Oral Abstract Session-03

Monday, March 10, 2025

123 - Genotypic Resistance in the African Paediatric CHAPAS-4 Trial of Second-Line Antiretroviral Therapy

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Genotypic resistance in the African paediatric CHAPAS-4 trial of second-line antiretroviral therapy

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*equal contribution

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Background

CHAPAS-4, a 4X2 open-label factorial randomised trial, demonstrated superior virological efficacy (VL<400 c/ml) at 96 weeks for:

dolutegravir (DTG)
vs
ritonavir-boosted lopinavir (LPV/r) and **atazanavir (ATV/r)**

and

tenofovir alafenamide (TAF) + emtricitabine (FTC)
vs
abacavir (ABC) or **zidovudine (ZDV)** + lamivudine (3TC)

for African children starting **2nd line** antiretroviral therapy (ART) after treatment failure on 1st line non-nucleoside reverse transcriptase inhibitor (NNRTI)-based ART[1,2]

*current standard-of-care (SOC)
** including novel pTAF/FTC formuation

1. medrxiv.org/content/10.1101/2024.04.12.24305333
2. medrxiv.org/content/10.1101/2024.04.12.24304337

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Methods

HIV-1 viral load (VL) tested at: screening, W48, 96 (real-time); 6, 24 & 72 (retrospectively)

At W96, samples with VL≥400 c/ml retrospectively sequenced for genotypic resistance (RT, PR, IN)

Baseline samples retrospectively sequenced (RT only)

Drug resistance mutations and resistance scores defined using Stanford algorithm (v9.5.1)

Resistance scores categorised into **susceptible**, **low**, **intermediate** or **high-level resistance**

Results – baseline NRTI resistance

Of **919** children, age 10 (range 3-15) years, 5.6 (IQR: 3.3-7.8) years on 1st line:

- **713** (78%) baseline sequencing
- **665** (93%) had M184V/I

Intermediate/high level resistance to allocated NRTI:

- **30%** (58/192) ABC
- **10%** (17/171) ZDV
- **15%** (53/350) TAF

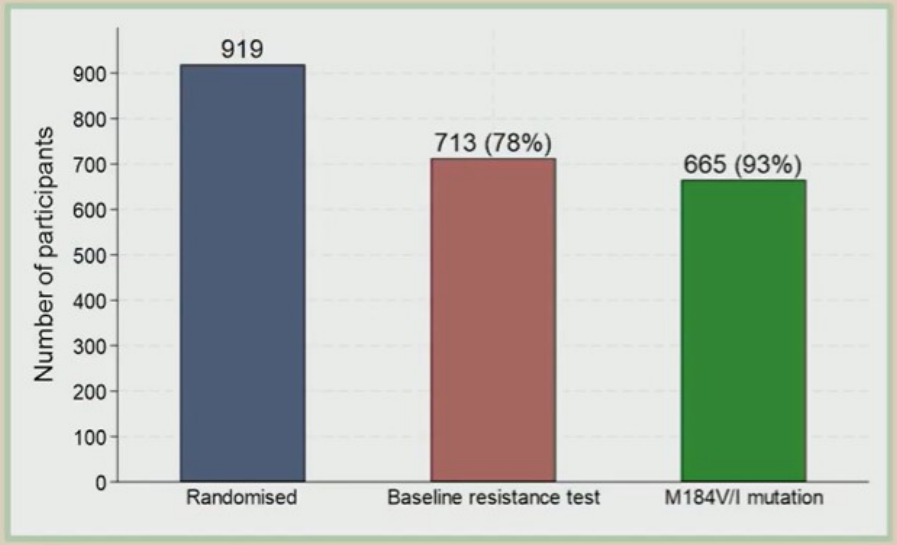

Figure 1: Baseline resistance testing

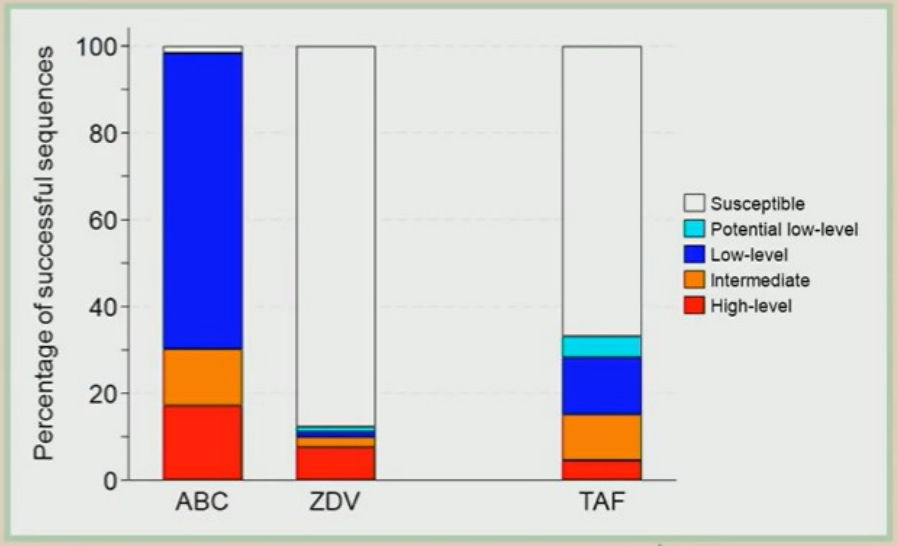

Figure 2: Baseline resistance scores to allocated NRTI

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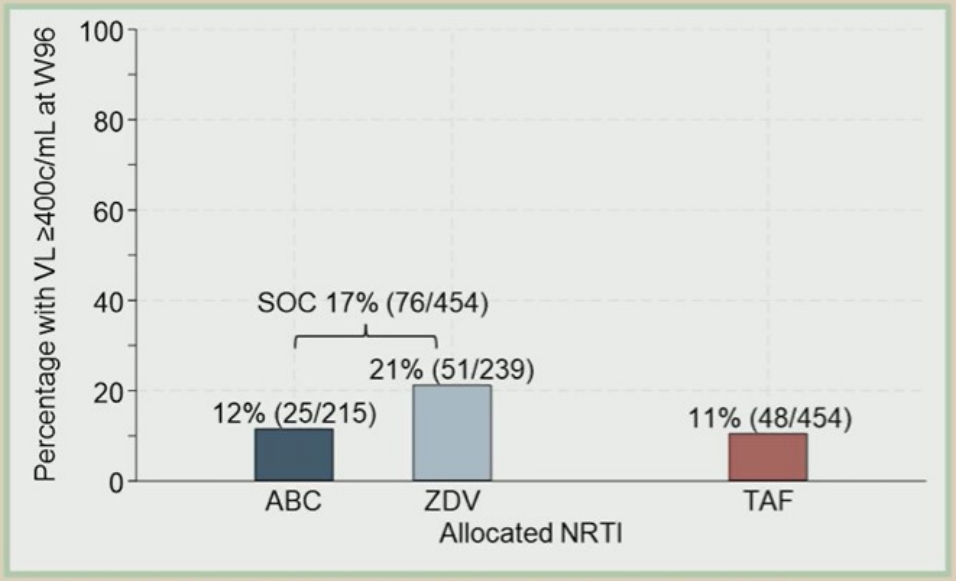
Results – 96 weeks VL ≥400c/ml



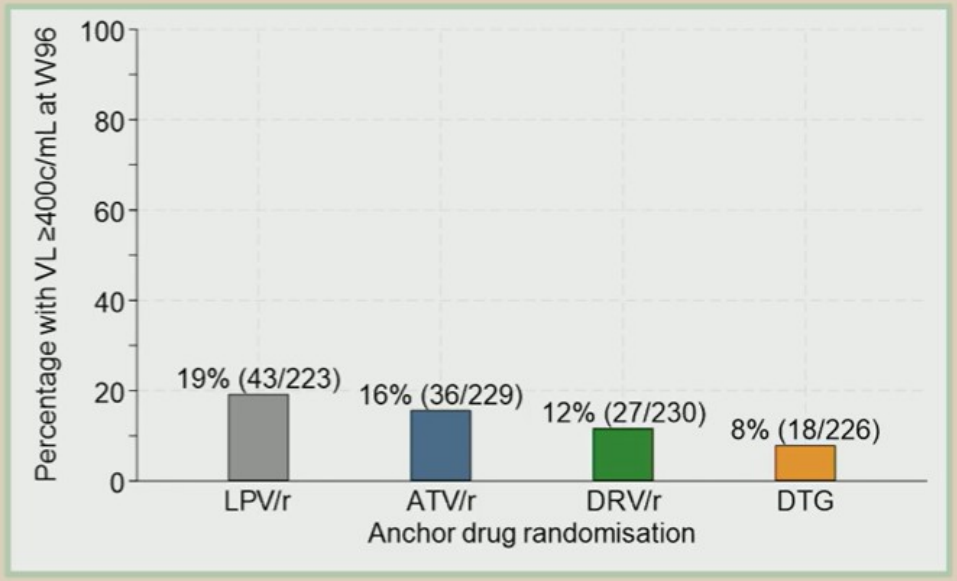


Figure 3: Viral load ≥400c/mL at week 96, by allocated NRTI and anchor drug

Overall, at W96, **14% (124/908)** had VL≥400c/ml

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Results – baseline NRTI resistance and VL≥400c/ml

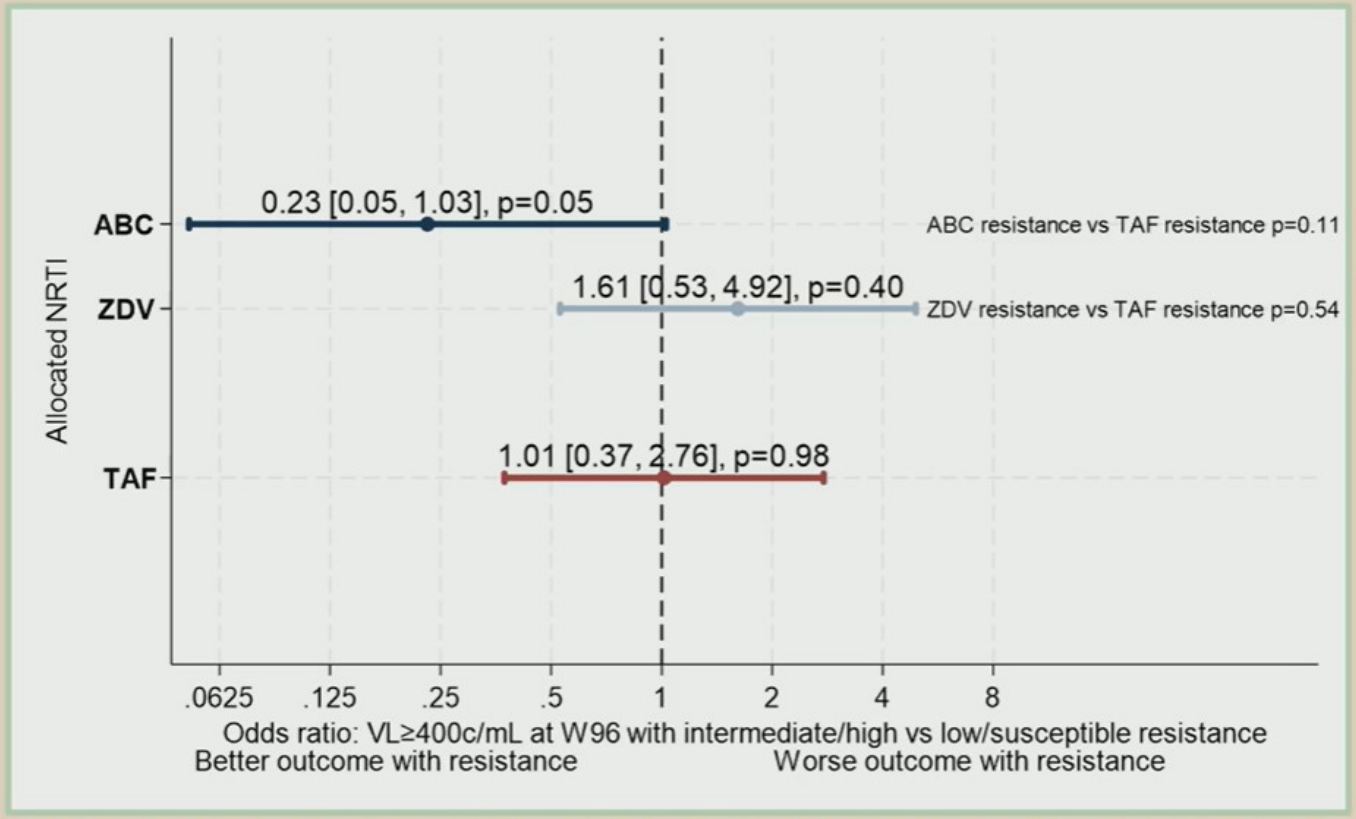

Figure 5: Odds ratios of viral load ≥ 400c/ml at week 96 in those with intermediate/high vs low/susceptible baseline resistance to allocated NRTI

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Results – 96 weeks NRTI resistance

At W96 - intermediate/high-level resistance to allocated NRTI

ABC	0% (0/17)
ZDV	14% (5/36)
TAF	9% (3/33)

At W96 - intermediate/high-level resistance to FTC/3TC

ABC	59% (10/17)
ZDV	78% (28/36)
TAF	36% (12/33)

Results – baseline vs 96W NRTI resistance

54% (67/124) children with VL≥400c/mL at W96 had RT sequencing at both baseline **and** W96

- **Resistance categorisation** to allocated NRTI **remained the same** in all (score worsened in 16)
- **3 children** (2 DTG/ZDV/3TC,1 LPV/r/ZDV/3TC) had emergent M184V

Results – 96 weeks anchor drug resistance

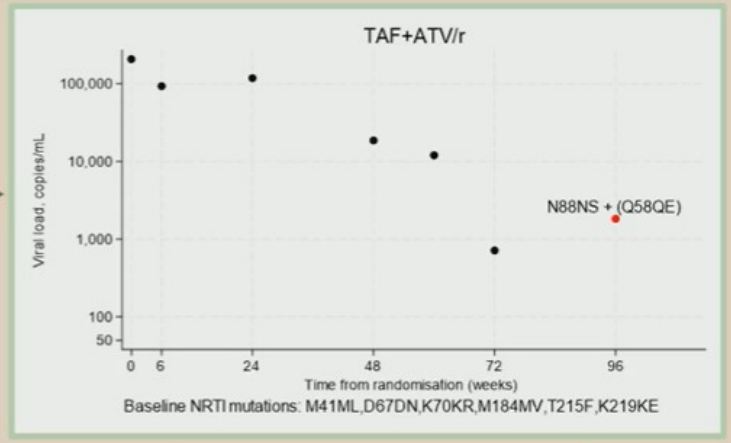
Intermediate/high-level resistance to anchor drug

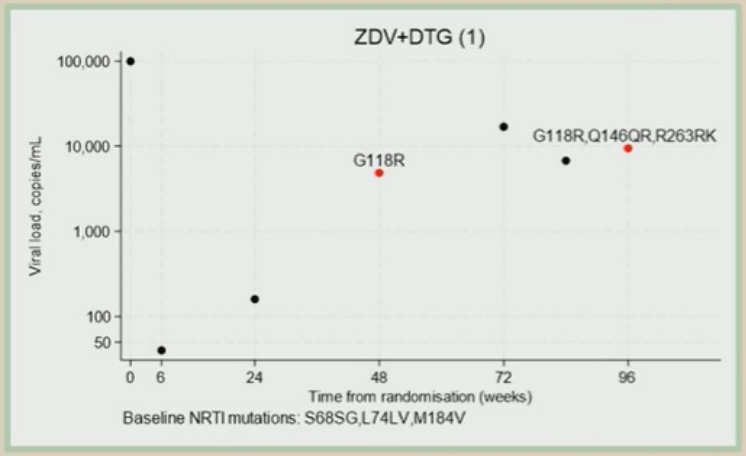
0% (0/29) LPV/r

4% (1/26) ATV/r (1 TAF/FTC)

0% (0/18) DRV/r

22% (2/9) DTG (2 ZDV/3TC)





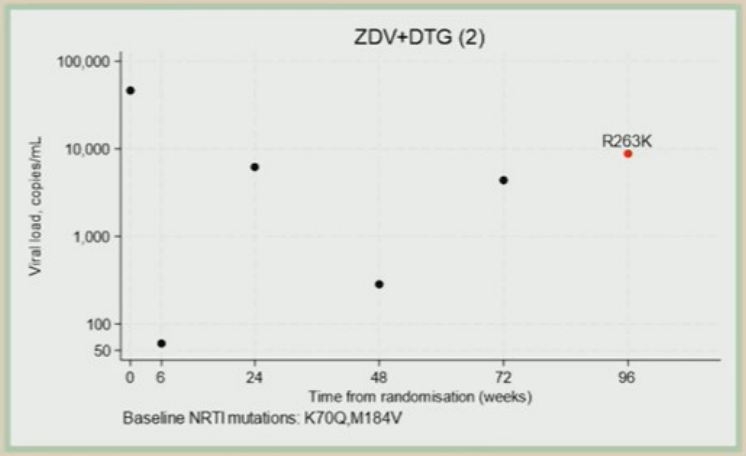


Figure 4: Participants with high-level resistance to anchor drug at week 96

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Conclusions

TAF resistance at baseline was less common than ABC resistance

No new intermediate/high-level resistance to allocated NRTI occurred

W96 intermediate/high-level anchor drug resistance was uncommon (2 DTG, 1 ATV/r)

As in second-line adult[1] and paediatric[2] trials, resistance to DTG occurred in children receiving ZDV

These results will inform second-line treatment guidelines for children

[1] Paton et al Lancet HIV 2022 [2] White et al Lancet HIV 2025

Acknowledgements

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