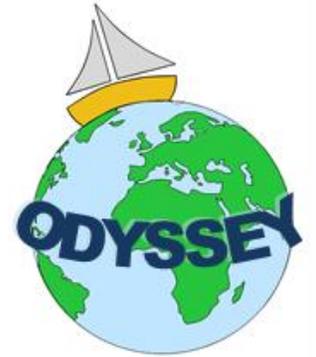




Penta

Child Health Research



Virological failures and genotypic resistance in children and adolescents randomised to dolutegravir-based ART vs. standard-of-care in the ODYSSEY trial

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ODYSSEY population at baseline (n=707)

Baseline characteristics

- Age, median [range]: 12.2 years [2.9-18]
- 49% female
- 88% African
- 27% WHO stage 3/4

Baseline ART

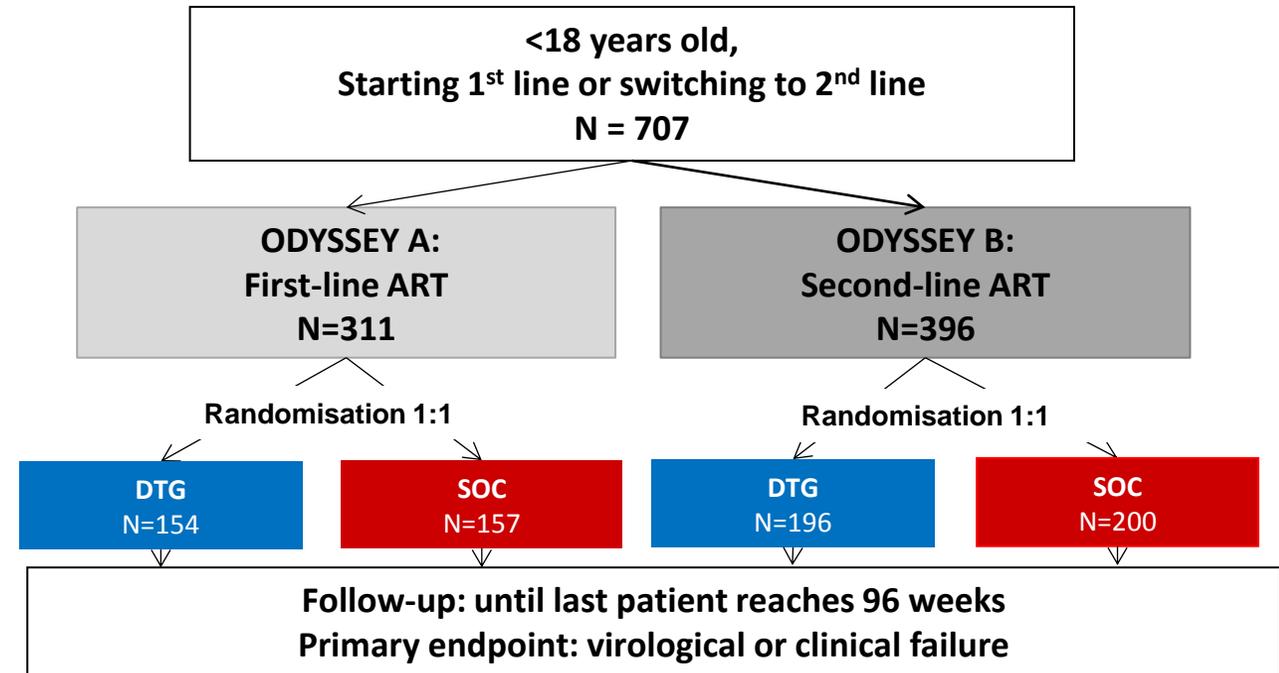
NRTI backbone

ODYSSEY A – first-line	ODYSSEY B – second-line
80% ABC+3TC	54% ABC+3TC
19% TDF+XTC	26% TDF+XTC
	19% ZDV+3TC

Third agents in the SOC arm

ODYSSEY A	92% EFV-based
ODYSSEY B	72% LPVr & 25% ATVr

- A randomised 96-week non-inferiority trial comparing **DTG-based ART with standard-of-care** in children **starting first- or second-line ART**
- **Main trial: children ≥ 14 kg**



Resistance sub-study

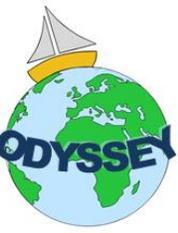


Participants with virological failure* by 96 weeks

	DTG	SOC
ODYSSEY A: first-line	11 (7%)	30 (19%)
ODYSSEY B: second-line	31 (16%)	40 (20%)

Definition: virological failure

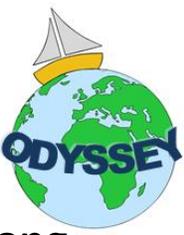
- <1 log drop at w24 and ART switch for treatment failure
- confirmed (x2) VL \geq 400 c/mL at any time after w36



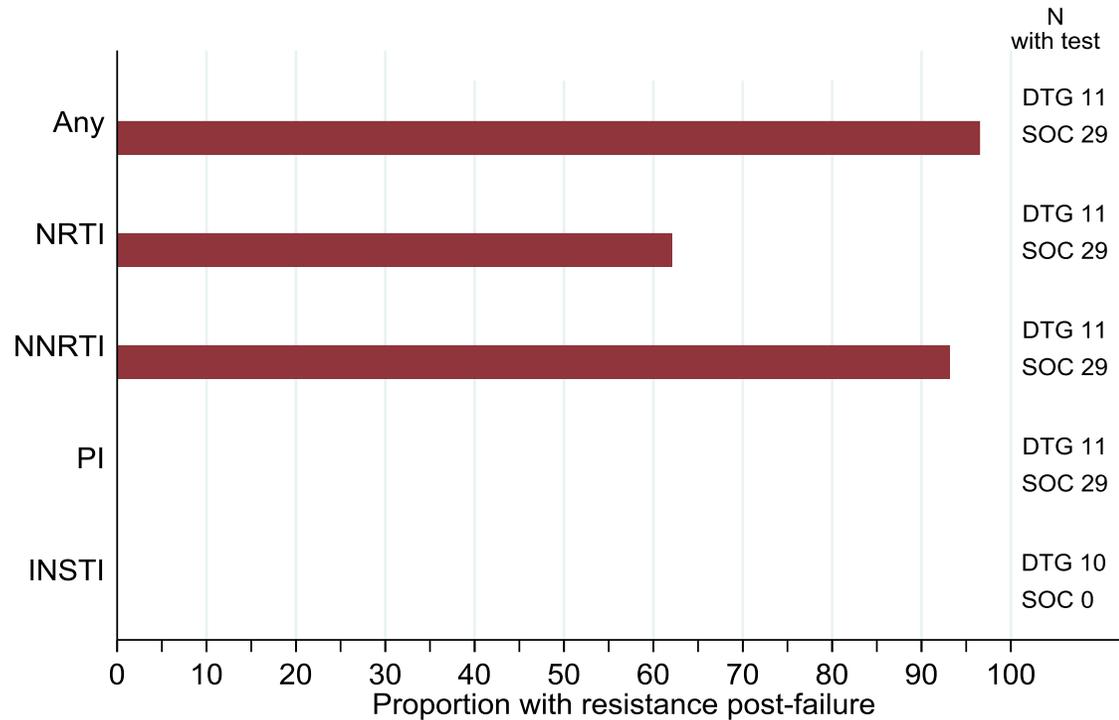
Resistance testing

- Participants with virological failure were retrospectively tested for post-failure resistance up to week 96 (Sanger sequencing)
- Requested the latest sample with $VL \geq 1000$ c/mL after failure and prior to treatment change (if occurred)
- Earlier samples, including baseline, were sequenced if ≥ 1 major IAS mutation was identified in post-failure sample
- Drug resistance mutations were defined according to IAS major mutations (2019)
- Drug susceptibility was defined according to the Stanford HIVdb algorithm 9.0

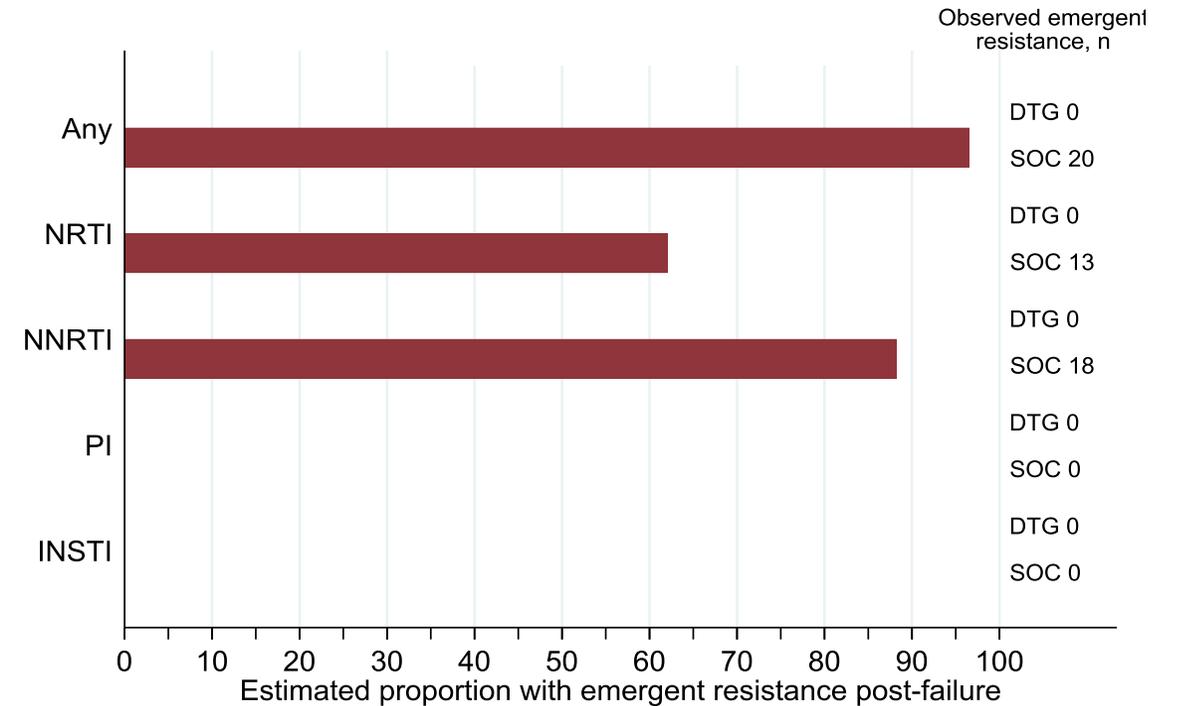
ODYSSEY A: Major resistance post-failure & emergent resistance on first-line



Proportion with resistance to drug-class post-failure



Estimated proportion with emergent resistance among those exposed to drug-class during ODYSSEY*



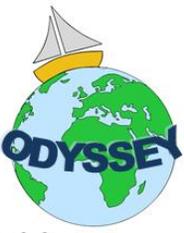
Resistance defined according to major IAS (2019) mutations

*Estimated proportion with emergent mutation calculated assuming same proportion of emergent resistance in those with no baseline test available



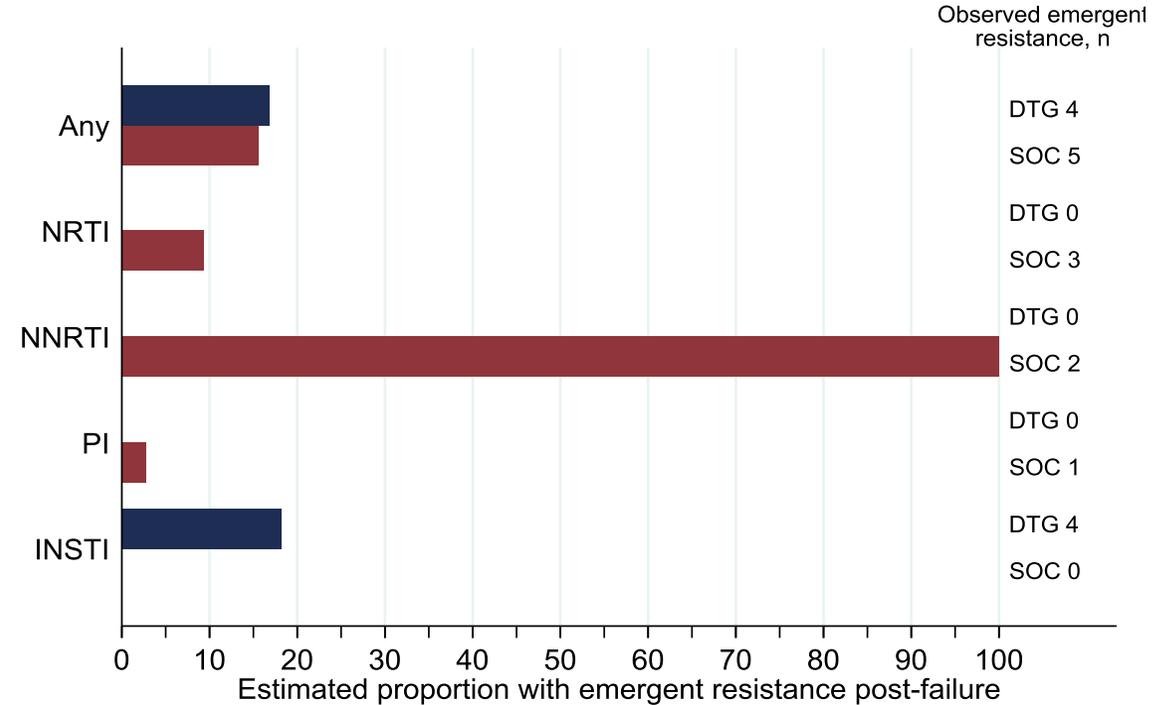
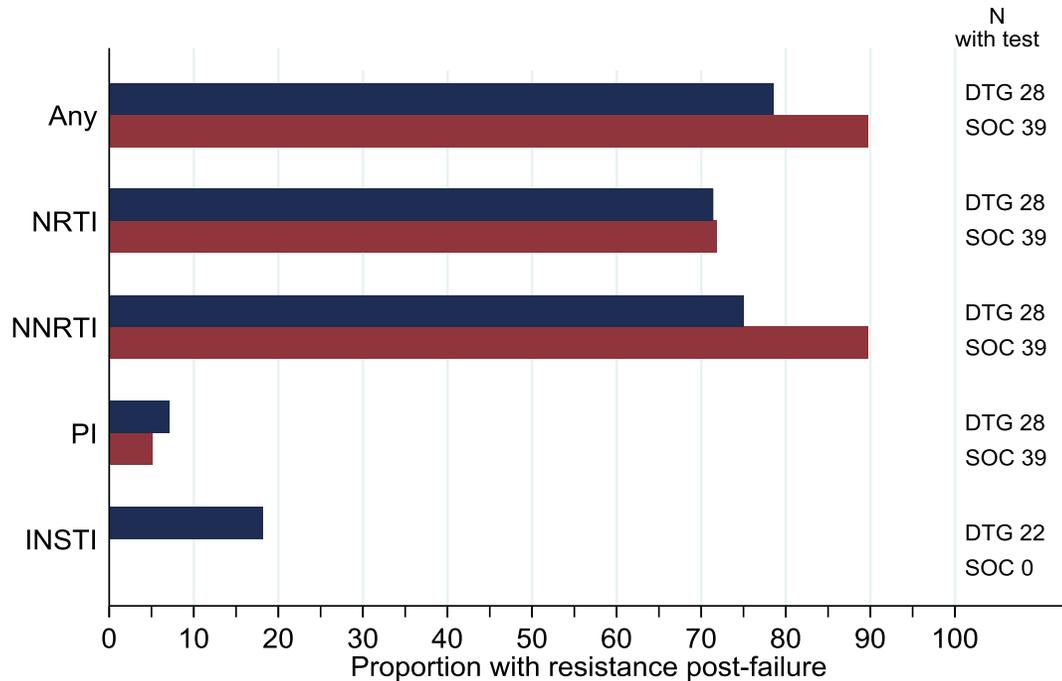
SOC third agent in resistance sub-study:
ODYSSEY A: 100% NNRTI

ODYSSEY B: Major resistance post-failure & emergent resistance on second-line



Proportion with resistance to drug-class post-failure

Estimated proportion with emergent resistance among those exposed to drug-class during ODYSSEY*

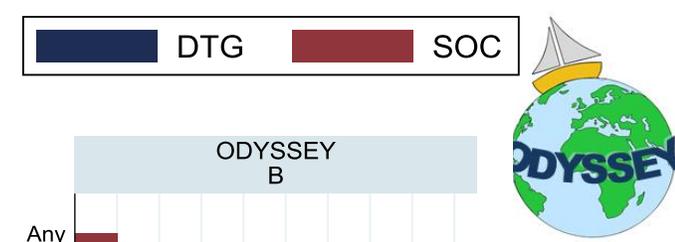


Resistance defined according to major IAS (2019) mutations
 *Estimated proportion with emergent mutation calculated assuming same proportion of emergent resistance in those with no baseline test available

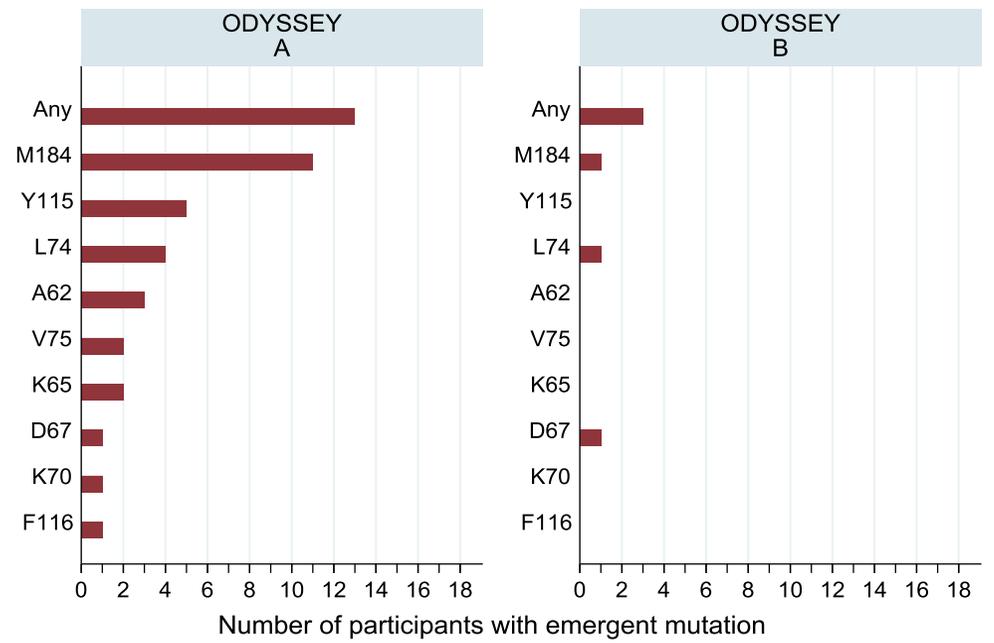


SOC third agent in resistance sub-study:
 ODYSSEY B: 92% PI, 8% NNRTI

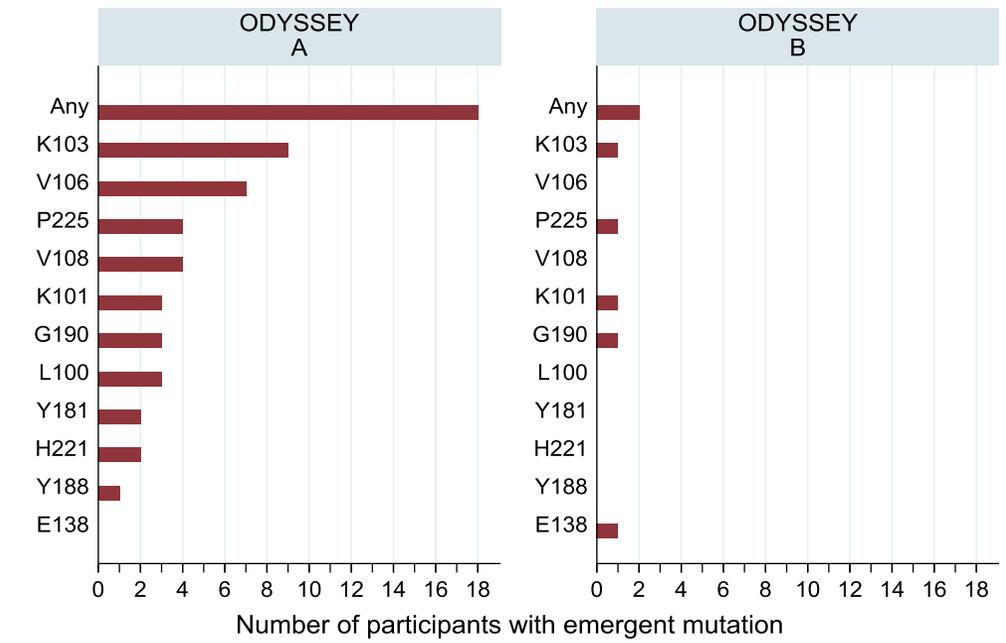
Emergent resistance mutations



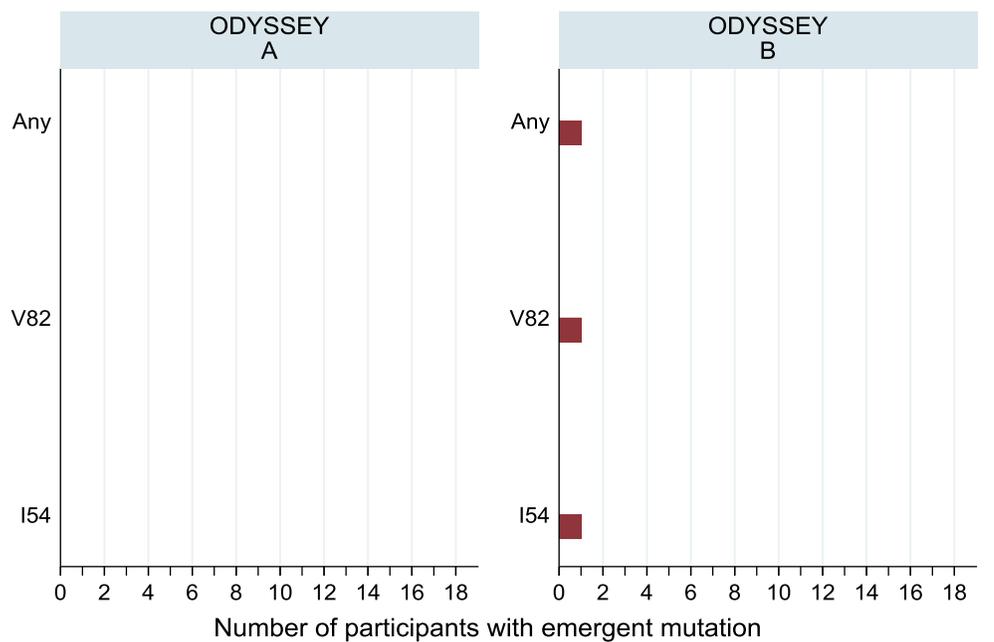
NRTI mutations



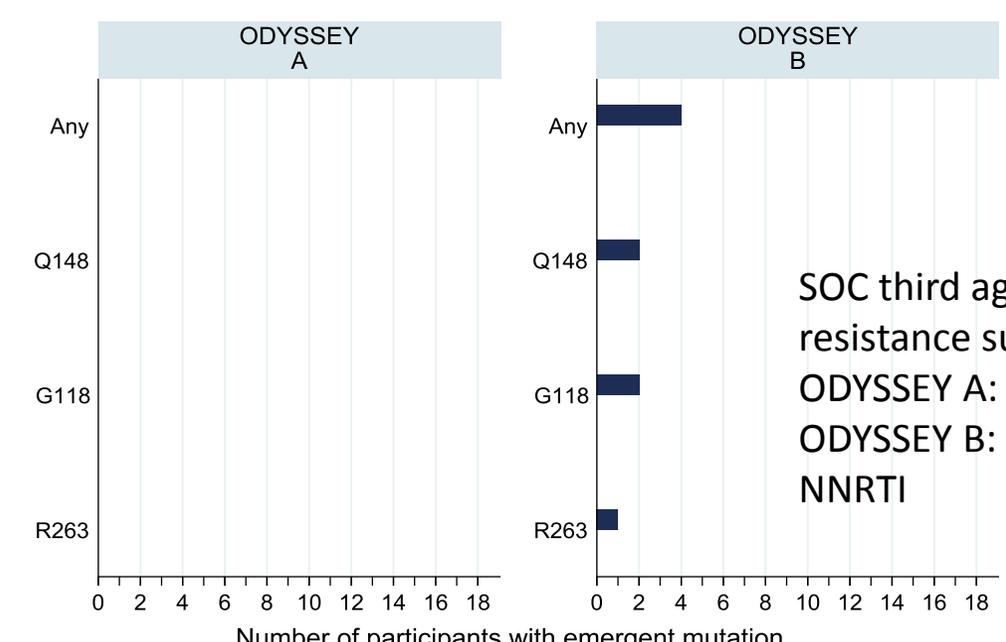
NNRTI mutations



PI mutations

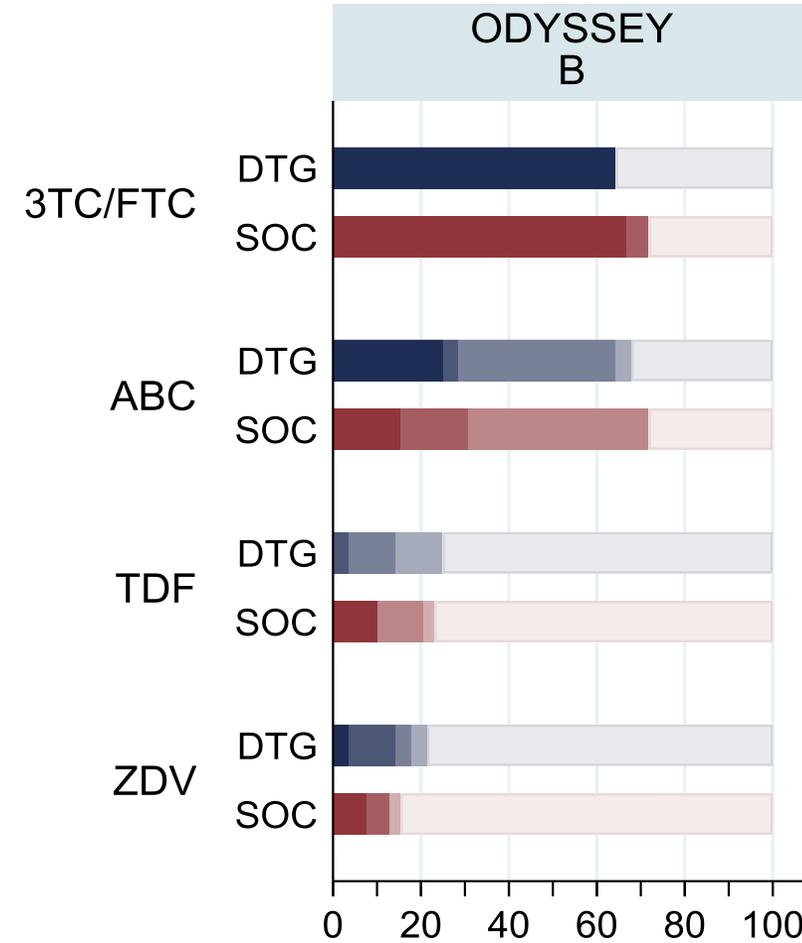
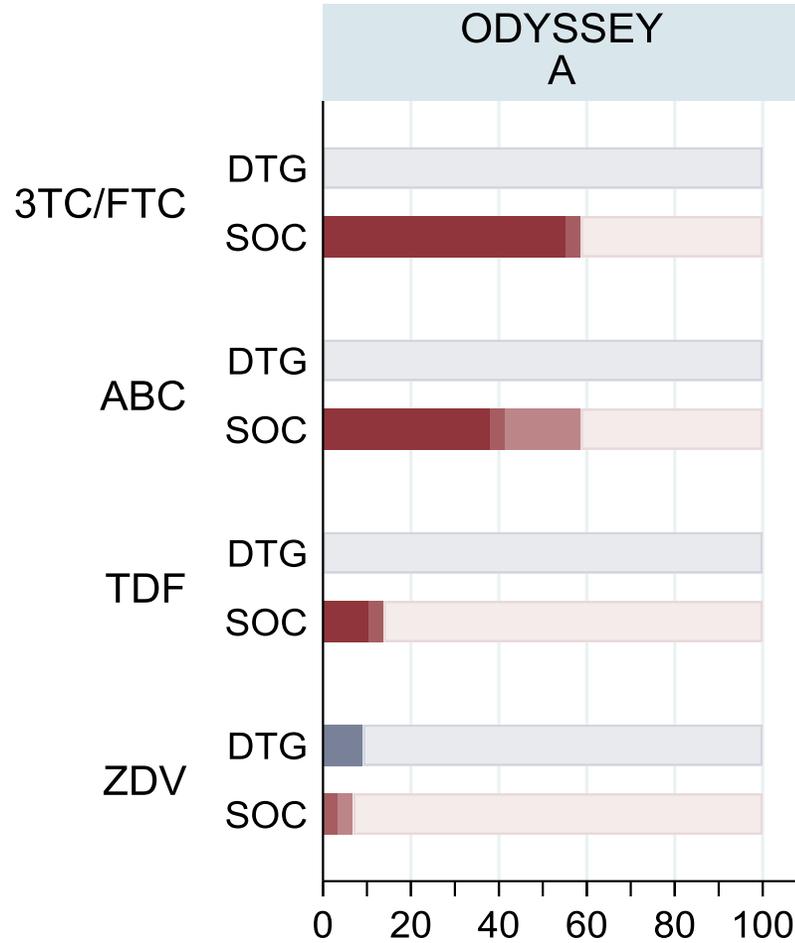
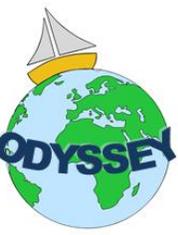


INSTI mutations



SOC third agent in resistance sub-study:
 ODYSSEY A: 100% NNRTI
 ODYSSEY B: 92% PI, 8% NNRTI

NRTI drug resistance – based on susceptibility scores



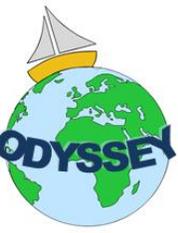
SOC third agent in resistance sub-study:
 ODYSSEY A: 100% NNRTI
 ODYSSEY B: 92% PI, 8% NNRTI

Resistance:



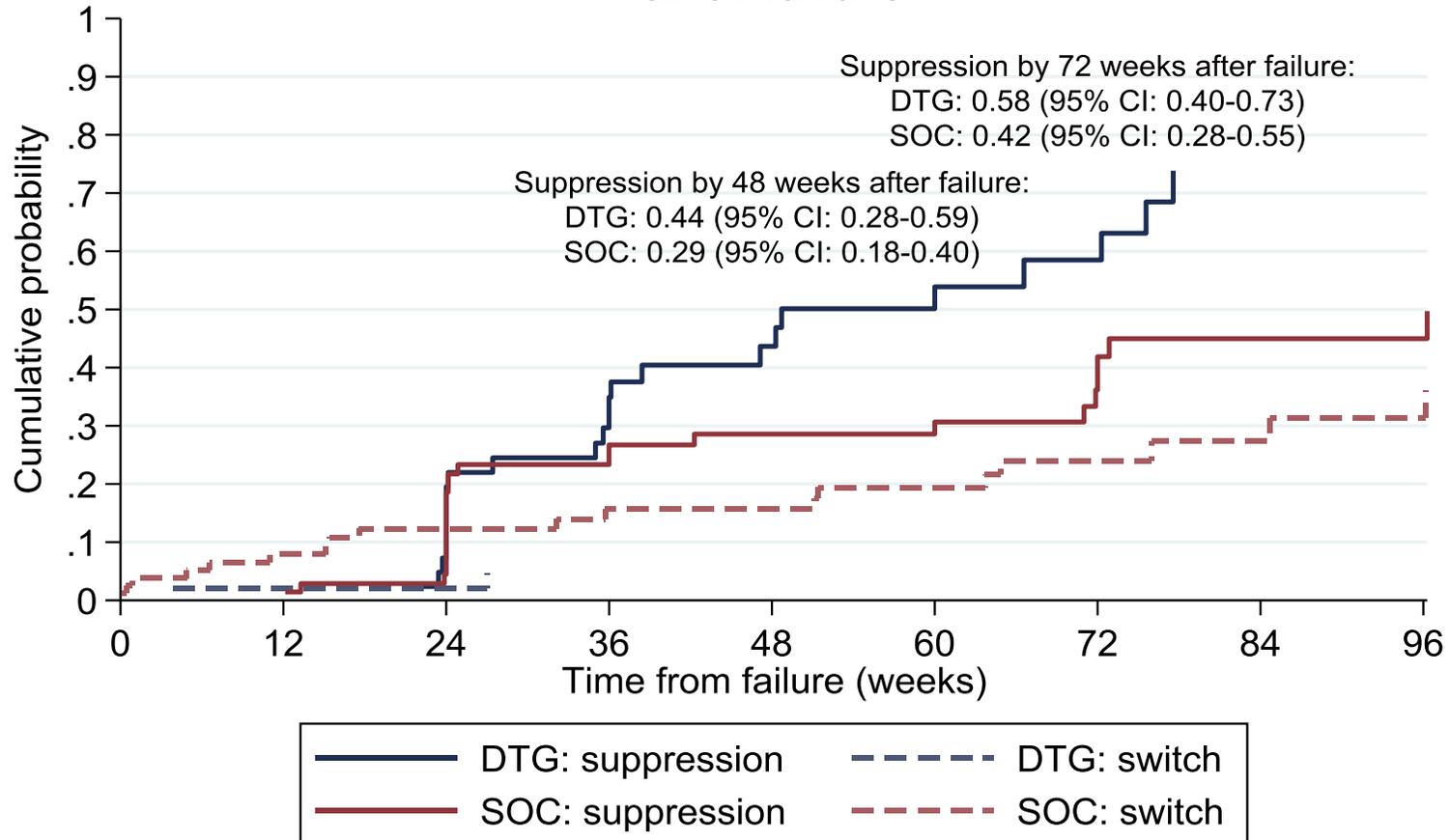
Estimated drug resistance predicted using Stanford HIVdb, version 9.0, including all resistance mutations





Time to re-suppression following 2 VLs $\geq 400\text{c/ml}$ (primary endpoint)

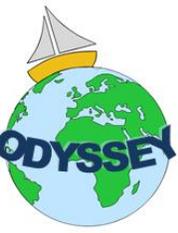
Cumulative probability of re-suppression/switch after failure



Suppression in DTG vs. SOC $p=0.047$

Suppression: 2 consecutive VLs $< 200\text{c/ml}$

Summary



- ODYSSEY demonstrated that DTG has a high genetic resistance barrier in children, preventing emergent resistance to NRTIs.
- We identified no post-failure resistance to any drug class amongst children initiating first-line DTG, significantly less than on first-line SOC.
- Among those on second-line DTG, there was no new NRTI resistance, however 4 children developed new INSTI resistance.
 - 3/4 were on zidovudine
- A high proportion of children re-suppress after virological rebound without ART switch, with marginally higher rates in DTG.
 - None of the children with INSTI resistance had re-suppressed by end of trial.
- These results support using DTG-containing regimens for children starting first-line or second-line ART, but ongoing adherence support is required, especially on second-line.

Thank you

- ODYSSEY participants
- ODYSSEY investigators
- Trial Management Team
- Trial Steering Committee
- Data Monitoring Committee
- Endpoint Review Committee
- Penta (sponsor)
- ViiV Healthcare (funder)
- Mylan



Smarter Studies
Global Impact
Better Health



The ODYSSEY Trial Team



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