EFFECTIVENESS OF DOLUTEGRAVIR IN PEOPLE ON RIFAMPIN-BASED TB TREATMENT

A5381/HAKIM Study

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BACKGROUND

• Tenofovir-lamivudine-dolutegravir (TLD) is the WHO preferred first-line regimen for people living with HIV.

• Rifampin is a key drug in TB treatment but is a potent inducer of metabolizing enzymes and drug efflux transporters, which lowers dolutegravir (DTG) concentrations.

• This drug-drug interaction can be overcome with an additional 50mg dose of DTG 12 hours later (TLD+50) in people receiving TB/HIV co-treatment.

OBJECTIVE

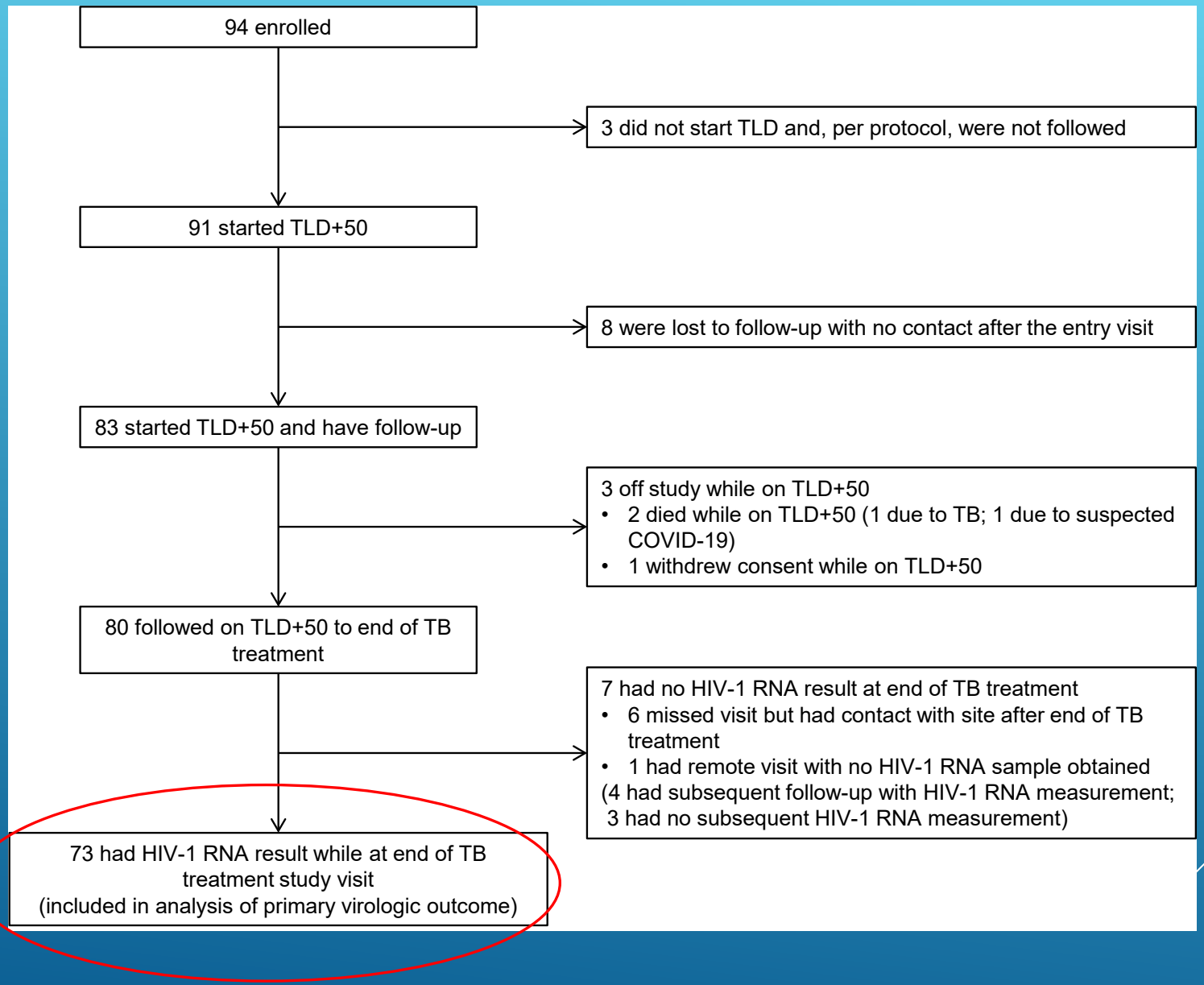
A5381 was an observational, longitudinal prospective cohort study to assess efficacy and emergence of HIV drug resistance following initiation of TLD for first- or second-line ART or start of concomitant TLD and Rifampin(Rif)-containing TB treatment.

POPULATION OF THE STUDY

12 sites in 6 countries and enrolled 1,339 participants.
18 years and older living with HIV who were initiating TB treatment.
Participants were divided into 4 study groups for enrollment and analysis.
Results reported in this analysis focus on Group 3 only

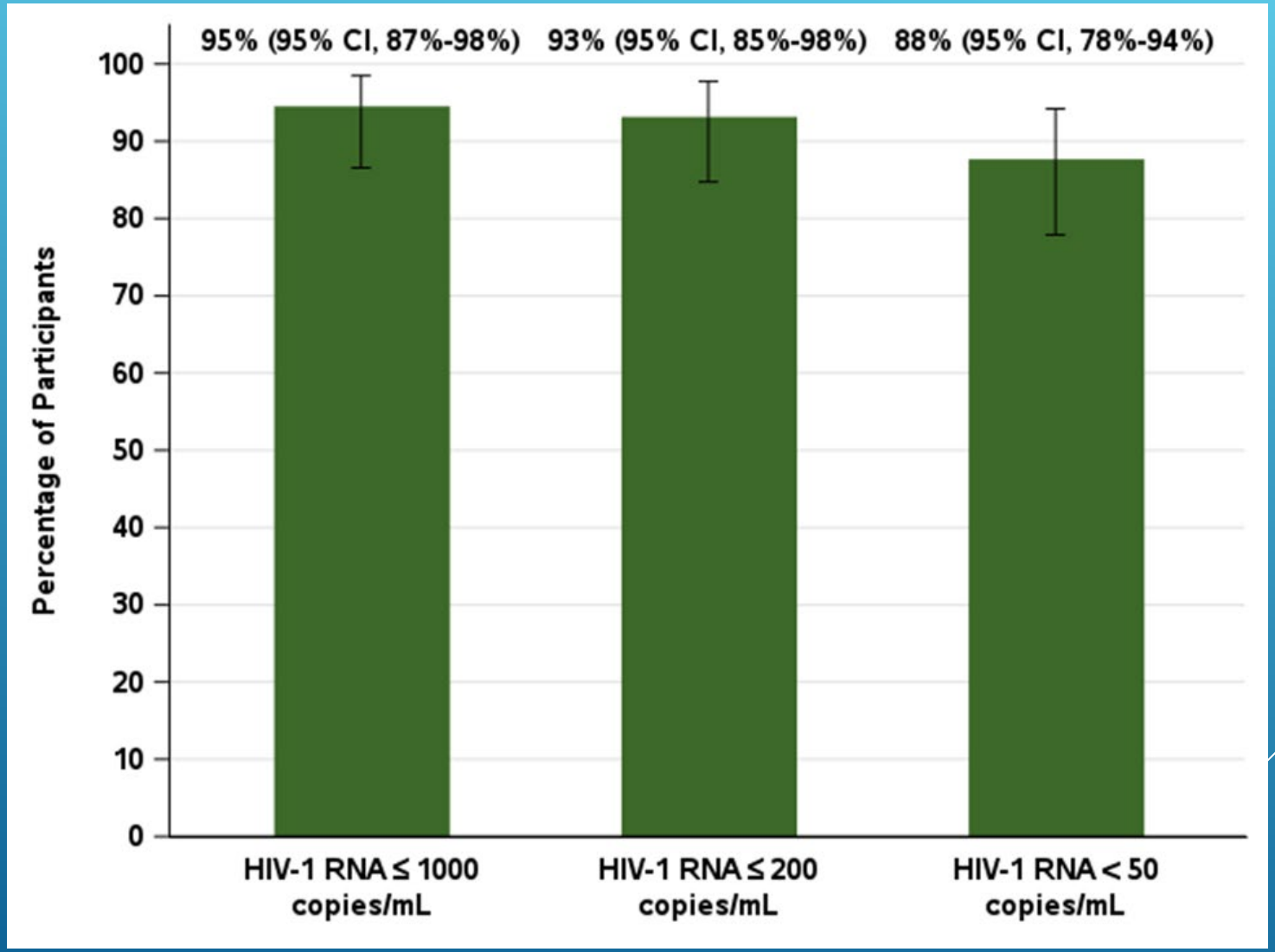
GROUP 1	GROUP 2	GROUP 3	GROUP 4
People switching to TLD after taking anti-HIV medication containing efavirenz or nevirapine	People switching to TLD after taking anti-HIV medication containing lopinavir or atazanavir	People taking TLD+50 and receiving medication for TB that includes Rifampin (must have been taking one or both medications at entry).	People starting TLD who have not taken anti-HIV medications before

PARTICIPANT ENROLLMENT



VIRAL SUPPRESSION AT END OF TB TREATMENT

Per Protocol Analysis (N=73)



KEY FINDINGS

- Rifampin-containing TB regimens are safe, well tolerated and effective in people with HIV on ART regimens including DTG.
- Concomitant rifampin-containing TB treatment and TLD with an extra 50mg of DTG (TLD+50) achieved viral suppression among 95% of people with TB/HIV in program settings.
- There was no DTG resistance among 4 participants with HIV-1 RNA >1000 cpm.
- There were 2 safety issues; 1 interrupted both TLD+50 and TB treatment due to jaundice. 1 stopped TB treatment due to drug-induced liver injury (resolved; Viral Load <50 cpm at end of TB treatment).

WHY IS THIS STUDY IMPORTANT?

- The study instills confidence in the use of DTG-based ART and Rif-based TB therapy in people with HIV/TB co-infection. Viral suppression can be achieved when receiving HIV/TB treatment, which is a huge milestone for TB and HIV treatment.
- It provides valuable data to clinicians and public health officials all over the world about the tolerability of concomitant RIF-containing TB treatment and TLD+50.

WHAT'S NEXT?

Routine program settings should continue current treatment with TLD+50 in people receiving TB/HIV co-treatment.