDF) triple-tape
- 300 patients receiving ZDV+3TC+TDF were enrolled in a virology substudy (retrospective), with on average, good virologic response at 24 weeks
- 300 patients – 100 each from 3 sites; 2 in Uganda and 1 in Zimbabwe
- Baseline genotypes are currently being sequenced

**RESULTS**

- Plasma HIV-1 RNA was assayed retrospectively in 300 adults with baseline CD4 <200 cells/mm\(^3\) from 3 sites in Uganda and Zimbabwe using the Roche Amplicor assay v1.5. All assays were performed on samples with HIV RNA >1000 c/ml at 24 weeks.

**CONCLUSION**

- ZDV+3TC+TDF maintains good virological efficacy from 24 to 48 weeks in advanced disease. In this population infected with HIV-1 subtypes A, C or D, M184V with or without TAMS was the most common route to resistance, whereas K65R was identified infrequently.

**HIV-1 VIRAL LOAD**

- No patient reached clinical/immunological criteria for failure (there were no switches to second-line therapy) before 48 weeks
- The proportion of HIV-1 RNA >1000 c/ml increased over time as expected, but remained low (4%, 6%, 9% and 16% of HIV-1 RNA results were >1000 c/ml at 12, 24, 36 and 48 weeks, respectively).
- At 24 weeks, viral suppression was independently significantly more likely in patients with higher baseline CD4: who were female: who were dual user: there was a trend towards lower chance of suppression (<400 c/ml) with higher baseline RNA, but the effect of baseline viral load was much weaker for suppression (<50 c/ml)

**HIV GENOTYPE at 24 WEEKS**

- 48 patients had HIV-1 RNA >1000 c/ml at 24 weeks
- 10 had insufficient sample for genotyping
- Genotypes were obtained from the remaining 38 samples
- It was possible to amplify both PR and RT in 18 samples, even with optimised primers
- 12 of these 18 samples had HIV-1 RNA >9000 c/ml
- 20 sequenced viruses (STAR1): 6 A, 8 C, 5 D, 1 D/A
- Only 3/20 (15%) patients had ever achieved HIV-1 RNA <50 c/ml (10/20 (50%) ever <400 c/ml)
- Only the patient with K65R alone had substituted d4T for ZDV (at week 14 for anaemia & neutropenia)
- No relationship between pattern of NRTI mutations and NNRTI resistance mutations: TAMs was the most common route to resistance, whereas K65R was identified infrequently.

**Virola loads and patient status over time**

**Viral suppression at 48 weeks**

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- No relationship between pattern of NRTI mutations and NNRTI resistance mutations:
- Subset of the 20 sequenced viruses (STAR1): 6 A, 8 C, 5 D, 1 D/A
- A & D from Uganda, C & D from Zimbabwe as expected
- 18/20 showed key NNRTI resistance mutations:
- With both patients who had mutations of d3ART (w/h-24 [pregnancy], w/h-20 [AE, renal impairment])

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