THE LANCET
HIV

## Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Amuge P, Lugemwa A, Wynne B, et al. Once-daily dolutegravir-based antiretroviral therapy in infants and children living with HIV from age 4 weeks: results from the below 14 kg cohort in the randomised ODYSSEY trial. *Lancet HIV* 2022; **9:** e638–48.

# Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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# S2 Primary and secondary outcome measures in ODYSSEY

| **Primary Efficacy Outcome** |
|---|
| Difference in proportion with clinical or virological failure by 96 weeks, defined as the first occurrence of any of the following components:<br>1. Insufficient virological response defined as <1 log10 drop at week 24 (or viral load ≥50c/mL at week 24 in a participant with viral load <500c/mL at baseline) and switch to second/third line antiretroviral therapy for treatment failure<br>2. Virological failure (defined as a viral load of greater than or equal to 400 copies/mL at or after week 36 confirmed by the next visit)<br>3. New or recurrent AIDS defining event (WHO 4) or severe WHO 3 event, confirmed by the Endpoint Review Committee<br>4. All-cause death |
| **Secondary efficacy outcomes** |
| Difference in proportion with clinical or virological failure (as defined above) by 48 weeks |
| Time to any new or recurrent AIDS defining event (WHO 4) or severe WHO 3 events, confirmed by the Endpoint Review Committee |
| Proportion of children with Viral Load <50 c/ml at 48 and 96 weeks |
| Proportion of children with Viral Load <400 c/ml at 48 and 96 weeks |
| Rate of HIV-associated events (WHO 4 and severe WHO 3) and death over 96 weeks |
| Change in CD4 count and percentage and CD4/CD8 ratio from baseline to weeks 48 and 96 |
| Proportion developing new resistance mutations |
| **Secondary safety outcomes** |
| Change in total cholesterol, triglycerides and lipid fractions (high-density lipoproteins**,** low-density lipoproteins) from baseline to weeks 48 and 96 (change in total cholesterol from baseline to week 96 will be used to formally assess superiority of dolutegravir-based regimen vs. standard-of-care) |
| Incidence of serious adverse events |
| Incidence of new clinical and laboratory grade 3 and 4 adverse events |
| Incidence of adverse events (of any grade) leading to treatment modification |
| **Other secondary outcomes** |
| Adherence and acceptability |

# S3 Statistical methods

## S3.1 Analysis populations

The <14kg cohort includes participants weighing <14kg, randomised after recruitment to the main trial was completed, with randomisations between the 5th July 2018 and the 26th August 2019. Follow-up was censored on 28th June 2021, when the last child in the <14kg cohort reached 96 weeks follow-up.

**Intent-to-treat population**

The intent-to-treat (ITT) population includes all randomised participants, except those considered randomised in error. Randomisation in error was judged by whether the participant met a major violation of the eligibility criteria, including the participant was randomised at a time when the dolutegravir dose was not known for the participant's weight (and participant not participating in PK); and did not depend on treatment allocation or post-randomisation follow-up.

Intent-to-treat analyses are performed on all participants in the ITT population and participants are analysed according to the study group to which they were randomised.

**Per protocol population**

Participants who did not meet the eligibility criteria or where there was a major protocol deviation, e.g. site prescribed incorrect drug, are excluded from this population. Changes to the third agent (i.e. the non-NRTI component, including adding an additional third agent) for toxicity, failure or pregnancy are defined as a change in therapy and participants are censored at this date. Any stop in regimen for >31 days is defined as stopping therapy and participants are censored at this date.

## S3.2 Primary endpoint

The primary outcome was the difference in the cumulative probability of virological or clinical failure by 96 weeks, estimated by Kaplan-Meier method using time to the first occurrence of any of the following components:

- Insufficient virological response defined as <1 log10 drop at week 24 (or not <50 at week 24 if VL<500c/ml at baseline) and switch to second/third-line treatment for treatment failure
- VL ≥400 c/ml at or after 36 weeks confirmed by repeat VL
- Death due to any cause
- Any new or recurrent AIDS defining event (WHO 4) or severe WHO 3 event, confirmed by the Endpoint Review Committee

The primary comparison was the DTG-based regimen versus SOC for the primary efficacy outcome in the combined population (first and second line) adjusted for first and second line (ODYSSEY A and B).

**Handling viral load data**

Participants were included in ODYSSEY both from sites where HIV RNA was routinely measured frequently and from sites where HIV RNA is routinely measured 6-12 monthly. In the latter case, HIV RNA was measured retrospectively on plasma samples stored at each clinic visit. Confirmatory HIV RNA measures were likely to be performed faster in sites where HIV RNA monitoring occurred routinely more often. The primary endpoint included confirmed HIV RNA≥400 c/ml after 36 weeks.

For consistency across sites, where 2 consecutive HIV RNA were ≥400c/ml, the date of the next scheduled visit following the first HIV RNA ≥400 (using schedule from randomisation) was used to calculate the time to the first confirmed viral load measurement ≥400c/ml (primary endpoint failure date), rather than the date of the confirmatory measure. Where a patient had an HIV RNA≥400c/ml and switched treatment for treatment failure without a confirmatory viral load before switch, the date of the next scheduled visit following the first HIV RNA ≥400c/ml was used for the first confirmed viral load measurement ≥400c/ml.

The primary endpoint included insufficient virological response by week 24, defined by less than a 1 log10 drop in viral load from baseline (or HIV RNA≥50c/ml at week 24 when baseline HIV RNA<500c/ml) with switch to second/third line treatment for treatment failure. A participant was considered a failure if they switched to second- or third-line treatment following insufficient virological response at week 24 without suppressing (VL<50c/ml) between week 24 and switching therapy. Date of switching therapy was used as the primary endpoint failure date.

**Analysis details for primary efficacy outcome**

In the <14kg cohort, time to clinical or virological failure (ODYSSEY A and B combined) was estimated using Kaplan Meier curves to estimate the proportion of children failing in each arm at any time up to the week 96 censoring date (96 weeks from date of randomisation). The survival curve for each combination of ODYSSEY A/B stratum and randomised group was calculated using a Cox model adjusting for ODYSSEY A/B stratum and randomised group. The average survival curve for each randomised group

was estimated as a weighted average of the corresponding stratum-specific survival curves, with weights proportional to the number of individuals in each stratum across both randomised groups at baseline. The mean of these differences at week 96 was the point estimate for the difference in overall survival function between DTG and SOC arm. As only 85 children were recruited weighing <14kg, confidence intervals for the proportions failing by treatment arm were estimated by bootstrap on the log(-log(S(t)) scale, assuming Normal theory. The confidence interval for the risk difference was estimated using bias-corrected bootstrap. Bootstrapping was sampled 1000 times and stratified by ODYSSEY A/B and treatment group.

In the main trial (children enrolled weighing ≥14kg) the treatment effect had been estimated similarly, although stratification was by: trial cohort (ODYSSEY A or B), routine availability of resistance tests (available or unavailable), abacavir and lamivudine NRTI backbone vs. other NRTI backbone.

The primary outcome was assessed using Bayesian analysis, including an interaction parameter to model the relationship between underlying treatment effects in the ≥14kg and <14kg subgroups. Prior to any results being shared outside of IDMC meetings, elicitation was used to obtain clinical opinions on the likely values of the interaction parameter. Expert clinical opinion was elicited from thirteen experienced paediatricians and demonstrated that substantial borrowing from the ≥14kg cohort was supported. Clinical experts chose on average to allocate a relative weight of 78% (reduced from 90% based on sample size) to data from children weighing ≥14kg in a Bayesian analysis of the cohort of children weighing <14kg. The total effective sample size in the Bayesian analysis was 386 children, providing 84% predictive power to exclude a difference of more than 10% between arms, whereas the 85 younger children weighing <14kg provided only 20% power in a standalone frequentist analysis.[2]

Frequentist analyses of the <14kg cohort alone is adjusted for ODYSSEY A/B. The pooled dataset (whereby all data were analysed together is stratified by weight band (≥/<14kg) in addition to the strata identified above for the ≥14kg group and antiretroviral treatment (ODYSSEY A/B) in the <14kg group, i.e. 10 strata:

- ≥14kg/ODYSSEY A/No Resistance Testing/Abacavir and lamivudine NRTI backbone;
- ≥14kg/ODYSSEY A/Resistance Testing/ Abacavir and lamivudine NRTI backbone;
- ≥14kg/ODYSSEY A/No Resistance Testing/other NRTI backbone;
- ≥14kg/ODYSSEY A/Resistance Testing/ other NRTI backbone;
- ≥14kg/ODYSSEY B/No Resistance Testing/Abacavir and lamivudine NRTI backbone;
- ≥14kg/ODYSSEY B/Resistance Testing/Abacavir and lamivudine NRTI backbone;
- ≥14kg/ODYSSEY B/No Resistance Testing/other NRTI backbone;
- ≥14kg/ODYSSEY B/Resistance Testing/other NRTI backbone;
- <14kg/ODYSSEY A;
- <14kg/ODYSSEY B.

The Kaplan-Meier plot for time to clinical or virological failure follows the KMunicate principles.[3] The risk table presented differs to that proposed initially by Morris et al., where here 'at-risk (no event)' includes those observed without event up to and including time t; 'censored' includes those censored before time t; and 'event' includes those with an event up to and including time t. Using this approach, we assume that the outcome is known before censoring where both occur on same day.

*1. Reference: Turkova A, White E, Mujuru HA, Kekitiinwa AR, Kityo CM, Violari A, et al. ODYSSEY: Dolutegravir For First- and Second-Line HIV Treatment in Children. New England Journal of Medicine. 2021.*
*2. Reference: Turner B, Ford D, Moore C, Gibb D, Turkova A, White I, et al. Analysing small groups within clinical trials, while borrowing information from larger groups. Abstract presented at the 40th Annual Conference of the International Society for Clinical Biostatics; July 16, 2019; Leuven, Belgium.*
*3. Reference: Morris TP, Jarvis CI, Cragg W, Phillips PPJ, Choodari-Oskooei B, Sydes MR. Proposals on Kaplan–Meier plots in medical research and a survey of stakeholder views: KMunicate. BMJ Open 2019;9:e030215. doi: 10.1136/bmjopen-2019-030215*

**Per protocol**

The per protocol analysis aimed to estimate the "while on treatment" effect,[4] by comparing the primary endpoint between arms in the per protocol population (described above in S3.1).

*4. Reference: ICH E9 (R1) addendum on estimands and sensitivity analysis in clinical trials to the guideline on statistical principles for clinical trials. EMA/CHMP/ICH/436221/2017*

**Sub-group analysis**

A sub-group analysis was completed by age at randomisation (</>=1 year).

## S3.3 FDA snapshot algorithm

### Definitions for FDA snapshot algorithm

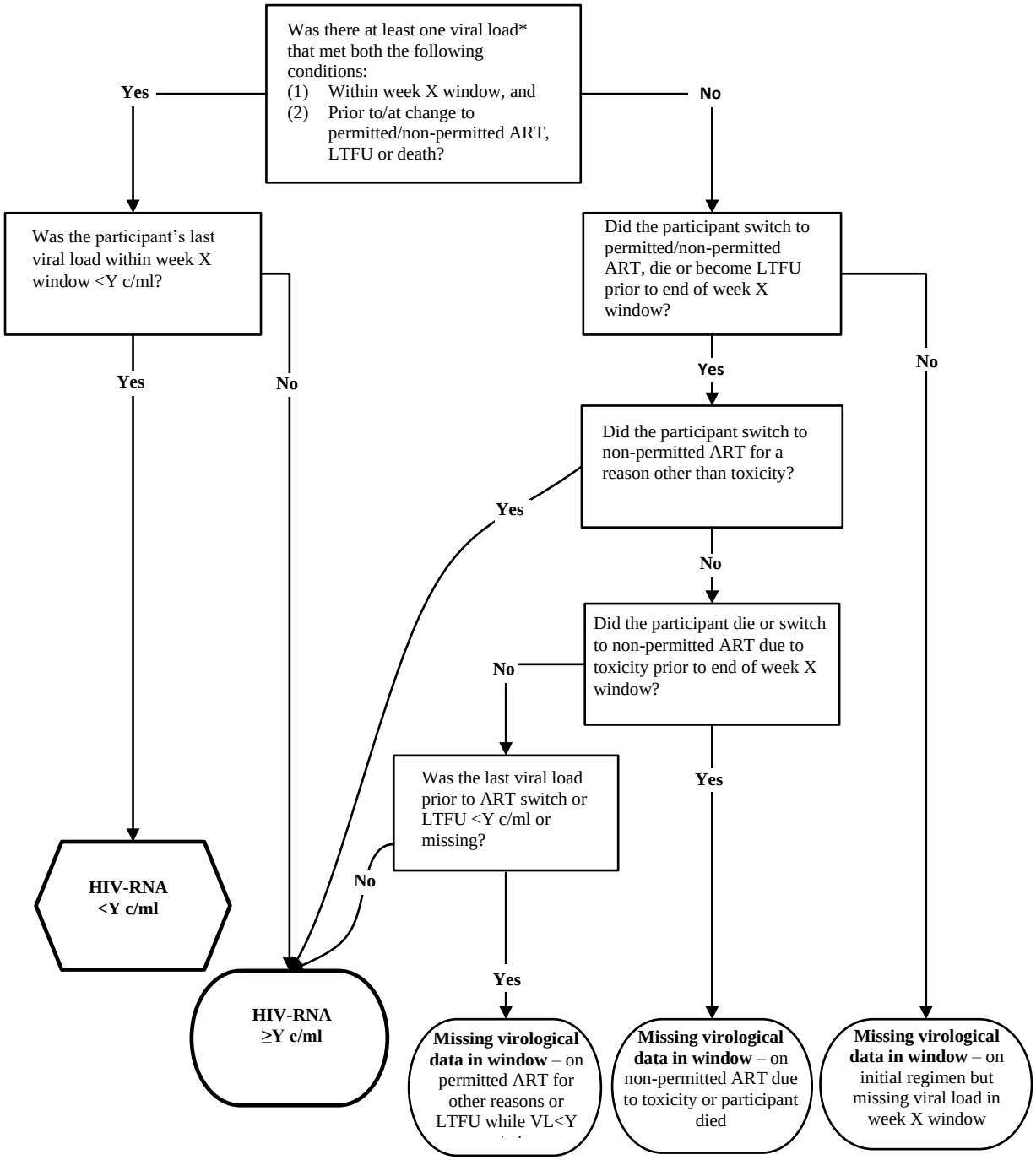
The FDA snapshot algorithm in ODYSSEY was used to compare virological suppression (<50 c/ml and <400 c/ml, indicated by Y) in DTG vs. SOC at weeks 48 and 96 (indicated by X).

Here we define changes to the initial ART regimen for the purposes of the FDA snapshot algorithm:

- **Strict initial regimen** - the strict initial regimen assigned at randomisation to ODYSSEY;
- **"Ignored" ART changes** – changes to NRTI backbone for increases in age/weight, simplification (including patient/carer decisions), and drug availability. Changes to 3rd agent are ignored when: (1) DTG arm – changes to the DTG dose for increases in age/weight; (2) SOC arm - changes to 3rd agent for simplification (including patient/carer decision), drug availability, and increases in weight.
- **"Permitted" ART changes** include: changes to NRTI backbone for any reason other than those listed above and treatment failure.
- **"Non-permitted" ART changes** include: (i) changes to the NRTI backbone in the initial regimen for treatment failure; (ii) changes to the third agent for treatment failure; (iii) changes to third agent for toxicity; or (iv) changes to the third agent for all reasons not listed in "Ignored ART changes".

Only post-baseline and on-treatment viral loads were used in the algorithm. Participants interrupting ART prior to or within week X window were assumed to remain on the regimen and were treated as a treatment switch when a new regimen (according to rules above) was initiated (although, viral loads off treatment were not used). In the case where a participant had multiple viral loads within week X window, the latest viral load was used in the FDA snapshot algorithm, provided it was on/prior to trial censoring date (28th June 2021).

## S3.4 Flowchart of the FDA snapshot algorithm




*Off ART viral loads will be excluded from algorithm.

### S3.5 Analysis of continuous outcomes

Changes in continuous outcomes were analysed using analysis of covariance, adjusting for baseline value and ODYSSEY A/B; average treatment differences through follow-up were estimated using mixed linear models with random effect for intercept and fixed effects for treatment arm, visit week and ODYSSEY A/B.

### S3.6 Analyses of clinical events

Clinical events (WHO severe stage 3 and stage 4 events and adverse events) were compared between arms using the hazard ratio for first event from a Cox proportional hazards regression model.

### S3.7 Definition of treatment change

The following are used to define substitutions and changes to initial ART regimens (Appendix, S13):

A strict initial regimen was defined as strictly the regimen allocated at trial entry.

A substituted initial regimen was defined as the strict initial regimen allowing for substitutions to the third agent of the regimen for reasons other than toxicity, treatment failure, pregnancy or major protocol deviation (e.g. site prescribing incorrect drug) or to the NRTI component for any reason. Permissible substitutions to the third agent included reasons for simplification, drug availability, patient/carer decision and increases in weight.

All reductions to NRTIs were also considered substituted initial regimen.

All changes to the third agent not defined above as a substitution to the initial regimen were considered a change from the initial treatment regimen. In the DTG arm, DTG should only be stopped for toxicity, failure or (at clinician's discretion) pregnancy.

Changes to the third agent for reasons of treatment failure were defined as switching to second line therapy in ODYSSEY A or third line therapy in ODYSSEY B.

Any interruptions or reductions to a regimen for less than or equal to 31 consecutive days were allowed; as long as the total number of drugs allocated in the regimen was not increased.

A stop to the initial regimen occurred when a patient interrupted their regimen or their third agent for >31 days.

### S3.8 Adjustment and testing multiple outcomes

Unless otherwise specified, adjusted analyses adjust for ODYSSEY A/B and are used in the paper. Unadjusted analyses are also presented through the Supplementary Appendix.

In accordance with the statistical analysis plan, we have made no adjustment to p-values or confidence intervals to allow for testing multiple secondary outcomes.

## S4 Impact of Covid-19

Due to the COVID-19 pandemic (March 2020 onwards), and uncertainty about how it would evolve, sites were advised that all participants would remain in randomised follow-up until the final participant recruited <14kg reached 96 weeks follow-up on the 28th June 2021. It was originally intended that participants recruited <14kg would exit randomised follow-up upon reaching week 96.

There may have been a slight excess of missed in person visits between 1st March-31st May 2020 (10 visits missed, 11% of expected visits) and 1st June-31st August 2020 (4 visits missed, 5% of expected visits) compared to the remainder of follow-up (total 2% of expected visits missed). Missed visits within the period 1st March-31st August 2020 were similar in both arms with 8 in DTG and 6 in SOC (DTG 10%; SOC 7%). Two of the 14 missed in-person visits were conducted over the phone (both in SOC).

In total, there were 11 participants with missed in person visits within the period 1st March-31st August 2020, 6 in DTG and 5 in SOC. Of these 11 participants, 1 in SOC was withdrawn (December 2019 for social problems) and 1 in DTG was lost to follow-up (December 2019 for carer relocation). In addition, one participant was withdrawn in August 2020 for moved area. None of these withdrawals or losses to follow-up appear to be related to COVID-19. Of the 9 participants with any missed in person visit within the period 1st March-31st August 2020 who remained in follow-up to the trial censoring date, only one participant missed more than one consecutive visit and they were suppressed at week 96. Drug supply was ensured where in person visits were missed.

## S5 Dolutegravir dosing throughout ODYSSEY

| | ODYSSEY v2.0* | ODYSSEY v3.0 | | ODYSSEY v4.0 | | ODYSSEY v5.0 onwards | |
|---|---|---|---|---|---|---|---|
| | Main trial participants | Main trial participants | WB PK substudy participants | Main trial participants | WB PK substudy participants | Main trial participants | WB PK substudy participants |
| 3-<6kg | - | - | | - | 5mg or 10mg DTψ | - | 5mg or 10mg DTψ |
| 6-<10kg | - | - | | - | 15mg DT | - | 15mg DT |
| 10-<14kg | - | - | | - | 20mg DT | - | 20mg DT |
| 14-<15kg | - | - | 25mg | 25mg→25mg DT§ | 25mg DT | 25mg DT | N/A |
| 15-<20kg | 20mg* | 20mg | | | | | |
| 20-<25kg | 25mg | 25mg | 25mg | 25mg→30mg DT or 50mg¥ | 30mg DT or 50mg† | 50mgπ | N/A |
| 25-<30kg | 25mg | 25mg→50mg** | 50mg | 25mg→50mg** | NA | 50mg | NA |
| 30-<35kg | 35mg | 35mg→50mg** | 50mg | 35mg→50mg** | NA | 50mg | NA |
| 35-<40kg | 35mg | 35mg→50mg** | 50mg | 35mg→50mg** | NA | 50mg | NA |
| ≥40kg | 50mg | 50mg | NA | 50mg | NA | 50mg | NA |

ψ Infants <6 months of age receive DTG 5mg QD while infants ≥6 months of age receive DTG 10mg QD, both as dispersible tablets.
* In May 2017 the EMA licensed the use of 20mg DTG in children 15 - <20kg and ≥6years, following this, children were able to be recruited in this weight and age-band.
** From 1st of April 2018, after ethics notification, sites following protocol version 3.0 and above were recommended to increase the DTG dose of children 25 - <40kg to 50mg FCT QD at their next scheduled study visit based on the results of the WB-PK2. WB-PK2 participants remained on DTG 50mg with ongoing follow-up. Non-PK participants recruited after implementation were initiated on the 50mg film-coated DTG dose.
† Both doses are examined in WB-PK1 part II substudy in this weight-band.
§ Children 15 - <20kg previously receiving DTG 20mg QD were changed to DTG film-coated 25mg tablets upon the approval of protocol v4.0. Subsequently all children 14-<20kg changed to DTG 25mg QD dispersible tablets following the review of WB-PK1 part I results and approval by the relevant ethical and regulatory authorities.
¥ Children 20 - <25kg previously receiving DTG 25mg QD as one 25mg film-coated tablet changed to either DTG 30mg QD dispersible tablets or DTG 50mg QD (film-coated tablet) depending on site following the review of WB-PK1 part I results and approval by the relevant ethical and regulatory authorities.
π Following the review of PK and safety data children 20-<25kg receiving DTG 30mg dispersible tablets should be switched to DTG 50mg film-coated tablets. Those who prefer to remain on DTG 30mg DT will be able to do so until they move weight band.
DT=dispersible, otherwise film coated tables

# S6 Enrolment and Eligibility

## S6.1 Screening and randomisation

| | Total | A | B |
|---|---|---|---|
| Screened | 102 | 80 | 22 |
| Randomised | 85 | 72 | 13 |
| Total ineligible | 17 | 8 | 9 |
| Reasons for ineligibility | | | |
| Failed at least one eligibility criterion | 14 | 5 | 9 |
| Died before enrolment | 1 | 1 | 0 |
| Other+ | 2 | 2 | 0 |

+1 ODYSSEY A participant's carer declined to participate due to the blood volumes required. 1 ODYSSEY A participant was not recruited as the protocol amendment allowing recruitment to this participant's weight group had not been approved at the site.

# S7 Baseline Demographics

## S7.1 Baseline characteristics

| | Total | | | A | | | B | | |
|---|---|---|---|---|---|---|---|---|---|
| | **DTG** | **SOC** | **Total** | **DTG** | **SOC** | **Total** | **DTG** | **SOC** | **Total** |
| **Participants randomised** | 42 | 43 | 85 | 35 | 37 | 72 | 7 | 6 | 13 |
| **Country** | | | | | | | | | |
| South Africa | 8 (19%) | 12 (28%) | 20 (24%) | 8 (23%) | 12 (32%) | 20 (28%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| Uganda | 22 (52%) | 21 (49%) | 43 (51%) | 17 (49%) | 16 (43%) | 33 (46%) | 5 (71%) | 5 (83%) | 10 (77%) |
| Zimbabwe | 12 (29%) | 10 (23%) | 22 (26%) | 10 (29%) | 9 (24%) | 19 (26%) | 2 (29%) | 1 (17%) | 3 (23%) |
| **Sex** | | | | | | | | | |
| male | 16 (38%) | 25 (58%) | 41 (48%) | 14 (40%) | 21 (57%) | 35 (49%) | 2 (29%) | 4 (67%) | 6 (46%) |
| female | 26 (62%) | 18 (42%) | 44 (52%) | 21 (60%) | 16 (43%) | 37 (51%) | 5 (71%) | 2 (33%) | 7 (54%) |
| **Age (years)** | | | | | | | | | |
| n | 42 | 43 | 85 | 35 | 37 | 72 | 7 | 6 | 13 |
| mean (SD) | 1.6 (1.2) | 1.5 (1.1) | 1.5 (1.2) | 1.3 (1.2) | 1.3 (1.1) | 1.3 (1.1) | 2.7 (0.5) | 2.7 (0.5) | 2.7 (0.5) |
| median | 1.3 | 1.5 | 1.4 | 1.2 | 1.1 | 1.1 | 2.6 | 2.7 | 2.6 |
| [IQR] | [0.5, 2.0] | [0.6, 2.1] | [0.6, 2.0] | [0.4, 2.0] | [0.5, 1.7] | [0.5, 1.9] | [2.1, 3.2] | [2.5, 2.9] | [2.5, 2.9] |
| [range] | [0.3-5.9] | [0.1-4.5] | [0.1-5.9] | [0.3-5.9] | [0.1-4.5] | [0.1-5.9] | [2.0-3.3] | [1.9-3.5] | [1.9-3.5] |
| <6months | 11 (26%) | 8 (19%) | 19 (22%) | 11 (31%) | 8 (22%) | 19 (26%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| 6months-<1year | 5 (12%) | 8 (19%) | 13 (15%) | 5 (14%) | 8 (22%) | 13 (18%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| 1-<3years | 22 (52%) | 22 (51%) | 44 (52%) | 17 (49%) | 17 (46%) | 34 (47%) | 5 (71%) | 5 (83%) | 10 (77%) |
| 3-<6years | 4 (10%) | 5 (12%) | 9 (11%) | 2 ( 6%) | 4 (11%) | 6 ( 8%) | 2 (29%) | 1 (17%) | 3 (23%) |
| **Weight (kg)+** | | | | | | | | | |
| n | 42 | 43 | 85 | 35 | 37 | 72 | 7 | 6 | 13 |
| mean (SD) | 8.0 (2.7) | 8.1 (3.0) | 8.1 (2.8) | 7.4 (2.5) | 7.7 (2.9) | 7.6 (2.7) | 10.7 (1.6) | 10.8 (1.6) | 10.7 (1.6) |
| median | 8.1 | 8.2 | 8.1 | 6.6 | 7.3 | 7.2 | 11.1 | 11.3 | 11.1 |
| [IQR] | [5.6, 10.0] | [5.2, 10.3] | [5.4, 10.0] | [5.3, 9.8] | [5.1, 9.7] | [5.1, 9.7] | [9.0, 12.0] | [9.7, 11.7] | [9.5, 11.7] |
| [range] | [3.8-13.0] | [3.4-13.4] | [3.4-13.4] | [3.8-13.0] | [3.4-13.4] | [3.4-13.4] | [8.8-13.0] | [8.0-12.5] | [8.0-13.0] |
| <6kg | 11 (26%) | 12 (28%) | 23 (27%) | 11 (31%) | 12 (32%) | 23 (32%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| 6-<10kg | 20 (48%) | 20 (47%) | 40 (47%) | 17 (49%) | 18 (49%) | 35 (49%) | 3 (43%) | 2 (33%) | 5 (38%) |
| 10-<14kg | 11 (26%) | 11 (26%) | 22 (26%) | 7 (20%) | 7 (19%) | 14 (19%) | 4 (57%) | 4 (67%) | 8 (62%) |
| **Height (cm)** | | | | | | | | | |
| n | 42 | 43 | 85 | 35 | 37 | 72 | 7 | 6 | 13 |
| mean (SD) | 71.9 (12.1) | 72.0 (11.5) | 71.9 (11.7) | 69.0 (10.8) | 70.6 (11.7) | 69.8 (11.3) | 86.4 (5.6) | 80.4 (4.4) | 83.6 (5.8) |
| median | 72.3 | 73.3 | 73.0 | 68.2 | 70.0 | 69.7 | 86.2 | 80.5 | 83.5 |
| [IQR] | [60.0, 80.3] | [62.0, 80.5] | [61.0, 80.3] | [58.8, 76.3] | [61.0, 78.2] | [59.5, 77.2] | [80.3, 91.0] | [78.0, 83.5] | [79.0, 86.2] |
| [range] | [53.5-93.8] | [50.0-93.4] | [50.0-93.8] | [53.5-93.8] | [50.0-93.4] | [50.0-93.8] | [79.0-93.8] | [74.0-86.2] | [74.0-93.8] |
| **Weight-for-Age*** | | | | | | | | | |
| n | 42 | 43 | 85 | 35 | 37 | 72 | 7 | 6 | 13 |
| mean (SD) | -2.3 (1.4) | -2.1 (1.7) | -2.2 (1.6) | -2.3 (1.4) | -2.1 (1.8) | -2.2 (1.6) | -1.8 (1.0) | -1.9 (1.7) | -1.9 (1.3) |
| median | -2.1 | -1.8 | -1.9 | -2.5 | -1.8 | -1.9 | -1.8 | -1.2 | -1.6 |
| [IQR] | [-3.4, -1.3] | [-3.7, -0.8] | [-3.4, -1.1] | [-3.5, -1.1] | [-3.4, -0.9] | [-3.5, -1.1] | [-2.8, -1.5] | [-3.7, -0.7] | [-2.8, -1.0] |
| [range] | [-5.1-0.3] | [-5.7-1.4] | [-5.7-1.4] | [-5.1-0.3] | [-5.7-1.4] | [-5.7-1.4] | [-3.0-0.0] | [-4.3--0.3] | [-4.3-0.0] |
| <-3 | 14 (33%) | 13 (30%) | 27 (32%) | 14 (40%) | 11 (30%) | 25 (35%) | 0 ( 0%) | 2 (33%) | 2 (15%) |
| -3-<-2 | 7 (17%) | 6 (14%) | 13 (15%) | 4 (11%) | 6 (16%) | 10 (14%) | 3 (43%) | 0 ( 0%) | 3 (23%) |
| -2-<0 | 18 (43%) | 21 (49%) | 39 (46%) | 15 (43%) | 17 (46%) | 32 (44%) | 3 (43%) | 4 (67%) | 7 (54%) |
| >=0 | 3 ( 7%) | 3 ( 7%) | 6 ( 7%) | 2 ( 6%) | 3 ( 8%) | 5 ( 7%) | 1 (14%) | 0 ( 0%) | 1 ( 8%) |
| **BMI-for-Age*** | | | | | | | | | |
| n | 42 | 43 | 85 | 35 | 37 | 72 | 7 | 6 | 13 |
| mean (SD) | -0.9 (1.4) | -0.9 (1.9) | -0.9 (1.7) | -0.9 (1.5) | -1.1 (1.9) | -1.0 (1.7) | -1.1 (1.0) | 0.6 (1.3) | -0.3 (1.4) |
| median | -1.1 | -0.7 | -0.8 | -1.1 | -0.8 | -0.9 | -1.4 | 0.3 | -0.0 |
| [IQR] | [-1.9, 0.2] | [-2.2, 0.3] | [-2.0, 0.2] | [-1.9, 0.2] | [-2.3, 0.2] | [-2.1, 0.2] | [-2.0, -0.0] | [0.0, 0.8] | [-1.4, 0.2] |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| [range] | [-3.6-1.9] | [-5.7-3.1] | [-5.7-3.1] | [-3.6-1.9] | [-5.7-2.3] | [-5.7-2.3] | [-2.3-0.2] | [-0.7-3.1] | [-2.3-3.1] |
| <-3 | 3 ( 7%) | 6 (14%) | 9 (11%) | 3 ( 9%) | 6 (16%) | 9 (13%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| -3-<-2 | 6 (14%) | 6 (14%) | 12 (14%) | 5 (14%) | 6 (16%) | 11 (15%) | 1 (14%) | 0 ( 0%) | 1 ( 8%) |
| -2-<0 | 20 (48%) | 14 (33%) | 34 (40%) | 15 (43%) | 13 (35%) | 28 (39%) | 5 (71%) | 1 (17%) | 6 (46%) |
| >=0 | 13 (31%) | 17 (40%) | 30 (35%) | 12 (34%) | 12 (32%) | 24 (33%) | 1 (14%) | 5 (83%) | 6 (46%) |
| **Weight-for-Height*** | | | | | | | | | |
| n | 41 | 43 | 84 | 34 | 37 | 71 | 7 | 6 | 13 |
| mean (SD) | -0.9 (1.4) | -0.9 (1.9) | -0.9 (1.7) | -0.8 (1.5) | -1.1 (1.9) | -1.0 (1.7) | -1.2 (0.9) | 0.1 (1.4) | -0.6 (1.3) |
| median | -0.7 | -0.8 | -0.8 | -0.5 | -1.1 | -0.8 | -1.5 | -0.1 | -0.7 |
| [IQR] | [-1.9, 0.1] | [-1.9, 0.5] | [-1.9, 0.3] | [-1.7, 0.3] | [-1.9, 0.5] | [-1.9, 0.3] | [-1.9, -0.4] | [-0.7, 0.4] | [-1.5, 0.1] |
| [range] | [-3.4-2.2] | [-5.4-2.6] | [-5.4-2.6] | [-3.4-2.2] | [-5.4-2.2] | [-5.4-2.2] | [-2.4-0.1] | [-1.5-2.6] | [-2.4-2.6] |
| <-3 | 3 ( 7%) | 5 (12%) | 8 (10%) | 3 ( 9%) | 5 (14%) | 8 (11%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| -3-<-2 | 6 (15%) | 4 ( 9%) | 10 (12%) | 5 (15%) | 4 (11%) | 9 (13%) | 1 (14%) | 0 ( 0%) | 1 ( 8%) |
| -2-<0 | 21 (51%) | 17 (40%) | 38 (45%) | 16 (47%) | 14 (38%) | 30 (42%) | 5 (71%) | 3 (50%) | 8 (62%) |
| >=0 | 11 (27%) | 17 (40%) | 28 (33%) | 10 (29%) | 14 (38%) | 24 (34%) | 1 (14%) | 3 (50%) | 4 (31%) |
| missing | 1 | 0 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| **Mode of infection** | | | | | | | | | |
| Mother to child | 42 (100%) | 42 (98%) | 84 (99%) | 35 (100%) | 36 (97%) | 71 (99%) | 7 (100%) | 6 (100%) | 13 (100%) |
| Unknown | 0 ( 0%) | 1 ( 2%) | 1 ( 1%) | 0 ( 0%) | 1 ( 3%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| **Ethnic origin** | | | | | | | | | |
| Black-African | 41 (98%) | 42 (98%) | 83 (98%) | 34 (97%) | 36 (97%) | 70 (97%) | 7 (100%) | 6 (100%) | 13 (100%) |
| Black-other | 0 ( 0%) | 1 ( 2%) | 1 ( 1%) | 0 ( 0%) | 1 ( 3%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| Mixed Black-White | 1 ( 2%) | 0 ( 0%) | 1 ( 1%) | 1 ( 3%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| **CD4%**** | | | | | | | | | |
| n | 41 | 40 | 81 | 34 | 34 | 68 | 7 | 6 | 13 |
| mean (SD) | 25 ( 12) | 22 ( 12) | 24 ( 12) | 25 ( 12) | 21 ( 11) | 23 ( 12) | 25 ( 12) | 28 ( 13) | 26 ( 12) |
| median | 24 | 23 | 23 | 24 | 22 | 23 | 28 | 26 | 27 |
| [IQR] | [ 17, 35] | [ 14, 30] | [ 16, 31] | [ 18, 35] | [ 13, 31] | [ 16, 32] | [ 13, 40] | [ 19, 28] | [ 15, 29] |
| [range] | [ 3- 46] | [ 1- 53] | [ 1- 53] | [ 3- 46] | [ 1- 43] | [ 1- 46] | [ 13- 40] | [ 14- 53] | [ 13- 53] |
| <10 | 3 ( 7%) | 8 (20%) | 11 (14%) | 3 ( 9%) | 8 (24%) | 11 (16%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| 10-<15 | 4 (10%) | 3 ( 8%) | 7 ( 9%) | 2 ( 6%) | 2 ( 6%) | 4 ( 6%) | 2 (29%) | 1 (17%) | 3 (23%) |
| 15-<20 | 9 (22%) | 4 (10%) | 13 (16%) | 8 (24%) | 3 ( 9%) | 11 (16%) | 1 (14%) | 1 (17%) | 2 (15%) |
| 20-<25 | 6 (15%) | 11 (28%) | 17 (21%) | 6 (18%) | 10 (29%) | 16 (24%) | 0 ( 0%) | 1 (17%) | 1 ( 8%) |
| 25-<30 | 7 (17%) | 3 ( 8%) | 10 (12%) | 5 (15%) | 1 ( 3%) | 6 ( 9%) | 2 (29%) | 2 (33%) | 4 (31%) |
| 30-<40 | 4 (10%) | 9 (23%) | 13 (16%) | 4 (12%) | 9 (26%) | 13 (19%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| >=40 | 8 (20%) | 2 ( 5%) | 10 (12%) | 6 (18%) | 1 ( 3%) | 7 (10%) | 2 (29%) | 1 (17%) | 3 (23%) |
| missing | 1 | 3 | 4 | 1 | 3 | 4 | 0 | 0 | 0 |
| **CD4 (cells/mm3)**** | | | | | | | | | |
| n | 41 | 40 | 81 | 34 | 34 | 68 | 7 | 6 | 13 |
| mean (SD) | 1671 (971) | 1425 (1108) | 1550 (1042) | 1685 (1013) | 1408 (1119) | 1547 (1068) | 1604 (800) | 1523 (1140) | 1567 (929) |
| median | 1639 | 1221 | 1391 | 1662 | 1221 | 1421 | 1639 | 1145 | 1315 |
| [IQR] | [1026, 2327] | [633, 1870] | [863, 2060] | [949, 2327] | [559, 1858] | [839, 2102] | [1026, 2558] | [863, 1882] | [976, 1882] |
| [range] | [ 67-4676] | [ 54-5300] | [ 54-5300] | [ 67-4676] | [ 54-5300] | [ 54-5300] | [510-2672] | [465-3638] | [465-3638] |
| 50-<100 | 1 ( 2%) | 4 (10%) | 5 ( 6%) | 1 ( 3%) | 4 (12%) | 5 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| 100-<200 | 2 ( 5%) | 0 ( 0%) | 2 ( 2%) | 2 ( 6%) | 0 ( 0%) | 2 ( 3%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| 200-<350 | 1 ( 2%) | 0 ( 0%) | 1 ( 1%) | 1 ( 3%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| 350-<500 | 1 ( 2%) | 3 ( 8%) | 4 ( 5%) | 1 ( 3%) | 2 ( 6%) | 3 ( 4%) | 0 ( 0%) | 1 (17%) | 1 ( 8%) |
| 500-<1000 | 5 (12%) | 7 (18%) | 12 (15%) | 4 (12%) | 5 (15%) | 9 (13%) | 1 (14%) | 2 (33%) | 3 (23%) |
| 1000-1500 | 8 (20%) | 11 (28%) | 19 (23%) | 6 (18%) | 10 (29%) | 16 (24%) | 2 (29%) | 1 (17%) | 3 (23%) |
| >=1500 | 23 (56%) | 15 (38%) | 38 (47%) | 19 (56%) | 13 (38%) | 32 (47%) | 4 (57%) | 2 (33%) | 6 (46%) |
| missing | 1 | 3 | 4 | 1 | 3 | 4 | 0 | 0 | 0 |
| **CD4/CD8 ratio**** | | | | | | | | | |
| n | 41 | 40 | 81 | 34 | 34 | 68 | 7 | 6 | 13 |
| mean (SD) | 0.7 (0.6) | 0.6 (0.5) | 0.7 (0.6) | 0.8 (0.7) | 0.6 (0.4) | 0.7 (0.6) | 0.7 (0.4) | 0.9 (0.9) | 0.8 (0.7) |
| median | 0.5 | 0.6 | 0.5 | 0.5 | 0.5 | 0.5 | 0.7 | 0.7 | 0.7 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| [IQR] | [0.3, 0.8] | [0.3, 0.8] | [0.3, 0.8] | [0.4, 0.8] | [0.3, 0.8] | [0.3, 0.8] | [0.2, 1.1] | [0.5, 0.8] | [0.3, 0.8] |
| [range] | [0.0-2.7] | [0.0-2.8] | [0.0-2.8] | [0.0-2.7] | [0.0-1.3] | [0.0-2.7] | [0.2-1.1] | [0.3-2.8] | [0.2-2.8] |
| >=1 | 10 (24%) | 7 (18%) | 17 (21%) | 8 (24%) | 6 (18%) | 14 (21%) | 2 (29%) | 1 (17%) | 3 (23%) |
| <1 | 31 (76%) | 33 (83%) | 64 (79%) | 26 (76%) | 28 (82%) | 54 (79%) | 5 (71%) | 5 (83%) | 10 (77%) |
| missing | 1 | 3 | 4 | 1 | 3 | 4 | 0 | 0 | 0 |
| **Log10 Viral load (copies/mL)**** | | | | | | | | | |
| n | 42 | 38 | 80 | 35 | 32 | 67 | 7 | 6 | 13 |
| mean (SD) | 5.1 (1.0) | 5.1 (1.1) | 5.1 (1.0) | 5.2 (1.0) | 5.3 (1.0) | 5.2 (1.0) | 4.8 (0.7) | 4.1 (1.1) | 4.5 (0.9) |
| median | 5.2 | 5.4 | 5.3 | 5.2 | 5.5 | 5.5 | 4.8 | 4.2 | 4.8 |
| [IQR] | [4.4, 5.8] | [4.8, 5.9] | [4.6, 5.9] | [4.4, 6.0] | [5.0, 5.9] | [4.8, 5.9] | [4.3, 5.2] | [3.3, 4.8] | [4.1, 4.9] |
| [range] | [2.7-6.6] | [2.1-7.0] | [2.1-7.0] | [2.7-6.6] | [2.1-7.0] | [2.1-7.0] | [4.1-6.1] | [2.9-5.6] | [2.9-6.1] |
| **Viral load (copies/mL)**** | | | | | | | | | |
| <400 | 0 ( 0%) | 1 ( 3%) | 1 ( 1%) | 0 ( 0%) | 1 ( 3%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| 400-<1,000 | 2 ( 5%) | 2 ( 5%) | 4 ( 5%) | 2 ( 6%) | 1 ( 3%) | 3 ( 4%) | 0 ( 0%) | 1 (17%) | 1 ( 8%) |
| 1,000-<10,000 | 2 ( 5%) | 4 (11%) | 6 ( 8%) | 2 ( 6%) | 2 ( 6%) | 4 ( 6%) | 0 ( 0%) | 2 (33%) | 2 (15%) |
| 10,000-<50,000 | 9 (21%) | 2 ( 5%) | 11 (14%) | 6 (17%) | 2 ( 6%) | 8 (12%) | 3 (43%) | 0 ( 0%) | 3 (23%) |
| 50,000-<100,000 | 4 (10%) | 3 ( 8%) | 7 ( 9%) | 2 ( 6%) | 1 ( 3%) | 3 ( 4%) | 2 (29%) | 2 (33%) | 4 (31%) |
| 100,000-<500,000 | 12 (29%) | 15 (39%) | 27 (34%) | 11 (31%) | 14 (44%) | 25 (37%) | 1 (14%) | 1 (17%) | 2 (15%) |
| 500,000-<1,000,000 | 5 (12%) | 6 (16%) | 11 (14%) | 5 (14%) | 6 (19%) | 11 (16%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| >=1,000,000 | 8 (19%) | 5 (13%) | 13 (16%) | 7 (20%) | 5 (16%) | 12 (18%) | 1 (14%) | 0 ( 0%) | 1 ( 8%) |
| missing | 0 | 5 | 5 | 0 | 5 | 5 | 0 | 0 | 0 |
| **History of WHO staging** | | | | | | | | | |
| stage1 | 20 (48%) | 16 (37%) | 36 (42%) | 18 (51%) | 14 (38%) | 32 (44%) | 2 (29%) | 2 (33%) | 4 (31%) |
| stage2 | 11 (26%) | 9 (21%) | 20 (24%) | 7 (20%) | 7 (19%) | 14 (19%) | 4 (57%) | 2 (33%) | 6 (46%) |
| stage3 | 6 (14%) | 8 (19%) | 14 (16%) | 6 (17%) | 8 (22%) | 14 (19%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| stage4 | 5 (12%) | 10 (23%) | 15 (18%) | 4 (11%) | 8 (22%) | 12 (17%) | 1 (14%) | 2 (33%) | 3 (23%) |
| **Total cholesterol (mg/dL)** | | | | | | | | | |
| n | 41 | 36 | 77 | 34 | 30 | 64 | 7 | 6 | 13 |
| mean (SD) | 124 ( 41) | 132 ( 32) | 128 ( 37) | 125 ( 38) | 130 ( 33) | 128 ( 36) | 119 ( 57) | 142 ( 26) | 129 ( 45) |
| median | 126 | 139 | 135 | 130 | 137 | 135 | 94 | 155 | 133 |
| [IQR] | [ 93, 148] | [106, 157] | [101, 154] | [ 95, 148] | [104, 154] | [101, 151] | [ 82, 162] | [115, 159] | [ 94, 159] |
| [range] | [ 50-220] | [ 65-188] | [ 50-220] | [ 50-194] | [ 65-188] | [ 50-194] | [ 51-220] | [104-163] | [ 51-220] |
| **Triglycerides (mg/dL)** | | | | | | | | | |
| n | 41 | 36 | 77 | 34 | 30 | 64 | 7 | 6 | 13 |
| mean (SD) | 153 (121) | 166 ( 86) | 159 (106) | 168 (127) | 159 ( 74) | 164 (105) | 81 ( 47) | 204 (134) | 137 (113) |
| median | 127 | 150 | 146 | 140 | 150 | 149 | 63 | 160 | 126 |
| [IQR] | [ 75, 181] | [112, 194] | [ 82, 181] | [ 80, 192] | [110, 177] | [ 94, 189] | [ 39, 141] | [126, 225] | [ 63, 149] |
| [range] | [ 29-642] | [ 58-462] | [ 29-642] | [ 35-642] | [ 58-408] | [ 35-642] | [ 29-147] | [ 90-462] | [ 29-462] |
| **HDL cholesterol (mg/dL)** | | | | | | | | | |
| n | 34 | 33 | 67 | 27 | 27 | 54 | 7 | 6 | 13 |
| mean (SD) | 35 ( 14) | 33 ( 15) | 34 ( 15) | 34 ( 15) | 35 ( 16) | 34 ( 15) | 39 ( 15) | 28 ( 7) | 34 ( 13) |
| median | 34 | 35 | 35 | 33 | 39 | 36 | 40 | 28 | 32 |
| [IQR] | [ 24, 43] | [ 24, 43] | [ 24, 43] | [ 20, 43] | [ 24, 44] | [ 24, 43] | [ 30, 52] | [ 21, 35] | [ 24, 40] |
| [range] | [ 8- 60] | [ 4- 67] | [ 4- 67] | [ 8- 58] | [ 4- 67] | [ 4- 67] | [ 16- 60] | [ 18- 36] | [ 16- 60] |
| **LDL cholesterol (mg/dL)** | | | | | | | | | |
| n | 37 | 35 | 72 | 30 | 29 | 59 | 7 | 6 | 13 |
| mean (SD) | 71 ( 32) | 69 ( 31) | 70 ( 31) | 72 ( 28) | 67 ( 31) | 69 ( 29) | 67 ( 49) | 77 ( 32) | 72 ( 41) |
| median | 65 | 75 | 68 | 68 | 75 | 69 | 46 | 76 | 51 |
| [IQR] | [ 48, 84] | [ 39, 91] | [ 46, 89] | [ 54, 84] | [ 39, 89] | [ 47, 88] | [ 33, 100] | [ 51, 107] | [ 44, 100] |
| [range] | [ 18-166] | [ 7-128] | [ 7-166] | [ 18-145] | [ 7-128] | [ 7-145] | [ 30-166] | [ 35-119] | [ 30-166] |
| **PMTCT Exposure** | | | | | | | | | |
| No | 19 (45%) | 23 (53%) | 42 (49%) | 16 (46%) | 22 (59%) | 38 (53%) | 3 (43%) | 1 (17%) | 4 (31%) |
| Yes | 22 (52%) | 16 (37%) | 38 (45%) | 18 (51%) | 13 (35%) | 31 (43%) | 4 (57%) | 3 (50%) | 7 (54%) |
| Not Known | 1 ( 2%) | 4 ( 9%) | 5 ( 6%) | 1 ( 3%) | 2 ( 5%) | 3 ( 4%) | 0 ( 0%) | 2 (33%) | 2 (15%) |

*WHO Child Growth Charts and WHO Reference 2007 Charts, version WHO. Metrics are considered missing if height-for-age is <-6/>6, weight-for-age <-6/>5, BMI for age <-5/>5.

+One participant was randomised at 9.7kg; site indicated that they would be dosed as 10-<14kg and therefore they were stratified in this weight-band but are included here according to their actual weight.
**Mean of measurement at screening and randomisation if both are available

## S7.2 Baseline characteristics: Antiretroviral exposure [ODYSSEY B Only]

| | B | | | | | |
|---|---|---|---|---|---|---|
| | **DTG** | | **SOC** | | **Total** | |
| **Participants randomised** | 7 | | 6 | | 13 | |
| **Number of different drugs ever received excluding PMTCT, median [range]** | | | | | | |
| n | 7 | | 6 | | 13 | |
| All classes | 3.0 | [3.0-3.0] | 3.0 | [1.0-3.0] | 3.0 | [1.0-3.0] |
| NRTI | 2.0 | [2.0-2.0] | 2.0 | [0.0-2.0] | 2.0 | [0.0-2.0] |
| NNRTI | 1.0 | [0.0-1.0] | 0.5 | [0.0-1.0] | 1.0 | [0.0-1.0] |
| PI | 0.0 | [0.0-1.0] | 0.5 | [0.0-1.0] | 0.0 | [0.0-1.0] |
| **ART Class Exposure+** | | | | | | |
| Monotherapy | 0 | ( 0%) | 1 | (17%) | 1 | ( 8%) |
| NRTI/NNRTI | 5 | (71%) | 2 | (33%) | 7 | (54%) |
| NRTI/PIs | 2 | (29%) | 3 | (50%) | 5 | (38%) |
| missing | 0 | | 0 | | 0 | |
| **Cumulative ART exposure (years), median [range]** | | | | | | |
| n | 7 | | 6 | | 13 | |
| All classes | 1.6 | [1.4-3.0] | 1.5 | [1.1-1.9] | 1.6 | [1.1-3.0] |
| NRTI | 1.6 | [1.4-3.0] | 1.5 | [0.0-1.9] | 1.6 | [0.0-3.0] |
| NNRTI | 1.4 | [0.0-3.0] | 0.5 | [0.0-1.7] | 1.4 | [0.0-3.0] |
| PI | 0.0 | [0.0-1.8] | 0.7 | [0.0-1.9] | 0.0 | [0.0-1.9] |
| **ART Regimen Class Prior to Randomisation+** | | | | | | |
| Monotherapy | 0 | ( 0%) | 1 | (17%) | 1 | ( 8%) |
| NRTI/NNRTI | 5 | (71%) | 2 | (33%) | 7 | (54%) |
| NRTI/PIs | 2 | (29%) | 3 | (50%) | 5 | (38%) |
| missing | 0 | | 0 | | 0 | |

+Site confirms that NVP was used as a monotherapy prior to the start of ODYSSEY for one participant.

# S8 Efficacy

## S8.1 Comparison of proportion with clinical or virological failure by 48 weeks

| | Total | | | A | | | B | | |
|---|---|---|---|---|---|---|---|---|---|
| | **DTG** | **SOC** | **DTG vs. SOC** | **DTG** | **SOC** | **DTG vs. SOC** | **DTG** | **SOC** | **DTG vs. SOC** |
| **Participants randomised** | 42 | 43 | | 35 | 37 | | 7 | 6 | |
| **Total participants meeting primary endpoint** | 7 (17%) | 15 (35%) | | 4 (11%) | 13 (35%) | | 3 (43%) | 2 (33%) | |
| Insufficient virological response | 0 (0%) | 0 (0%) | | 0 (0%) | 0 (0%) | | 0 (0%) | 0 (0%) | |
| Confirmed VL>=400 copies/mL | 4 (10%) | 11 (26%) | | 2 ( 6%) | 9 (24%) | | 2 (29%) | 2 (33%) | |
| Severe WHO 3 | 0 (0%) | 0 (0%) | | 0 (0%) | 0 (0%) | | 0 (0%) | 0 (0%) | |
| WHO 4 | 1 ( 2%) | 1 ( 2%) | | 0 ( 0%) | 1 ( 3%) | | 1 (14%) | 0 ( 0%) | |
| Death | 2 ( 5%) | 3 ( 7%) | | 2 ( 6%) | 3 ( 8%) | | 0 ( 0%) | 0 ( 0%) | |
| **Unadjusted estimated probability of failure** | 0.18 | 0.34 | | 0.13 | 0.34 | | 0.44 | 0.33 | |
| [95%CI] | [0.08, 0.37] | [0.22, 0.50] | | [0.01, 0.89] | [0.21, 0.52] | | [0.01, 1.00] | [0.00, 1.00] | |
| Difference (DTG-SOC) | | | -0.16 | | | -0.22 | | | 0.11 |
| [95%CI] | | | [-0.32, 0.01] | | | [-0.40, -0.03] | | | [-0.44, 0.57] |
| P-value** | | | 0.070 | | | 0.023 | | | 0.65 |
| **Adjusted* estimated probability of failure** | 0.18 | 0.34 | | | | | | | |
| [95%CI] | [0.07, 0.44] | [0.22, 0.50] | | | | | | | |
| Difference (DTG-SOC) | | | -0.16 | | | | | | |
| [95%CI] | | | [-0.35, -0.00] | | | | | | |
| P-value** | | | 0.063 | | | | | | |
| **A/B x arm interaction+** | 0.21 | | | | | . | | | |

*Adjusted for ODYSSEY A and B strata only in Total. Analysis conducted using same approach as analysis of primary endpoint at 96 weeks in <14kg cohort (see S3.2 statistical methods)
+Z-test

## S8.2 Incidence of clinical or virological failure by 48 weeks

| | Total | | | A | | | B | | |
|---|---|---|---|---|---|---|---|---|---|
| | **DTG** | **SOC** | **DTG vs SOC** | **DTG** | **SOC** | **DTG vs SOC** | **DTG** | **SOC** | **DTG vs SOC** |
| **Participants randomised** | 42 | 43 | | 35 | 37 | | 7 | 6 | |
| **Total participants meeting primary endpoint** | 7 (17%) | 15 (35%) | | 4 (11%) | 13 (35%) | | 3 (43%) | 2 (33%) | |
| **Person years** | 35 | 36 | | 29 | 31 | | 6 | 6 | |
| **Event rate (per 100 person years)** | 20 | 42 | | 14 | 43 | | 53 | 36 | |
| (95% CI) | ( 9, 42) | (25, 69) | | ( 5, 36) | (25, 73) | | (17, 163) | ( 9, 145) | |
| **Unadjusted Hazard ratio** | | | 0.48 | | | 0.32 | | | 1.46 |
| (95% CI) | | | (0.20, 1.19) | | | (0.11, 0.99) | | | (0.24, 8.71) |
| P-value | | | 0.11 | | | 0.048 | | | 0.68 |
| **Adj. hazard ratio*** | | | 0.48 | | | | | | |
| (95% CI) | | | (0.20, 1.18) | | | | | | |
| P-value | | | 0.11 | | | | | | |
| **A/B x arm interaction+** | 0.16 | | | | | | | | |

*Adjusted for ODYSSEY A and B strata only in Total.

+Z-test

Note: Hazard ratios from Cox regression models presented as an alternative analysis to the comparison of proportion with clinical or virological failure (see table above)

## S8.3 Comparison of proportion with clinical or virological failure by 96 weeks

| | Total | | | A | | | B | | |
|---|---|---|---|---|---|---|---|---|---|
| | **DTG** | **SOC** | **DTG vs. SOC** | **DTG** | **SOC** | **DTG vs. SOC** | **DTG** | **SOC** | **DTG vs. SOC** |
| **Participants randomised** | 42 | 43 | | 35 | 37 | | 7 | 6 | |
| **Total participants meeting primary endpoint** | 12 (29%) | 21 (49%) | | 9 (26%) | 17 (46%) | | 3 (43%) | 4 (67%) | |
| Insufficient virological response | 0 (0%) | 0 (0%) | | 0 (0%) | 0 (0%) | | 0 (0%) | 0 (0%) | |
| Confirmed VL>=400 copies/mL | 9 (21%) | 16 (37%) | | 7 (20%) | 13 (35%) | | 2 (29%) | 3 (50%) | |
| Severe WHO 3 | 0 (0%) | 0 (0%) | | 0 (0%) | 0 (0%) | | 0 (0%) | 0 (0%) | |
| WHO 4 | 1 ( 2%) | 1 ( 2%) | | 0 ( 0%) | 1 ( 3%) | | 1 (14%) | 0 ( 0%) | |
| Death | 2 ( 5%) | 4 ( 9%) | | 2 ( 6%) | 3 ( 8%) | | 0 ( 0%) | 1 (17%) | |
| **Unadjusted estimated probability of failure** | 0.31 | 0.48 | | 0.27 | 0.46 | | 0.48 | 0.60 | |
| [95%CI] | [0.19, 0.48] | [0.35, 0.63] | | [0.15, 0.47] | [0.32, 0.63] | | [0.01, 1.00] | [0.17, 0.99] | |
| Difference (DTG-SOC) | | | -0.18 | | | -0.19 | | | -0.12 |
| [95%CI] | | | [-0.37, 0.01] | | | [-0.41, 0.01] | | | [-0.61, 0.37] |
| P-value** | | | 0.071 | | | 0.079 | | | 0.61 |
| **Adjusted* estimated probability of failure** | 0.31 | 0.48 | | | | | | | |
| [95%CI] | [0.18, 0.48] | [0.35, 0.63] | | | | | | | |
| Difference (DTG-SOC) | | | -0.18 | | | | | | |
| [95%CI] | | | [-0.36, 0.02] | | | | | | |
| P-value** | | | 0.057 | | | | | | |
| **A/B x arm interaction+** | 0.81 | | | | | . | | | |

*Adjusted for ODYSSEY A and B strata only in Total. Analysis conducted of primary endpoint in <14kg cohort at 96 weeks (see S3.2 statistical methods)

+Z-test

## S8.4 Incidence of clinical or virological failure by 96 weeks (alternative approach to analysis of primary endpoint)

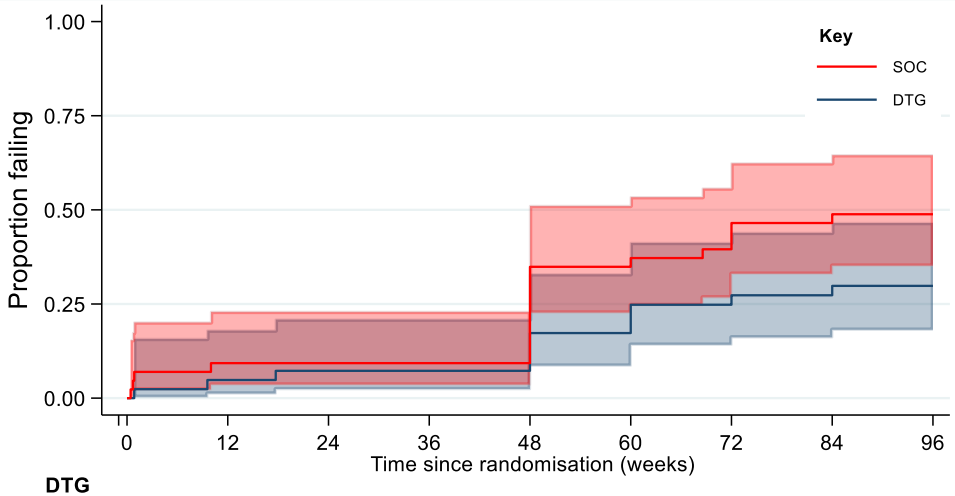
| | Total | | | A | | | B | | |
|---|---|---|---|---|---|---|---|---|---|
| | **DTG** | **SOC** | **DTG vs SOC** | **DTG** | **SOC** | **DTG vs SOC** | **DTG** | **SOC** | **DTG vs SOC** |
| **Participants randomised** | 42 | 43 | | 35 | 37 | | 7 | 6 | |
| **Total participants meeting primary endpoint** | 12 (29%) | 21 (49%) | | 9 (26%) | 17 (46%) | | 3 (43%) | 4 (67%) | |
| **Person years** | 63 | 59 | | 53 | 51 | | 9 | 8 | |
| **Event rate (per 100 person years)** | 19 | 36 | | 17 | 33 | | 32 | 49 | |
| (95% CI) | (11, 34) | (23, 55) | | ( 9, 32) | (21, 54) | | (10, 99) | (18, 130) | |
| **Unadjusted Hazard ratio** | | | 0.55 | | | 0.52 | | | 0.70 |
| (95% CI) | | | (0.27, 1.13) | | | (0.23, 1.16) | | | (0.16, 3.15) |
| P-value | | | 0.10 | | | 0.11 | | | 0.65 |
| **Adj. hazard ratio*** | | | 0.55 | | | | | | |
| (95% CI) | | | (0.27, 1.12) | | | | | | |
| P-value | | | 0.10 | | | | | | |
| **A/B x arm interaction+** | 0.74 | | | | | | | | |

*Adjusted for ODYSSEY A and B strata only in Total.

+Z-test

Note: Hazard ratios from Cox regression models presented as an alternative analysis to the comparison of proportion with clinical or virological failure (see table above)

## S8.5 Time to clinical or virological failure




| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **DTG** | | | | | | | | | |
| At-risk (no event) | 42 | 39 | 38 | 37 | 33 | 30 | 29 | 28 | 28 |
| Censored | 0 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 |
| Event | 0 | 2 | 3 | 3 | 7 | 10 | 11 | 12 | 12 |
| **SOC** | | | | | | | | | |
| At-risk (no event) | 43 | 39 | 39 | 39 | 28 | 27 | 23 | 22 | 22 |
| Censored | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Event | 0 | 4 | 4 | 4 | 15 | 16 | 20 | 21 | 21 |

HR=0.55 (0.27, 1.12) p=0.10 log rank p=0.081

## S8.6 Comparison of proportion with clinical or virological failure by 96 weeks

| | Analysis | Difference (DTG-SOC) | | p-value* |
|---|---|---|---|---|
| Difference (DTG-SOC) [95%CI] | <14kg Bayesian Analysis | -0.102 | [-0.187,-0.016] | 0.020 |
| | <14kgs | -0.177 | [-0.356,0.023] | 0.057 |
| | ≥14kgs | -0.080 | [-0.142,-0.031] | 0.0039 |
| | Pooled Analysis | -0.092 | [-0.144,-0.034] | 0.0010 |
| Test of Heterogeneity between above and below 14kgs | P-Value | 0.32 | | |

*bootstrapped p-values in <14kgs, ≥14kgs, and pooled analyses; z test for significance of the effect size in <14kg Bayesian analysis

## S8.7 Comparison of proportion of participants with HIV-1 RNA <50c/ml at 48 weeks

| | | Total | | A | | B | |
|---|---|---|---|---|---|---|---|
| | | **DTG** | **SOC** | **DTG** | **SOC** | **DTG** | **SOC** |
| **Participants randomised** | | 42 | 43 | 35 | 37 | 7 | 6 |
| HIV-1 RNA <50c/mL at 48 weeks | | 15 | 19 | 12 | 18 | 3 | 1 |
| HIV-1 RNA >=50c/mL at 48 weeks | | 19 | 20 | 15 | 15 | 4 | 5 |
| **Unadjusted** | Proportion<50c/mL | 44 | 49 | 44 | 55 | 43 | 17 |
| | [95%Confidence Interval] | [28, 61] | [33, 65] | [27, 64] | [37, 71] | [10, 83] | [ 1, 77] |
| | Treatment Difference (DTG-SOC) | -5 | | -10 | | 26 | |
| | [95% Confidence Interval] | [-28, 18] | | [-35, 15] | | [-21, 73] | |
| | P-value+ | 0.69 | | 0.44 | | 0.31 | |
| **Adjusted#** | Estimated Difference (DTG-SOC) | -4 | | | | | |
| | [95% Confidence Interval] | [-26, 19] | | | | | |
| | P-value | 0.76 | | | | | |

+P-value for total population and A/B stratum-specific p-values derived from chi-squared test

#Logistic regression adjusted for ODYSSEY A and B strata. Difference between arms in proportion is marginal risk difference from logistic regression model

## S8.8 Comparison of proportion of participants with HIV-1 RNA <400c/ml at 48 weeks

| | | Total | | A | | B | |
|---|---|---|---|---|---|---|---|
| | | **DTG** | **SOC** | **DTG** | **SOC** | **DTG** | **SOC** |
| **Participants randomised** | | 42 | 43 | 35 | 37 | 7 | 6 |
| HIV-1 RNA <400c/mL at 48 weeks | | 25 | 27 | 21 | 23 | 4 | 4 |
| HIV-1 RNA >=400c/mL at 48 weeks | | 9 | 12 | 6 | 10 | 3 | 2 |
| | [95%Confidence Interval] | [56, 86] | [53, 82] | [57, 90] | [52, 83] | [17, 90] | [18, 95] |
| | Treatment Difference (DTG-SOC) | 4 | | 8 | | -10 | |
| | [95% Confidence Interval] | [-16, 25] | | [-14, 30] | | [-62, 43] | |
| | P-value+ | 0.69 | | 0.48 | | 0.72 | |
| **Adjusted#** | Estimated Difference (DTG-SOC) | 5 | | | | | |
| | [95% Confidence Interval] | [-16, 26] | | | | | |
| | P-value | 0.64 | | | | | |

+P-value for total population and A/B stratum-specific p-values derived from chi-squared test

#Logistic regression adjusted for ODYSSEY A and B strata. Difference between arms in proportion is marginal risk difference from logistic regression model

## S8.9 Comparison of proportion of participants with HIV-1 RNA <50c/ml at 96 weeks

| | | Total | | A | | B | |
|---|---|---|---|---|---|---|---|
| | | **DTG** | **SOC** | **DTG** | **SOC** | **DTG** | **SOC** |
| **Participants randomised** | | 42 | 43 | 35 | 37 | 7 | 6 |
| HIV-1 RNA <50c/mL at 96 weeks | | 27 | 19 | 23 | 18 | 4 | 1 |
| HIV-1 RNA >=50c/mL at 96 weeks | | 8 | 17 | 5 | 13 | 3 | 4 |
| | [95%Confidence Interval] | [60, 88] | [36, 69] | [63, 93] | [40, 74] | [17, 90] | [ 1, 85] |
| | Treatment Difference (DTG-SOC) | 24 | | 24 | | 37 | |
| | [95% Confidence Interval] | [ 3, 46] | | [ 2, 47] | | [-14, 88] | |
| | P-value+ | 0.032 | | 0.045 | | 0.20 | |
| **Adjusted#** | Estimated Difference (DTG-SOC) | 26 | | | | | |
| | [95% Confidence Interval] | [ 6, 47] | | | | | |
| | P-value | 0.021 | | | | | |

+P-value for total population and A/B stratum-specific p-values derived from chi-squared test

#Logistic regression adjusted for ODYSSEY A and B strata. Difference between arms in proportion is marginal risk difference from logistic regression model

## S8.10 Comparison of proportion of participants with HIV-1 RNA <400 c/ml at 96 weeks

| | | Total | | A | | B | |
|---|---|---|---|---|---|---|---|
| | | **DTG** | **SOC** | **DTG** | **SOC** | **DTG** | **SOC** |
| **Participants randomised** | | 42 | 43 | 35 | 37 | 7 | 6 |
| HIV-1 RNA <400c/mL at 96 weeks | | 33 | 26 | 26 | 23 | 7 | 3 |
| HIV-1 RNA >=400c/mL at 96 weeks | | 3 | 10 | 3 | 8 | 0 | 2 |
| **Unadjusted** | Proportion<400c/mL | 92 | 72 | 90 | 74 | 100 | 60 |
| | [95%Confidence Interval] | [76, 97] | [55, 85] | [71, 97] | [55, 87] | [ ., .] | [11, 95] |
| | Treatment Difference (DTG-SOC) | 19 | | 15 | | 40 | |
| | [95% Confidence Interval] | [ 2, 37] | | [-4, 34] | | [-3, 83] | |
| | P-value+ | 0.032 | | 0.12 | | 0.067 | |
| **Adjusted#** | Estimated Difference (DTG-SOC) | 19 | | | | | |
| | [95% Confidence Interval] | [ 2, 37] | | | | | |
| | P-value | 0.038 | | | | | |

+P-value for total population and A/B stratum-specific p-values derived from chi-squared test

#Logistic regression adjusted for ODYSSEY A and B strata. Difference between arms in proportion is marginal risk difference from logistic regression model

## S8.11 FDA snapshot algorithm - comparison of proportion of participants with HIV-1 RNA <50c/ml at 48 weeks

| | | Total | | A | | B | |
|---|---|---|---|---|---|---|---|
| | | **DTG** | **SOC** | **DTG** | **SOC** | **DTG** | **SOC** |
| **Participants randomised** | | 42 | 43 | 35 | 37 | 7 | 6 |
| **HIV-RNA<50 c/ml (Total participants)** | | 15 | 19 | 12 | 18 | 3 | 1 |
| | Proportion | 36% | 44% | 34% | 49% | 43% | 17% |
| | Treatment difference (DTG-SOC) | -8 | | -14 | | 26 | |
| | [95% Confidence Interval] | [-29, 12] | | [-37, 8] | | [-21, 73] | |
| | Unadjusted P-value+ | 0.43 | | 0.22 | | 0.31 | |
| | Adjusted p-value# | 0.44 | | | | | |
| **HIV-RNA>=50 c/ml (Total participants)** | | 19 | 20 | 15 | 15 | 4 | 5 |
| | Proportion | 45% | 47% | 43% | 41% | 57% | 83% |
| | Treatment difference (DTG-SOC) | -1 | | 2 | | -26 | |
| | [95% Confidence Interval] | [-22, 20] | | [-20, 25] | | [-73, 21] | |
| | Unadjusted P-value+ | 0.91 | | 0.84 | | 0.31 | |
| | Adjusted p-value# | 0.85 | | | | | |
| Components of HIV-RNA>=50 c/ml | | | | | | | |
| | HIV-RNA >=50 c/ml - in window | 18 | 20 | 14 | 15 | 4 | 5 |
| | VL>=50 c/ml prior to permitted switch or LTFU | 1 | 0 | 1 | 0 | 0 | 0 |
| **Missing VL in week 48 window (Total participants)** | | 8 | 4 | 8 | 4 | 0 | 0 |
| | Proportion | 19% | 9% | 23% | 11% | 0% | 0% |
| | VL<50 c/ml prior to permitted switch or LTFU | 1 | 0 | 1 | 0 | 0 | 0 |
| | On non-permitted ART due to toxicity or died | 2 | 3 | 2 | 3 | 0 | 0 |
| | Initial regimen but no VL in window | 5 | 1 | 5 | 1 | 0 | 0 |

+P-value for total population and A/B stratum-specific p-values derived from chi-squared test
#Logistic regression p-value adjusted for ODYSSEY A and B strata

## S8.12 FDA snapshot algorithm - comparison of proportion of participants with HIV-1 RNA <400 c/ml at 48 weeks

| | | Total | | A | | B | |
|---|---|---|---|---|---|---|---|
| | | **DTG** | **SOC** | **DTG** | **SOC** | **DTG** | **SOC** |
| **Participants randomised** | | 42 | 43 | 35 | 37 | 7 | 6 |
| **HIV-RNA<400 c/ml (Total participants)** | | 25 | 27 | 21 | 23 | 4 | 4 |
| | Proportion | 60% | 63% | 60% | 62% | 57% | 67% |
| | Treatment difference (DTG-SOC) | -3 | | -2 | | -10 | |
| | [95% Confidence Interval] | [-24, 17] | | [-25, 20] | | [-62, 43] | |
| | Unadjusted P-value+ | 0.76 | | 0.85 | | 0.72 | |
| | Adjusted p-value# | .76 | | | | | |
| **HIV-RNA>=400 c/ml (Total participants)** | | 9 | 12 | 6 | 10 | 3 | 2 |
| | Proportion | 21% | 28% | 17% | 27% | 43% | 33% |
| | Treatment difference (DTG-SOC) | -6 | | -10 | | 10 | |
| | [95% Confidence Interval] | [-25, 12] | | [-29, 9] | | [-43, 62] | |
| | Unadjusted P-value+ | 0.49 | | 0.31 | | 0.72 | |
| | Adjusted p-value# | 0.46 | | | | | |
| Components of HIV-RNA>=400 c/ml | | | | | | | |
| | HIV-RNA >=400 c/ml - in window | 8 | 12 | 5 | 10 | 3 | 2 |
| | VL>=400 c/ml prior to permitted switch or LTFU | 1 | 0 | 1 | 0 | 0 | 0 |
| **Missing VL in week 48 window (Total participants)** | | 8 | 4 | 8 | 4 | 0 | 0 |
| | Proportion | 19% | 9% | 23% | 11% | 0% | 0% |
| | VL<400 c/ml prior to permitted switch or LTFU | 1 | 0 | 1 | 0 | 0 | 0 |
| | On non-permitted ART due to toxicity or died | 2 | 3 | 2 | 3 | 0 | 0 |
| | Initial regimen but no VL in window | 5 | 1 | 5 | 1 | 0 | 0 |

+P-value for total population and A/B stratum-specific p-values derived from chi-squared test
#Logistic regression p-value adjusted for ODYSSEY A and B strata

## S8.13 FDA snapshot algorithm - comparison of proportion of participants with HIV-1 RNA <50 c/ml at 96 weeks

| | | Total | | A | | B | |
|---|---|---|---|---|---|---|---|
| | | **DTG** | **SOC** | **DTG** | **SOC** | **DTG** | **SOC** |
| **Participants randomised** | | 42 | 43 | 35 | 37 | 7 | 6 |
| **HIV-RNA<50 c/ml (Total participants)** | | 27 | 18 | 23 | 17 | 4 | 1 |
| | Proportion | 64% | 42% | 66% | 46% | 57% | 17% |
| | Treatment difference (DTG-SOC) | 22 | | 20 | | 40 | |
| | [95% Confidence Interval] | [ 2, 43] | | [-3, 42] | | [-7, 88] | |
| | Unadjusted P-value+ | 0.038 | | 0.092 | | 0.13 | |
| | Adjusted p-value# | 0.035 | | | | | |
| **HIV-RNA>=50 c/ml (Total participants)** | | 8 | 18 | 6 | 14 | 2 | 4 |
| | Proportion | 19% | 42% | 17% | 38% | 29% | 67% |
| | Treatment difference (DTG-SOC) | -23 | | -21 | | -38 | |
| | [95% Confidence Interval] | [-42, -4] | | [-41, -1] | | [-89, 12] | |
| | Unadjusted P-value+ | 0.022 | | 0.050 | | 0.17 | |
| | Adjusted p-value# | 0.021 | | | | | |
| Components of HIV-RNA>=50 c/ml | | | | | | | |
| | HIV-RNA >=50 c/ml - in window | 7 | 12 | 5 | 9 | 2 | 3 |
| | Non-permitted ART (other than toxicity) | 0 | 5 | 0 | 4 | 0 | 1 |
| | VL>=50 c/ml prior to permitted switch or LTFU | 1 | 1 | 1 | 1 | 0 | 0 |
| **Missing VL in week 96 window (Total participants)** | | 7 | 7 | 6 | 6 | 1 | 1 |
| | Proportion | 17% | 16% | 17% | 16% | 14% | 17% |
| | VL<50 c/ml prior to permitted switch or LTFU | 2 | 0 | 2 | 0 | 0 | 0 |
| | On non-permitted ART due to toxicity or died | 2 | 4 | 2 | 3 | 0 | 1 |
| | Initial regimen but no VL in window | 3 | 3 | 2 | 3 | 1 | 0 |

+P-value for total population and A/B stratum-specific p-values derived from chi-squared test

#Logistic regression p-value adjusted for ODYSSEY A and B strata

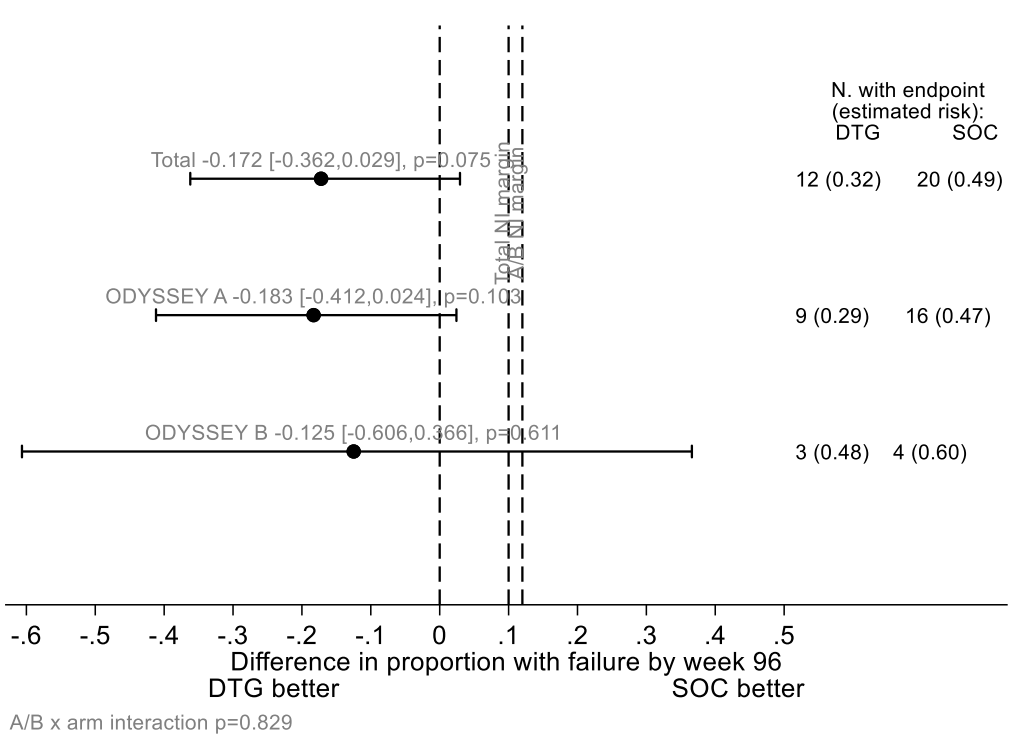
## S8.14 FDA snapshot algorithm - comparison of proportion of participants with HIV-1 RNA <400 c/ml at 96 weeks

| | | Total | | A | | B | |
|---|---|---|---|---|---|---|---|
| | | **DTG** | **SOC** | **DTG** | **SOC** | **DTG** | **SOC** |
| **Participants randomised** | | 42 | 43 | 35 | 37 | 7 | 6 |
| **HIV-RNA<400 c/ml (Total participants)** | | 32 | 22 | 26 | 20 | 6 | 2 |
| | Proportion | 76% | 51% | 74% | 54% | 86% | 33% |
| | Treatment difference (DTG-SOC) | 25 | | 20 | | 52 | |
| | [95% Confidence Interval] | [ 5, 45] | | [-1, 42] | | [ 7, 98] | |
| | Unadjusted P-value+ | .017 | | .074 | | .053 | |
| | Adjusted p-value# | .018 | | | | | |
| **HIV-RNA>=400 c/ml (Total participants)** | | 4 | 14 | 4 | 11 | 0 | 3 |
| | Proportion | 10% | 33% | 11% | 30% | 0% | 50% |
| | Treatment difference (DTG-SOC) | -23 | | -18 | | -50 | |
| | [95% Confidence Interval] | [-40, -6] | | [-36, -0] | | [-90, -10] | |
| | Unadjusted P-value+ | 0.0094 | | 0.056 | | 0.033 | |
| | Adjusted p-value# | 0.013 | | | | | |
| Components of HIV-RNA>=400 c/ml | | | | | | | |
| | HIV-RNA >=400 c/ml - in window | 3 | 8 | 3 | 6 | 0 | 2 |
| | Non-permitted ART (other than toxicity) | 0 | 5 | 0 | 4 | 0 | 1 |
| | VL>=400 c/ml prior to permitted switch or LTFU | 1 | 1 | 1 | 1 | 0 | 0 |
| **Missing VL in week 96 window (Total participants)** | | 6 | 7 | 5 | 6 | 1 | 1 |
| | Proportion | 14% | 16% | 14% | 16% | 14% | 17% |
| | VL<400 c/ml prior to permitted switch or LTFU | 2 | 0 | 2 | 0 | 0 | 0 |
| | On non-permitted ART due to toxicity or died | 2 | 4 | 2 | 3 | 0 | 1 |
| | Initial regimen but no VL in window | 2 | 3 | 1 | 3 | 1 | 0 |

+P-value for total population and A/B stratum-specific p-values derived from chi-squared test

#Logistic regression p-value adjusted for ODYSSEY A and B strata

## S8.15 Per-protocol analysis




Note: 1 participant was censored prior to meeting the primary endpoint due to ART discontinuation for >31days.

## S8.16 Total population - Subgroup analyses for primary endpoint

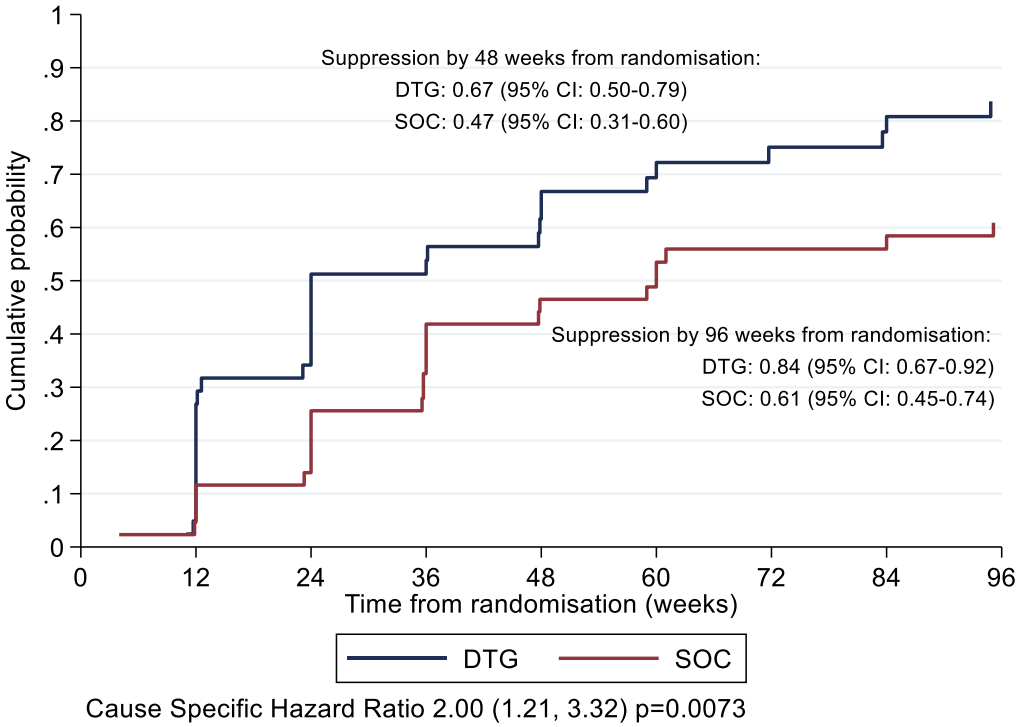
| | DTG | | | | SOC | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Participants randomised** | **Total participants meeting primary endpoint** | **Person-years** | **Event rate (95% CI)** | **Participants randomised** | **Total participants meeting primary endpoint** | **Person-years** | **Event rate (95% CI)** | **Hazard ratio (95% CI)** | **p-value** | **Adjusted hazard ratio (95% CI)** | **p-value** | **p-value (interaction)** |
| **Age at baseline** | | | | | | | | | | | | | |
| <1 year | 16 | 4 (25.0%) | 26 | 15.2 (5.7, 40.5) | 16 | 11 (68.8%) | 18 | 62.2 (34.4, 112.3) | 0.26 (0.08, 0.82) | 0.022 | 0.26 (0.08, 0.82) | 0.021 | 0.11 |
| >=1 year | 26 | 8 (30.8%) | 36 | 22.0 (11.0, 43.9) | 27 | 10 (37.0%) | 41 | 24.2 (13.0, 44.9) | 0.92 (0.36, 2.32) | 0.85 | 0.87 (0.34, 2.22) | 0.77 | |

## S8.17 ODYSSEY A - Subgroup analyses for primary endpoint

| | DTG | | | | SOC | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Participants randomised** | **Total participants meeting primary endpoint** | **Person-years** | **Event rate (95% CI)** | **Participants randomised** | **Total participants meeting primary endpoint** | **Person-years** | **Event rate (95% CI)** | **Hazard ratio (95% CI)** | **p-value** | **p-value (interaction)** |
| **Age at baseline** | | | | | | | | | | | |
| <1 year | 16 | 4 (25.0%) | 26 | 15.2 (5.7, 40.5) | 16 | 11 (68.8%) | 18 | 62.2 (34.4, 112.3) | 0.26 (0.08, 0.81) | 0.021 | 0.10 |
| >=1 year | 19 | 5 (26.3%) | 27 | 18.5 (7.7, 44.5) | 21 | 6 (28.6%) | 33 | 18.1 (8.1, 40.3) | 1.02 (0.31, 3.34) | 0.98 | |

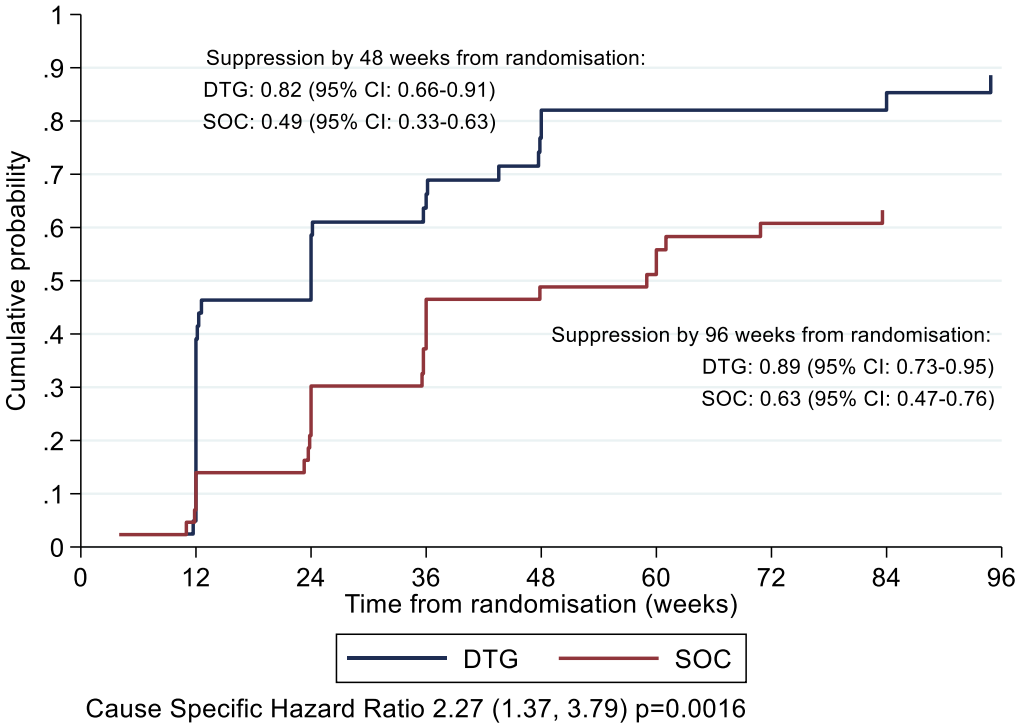
Please note no participants in ODYSSEY B were <1 year at baseline.

**S8.18 Cumulative probability of suppression by treatment group (suppression defined as two consecutive viral loads <200cp/ml)**




Suppression defined as two consecutive viral loads <200c/mL. Treating switch from initial trial regimen or switch in backbone for failure and death as competing risks

**S8.19 Cumulative probability of suppression by treatment group (suppression defined as two consecutive viral loads <400cp/ml)**




Suppression defined as two consecutive viral loads <400c/mL. Treating switch from initial trial regimen or switch in backbone for failure and death as competing risks

## S8.20 Rate of clinical events to trial censoring date: WHO 4, severe WHO 3 and death

| | Total | | | A | | | B | | |
|---|---|---|---|---|---|---|---|---|---|
| | **DTG** | **SOC** | **Total** | **DTG** | **SOC** | **Total** | **DTG** | **SOC** | **Total** |
| **Participants randomised and included** | 42 | 43 | 85 | 35 | 37 | 72 | 7 | 6 | 13 |
| Person years | 93 | 95 | 188 | 76 | 81 | 156 | 18 | 14 | 32 |
| **Total number of events [Number of participants]** | 3 [3] | 6 [6] | 9 [9] | 2 [2] | 5 [5] | 7 [7] | 1 [1] | 1 [1] | 2 [2] |
| Severe WHO 3 | 0 [0] | 0 [0] | 0 [0] | 0 [0] | 0 [0] | 0 [0] | 0 [0] | 0 [0] | 0 [0] |
| WHO 4 | 1 [1] | 2 [2] | 3 [3] | 0 [0] | 2 [2] | 2 [2] | 1 [1] | 0 [0] | 1 [1] |
| Death | 2 [2] | 4 [4] | 6 [6] | 2 [2] | 3 [3] | 5 [5] | 0 [0] | 1 [1] | 1 [1] |
| **Number of events [Number of children]** | | | | | | | | | |
| **Infectious Disease** | 0 [0] | 5 [5] | 5 [5] | 0 [0] | 4 [4] | 4 [4] | 0 [0] | 1 [1] | 1 [1] |
| Gastroenteritis * | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] | 0 [0] | 1 [1] | 1 [1] |
| Pneumonia no organism identified, aspiration pneumonia * | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Tuberculosis - abdominal | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Tuberculosis - disseminated/miliary | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Tuberculosis - pulmonary - smear negative or not done+Severe malnutrition * | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| **Non HIV related deaths** | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Traumatic * | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| **Systemic** | 2 [2] | 1 [1] | 3 [3] | 1 [1] | 1 [1] | 2 [2] | 1 [1] | 0 [0] | 1 [1] |
| Chest infection+Severe malnutrition | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] | 1 [1] | 0 [0] | 1 [1] |
| Kwashiorkor * | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Severe malnutrition * | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| **Event rate (all events)** | | | | | | | | | |
| Event rate (per 100 person years) | 3.2 | 6.3 | 4.8 | 2.6 | 6.2 | 4.5 | 5.6 | 7.1 | 6.3 |
| (95% CI) | (1.0, 10.0) | (2.8, 14.1) | (2.5, 9.2) | (0.7, 10.6) | (2.6, 14.9) | (2.1, 9.4) | (0.8, 40.0) | (1.0, 50.2) | (1.6, 25.1) |
| Unadjusted Rate ratio | 0.51 | 1 (ref) | | 0.43 | 1 (ref) | | 0.80 | 1 (ref) | |
| (95% CI) | (0.12, 2.07) | - | | (0.08, 2.32) | - | | (0.05, 12.27) | | |
| P-value | | | 0.34 | | | 0.32 | | | 0.87 |
| Adj. Rate ratio+ | 0.50 | 1 (ref) | | | | | | | |
| (95% CI) | (0.12, 2.01) | | | | | | | | |
| P-value | | | 0.33 | | | | | | |
| **Time to first event (WHO 4, severe WHO 3 or death)** | | | | | | | | | |
| Unadjusted Hazard ratio | 0.50 | 1 (ref) | | 0.41 | 1 (ref) | | 0.93 | 1 (ref) | |
| (95% CI) | (0.13, 2.02) | - | | (0.08, 2.11) | - | | (0.06, 14.83) | | |
| P-value | | | 0.33 | | | 0.29 | | | 0.96 |
| Adj. hazard ratio+ | 0.50 | 1 (ref) | | | | | | | |
| (95% CI) | (0.13, 2.00) | | | | | | | | |
| P-value | | | 0.33 | | | | | | |
| A/B x arm interaction | 0.6245 | | | | | | | | |

*Resulted in death

+Adjusted for ODYSSEY A and B strata in total.

## S8.21 Rate of clinical events to week 96: WHO 4, severe WHO 3 and death

| | Total | | | A | | | B | | |
|---|---|---|---|---|---|---|---|---|---|
| | **DTG** | **SOC** | **Total** | **DTG** | **SOC** | **Total** | **DTG** | **SOC** | **Total** |
| **Participants randomised and included** | 42 | 43 | 85 | 35 | 37 | 72 | 7 | 6 | 13 |
| Person years | 70 | 73 | 143 | 57 | 62 | 120 | 13 | 11 | 23 |
| **Total number of events [Number of participants]** | 3 [3] | 6 [6] | 9 [9] | 2 [2] | 5 [5] | 7 [7] | 1 [1] | 1 [1] | 2 [2] |
| Severe WHO 3 | 0 [0] | 0 [0] | 0 [0] | 0 [0] | 0 [0] | 0 [0] | 0 [0] | 0 [0] | 0 [0] |
| WHO 4 | 1 [1] | 2 [2] | 3 [3] | 0 [0] | 2 [2] | 2 [2] | 1 [1] | 0 [0] | 1 [1] |
| Death | 2 [2] | 4 [4] | 6 [6] | 2 [2] | 3 [3] | 5 [5] | 0 [0] | 1 [1] | 1 [1] |
| **Number of events [Number of children]** | | | | | | | | | |
| **Infectious Disease** | 0 [0] | 5 [5] | 5 [5] | 0 [0] | 4 [4] | 4 [4] | 0 [0] | 1 [1] | 1 [1] |
| Gastroenteritis * | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] | 0 [0] | 1 [1] | 1 [1] |
| Pneumonia no organism identified, aspiration pneumonia * | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Tuberculosis - abdominal | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Tuberculosis - disseminated/miliary | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Tuberculosis - pulmonary - smear negative or not done+Severe malnutrition * | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| **Non HIV related deaths** | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Traumatic * | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| **Systemic** | 2 [2] | 1 [1] | 3 [3] | 1 [1] | 1 [1] | 2 [2] | 1 [1] | 0 [0] | 1 [1] |
| Chest infection+Severe malnutrition | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] | 1 [1] | 0 [0] | 1 [1] |
| Kwashiorkor * | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Severe malnutrition * | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| **Event rate (all events)** | | | | | | | | | |
| Event rate (per 100 person years) | 4.3 | 8.3 | 6.3 | 3.5 | 8.1 | 5.9 | 7.8 | 9.5 | 8.5 |
| (95% CI) | (1.4, 13.2) | (3.7, 18.4) | (3.3, 12.1) | (0.9, 13.9) | (3.4, 19.3) | (2.8, 12.3) | (1.1, 55.1) | (1.3, 67.5) | (2.1, 34.2) |
| Unadjusted Rate ratio | 0.52 | 1 (ref) | | 0.43 | 1 (ref) | | 0.82 | 1 (ref) | |
| (95% CI) | (0.13, 2.10) | - | | (0.08, 2.33) | - | | (0.05, 12.37) | | |
| P-value | | | 0.36 | | | 0.33 | | | 0.88 |
| Adj. Rate ratio+ | 0.51 | 1 (ref) | | | | | | | |
| (95% CI) | (0.13, 2.03) | | | | | | | | |
| P-value | | | 0.34 | | | | | | |
| **Time to first event (WHO 4, severe WHO 3 or death)** | | | | | | | | | |
| Unadjusted Hazard ratio | 0.50 | 1 (ref) | | 0.41 | 1 (ref) | | 0.93 | 1 (ref) | |
| (95% CI) | (0.13, 2.02) | - | | (0.08, 2.11) | - | | (0.06, 14.83) | | |
| P-value | | | 0.33 | | | 0.29 | | | 0.96 |
| Adj. hazard ratio+ | 0.50 | 1 (ref) | | | | | | | |
| (95% CI) | (0.13, 2.00) | | | | | | | | |
| P-value | | | 0.33 | | | | | | |
| A/B x arm interaction | 0.6245 | | | | | | | | |

*Resulted in death

+Adjusted for ODYSSEY A and B strata in total. Unadjusted in A and B comparison therefore identical to the unadjusted

## S8.22 Details of WHO 3 (Severe) or 4 events or deaths during follow-up

| ID | A/B | Treatment arm | ART regimen at event | Grade | Age (Weeks) | Event Week | Event | Type |
|---|---|---|---|---|---|---|---|---|
| 1 | A | DTG | ABC 3TC DTG | 4 | 67 | 0 [6days] | Kwashiorkor | Death |
| 2 | A | DTG | ABC 3TC DTG | 4 | 34 | 17 | Traumatic | Death |
| 3 | B | DTG | ZDV 3TC DTG | 4 | 162 | 9 | Chest infection+Severe malnutrition | WHO4 |
| 4 | A | SOC | ABC 3TC EFV | 3 | 257 | 53 | Tuberculosis - abdominal | WHO4 |
| 5 | A | SOC | ABC 3TC LOP | 4 | 28 | 0 [5days] | Pneumonia no organism identified, aspiration pneumonia | Death |
| 6 | A | SOC | ABC 3TC LOP | 2 | 7 | 0 [3days] | Tuberculosis - disseminated/miliary | WHO4 |
| 7 | A | SOC | ABC 3TC LOP | 4 | 64 | 0 [6days] | Severe malnutrition | Death |
| 8 | A | SOC | ABC 3TC NVP | 4 | 37 | 10 | Tuberculosis - pulmonary - smear negative or not done+Severe malnutrition | Death |
| 9 | B | SOC | ABC 3TC LOP | 4 | 219 | 68 | Gastroenteritis | Death |

ID 1, 7, and 8 had their WHO 4 condition (kwashiorkor, severe malnutrition and severe malnutrition respectively) pre-exisiting prior to randomisation, therefore the event in follow-up is death

## S8.23 Genotypic resistance comparing dolutegravir-based ART versus standard of care#

| | ODYSSEY A | | | | ODYSSEY B | | | |
|---|---|---|---|---|---|---|---|---|
| | DTG | | SOC | | DTG | | SOC | |
| **Participants with virological failure by 96 weeks^** | 7 | (20%) | 13 | (35%) | 2 | (29%) | 3 | (50%) |
| **Participants with resistance post-failure ≀** | | | | | | | | |
| Any | 6/6 | (100%) | 12/12 | (100%) | 2/2 | (100%) | 3/3 | (100%) |
| NRTI | 1/6 | (17%) | 10/12 | (83%) | 1/2 | (50%) | 3/3 | (100%) |
| NNRTI | 6/6 | (100%) | 11/12 | (92%) | 2/2 | (100%) | 3/3 | (100%) |
| PI | 0/6 | (0%) | 2/12 | (17%) | 0/2 | (0%) | 0/3 | (0%) |
| INSTI | 0/5 | (0%) | - | - | 1/2** | (50%) | - | - |

≀ Major IAS-USA drug resistance mutations defined according to 2019 update of the IAS-USA drug resistance mutations.[19] Percentage with resistance post-failure, of those with virological failure by week 96 and post-failure resistance test available for drug-class ('-' indicates integrase gene not sequenced for SOC arm).

**1 participant with INSTI resistance developed Asn155Asn/His mutation

^25 participants met a virological endpoint by week 96 (confirmed viral load≥400 c/mL after week 36 [n=25] or lack of virological response by week 24 followed by ART switch [n=0])

#Note: due to low availability of baseline resistance tests, proportion with emergent drug resistance could not be estimated

**DTG**, dolutegravir; **SOC**, standard of care; **NRTI**, Nucleoside reverse transcriptase inhibitors; **NNRTI**, Non-nucleoside reverse transcriptase inhibitors; **PI**, protease inhibitor; **INSTI**, Integrase Strand Transfer Inhibitor; **IAS-USA**, International AIDS Society-USA; **c/ml**, copies per millilitre; **ART**, antiretroviral therapy

## S8.24 Resistance mutations identified post-failure in participants*

| | DTG | SOC |
|---|---|---|
| **ODYSSEY A** | | |
| **NRTI** | | |
| Any NRTI | 1/6 | 10/12 |
| M41 | 0 | 1 |
| K65 | 0 | 1 |
| D67 | 1 | 1 |
| K70 | 1 | 0 |
| L74 | 0 | 2 |
| Y115 | 0 | 1 |
| M184 | 1 | 9 |
| L210 | 0 | 1 |
| T215 | 0 | 1 |
| K219 | 1 | 2 |
| **NNRTI** | | |
| Any NNRTI | 6/6 | 11/12 |
| K101 | 1 | 1 |
| K103 | 5 | 8 |
| V106 | 1 | 1 |
| E138 | 0 | 1 |
| Y181 | 2 | 4 |
| Y188 | 0 | 2 |
| G190 | 0 | 3 |
| H221 | 1 | 2 |
| P225 | 1 | 1 |
| **PI** | | |
| Any PI | 0/6 | 2/12 |
| M46 | 0 | 1 |
| I47 | 0 | 1 |
| Q58 | 0 | 1 |
| I84 | 0 | 1 |
| **INSTI** | | |
| Any INSTI | 0/5 | - |
| **ODYSSEY B** | | |
| **NRTI** | | |
| Any NRTI | 1/2 | 3/3 |
| D67 | 1 | 0 |
| K70 | 1 | 0 |
| M184 | 1 | 3 |
| K219 | 1 | 0 |
| **NNRTI** | | |
| Any NNRTI | 2/2 | 3/3 |
| K101 | 0 | 1 |
| K103 | 1 | 3 |
| V106 | 1 | 0 |
| E138 | 1 | 0 |
| Y181 | 1 | 0 |
| G190 | 0 | 1 |
| **PI** | | |
| Any PI | 0/2 | 0/3 |
| **INSTI** | | |
| Any INSTI** | 1/2 | - |

| | | |
|---|---|---|
| N155 | 1 | - |

*Reported for participants for whom a resistance test was available post-failure.

**1 participant with INSTI resistance: 1 N155NH.

Each participant may have one or more mutation to one or more drug class.

- indicates gene not sequenced.

## S8.25 Treatment emergent resistance mutations post-failure in participants exposed to drug-class*

| | DTG | SOC |
|---|---|---|
| **ODYSSEY A** | | |
| **NRTI** | | |
| Any NRTI | - | 5/5 |
| L74 | - | 1 |
| M184 | - | 3 |
| L210 | - | 1 |
| K219 | - | 1 |
| **NNRTI** | | |
| Any NNRTI | - | - |
| **PI** | | |
| Any PI | - | 1/1 |
| I47 | - | 1 |
| **INSTI** | | |
| Any INSTI | 0/5 | - |
| **ODYSSEY B** | | |
| **NRTI** | | |
| Any NRTI | 1/1 | - |
| D67 | 1 | - |
| K70 | 1 | - |
| **NNRTI** | | |
| Any NNRTI | - | - |
| **PI** | | |
| Any PI | - | - |
| **INSTI** | | |
| Any INSTI** | 1/2 | - |
| N155 | 1 | - |

*Reported for participants for whom a resistance test was available post-failure and at baseline and exposed to drug-class during trial. Note: IN gene was only sequenced during follow-up (not at baseline due to lack of prior INSTI exposure) and therefore INSTI resistance identified post-failure is classified as emergent.

**1 participant with INSTI resistance: 1 N155NH.

Each participant may have one or more mutation to one or more drug class.

- indicates no participants with virological failure, exposed to drug-class, and gene sequenced at baseline and post-failure.

# S9 Immunology

Note: ODYSSEY B is not presented here due to having few participants

Throughout this section, n refers to the number of participants with available measurement at each visit week. Numbers in models may be lower where there are missing data at baseline.

## S9.1 Total population - Changes in CD4 count over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | | Adjusted Difference** | | | | Interaction++ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p | mean | (SE) | [95% CI] | p | p |
| 4 | 36 | 334 | (104) | 36 | 235 | (105) | 99 | (148) | [-197, 395] | 0.51 | 109 | (145) | [-180, 398] | 0.45 | 0.95 |
| 12 | 36 | 269 | (134) | 39 | 198 | (132) | 71 | (190) | [-307, 450] | 0.71 | 72 | (190) | [-307, 452] | 0.70 | 0.69 |
| 24 | 36 | 283 | (116) | 37 | 133 | (114) | 150 | (163) | [-176, 475] | 0.36 | 158 | (163) | [-167, 483] | 0.34 | 1 |
| 48 | 32 | 368 | (152) | 38 | 239 | (141) | 129 | (208) | [-287, 545] | 0.54 | 165 | (202) | [-238, 567] | 0.42 | 0.78 |
| 72 | 34 | 106 | (128) | 34 | 32 | (126) | 74 | (180) | [-285, 433] | 0.68 | 78 | (182) | [-285, 441] | 0.67 | 0.94 |
| 96 | 36 | 72 | (116) | 35 | 51 | (118) | 21 | (167) | [-313, 355] | 0.90 | 30 | (169) | [-308, 368] | 0.86 | 0.48 |
| Average treatment differences through follow-up+ | | | | | | | 114 | (119) | [-119, 346] | 0.34 | 122 | (116) | [-106, 350] | 0.29 | 0.95 |

## S9.2 ODYSSEY A - changes in CD4 count over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p |
| 4 | 29 | 406 | (120) | 30 | 312 | (119) | 94 | (170) | [-247 434] | 0.58 |
| 12 | 30 | 319 | (158) | 33 | 225 | (156) | 94 | (224) | [-355 542] | 0.68 |
| 24 | 29 | 331 | (136) | 31 | 177 | (131) | 154 | (189) | [-226 534] | 0.42 |
| 48 | 25 | 516 | (179) | 32 | 331 | (160) | 186 | (242) | [-299 670] | 0.45 |
| 72 | 27 | 122 | (157) | 29 | 47 | (149) | 75 | (216) | [-359 510] | 0.73 |
| 96 | 29 | 58 | (133) | 31 | 97 | (129) | -39 | (187) | [-415 336] | 0.83 |
| Average treatment differences through follow-up+ | | | | | | | 116 | (135) | [-148, 379] | 0.39 |

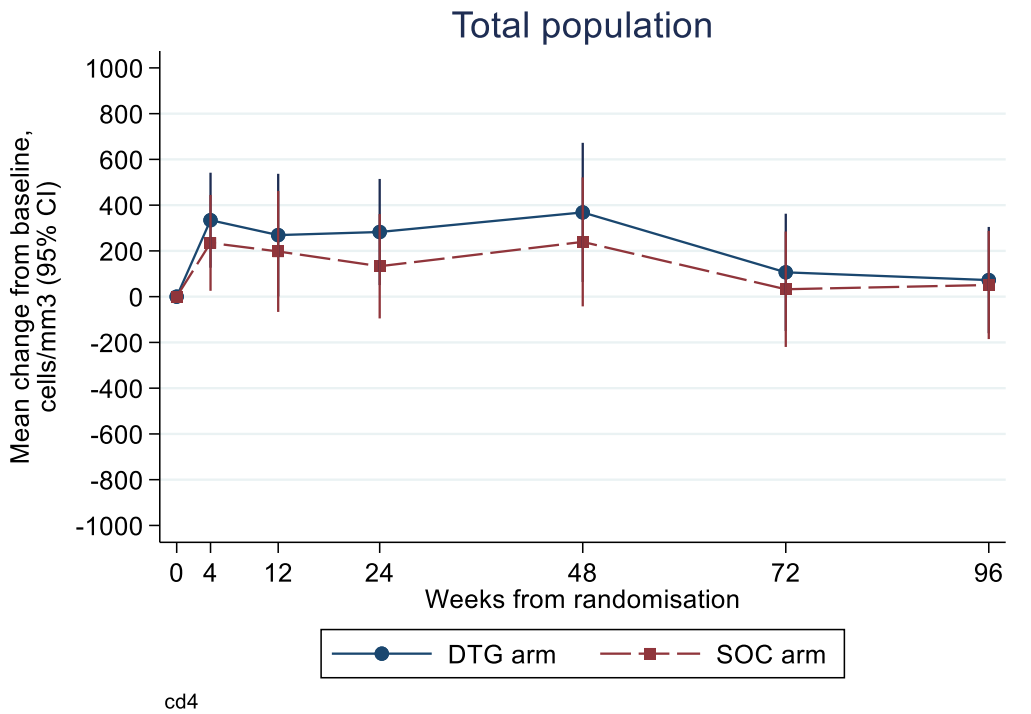
*Change calculated using normal regression adjusting for baseline only. Presenting mean change from a baseline of 1549.8 in total and 1546.6 in A.

**Normal regression adjusting for baseline and ODYSSEY A/B strata.

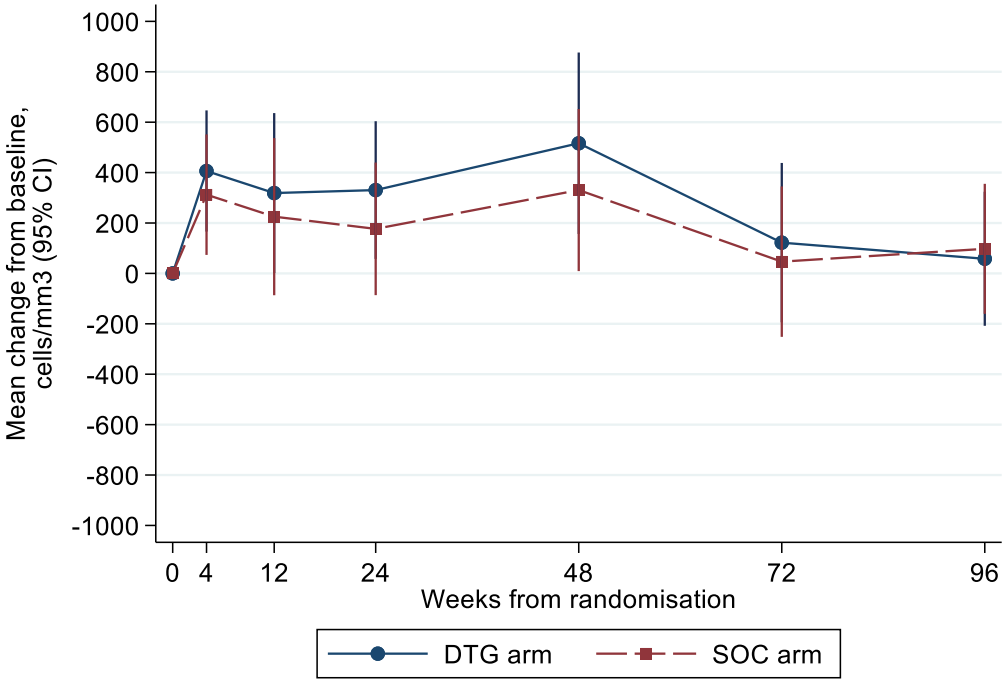
+Linear mixed models fitted with random intercept and fixed effects for treatment group, study visit and adjustment covariates (baseline CD4 count and ODYSSEY A/B strata (total population only))

++ Test of heterogeneity of treatment effect between ODYSSEY A/B

**S9.3 Total population - Changes in CD4 count over follow-up**



## S9.4 ODYSSEY A - changes in CD4 count over follow-up



## S9.5 Total population - Changes in CD4 percentage over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | | Adjusted Difference** | | | | Interaction++ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p | mean | (SE) | [95% CI] | p | p |
| 4 | 36 | 3.3 | (1.4) | 36 | 3.1 | (1.4) | 0.2 | (2.0) | [-3.8, 4.2] | 0.91 | 0.3 | (2.0) | [-3.7, 4.2] | 0.90 | 0.95 |
| 12 | 36 | 3.2 | (1.4) | 39 | 3.0 | (1.4) | 0.2 | (2.0) | [-3.7, 4.2] | 0.92 | 0.2 | (2.0) | [-3.8, 4.2] | 0.92 | 0.43 |
| 24 | 36 | 5.6 | (1.3) | 37 | 3.8 | (1.3) | 1.8 | (1.9) | [-1.9, 5.5] | 0.33 | 1.8 | (1.9) | [-1.9, 5.5] | 0.34 | 0.68 |
| 48 | 32 | 8.3 | (1.6) | 38 | 4.3 | (1.5) | 4.0 | (2.2) | [-0.4, 8.4] | 0.074 | 4.1 | (2.2) | [-0.3, 8.5] | 0.065 | 0.88 |
| 72 | 34 | 9.2 | (1.7) | 34 | 5.6 | (1.6) | 3.6 | (2.3) | [-1.0, 8.2] | 0.12 | 3.7 | (2.3) | [-0.9, 8.4] | 0.11 | 0.93 |
| 96 | 36 | 13.2 | (1.6) | 35 | 8.5 | (1.7) | 4.8 | (2.3) | [0.1, 9.4] | 0.047 | 4.7 | (2.4) | [-0.1, 9.4] | 0.053 | 0.37 |
| Average treatment differences through follow-up+ | | | | | | | 2.7 | (1.6) | [-0.3, 5.8] | 0.082 | 2.7 | (1.6) | [-0.3, 5.8] | 0.080 | 0.71 |

## S9.6 ODYSSEY A - changes in CD4 percentage over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p |
| 4 | 29 | 3.8 | (1.7) | 30 | 3.4 | (1.7) | 0.4 | (2.4) | [-4.4 5.3] | 0.86 |
| 12 | 30 | 2.8 | (1.7) | 33 | 3.3 | (1.6) | -0.5 | (2.4) | [-5.2 4.2] | 0.84 |
| 24 | 29 | 5.2 | (1.5) | 31 | 3.8 | (1.5) | 1.5 | (2.1) | [-2.8 5.7] | 0.49 |
| 48 | 25 | 9.0 | (2.0) | 32 | 4.9 | (1.7) | 4.1 | (2.6) | [-1.2 9.4] | 0.12 |
| 72 | 27 | 9.8 | (2.1) | 29 | 6.0 | (1.9) | 3.8 | (2.8) | [-1.8 9.5] | 0.18 |
| 96 | 29 | 12.7 | (2.0) | 31 | 9.0 | (1.9) | 3.7 | (2.8) | [-2.0 9.3] | 0.20 |
| Average treatment differences through follow-up+ | | | | | | | 2.5 | (1.9) | [-1.1, 6.1] | 0.18 |

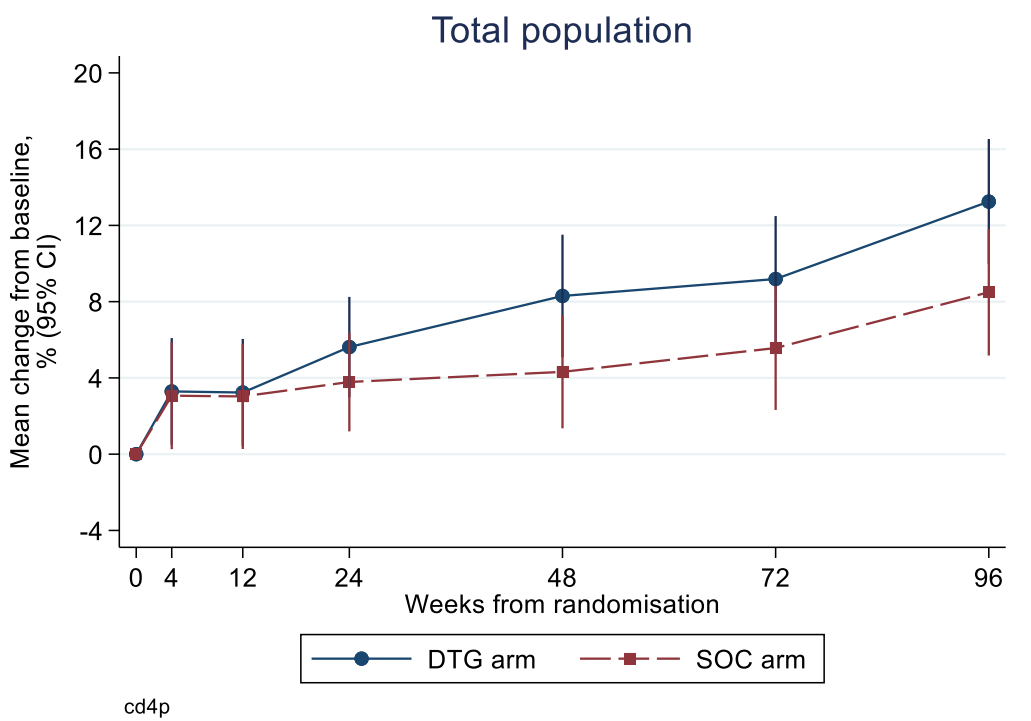
*Change calculated using normal regression adjusting for baseline only. Presenting mean change from a baseline of 23.6 in total and 23.1 in A.

**Normal regression adjusting for baseline and ODYSSEY A/B strata.

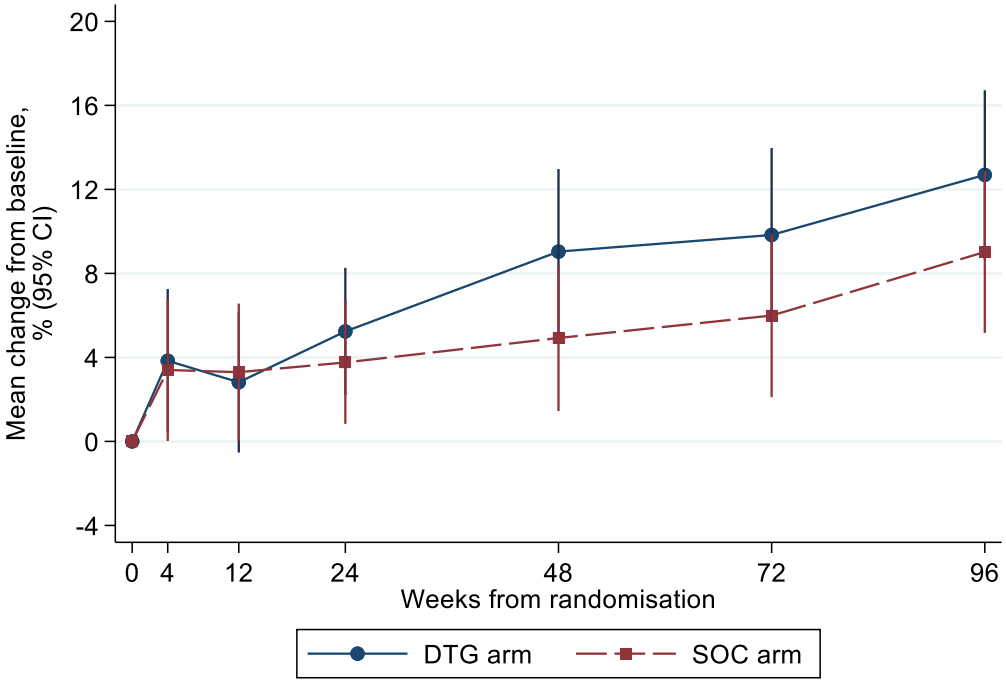
+Linear mixed models fitted with random intercept and fixed effects for treatment group, study visit and adjustment covariates (baseline CD4 percentage and ODYSSEY A/B strata (total population only))

++ Test of heterogeneity of treatment effect between ODYSSEY A/B

**S9.7 Total population - Changes in CD4 percentage over follow-up**



## S9.8 ODYSSEY A - changes in CD4 percentage over follow-up



## S9.9 Total population - Changes in CD4/CD8 ratio over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | | Adjusted Difference** | | | | Interaction++ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p | mean | (SE) | [95% CI] | p | p |
| 4 | 36 | 0.17 | (0.08) | 36 | 0.30 | (0.08) | -0.13 | (0.12) | [-0.36, 0.10] | 0.26 | -0.13 | (0.11) | [-0.36, 0.10] | 0.27 | 0.43 |
| 12 | 36 | 0.12 | (0.06) | 39 | 0.15 | (0.06) | -0.03 | (0.09) | [-0.20, 0.15] | 0.75 | -0.03 | (0.09) | [-0.21, 0.15] | 0.75 | 0.28 |
| 24 | 36 | 0.37 | (0.08) | 37 | 0.20 | (0.07) | 0.17 | (0.11) | [-0.05, 0.38] | 0.12 | 0.17 | (0.11) | [-0.05, 0.38] | 0.12 | 0.64 |
| 48 | 32 | 0.46 | (0.08) | 38 | 0.26 | (0.08) | 0.19 | (0.11) | [-0.03, 0.42] | 0.090 | 0.21 | (0.11) | [-0.01, 0.43] | 0.066 | 0.56 |
| 72 | 34 | 0.49 | (0.09) | 34 | 0.26 | (0.09) | 0.24 | (0.12) | [-0.01, 0.49] | 0.062 | 0.25 | (0.12) | [0.00, 0.50] | 0.048 | 0.56 |
| 96 | 36 | 0.57 | (0.07) | 35 | 0.44 | (0.07) | 0.14 | (0.10) | [-0.07, 0.34] | 0.18 | 0.14 | (0.10) | [-0.06, 0.35] | 0.17 | 0.10 |
| Average treatment differences through follow-up+ | | | | | | | 0.09 | (0.07) | [-0.04, 0.23] | 0.18 | 0.10 | (0.07) | [-0.04, 0.23] | 0.17 | 0.21 |

## S9.10 ODYSSEY A - changes in CD4/CD8 ratio over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p |
| 4 | 29 | 0.19 | (0.10) | 30 | 0.36 | (0.10) | -0.17 | (0.14) | [-0.45 0.11] | 0.23 |
| 12 | 30 | 0.10 | (0.07) | 33 | 0.18 | (0.07) | -0.07 | (0.10) | [-0.28 0.14] | 0.50 |
| 24 | 29 | 0.35 | (0.09) | 31 | 0.22 | (0.08) | 0.13 | (0.12) | [-0.12 0.38] | 0.30 |
| 48 | 25 | 0.48 | (0.09) | 32 | 0.33 | (0.08) | 0.15 | (0.13) | [-0.10 0.40] | 0.24 |
| 72 | 27 | 0.51 | (0.11) | 29 | 0.32 | (0.10) | 0.19 | (0.15) | [-0.10 0.49] | 0.19 |
| 96 | 29 | 0.55 | (0.09) | 31 | 0.49 | (0.08) | 0.06 | (0.12) | [-0.18 0.30] | 0.63 |
| Average treatment differences through follow-up+ | | | | | | | 0.05 | (0.08) | [-0.11, 0.21] | 0.56 |

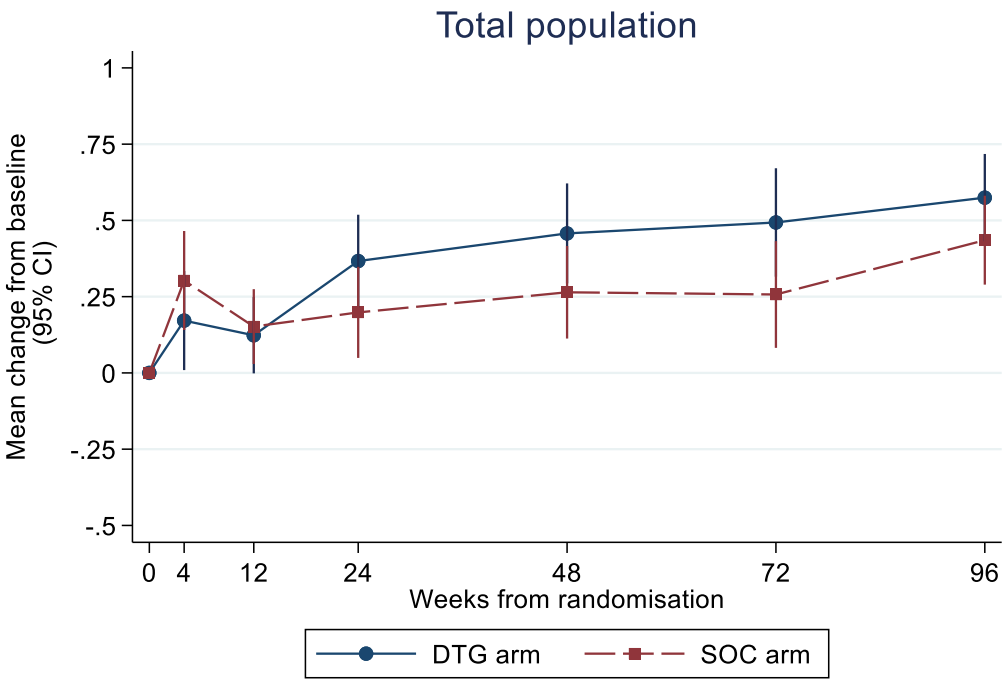
*Change calculated using normal regression adjusting for baseline only. Presenting mean change from a baseline of 0.7 in total and 0.7 in A.

**Normal regression adjusting for baseline and ODYSSEY A/B strata.

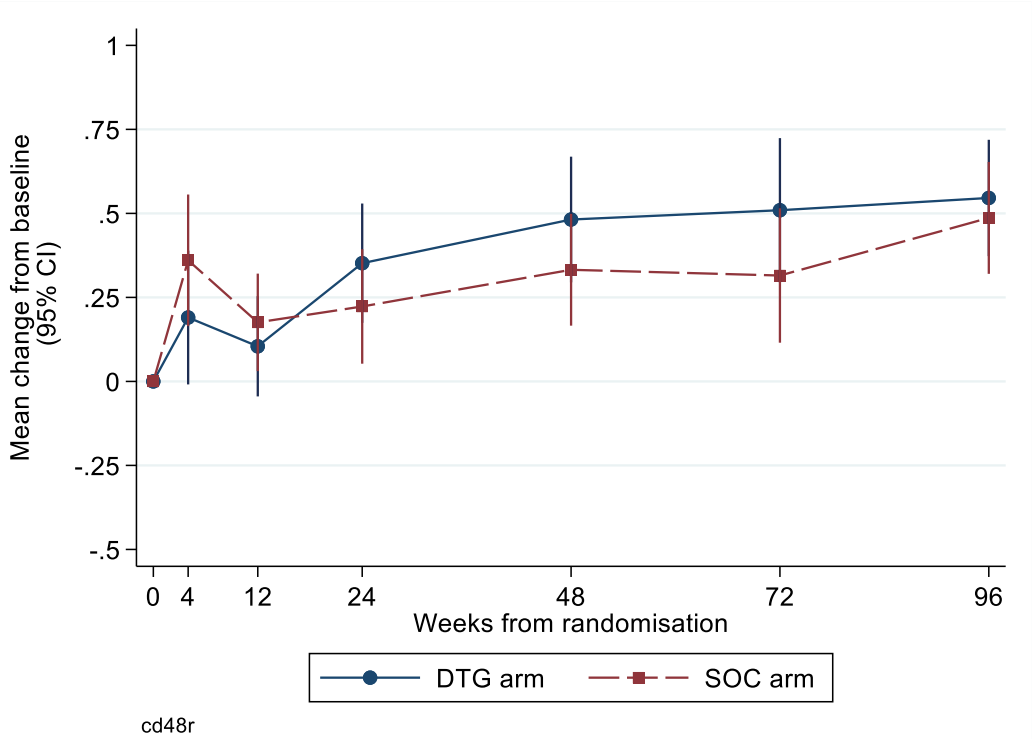
+Linear mixed models fitted with random intercept and fixed effects for treatment group, study visit and adjustment covariates (baseline CD4/CD8 ratio and ODYSSEY A/B strata (total population only))

++ Test of heterogeneity of treatment effect between ODYSSEY A/B

**S9.11 Total population - Changes in CD4/CD8 ratio over follow-up**



**S9.12 ODYSSEY A - changes in CD4/CD8 ratio over follow-up**



# S10 Lipids

Note: ODYSSEY B is not presented here due to having few participants

Throughout this section, n refers to the number of participants with available measurement at each visit week. Numbers in models may be lower where there are missing data at baseline.

## S10.1 Total population - Total cholesterol changes over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | | Adjusted Difference** | | | | Interaction++ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p | mean | (SE) | [95% CI] | p | p |
| 48 | 34 | 1.7 | (4.8) | 38 | 14.7 | (4.8) | -13.0 | (6.8) | [-26.6, 0.6] | 0.061 | -12.6 | (6.7) | [-26.0, 0.9] | 0.067 | 0.62 |
| 96 | 36 | 4.5 | (5.6) | 36 | 29.6 | (5.9) | -25.2 | (8.2) | [-41.5, -8.9] | 0.0030 | -24.4 | (8.0) | [-40.3, -8.5] | 0.0032 | 0.25 |
| Average treatment differences through follow-up+ | | | | | | | -18.6 | (6.0) | [-30.4, -6.7] | 0.0021 | -18.2 | (5.8) | [-29.6, -6.8] | 0.0018 | 0.34 |

## S10.2 ODYSSEY A - Total cholesterol changes over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p |
| 48 | 27 | 4.0 | (5.4) | 32 | 18.4 | (5.3) | -14.4 | (7.6) | [-29.6, 0.8] | 0.063 |
| 96 | 29 | 6.8 | (6.2) | 31 | 35.4 | (6.5) | -28.6 | (9.0) | [-46.7, -10.5] | 0.0026 |
| Average treatment differences through follow-up+ | | | | | | | -21.0 | (6.6) | [-33.8, -8.1] | 0.0014 |

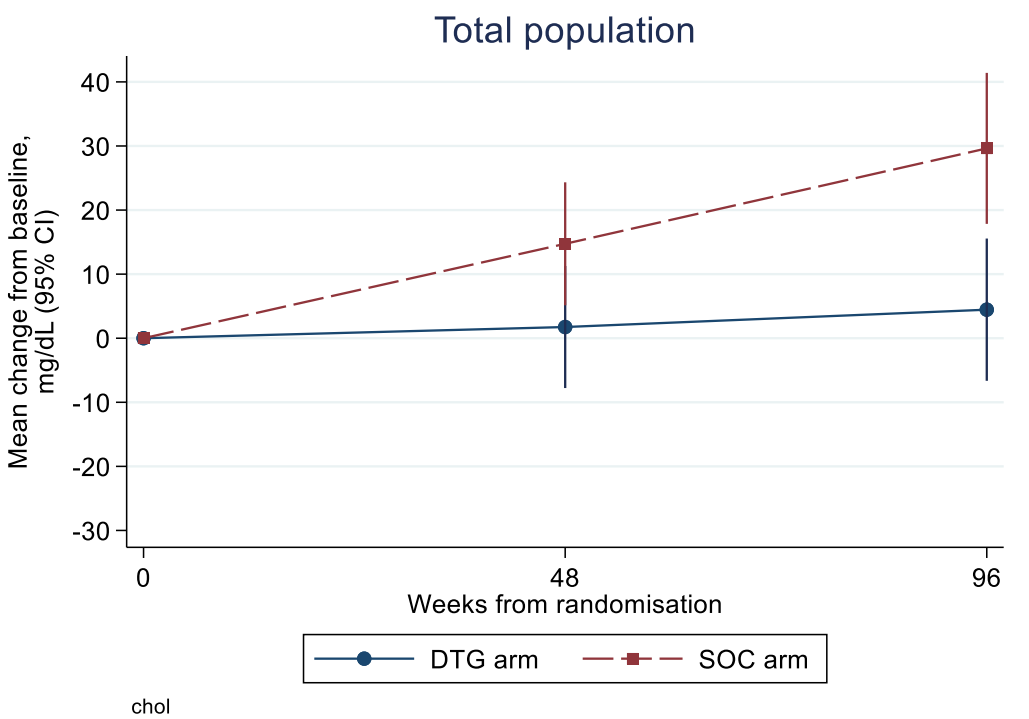
*Change calculated using normal regression adjusting for baseline only. Presenting mean change from a baseline of 127.9 in total and 127.7 in A.

**Normal regression adjusting for baseline and ODYSSEY A/B strata.

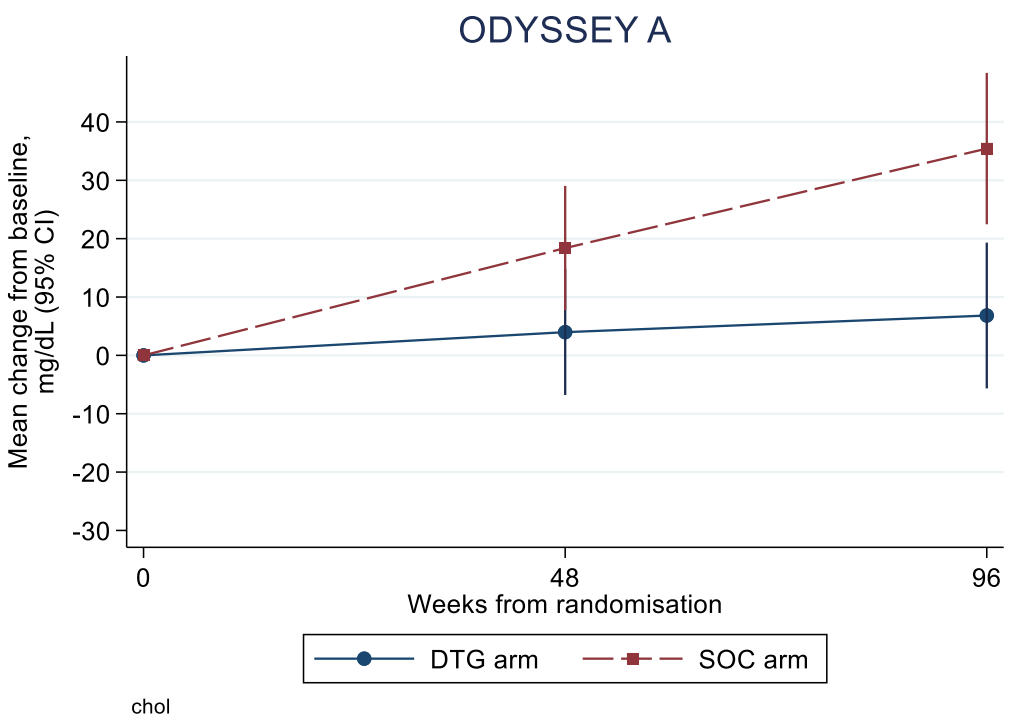
+Linear mixed models fitted with random intercept and fixed effects for treatment group, study visit and adjustment covariates (baseline Total cholesterol and ODYSSEY A/B strata (total population only))

++ Test of heterogeneity of treatment effect between ODYSSEY A/B

**S10.3 Total population - changes in Total cholesterol over follow-up**



**S10.4 ODYSSEY A - changes in Total cholesterol over follow-up**



## S10.5 Total population - LDL cholesterol changes over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | | Adjusted Difference** | | | | Interaction++ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p | mean | (SE) | [95% CI] | p | p |
| 48 | 34 | -2.5 | (3.9) | 38 | 13.6 | (3.7) | -16.1 | (5.4) | [-26.9, -5.4] | 0.0040 | -16.0 | (5.4) | [-26.8, -5.1] | 0.0046 | 0.79 |
| 96 | 36 | -3.2 | (5.1) | 36 | 22.4 | (5.3) | -25.7 | (7.4) | [-40.4, -11.0] | >0.0001 | -24.9 | (7.3) | [-39.5, -10.4] | 0.0011 | 0.35 |
| Average treatment differences through follow-up+ | | | | | | | -20.3 | (5.2) | [-30.4, -10.1] | >0.0001 | -20.0 | (5.1) | [-30.0, -9.9] | >0.0001 | 0.76 |

## S10.6 ODYSSEY A - LDL cholesterol changes over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p |
| 48 | 27 | -1.3 | (4.2) | 32 | 14.0 | (3.9) | -15.3 | (5.7) | [-26.9, -3.8] | 0.010 |
| 96 | 29 | -1.1 | (6.1) | 31 | 27.1 | (6.1) | -28.2 | (8.6) | [-45.5, -11.0] | 0.0019 |
| Average treatment differences through follow-up+ | | | | | | | -20.7 | (6.0) | [-32.4, -9.0] | 0.00051 |

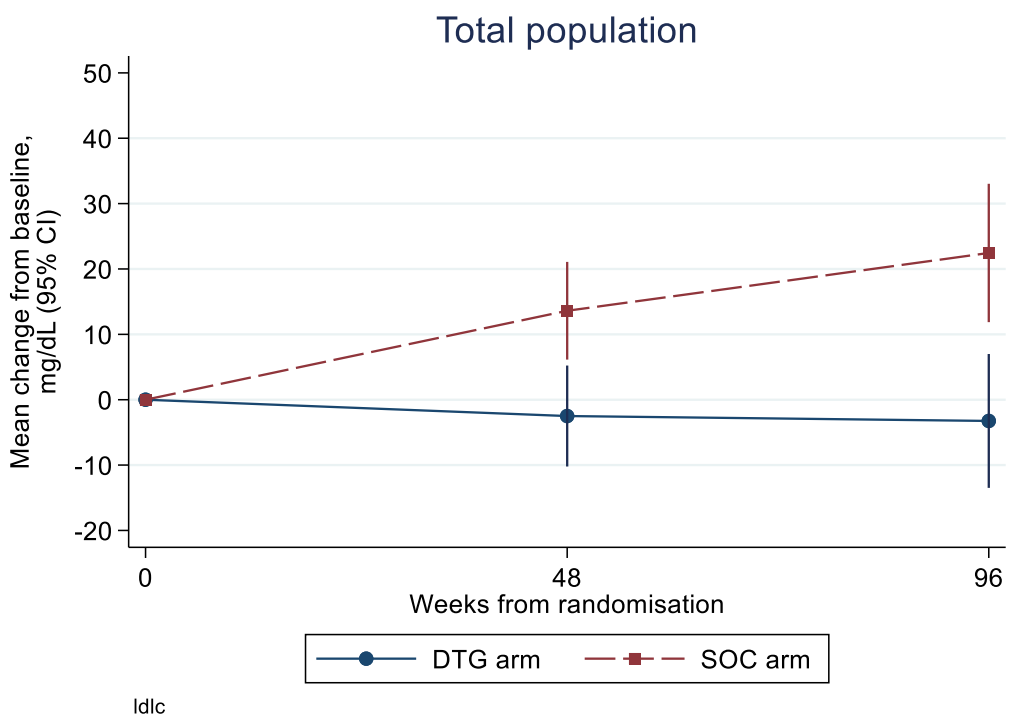
*Change calculated using normal regression adjusting for baseline only. Presenting mean change from a baseline of 69.8 in total and 69.4 in A.

**Normal regression adjusting for baseline and ODYSSEY A/B strata.

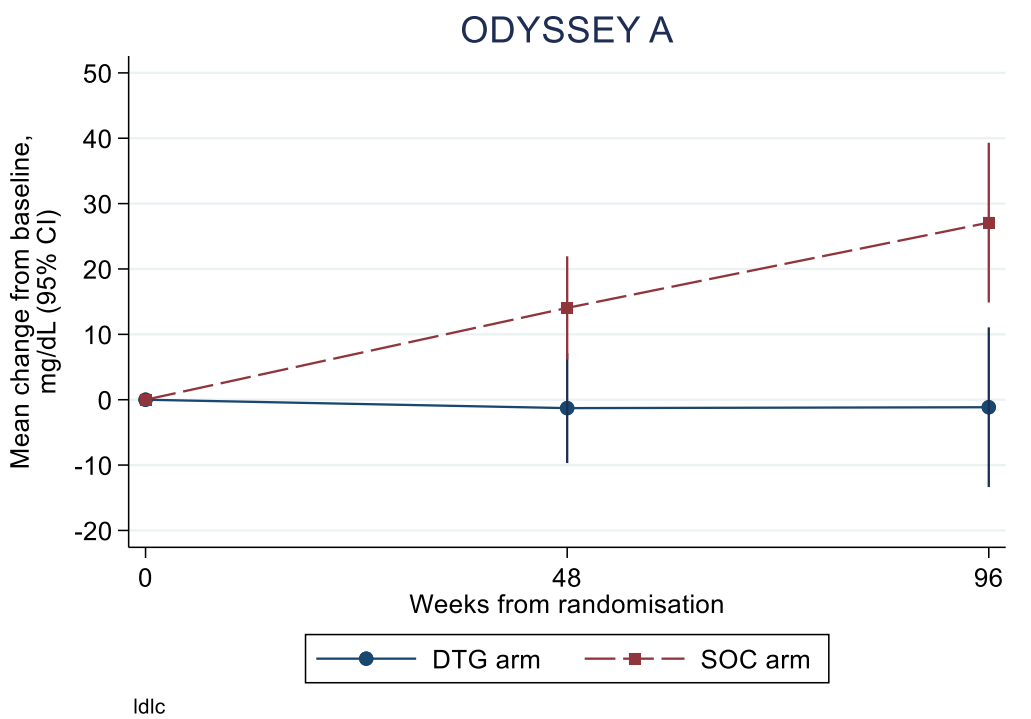
+Linear mixed models fitted with random intercept and fixed effects for treatment group, study visit and adjustment covariates (baseline LDL cholesterol and ODYSSEY A/B strata (total population only))

++ Test of heterogeneity of treatment effect between ODYSSEY A/B

**S10.7 Total population - changes in LDL cholesterol over follow-up**



**S10.8 ODYSSEY A - changes in LDL cholesterol over follow-up**



## S10.9 Total population - HDL cholesterol changes over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | | Adjusted Difference** | | | | Interaction++ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p | mean | (SE) | [95% CI] | p | p |
| 48 | 34 | 9.0 | (2.5) | 38 | 10.2 | (2.4) | -1.2 | (3.5) | [-8.2, 5.9] | 0.74 | -1.2 | (3.6) | [-8.3, 5.9] | 0.74 | 0.18 |
| 96 | 36 | 13.0 | (2.6) | 36 | 16.5 | (2.7) | -3.6 | (3.7) | [-11.0, 3.9] | 0.35 | -3.0 | (3.6) | [-10.3, 4.3] | 0.41 | 0.17 |
| Average treatment differences through follow-up+ | | | | | | | -2.3 | (2.6) | [-7.3, 2.7] | 0.37 | -2.1 | (2.5) | [-7.0, 2.9] | 0.41 | 0.97 |

## S10.10 ODYSSEY A - HDL cholesterol changes over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p |
| 48 | 27 | 10.2 | (2.9) | 32 | 8.9 | (2.7) | 1.2 | (4.0) | [-6.8, 9.3] | 0.76 |
| 96 | 29 | 13.6 | (2.9) | 31 | 19.2 | (2.8) | -5.6 | (4.0) | [-13.6, 2.4] | 0.17 |
| Average treatment differences through follow-up+ | | | | | | | -2.1 | (2.8) | [-7.6, 3.3] | 0.44 |

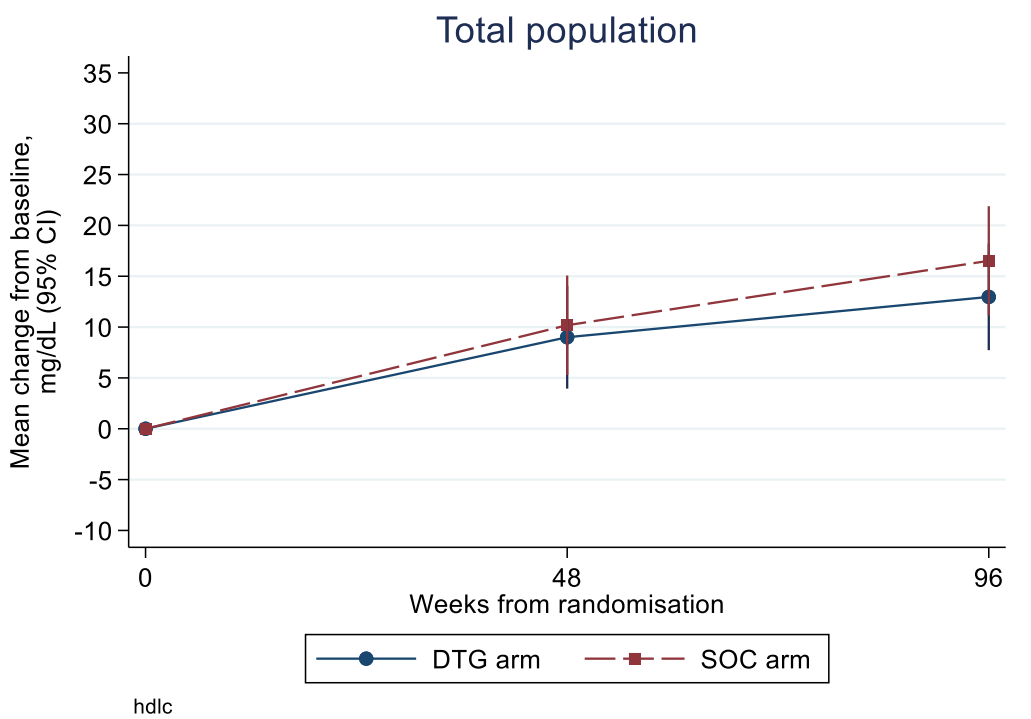
*Change calculated using normal regression adjusting for baseline only. Presenting mean change from a baseline of 34.0 in total and 34.1 in A.

**Normal regression adjusting for baseline and ODYSSEY A/B strata.

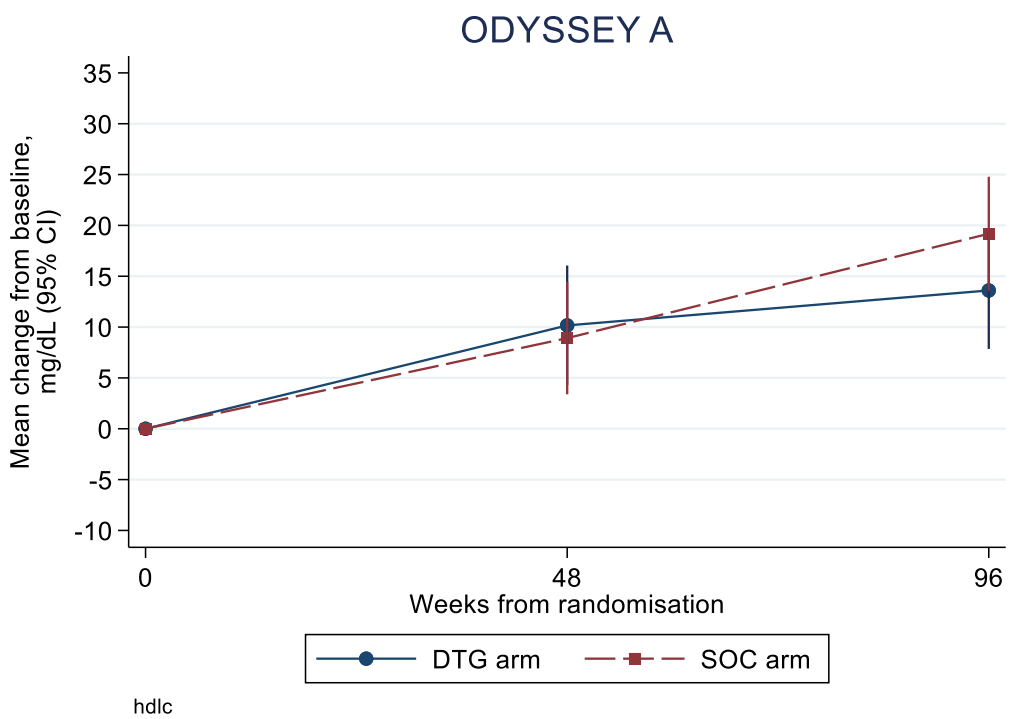
+Linear mixed models fitted with random intercept and fixed effects for treatment group, study visit and adjustment covariates (baseline HDL cholesterol and ODYSSEY A/B strata (total population only))

++ Test of heterogeneity of treatment effect between ODYSSEY A/B

**S10.11 Total population - changes in HDL cholesterol over follow-up**



**S10.12 ODYSSEY A - changes in HDL cholesterol over follow-up**



## S10.13 Total population - Triglycerides changes over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | | Adjusted Difference** | | | | Interaction++ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p | mean | (SE) | [95% CI] | p | p |
| 48 | 33 | -0.9 | (14.9) | 37 | -28.5 | (14.7) | 27.6 | (21.0) | [-14.5, 69.6] | 0.19 | 28.1 | (21.0) | [-13.9, 70.1] | 0.19 | 0.23 |
| 96 | 34 | -39.8 | (10.5) | 34 | -30.3 | (10.9) | -9.5 | (15.3) | [-40.0, 21.1] | 0.54 | -9.0 | (15.3) | [-39.6, 21.7] | 0.56 | 0.73 |
| Average treatment differences through follow-up+ | | | | | | | 9.9 | (13.9) | [-17.4, 37.2] | 0.48 | 10.4 | (13.8) | [-16.6, 37.4] | 0.45 | 0.42 |

## S10.14 ODYSSEY A - Triglycerides changes over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p |
| 48 | 26 | -4.7 | (16.0) | 31 | -21.1 | (15.6) | 16.4 | (22.3) | [-28.4, 61.2] | 0.46 |
| 96 | 27 | -39.2 | (12.4) | 29 | -32.7 | (12.7) | -6.5 | (17.7) | [-42.2, 29.1] | 0.71 |
| Average treatment differences through follow-up+ | | | | | | | 5.7 | (15.4) | [-24.5, 35.9] | 0.71 |

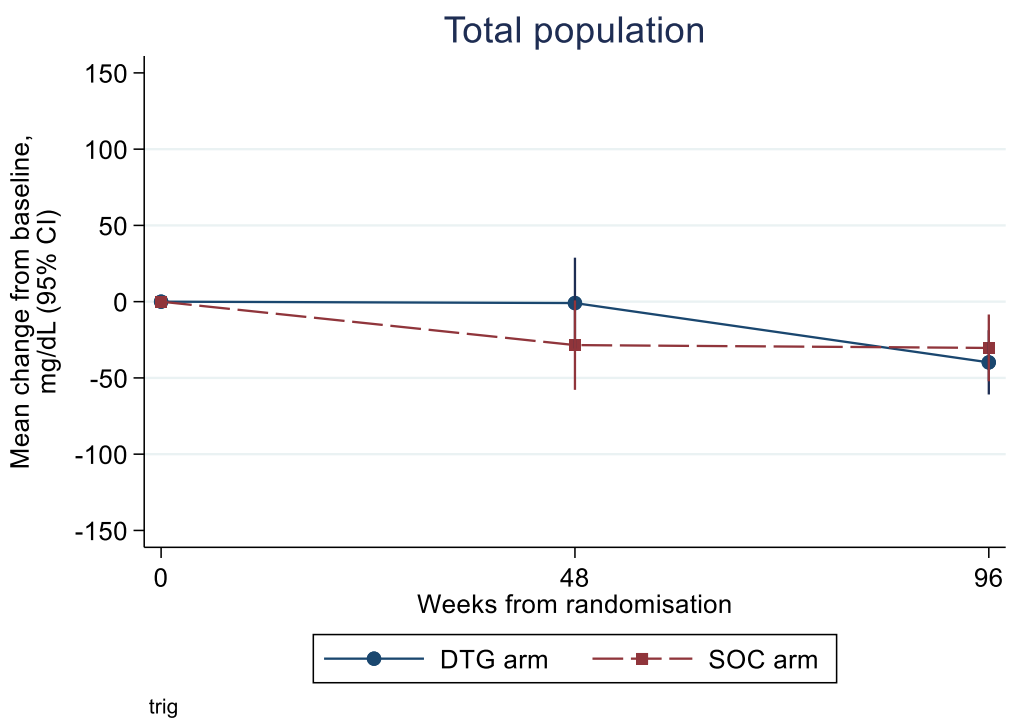
*Change calculated using normal regression adjusting for baseline only. Presenting mean change from a baseline of 159.2 in total and 163.6 in A.

**Normal regression adjusting for baseline and ODYSSEY A/B strata.

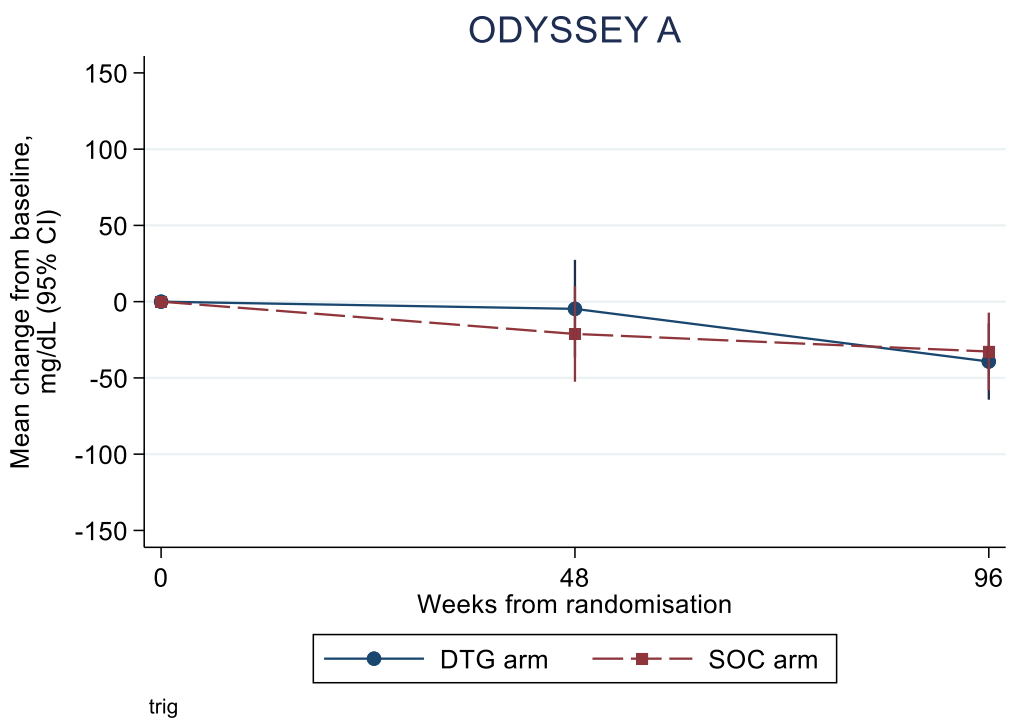
+Linear mixed models fitted with random intercept and fixed effects for treatment group, study visit and adjustment covariates (baseline Triglycerides and ODYSSEY A/B strata (total population only))

++ Test of heterogeneity of treatment effect between ODYSSEY A/B

**S10.15 Total population - changes in Triglycerides over follow-up**



**S10.16 ODYSSEY A - changes in Triglycerides over follow-up**



## S10.17 Total population - Glucose changes over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | | Adjusted Difference** | | | | Interaction++ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p | mean | (SE) | [95% CI] | p | p |
| 48 | 31 | 1.0 | (2.8) | 37 | -0.7 | (2.7) | 1.7 | (3.9) | [-6.0, 9.5] | 0.66 | 1.9 | (3.9) | [-5.8, 9.7] | 0.62 | 0.51 |
| 96 | 33 | -0.7 | (2.2) | 34 | 4.8 | (2.4) | -5.5 | (3.3) | [-12.0, 1.0] | 0.098 | -5.4 | (3.3) | [-12.0, 1.2] | 0.11 | 0.17 |
| Average treatment differences through follow-up+ | | | | | | | -2.0 | (2.6) | [-7.0, 3.0] | 0.43 | -1.8 | (2.5) | [-6.8, 3.1] | 0.47 | 0.77 |

## S10.18 ODYSSEY A - Glucose changes over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p |
| 48 | 24 | 1.6 | (3.2) | 31 | 1.0 | (3.1) | 0.6 | (4.4) | [-8.3, 9.4] | 0.90 |
| 96 | 26 | 0.5 | (2.5) | 29 | 3.9 | (2.7) | -3.4 | (3.7) | [-10.7, 4.0] | 0.36 |
| Average treatment differences through follow-up+ | | | | | | | -1.5 | (2.8) | [-7.0, 3.9] | 0.58 |

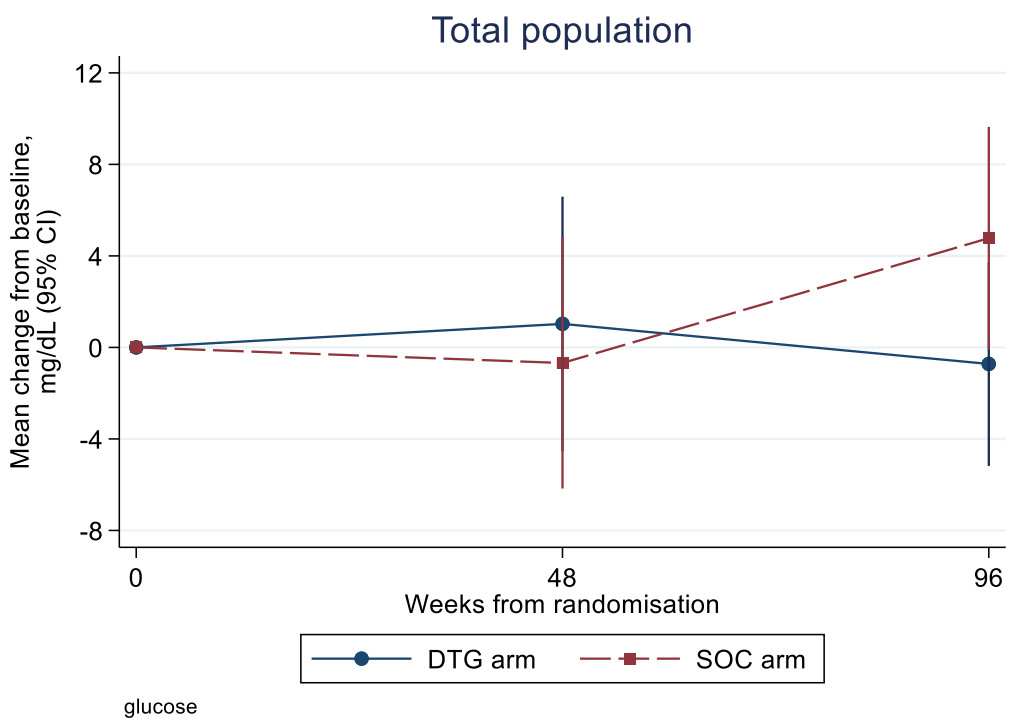
*Change calculated using normal regression adjusting for baseline only. Presenting mean change from a baseline of 81.7 in total and 82.3 in A.

**Normal regression adjusting for baseline and ODYSSEY A/B strata.

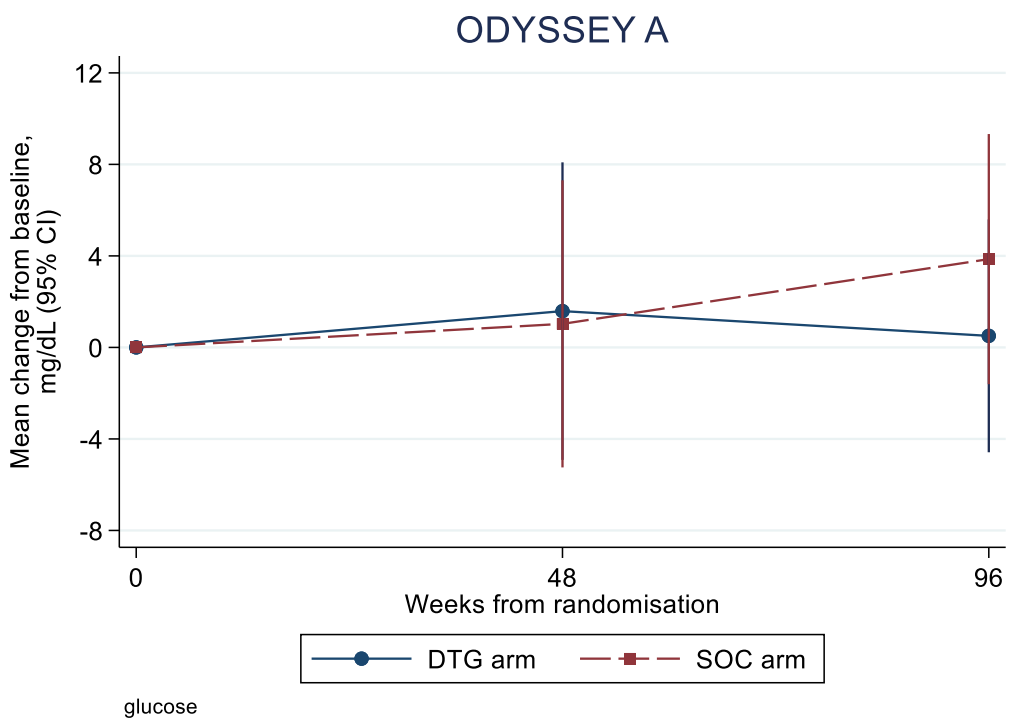
+Linear mixed models fitted with random intercept and fixed effects for treatment group, study visit and adjustment covariates (baseline Glucose and ODYSSEY A/B strata (total population only))

++ Test of heterogeneity of treatment effect between ODYSSEY A/B

**S10.19 Total population - changes in Glucose over follow-up**



**S10.20 ODYSSEY A - changes in Glucose over follow-up**




glucose

# S11 Adverse Events

## S11.1 Serious Adverse Events (SAEs) to trial censoring date by SAE type*

| | Total | | | A | | | B | | |
|---|---|---|---|---|---|---|---|---|---|
| | **DTG** | **SOC** | **Total** | **DTG** | **SOC** | **Total** | **DTG** | **SOC** | **Total** |
| **Participants randomised and included** | 42 | 43 | 85 | 35 | 37 | 72 | 7 | 6 | 13 |
| Number of events [Number of participants] | 15 [11] | 19 [11] | 34 [22] | 13 [10] | 18 [10] | 31 [20] | 2 [1] | 1 [1] | 3 [2] |
| Death | 2 [2] | 4 [4] | 6 [6] | 2 [2] | 3 [3] | 5 [5] | 0 [0] | 1 [1] | 1 [1] |
| Hospitalisation | 12 [9] | 14 [7] | 26 [16] | 10 [8] | 14 [7] | 24 [15] | 2 [1] | 0 [0] | 2 [1] |
| Other | 1 [1] | 1 [1] | 2 [2] | 1 [1] | 1 [1] | 2 [2] | 0 [0] | 0 [0] | 0 [0] |

*Non-overlapping categories, worst taken.

## S11.2 Serious Adverse Events to trial censoring date

| | Total | | | A | | | B | | |
|---|---|---|---|---|---|---|---|---|---|
| | DTG | SOC | Total | DTG | SOC | Total | DTG | SOC | Total |
| **Participants randomised and included** | 42 | 43 | 85 | 35 | 37 | 72 | 7 | 6 | 13 |
| **Person years** | 93 | 95 | 188 | 76 | 81 | 156 | 18 | 14 | 32 |
| **Number of events [Number of young people]** | 15 [11] | 19 [11] | 34 [22] | 13 [10] | 18 [10] | 31 [20] | 2 [1] | 1 [1] | 3 [2] |
| **Biochemical** | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Raised liver enzymes | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| **Haematological** | 1 [1] | 1 [1] | 2 [2] | 1 [1] | 1 [1] | 2 [2] | 0 [0] | 0 [0] | 0 [0] |
| Thrombocytopenia | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Thrombocytopenia+Neutropenia | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| **Infectious Disease** | 10 [9] | 16 [9] | 26 [18] | 9 [8] | 15 [8] | 24 [16] | 1 [1] | 1 [1] | 2 [2] |
| Acute diarrhoea not investigated+Dehydration | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Bronchiolitis | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Chest infection | 1 [1] | 1 [1] | 2 [2] | 0 [0] | 1 [1] | 1 [1] | 1 [1] | 0 [0] | 1 [1] |
| Chronic diarrhoea with no pathogen | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Encephalitis - presumed infectious | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Gastroenteritis | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Gastroenteritis * | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] | 0 [0] | 1 [1] | 1 [1] |
| Measles | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Measles+Chest infection | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| P falciparum malaria | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Pneumonia - other bacterial | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Pneumonia no organism identified, aspiration pneumonia | 1 [1] | 1 [1] | 2 [2] | 1 [1] | 1 [1] | 2 [2] | 0 [0] | 0 [0] | 0 [0] |
| Pneumonia no organism identified, aspiration pneumonia * | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Pneumonia no organism identified, aspiration pneumonia+Acute otitis media | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Presumed septicaemia/bacteremia - no organism | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Pyogenic meningitis - organism | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Tuberculosis - abdominal | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Tuberculosis - disseminated/miliary | 0 [0] | 2 [1] | 2 [1] | 0 [0] | 2 [1] | 2 [1] | 0 [0] | 0 [0] | 0 [0] |
| Tuberculosis - pulmonary - smear negative or not done | 1 [1] | 1 [1] | 2 [2] | 1 [1] | 1 [1] | 2 [2] | 0 [0] | 0 [0] | 0 [0] |
| Tuberculosis - pulmonary - smear negative or not done+Severe malnutrition | 0 [0] | 2 [1] | 2 [1] | 0 [0] | 2 [1] | 2 [1] | 0 [0] | 0 [0] | 0 [0] |
| Tuberculosis - pulmonary - smear negative or not done+Severe malnutrition * | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| **Non HIV related deaths** | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Traumatic * | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| **Systemic** | 3 [3] | 1 [1] | 4 [4] | 2 [2] | 1 [1] | 3 [3] | 1 [1] | 0 [0] | 1 [1] |
| Chest infection+Severe malnutrition | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] | 1 [1] | 0 [0] | 1 [1] |
| Kwashiorkor | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Kwashiorkor * | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Severe malnutrition * | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| **Event rate (all events)** | | | | | | | | | |
| Event rate (per 100 person years) | 16.1 | 20.0 | 18.1 | 17.2 | 22.3 | 19.8 | 11.3 | 7.1 | 9.4 |
| (95% CI) | (9.7, 26.6) | (12.8, 31.4) | (12.9, 25.3) | (10.0, 29.6) | (14.0, 35.4) | (13.9, 28.2) | (2.8, 45.0) | (1.0, 50.2) | (3.0, 29.2) |
| Unadjusted Rate ratio | 0.80 | 1 (ref) | | 0.77 | 1 (ref) | | 1.59 | 1 (ref) | |
| (95% CI) | (0.32, 2.04) | - | | (0.29, 2.06) | - | | (0.10, 24.54) | | |
| P-value | | | 0.64 | | | 0.61 | | | 0.74 |
| Adj. Rate ratio** | 0.82 | 1 (ref) | | | | | | | |
| (95% CI) | (0.32, 2.08) | - | | | | | | | |
| P-value | | | 0.68 | | | | | | |
| **Time to first event** | | | | | | | | | |
| Unadjusted Hazard ratio | 1.06 | 1 (ref) | | 1.09 | 1 (ref) | | 0.93 | 1 (ref) | |
| (95% CI) | (0.46, 2.45) | - | | (0.45, 2.62) | - | | (0.06, 14.83) | - | |
| P-value | | | 0.89 | | | 0.85 | | | 0.96 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Adj. hazard ratio** | 1.08 | 1 (ref) | | | | | | | |
| (95% CI) | (0.47, 2.49) | - | | | | | | | |
| P-value | | | 0.86 | | | | | | |
| A/B x arm interaction | 0.90 | | | | | | | | |

*Resulted in death

**Adjusted for ODYSSEY A and B strata in total.

## S11.3 Grade 3 or above clinical and laboratory adverse events to trial censoring date

| | Total | | | | | | A | | | | | | B | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | DTG | | SOC | | Total | | DTG | | SOC | | Total | | DTG | | SOC | | Total | |
| **Participants randomised and included** | 42 | | 43 | | 85 | | 35 | | 37 | | 72 | | 7 | | 6 | | 13 | |
| **Person years** | 93 | | 95 | | 188 | | 76 | | 81 | | 156 | | 18 | | 14 | | 32 | |
| **Number of events [Number of young people]** | 36 | [19] | 34 | [21] | 70 | [40] | 29 | [17] | 33 | [20] | 62 | [37] | 7 | [2] | 1 | [1] | 8 | [3] |
| **Biochemical** | 4 | [4] | 3 | [2] | 7 | [6] | 3 | [3] | 3 | [2] | 6 | [5] | 1 | [1] | 0 | [0] | 1 | [1] |
| Raised ALT | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Raised AST | 2 | [2] | 0 | [0] | 2 | [2] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] |
| Raised alkaline phosphatase (ALK) | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Raised cholesterol | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Raised liver enzymes | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Raised triglycerides | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| **Haematological** | 12 | [10] | 13 | [12] | 25 | [22] | 10 | [8] | 13 | [12] | 23 | [20] | 2 | [2] | 0 | [0] | 2 | [2] |
| Anaemia with no clinical symptoms | 6 | [6] | 8 | [8] | 14 | [14] | 5 | [5] | 8 | [8] | 13 | [13] | 1 | [1] | 0 | [0] | 1 | [1] |
| Leucopenia | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Neutropenia | 3 | [3] | 1 | [1] | 4 | [4] | 2 | [2] | 1 | [1] | 3 | [3] | 1 | [1] | 0 | [0] | 1 | [1] |
| Thrombocytopenia | 3 | [3] | 3 | [3] | 6 | [6] | 3 | [3] | 3 | [3] | 6 | [6] | 0 | [0] | 0 | [0] | 0 | [0] |
| **Hepatic** | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| drug induced liver injury | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| **Infectious Disease** | 15 | [11] | 15 | [11] | 30 | [22] | 12 | [9] | 14 | [10] | 26 | [19] | 3 | [2] | 1 | [1] | 4 | [3] |
| Acute diarrhoea not investigated | 2 | [2] | 0 | [0] | 2 | [2] | 2 | [2] | 0 | [0] | 2 | [2] | 0 | [0] | 0 | [0] | 0 | [0] |
| Acute otitis media | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Bronchiolitis | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Chest infection | 3 | [2] | 1 | [1] | 4 | [3] | 1 | [1] | 1 | [1] | 2 | [2] | 2 | [1] | 0 | [0] | 2 | [1] |
| Chronic diarrhoea not investigated | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Chronic diarrhoea with no pathogen | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Encephalitis - presumed infectious | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Gastroenteritis | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Gastroenteritis * | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] | 0 | [0] | 1 | [1] | 1 | [1] |
| Hepatitis A | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] | 1 | [1] | 0 | [0] | 1 | [1] |
| Internal abscess | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Measles | 1 | [1] | 1 | [1] | 2 | [2] | 1 | [1] | 1 | [1] | 2 | [2] | 0 | [0] | 0 | [0] | 0 | [0] |
| P falciparum malaria | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Pneumonia - other bacterial | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Pneumonia no organism identified, aspiration pneumonia | 2 | [2] | 0 | [0] | 2 | [2] | 2 | [2] | 0 | [0] | 2 | [2] | 0 | [0] | 0 | [0] | 0 | [0] |
| Pneumonia no organism identified, aspiration pneumonia * | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Presumed septicaemia/bacteremia - no organism | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Pyogenic meningitis - organism | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Tuberculosis - abdominal | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Tuberculosis - disseminated/miliary | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Tuberculosis - pulmonary - smear negative or not done | 1 | [1] | 2 | [2] | 3 | [3] | 1 | [1] | 2 | [2] | 3 | [3] | 0 | [0] | 0 | [0] | 0 | [0] |
| Tuberculosis - pulmonary - smear negative or not done * | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| **Non HIV related deaths** | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Traumatic * | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| **Systemic** | 4 | [4] | 2 | [2] | 6 | [6] | 3 | [3] | 2 | [2] | 5 | [5] | 1 | [1] | 0 | [0] | 1 | [1] |
| Dehydration | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Kwashiorkor | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Kwashiorkor * | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Severe malnutrition | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] | 1 | [1] | 0 | [0] | 1 | [1] |
| Severe malnutrition * | 0 | [0] | 2 | [2] | 2 | [2] | 0 | [0] | 2 | [2] | 2 | [2] | 0 | [0] | 0 | [0] | 0 | [0] |
| **Event rate (all events)** | | | | | | | | | | | | | | | | | | |
| Event rate (per 100 person years) | 38.5 | | 35.8 | | 37.2 | | 38.3 | | 40.8 | | 39.6 | | 39.4 | | 7.1 | | 25.1 | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| (95% CI) | (27.8, 53.4) | (25.6, 50.1) | (29.4, 47.0) | (26.6, 55.2) | (29.0, 57.4) | (30.9, 50.8) | (18.8, 82.7) | (1.0, 50.2) | (12.5, 50.2) |
| Unadjusted Rate ratio | 1.08 | 1 (ref) | | 0.94 | 1 (ref) | | 5.57 | 1 (ref) | |
| (95% CI) | (0.59, 1.96) | - | | (0.51, 1.73) | - | | (0.53, 58.84) | - | |
| P-value | | | 0.81 | | | 0.84 | | | 0.15 |
| Adj. Rate ratio** | 1.09 | 1 (ref) | | | | | | | |
| (95% CI) | (0.61, 1.97) | - | | | | | | | |
| P-value | | | 0.76 | | | | | | |
| **Time to first event** | | | | | | | | | |
| Unadjusted Hazard ratio | 0.92 | 1 (ref) | | 0.88 | 1 (ref) | | 2.03 | 1 (ref) | |
| (95% CI) | (0.50, 1.72) | - | | (0.46, 1.68) | - | | (0.18, 22.45) | - | |
| P-value | | | 0.80 | | | 0.70 | | | 0.57 |
| Adj. hazard ratio** | 0.93 | 1 (ref) | | | | | | | |
| (95% CI) | (0.50, 1.74) | - | | | | | | | |
| P-value | | | 0.83 | | | | | | |
| A/B x arm interaction | 0.55 | | | | | | | | |

*Resulted in death

**Adjusted for ODYSSEY A and B strata in total.

## S11.4 Adverse events leading to ART modification (any grade) to trial censoring date

| | Total | | | A | | | B | | |
|---|---|---|---|---|---|---|---|---|---|
| | **DTG** | **SOC** | **Total** | **DTG** | **SOC** | **Total** | **DTG** | **SOC** | **Total** |
| **Participants randomised and included** | 42 | 43 | 85 | 35 | 37 | 72 | 7 | 6 | 13 |
| **Person years** | 93 | 95 | 188 | 76 | 81 | 156 | 18 | 14 | 32 |
| **Number of events [Number of young people+]** | 0 [0] | 2 [2] | 2 [2] | 0 [0] | 2 [2] | 2 [2] | 0 [0] | 0 [0] | 0 [0] |
| **Biochemical** | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Raised liver enzymes | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| **Gastrointestinal** | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Vomiting | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |

+ Raised Liver Enzymes - Event is considered ART modifying as the event led to the participant stopping their ART regimen. The participant did subsequently re-start the same ART and hence is not contained within the table of treatment changes. Vomiting - Event led to substitution of 3rd agent due to adverse event.

## S11.5 Serious Adverse Events (SAEs) to week 96 by SAE type*

| | Total | | | A | | | B | | |
|---|---|---|---|---|---|---|---|---|---|
| | **DTG** | **SOC** | **Total** | **DTG** | **SOC** | **Total** | **DTG** | **SOC** | **Total** |
| **Participants randomised and included** | 42 | 43 | 85 | 35 | 37 | 72 | 7 | 6 | 13 |
| Number of events [Number of participants] | 15 [11] | 19 [11] | 34 [22] | 13 [10] | 18 [10] | 31 [20] | 2 [1] | 1 [1] | 3 [2] |
| Death | 2 [2] | 4 [4] | 6 [6] | 2 [2] | 3 [3] | 5 [5] | 0 [0] | 1 [1] | 1 [1] |
| Hospitalisation | 12 [9] | 14 [7] | 26 [16] | 10 [8] | 14 [7] | 24 [15] | 2 [1] | 0 [0] | 2 [1] |
| Other | 1 [1] | 1 [1] | 2 [2] | 1 [1] | 1 [1] | 2 [2] | 0 [0] | 0 [0] | 0 [0] |

*Non-overlapping categories, worst taken.

## S11.6 Serious Adverse Events to week 96

| | Total | | | | | | A | | | | | | B | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | DTG | | SOC | | Total | | DTG | | SOC | | Total | | DTG | | SOC | | Total | |
| **Participants randomised and included** | 42 | | 43 | | 85 | | 35 | | 37 | | 72 | | 7 | | 6 | | 13 | |
| **Person years** | 70 | | 73 | | 143 | | 57 | | 62 | | 120 | | 13 | | 11 | | 23 | |
| **Number of events [Number of young people]** | 15 | [11] | 19 | [11] | 34 | [22] | 13 | [10] | 18 | [10] | 31 | [20] | 2 | [1] | 1 | [1] | 3 | [2] |
| **Biochemical** | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Raised liver enzymes | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| **Haematological** | 1 | [1] | 1 | [1] | 2 | [2] | 1 | [1] | 1 | [1] | 2 | [2] | 0 | [0] | 0 | [0] | 0 | [0] |
| Thrombocytopenia | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Thrombocytopenia+Neutropenia | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| **Infectious Disease** | 10 | [9] | 16 | [9] | 26 | [18] | 9 | [8] | 15 | [8] | 24 | [16] | 1 | [1] | 1 | [1] | 2 | [2] |
| Acute diarrhoea not investigated+Dehydration | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Bronchiolitis | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Chest infection | 1 | [1] | 1 | [1] | 2 | [2] | 0 | [0] | 1 | [1] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] |
| Chronic diarrhoea with no pathogen | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Encephalitis - presumed infectious | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Gastroenteritis | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Gastroenteritis * | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] | 0 | [0] | 1 | [1] | 1 | [1] |
| Measles | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Measles+Chest infection | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| P falciparum malaria | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Pneumonia - other bacterial | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Pneumonia no organism identified, aspiration pneumonia | 1 | [1] | 1 | [1] | 2 | [2] | 1 | [1] | 1 | [1] | 2 | [2] | 0 | [0] | 0 | [0] | 0 | [0] |
| Pneumonia no organism identified, aspiration pneumonia * | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Pneumonia no organism identified, aspiration pneumonia+Acute otitis media | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Presumed septicaemia/bacteremia - no organism | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Pyogenic meningitis - organism | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Tuberculosis - abdominal | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Tuberculosis - disseminated/miliary | 0 | [0] | 2 | [1] | 2 | [1] | 0 | [0] | 2 | [1] | 2 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Tuberculosis - pulmonary - smear negative or not done | 1 | [1] | 1 | [1] | 2 | [2] | 1 | [1] | 1 | [1] | 2 | [2] | 0 | [0] | 0 | [0] | 0 | [0] |
| Tuberculosis - pulmonary - smear negative or not done+Severe malnutrition | 0 | [0] | 2 | [1] | 2 | [1] | 0 | [0] | 2 | [1] | 2 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Tuberculosis - pulmonary - smear negative or not done+Severe malnutrition * | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| **Non HIV related deaths** | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Traumatic * | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| **Systemic** | 3 | [3] | 1 | [1] | 4 | [4] | 2 | [2] | 1 | [1] | 3 | [3] | 1 | [1] | 0 | [0] | 1 | [1] |
| Chest infection+Severe malnutrition | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] | 1 | [1] | 0 | [0] | 1 | [1] |
| Kwashiorkor | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Kwashiorkor * | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Severe malnutrition * | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| **Event rate (all events)** | | | | | | | | | | | | | | | | | | |
| Event rate (per 100 person years) | 21.3 | | 26.2 | | 23.8 | | 22.6 | | 29.0 | | 25.9 | | 15.5 | | 9.5 | | 12.8 | |
| (95% CI) | (12.9, 35.4) | | (16.7, 41.0) | | (17.0, 33.3) | | (13.1, 39.0) | | (18.3, 46.0) | | (18.2, 36.9) | | (3.9, 62.1) | | (1.3, 67.5) | | (4.1, 39.8) | |
| Unadjusted Rate ratio | 0.81 | | 1 (ref) | | | | 0.78 | | 1 (ref) | | | | 1.63 | | 1 (ref) | | | |
| (95% CI) | (0.32, 2.05) | | - | | | | (0.30, 2.06) | | - | | | | (0.11, 24.75) | | | | | |
| P-value | | | | | 0.66 | | | | | | 0.62 | | | | | | 0.72 | |
| Adj. Rate ratio** | 0.83 | | 1 (ref) | | | | | | | | | | | | | | | |
| (95% CI) | (0.33, 2.08) | | - | | | | | | | | | | | | | | | |
| P-value | | | | | 0.69 | | | | | | | | | | | | | |
| **Time to first event** | | | | | | | | | | | | | | | | | | |
| Unadjusted Hazard ratio | 1.06 | | 1 (ref) | | | | 1.09 | | 1 (ref) | | | | 0.93 | | 1 (ref) | | | |
| (95% CI) | (0.46, 2.45) | | - | | | | (0.45, 2.62) | | - | | | | (0.06, 14.83) | | - | | | |
| P-value | | | | | 0.89 | | | | | | 0.85 | | | | | | 0.96 | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Adj. hazard ratio** | 1.08 | 1 (ref) | | | | | | | |
| (95% CI) | (0.47, 2.49) | - | | | | | | | |
| P-value | | | 0.86 | | | | | | |
| A/B x arm interaction | 0.90 | | | | | | | | |

*Resulted in death

**Adjusted for ODYSSEY A and B strata in total.

## S11.7 Grade 3 or above clinical and laboratory adverse events to week 96

| | Total | | | | | | A | | | | | | B | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | DTG | | SOC | | Total | | DTG | | SOC | | Total | | DTG | | SOC | | Total | |
| **Participants randomised and included** | 42 | | 43 | | 85 | | 35 | | 37 | | 72 | | 7 | | 6 | | 13 | |
| **Person years** | 70 | | 73 | | 143 | | 57 | | 62 | | 120 | | 13 | | 11 | | 23 | |
| **Number of events [Number of young people]** | 35 | [18] | 33 | [20] | 68 | [38] | 28 | [16] | 32 | [19] | 60 | [35] | 7 | [2] | 1 | [1] | 8 | [3] |
| **Biochemical** | 4 | [4] | 3 | [2] | 7 | [6] | 3 | [3] | 3 | [2] | 6 | [5] | 1 | [1] | 0 | [0] | 1 | [1] |
| Raised ALT | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Raised AST | 2 | [2] | 0 | [0] | 2 | [2] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] |
| Raised alkaline phosphatase (ALK) | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Raised cholesterol | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Raised liver enzymes | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Raised triglycerides | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| **Haematological** | 11 | [9] | 12 | [11] | 23 | [20] | 9 | [7] | 12 | [11] | 21 | [18] | 2 | [2] | 0 | [0] | 2 | [2] |
| Anaemia with no clinical symptoms | 6 | [6] | 8 | [8] | 14 | [14] | 5 | [5] | 8 | [8] | 13 | [13] | 1 | [1] | 0 | [0] | 1 | [1] |
| Leucopenia | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Neutropenia | 3 | [3] | 1 | [1] | 4 | [4] | 2 | [2] | 1 | [1] | 3 | [3] | 1 | [1] | 0 | [0] | 1 | [1] |
| Thrombocytopenia | 2 | [2] | 2 | [2] | 4 | [4] | 2 | [2] | 2 | [2] | 4 | [4] | 0 | [0] | 0 | [0] | 0 | [0] |
| **Hepatic** | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| drug induced liver injury | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| **Infectious Disease** | 15 | [11] | 15 | [11] | 30 | [22] | 12 | [9] | 14 | [10] | 26 | [19] | 3 | [2] | 1 | [1] | 4 | [3] |
| Acute diarrhoea not investigated | 2 | [2] | 0 | [0] | 2 | [2] | 2 | [2] | 0 | [0] | 2 | [2] | 0 | [0] | 0 | [0] | 0 | [0] |
| Acute otitis media | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Bronchiolitis | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Chest infection | 3 | [2] | 1 | [1] | 4 | [3] | 1 | [1] | 1 | [1] | 2 | [2] | 2 | [1] | 0 | [0] | 2 | [1] |
| Chronic diarrhoea not investigated | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Chronic diarrhoea with no pathogen | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Encephalitis - presumed infectious | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Gastroenteritis | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Gastroenteritis * | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] | 0 | [0] | 1 | [1] | 1 | [1] |
| Hepatitis A | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] | 1 | [1] | 0 | [0] | 1 | [1] |
| Internal abscess | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Measles | 1 | [1] | 1 | [1] | 2 | [2] | 1 | [1] | 1 | [1] | 2 | [2] | 0 | [0] | 0 | [0] | 0 | [0] |
| P falciparum malaria | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Pneumonia - other bacterial | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Pneumonia no organism identified, aspiration pneumonia | 2 | [2] | 0 | [0] | 2 | [2] | 2 | [2] | 0 | [0] | 2 | [2] | 0 | [0] | 0 | [0] | 0 | [0] |
| Pneumonia no organism identified, aspiration pneumonia * | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Presumed septicaemia/bacteremia - no organism | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Pyogenic meningitis - organism | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Tuberculosis - abdominal | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Tuberculosis - disseminated/miliary | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Tuberculosis - pulmonary - smear negative or not done | 1 | [1] | 2 | [2] | 3 | [3] | 1 | [1] | 2 | [2] | 3 | [3] | 0 | [0] | 0 | [0] | 0 | [0] |
| Tuberculosis - pulmonary - smear negative or not done * | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| **Non HIV related deaths** | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Traumatic * | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| **Systemic** | 4 | [4] | 2 | [2] | 6 | [6] | 3 | [3] | 2 | [2] | 5 | [5] | 1 | [1] | 0 | [0] | 1 | [1] |
| Dehydration | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Kwashiorkor | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Kwashiorkor * | 1 | [1] | 0 | [0] | 1 | [1] | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] |
| Severe malnutrition | 1 | [1] | 0 | [0] | 1 | [1] | 0 | [0] | 0 | [0] | 0 | [0] | 1 | [1] | 0 | [0] | 1 | [1] |
| Severe malnutrition * | 0 | [0] | 2 | [2] | 2 | [2] | 0 | [0] | 2 | [2] | 2 | [2] | 0 | [0] | 0 | [0] | 0 | [0] |
| **Event rate (all events)** | | | | | | | | | | | | | | | | | | |
| Event rate (per 100 person years) | 49.8 | | 45.5 | | 47.6 | | 48.7 | | 51.5 | | 50.2 | | 54.4 | | 9.5 | | 34.2 | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| (95% CI) | (35.7, 69.3) | (32.3, 63.9) | (37.5, 60.3) | (33.6, 70.6) | (36.4, 72.9) | (39.0, 64.6) | (25.9, 114.0) | (1.3, 67.5) | (17.1, 68.4) |
| Unadjusted Rate ratio | 1.09 | 1 (ref) | | 0.95 | 1 (ref) | | 5.71 | 1 (ref) | |
| (95% CI) | (0.59, 2.02) | - | | (0.50, 1.77) | - | | (0.57, 57.77) | - | |
| P-value | | | 0.77 | | | 0.86 | | | 0.14 |
| Adj. Rate ratio** | 1.11 | 1 (ref) | | | | | | | |
| (95% CI) | (0.61, 2.03) | - | | | | | | | |
| P-value | | | 0.74 | | | | | | |
| **Time to first event** | | | | | | | | | |
| Unadjusted Hazard ratio | 0.93 | 1 (ref) | | 0.88 | 1 (ref) | | 2.03 | 1 (ref) | |
| (95% CI) | (0.49, 1.75) | - | | (0.45, 1.71) | - | | (0.18, 22.45) | - | |
| P-value | | | 0.82 | | | 0.71 | | | 0.57 |
| Adj. hazard ratio** | 0.94 | 1 (ref) | | | | | | | |
| (95% CI) | (0.50, 1.77) | - | | | | | | | |
| P-value | | | 0.84 | | | | | | |
| A/B x arm interaction | 0.54 | | | | | | | | |

*Resulted in death

**Adjusted for ODYSSEY A and B strata in total.

## S11.8 Adverse events leading to ART modification (any grade) to week 96

| | Total | | | A | | | B | | |
|---|---|---|---|---|---|---|---|---|---|
| | **DTG** | **SOC** | **Total** | **DTG** | **SOC** | **Total** | **DTG** | **SOC** | **Total** |
| **Participants randomised and included** | 42 | 43 | 85 | 35 | 37 | 72 | 7 | 6 | 13 |
| **Person years** | 70 | 73 | 143 | 57 | 62 | 120 | 13 | 11 | 23 |
| **Number of events [Number of young people+]** | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| **Biochemical** | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |
| Raised liver enzymes | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 1 [1] | 1 [1] | 0 [0] | 0 [0] | 0 [0] |

+ Raised Liver Enzymes - Event is considered ART modifying as the event led to the participant stopping their ART regimen. The participant did subsequently re-start the same ART and hence is not contained within the table of treatment changes.

# S12 Patient Reported Outcomes

Note: ODYSSEY B is not presented here due to having few participants

## S12.1 Summary of carer reported adherence

| | Total | | | A | | |
|---|---|---|---|---|---|---|
| | **DTG** | **SOC** | **Total** | **DTG** | **SOC** | **Total** |
| **Participants randomised** | 42 | 43 | 85 | 35 | 37 | 72 |
| **Dose missed in the last week #missed [#questionnaires completed]** | | | | | | |
| Week 4 | 3 [40] | 5 [38] | 8 [78] | 3 [33] | 4 [32] | 7 [65] |
| Week 12 | 4 [40] | 5 [38] | 9 [78] | 4 [33] | 4 [33] | 8 [66] |
| Week 24 | 2 [38] | 4 [39] | 6 [77] | 1 [31] | 3 [33] | 4 [64] |
| Week 36 | 5 [36] | 6 [40] | 11 [76] | 4 [29] | 6 [34] | 10 [63] |
| Week 48 | 3 [34] | 7 [36] | 10 [70] | 3 [27] | 7 [31] | 10 [58] |
| Week 60 | 4 [35] | 2 [34] | 6 [69] | 3 [28] | 2 [28] | 5 [56] |
| Week 72 | 4 [35] | 5 [35] | 9 [70] | 3 [28] | 4 [30] | 7 [58] |
| Week 84 | 2 [34] | 3 [33] | 5 [67] | 1 [27] | 3 [29] | 4 [56] |
| Week 96 | 4 [34] | 6 [38] | 10 [72] | 2 [27] | 6 [33] | 8 [60] |
| Week 108 | 5 [33] | 4 [30] | 9 [63] | 4 [26] | 3 [26] | 7 [52] |
| Week 120 | 4 [25] | 3 [22] | 7 [47] | 1 [21] | 3 [18] | 4 [39] |
| Week 132 | 1 [14] | 3 [14] | 4 [28] | 1 [11] | 2 [11] | 3 [22] |
| Total # of reports of dose missed in the last week over follow-up (% of all follow-up questionnaires) | 42 (10%) | 53 (13%) | 95 (12%) | 31 (10%) | 47 (14%) | 78 (12%) |
| # of participants reporting at >=1 follow-up visit | 25 (61%) | 30 (73%) | 55 (67%) | 21 (62%) | 25 (71%) | 46 (67%) |
| P-value* | | | 0.50 | | | 0.49 |
| **Dose missed in the last month #missed [#questionnaires completed]** | | | | | | |
| Week 4 | 2 [40] | 3 [38] | 5 [78] | 2 [33] | 2 [32] | 4 [65] |
| Week 12 | 3 [39] | 8 [39] | 11 [78] | 2 [32] | 7 [33] | 9 [65] |
| Week 24 | 4 [38] | 4 [39] | 8 [77] | 2 [31] | 4 [33] | 6 [64] |
| Week 36 | 4 [36] | 5 [40] | 9 [76] | 4 [29] | 4 [34] | 8 [63] |
| Week 48 | 3 [34] | 7 [36] | 10 [70] | 3 [27] | 7 [31] | 10 [58] |
| Week 60 | 5 [35] | 3 [34] | 8 [69] | 4 [28] | 3 [28] | 7 [56] |
| Week 72 | 5 [35] | 6 [35] | 11 [70] | 4 [28] | 6 [30] | 10 [58] |
| Week 84 | 4 [33] | 3 [33] | 7 [66] | 4 [27] | 3 [29] | 7 [56] |
| Week 96 | 3 [35] | 5 [38] | 8 [73] | 3 [28] | 5 [33] | 8 [61] |
| Week 108 | 3 [33] | 6 [30] | 9 [63] | 3 [26] | 5 [26] | 8 [52] |
| Week 120 | 2 [25] | 4 [22] | 6 [47] | 1 [21] | 3 [18] | 4 [39] |
| Week 132 | 1 [14] | 0 [14] | 1 [28] | 1 [11] | 0 [11] | 1 [22] |
| Total # of reports of dose missed in the last week over follow-up (% of all follow-up questionnaires) | 39 (10%) | 55 (14%) | 94 (12%) | 33 (10%) | 50 (14%) | 83 (12%) |
| # of participants reporting at >=1 follow-up visit | 22 (54%) | 26 (63%) | 48 (59%) | 18 (53%) | 22 (63%) | 40 (58%) |
| P-value* | | | 0.27 | | | 0.35 |

*Mixed logistic regression model with a random effect for participant and fixed effects for treatment arm, visit week and ODYSSEY A/B (total population only).

## S12.2 Summary of carer reported acceptability of treatment during follow-up

| | Total | | | A | | |
|---|---|---|---|---|---|---|
| | **DTG** | **SOC** | **Total** | **DTG** | **SOC** | **Total** |
| Participants randomised | 42 | 43 | 85 | 35 | 37 | 72 |
| **Problems with taste/does not like taste #with a problem [#questionnaires completed]** | | | | | | |
| Week 4 | 5 [35] | 6 [32] | 11 [67] | 5 [29] | 6 [27] | 11 [56] |
| Week 12 | 5 [34] | 8 [32] | 13 [66] | 5 [27] | 8 [27] | 13 [54] |
| Week 24 | 3 [35] | 3 [34] | 6 [69] | 3 [28] | 3 [29] | 6 [57] |
| Week 48 | 3 [30] | 3 [31] | 6 [61] | 3 [23] | 3 [25] | 6 [48] |
| Week 72 | 3 [32] | 4 [33] | 7 [65] | 3 [26] | 4 [28] | 7 [54] |
| Week 96 | 4 [33] | 2 [37] | 6 [70] | 3 [27] | 2 [32] | 5 [59] |
| Week 120 | 1 [24] | 1 [19] | 2 [43] | 1 [19] | 1 [15] | 2 [34] |
| Total # of reports of problems over follow-up (% of all follow-up questionnaires) | 24 (10%) | 28 (12%) | 52 (11%) | 23 (13%) | 28 (15%) | 51 (14%) |
| # of participants reporting at >=1 follow-up visit | 13 (32%) | 14 (34%) | 27 (33%) | 12 (35%) | 14 (40%) | 26 (38%) |
| P-value* | | | 0.78 | | | 0.62 |
| **Problems with swallowing/not easy to swallow #with a problem [#questionnaires completed]** | | | | | | |
| Week 4 | 3 [35] | 6 [32] | 9 [67] | 3 [29] | 6 [27] | 9 [56] |
| Week 12 | 4 [34] | 4 [32] | 8 [66] | 4 [27] | 4 [27] | 8 [54] |
| Week 24 | 2 [35] | 2 [34] | 4 [69] | 2 [28] | 2 [29] | 4 [57] |
| Week 48 | 2 [30] | 0 [31] | 2 [61] | 2 [23] | 0 [25] | 2 [48] |
| Week 72 | 2 [32] | 1 [33] | 3 [65] | 2 [26] | 1 [28] | 3 [54] |
| Week 96 | 0 [33] | 2 [35] | 2 [68] | 0 [27] | 1 [30] | 1 [57] |
| Week 120 | 0 [24] | 0 [18] | 0 [42] | 0 [19] | 0 [14] | 0 [33] |
| Total # of reports of problems over follow-up (% of all follow-up questionnaires) | 13 ( 6%) | 17 ( 8%) | 30 ( 7%) | 13 ( 7%) | 16 ( 9%) | 29 ( 8%) |
| # of participants reporting at >=1 follow-up visit | 10 (24%) | 13 (32%) | 23 (28%) | 10 (29%) | 12 (34%) | 22 (32%) |
| P-value* | | | 0.51 | | | 0.68 |

*Mixed logistic regression model with a random effect for participant and fixed effects for treatment arm, visit week and ODYSSEY A/B (total population only).

# S13 Antiretroviral Therapy

## S13.1 Summary of initial SOC treatment regimens

| | | Total | | A | | B | |
|---|---|---|---|---|---|---|---|
| | | SOC | | SOC | | SOC | |
| **Participants randomised** | | 43 | | 37 | | 6 | |
| **ART regimen** | | | | | | | |
| **Non-NRTI component** | NRTI component | | | | | | |
| EFV | ABC 3TC | 4 | ( 9%) | 4 | (11%) | 0 | (%) |
| LOP | ABC 3TC | 30 | (70%) | 29 | (78%) | 1 | (17%) |
| LOP | ZDV 3TC | 2 | ( 5%) | 0 | (0%) | 2 | (33%) |
| NVP | ABC 3TC | 3 | ( 7%) | 3 | ( 8%) | 0 | (%) |
| NVP | ZDV 3TC | 2 | ( 5%) | 1 | ( 3%) | 1 | (17%) |
| RAL | ZDV 3TC | 2 | ( 5%) | 0 | (0%) | 2 | (33%) |

## S13.2 Summary of initial DTG regimens

| | | Total | | A | | B | |
|---|---|---|---|---|---|---|---|
| | | DTG | | DTG | | DTG | |
| **Participants randomised** | | 42 | | 35 | | 7 | |
| **ART regimen** | | | | | | | |
| **Non-NRTI component** | NRTI component | | | | | | |
| DTG | ABC 3TC | 38 | (90%) | 35 | (100%) | 3 | (43%) |
| DTG | ZDV 3TC | 4 | (10%) | | | 4 | (57%) |

## S13.3 Definitions of Treatment Regimens

1st ODYSSEY Regimen: Can either be strictly the regimen allocated at trial entry or initial regimen allowing for NRTI substitutions or reductions for any reason and/or third agent substitutions for reasons other than toxicity, treatment failure, pregnancy or a major protocol deviation (these include simplification, drug availability, patient/carer decision and increases in weight).

2nd ODYSSEY Regimen: Participants will considered to be on their second ODYSSEY regimen if changed the third agent in initial regimen for reasons of toxicity, treatment failure, pregnancy or a major protocol deviation.

3rd ODYSSEY Regimen: Participants will considered to be on their third ODYSSEY regimen if changed the third agent in their second regimen for reasons of toxicity, treatment failure, pregnancy or a major protocol deviation.

## S13.4 Treatment regimen at last visit

| | Total | | | | | | A | | | | | | B | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | DTG | | SOC | | Total | | DTG | | SOC | | Total | | DTG | | SOC | | Total | |
| **Participants randomised** | 42 | | 43 | | 85 | | 35 | | 37 | | 72 | | 7 | | 6 | | 13 | |
| **ODYSSEY regimen at last visit, number of participants (%):** | | | | | | | | | | | | | | | | | | |
| 1st:strict initial | 41 | (98%) | 37 | (86%) | 78 | (92%) | 34 | (97%) | 32 | (86%) | 66 | (92%) | 7 | (100%) | 5 | (83%) | 12 | (92%) |
| 1st:NRTI substitution/reduction | 0 | ( 0%) | 1 | ( 2%) | 1 | ( 1%) | 0 | ( 0%) | 1 | ( 3%) | 1 | ( 1%) | 0 | ( 0%) | 0 | ( 0%) | 0 | ( 0%) |
| 1st:substitution 3rd agent | 0 | ( 0%) | 1 | ( 2%) | 1 | ( 1%) | 0 | ( 0%) | 1 | ( 3%) | 1 | ( 1%) | 0 | ( 0%) | 0 | ( 0%) | 0 | ( 0%) |
| 2nd regimen | 0 | ( 0%) | 4 | ( 9%) | 4 | ( 5%) | 0 | ( 0%) | 3 | ( 8%) | 3 | ( 4%) | 0 | ( 0%) | 1 | (17%) | 1 | ( 8%) |
| Stopped | 1 | ( 2%) | 0 | ( 0%) | 1 | ( 1%) | 1 | ( 3%) | 0 | ( 0%) | 1 | ( 1%) | 0 | ( 0%) | 0 | ( 0%) | 0 | ( 0%) |

The following two tables present all ART changes from strict initial regimen and stops of >31 days. Stops of ART of <=31 days are ignored here.

## S13.5 Details of Changes to Treatment Regimens for Toxicity or Treatment Failure

| ID | Arm | Treatment | Date of Change | Week | ART Regimen | Treatment Line | Reason for Change |
|---|---|---|---|---|---|---|---|
| 5 | A | SOC | 15nov2018 | - | ABC 3TC LOP | 1st:Strict initial | Start ODYSSEY Trial |
| 5 | A | SOC | 18feb2020 | 65 | ZDV 3TC LOP | 1st:NRTI substitution/reduction | Treatment failure |
| 6 | A | SOC | 19feb2019 | - | ABC 3TC NVP | 1st:Strict initial | Start ODYSSEY Trial |
| 6 | A | SOC | 28feb2020 | 53 | ABC 3TC EFV | 1st:substitution 3rd agent | TB |
| 6 | A | SOC | 12oct2020 | 85 | ZDV 3TC LOP | 2nd: treatment failure | Treatment failure |
| 7 | A | SOC | 16aug2018 | - | ABC 3TC EFV | 1st:Strict initial | Start ODYSSEY Trial |
| 7 | A | SOC | 25feb2021 | 132 | ABC 3TC LOP | 1st:substitution 3rd agent | Change in National Guidelines |
| 7 | A | SOC | 03mar2021 | 132 | ABC 3TC EFV | 2nd: toxicity | Adverse event |
| 8 | A | SOC | 24jan2019 | - | ABC 3TC LOP | 1st:Strict initial | Start ODYSSEY Trial |
| 8 | A | SOC | 25jun2020 | 74 | ZDV 3TC RAL | 2nd: treatment failure | Treatment failure |
| 9 | A | SOC | 07jun2019 | - | ABC 3TC LOP | 1st:Strict initial | Start ODYSSEY Trial |
| 9 | A | SOC | 22jun2019 | 2 | - | stopped | Adverse event |
| 9 | A | SOC | 27aug2019 | 11 | ABC 3TC LOP | 1st:Strict initial | Restart previous ART |
| 10 | A | SOC | 26aug2019 | - | ABC 3TC LOP | 1st:Strict initial | Start ODYSSEY Trial |
| 10 | A | SOC | 01nov2019 | 9 | - | stopped | Adverse event |
| 10 | A | SOC | 08feb2020 | 23 | ABC 3TC LOP | 1st:Strict initial | Restart previous ART |
| 13 | B | SOC | 06nov2018 | - | ZDV 3TC NVP | 1st:Strict initial | Start ODYSSEY Trial |
| 13 | B | SOC | 01sep2020 | 95 | ZDV 3TC LOP | 2nd: treatment failure | Treatment failure |

ID 7 – Participant switched from efavrenz to lopinavir due to a change in national guidelines and subsequently changed back to their initial regimen of efavrenz due to an adverse event and are hence considered to be on their second regimen

## S13.6 Details of Other Changes to Treatment Regimens

| ID | Arm | Treatment | Date of Change | Week | ART Regimen | Treatment Line | Reason for Change |
|---|---|---|---|---|---|---|---|
| 1 | A | DTG | 12jul2018 | - | ABC 3TC DTG | 1st:Strict initial | Start ODYSSEY Trial |
| 1 | A | DTG | 07aug2018 | 3 | - | stopped | Missed/Forgot/Compliance |
| 2 | A | DTG | 15jan2019 | - | ABC 3TC DTG | 1st:Strict initial | Start ODYSSEY Trial |
| 2 | A | DTG | 16dec2019 | 47 | - | stopped | Patient/carer decision |
| 2 | A | DTG | 12mar2020 | 60 | ABC 3TC DTG | 1st:Strict initial | Restart previous ART |
| 3 | A | DTG | 30jan2019 | - | ABC 3TC DTG | 1st:Strict initial | Start ODYSSEY Trial |
| 3 | A | DTG | 19jun2020 | 72 | - | stopped | Unable/failed to attend clinic |
| 3 | A | DTG | 27jul2020 | 77 | ABC 3TC DTG | 1st:Strict initial | Unable/failed to attend clinic |
| 4 | A | DTG | 13feb2019 | - | ABC 3TC DTG | 1st:Strict initial | Start ODYSSEY Trial |
| 4 | A | DTG | 24oct2019 | 36 | - | stopped | Unable/failed to attend clinic |
| 4 | A | DTG | 07sep2020 | 81 | ABC 3TC DTG | 1st:Strict initial | Unable/failed to attend clinic |
| 11 | A | SOC | 25jul2018 | - | ZDV 3TC NVP | 1st:Strict initial | Start ODYSSEY Trial |
| 11 | A | SOC | 11dec2019 | 72 | ZDV 3TC DTG | 1st:substitution 3rd agent | TB |
| 12 | A | SOC | 31jul2018 | - | ABC 3TC EFV | 1st:Strict initial | Start ODYSSEY Trial |
| 12 | A | SOC | 15aug2018 | 2 | - | stopped | Unable/failed to attend clinic |
| 12 | A | SOC | 22oct2018 | 11 | ABC 3TC EFV | 1st:Strict initial | Restart previous ART |

ID 1 - participant was considered as stopped ART at their last visit, they subsequently withdrew

# S14 Anthropometric measures

Note: ODYSSEY B is not presented here due to having few participants

Throughout this section, n refers to the number of participants with available measurement at each visit week. Numbers in models may be lower where there are missing data at baseline.

## S14.1 Total population - Height (cm) change over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | | Adjusted Difference** | | | | Interaction++ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p | mean | (SE) | [95% CI] | p | p |
| 12 | 39 | 3.2 | (0.3) | 40 | 2.6 | (0.3) | 0.6 | (0.4) | [-0.2, 1.3] | 0.12 | 0.6 | (0.4) | [-0.2, 1.3] | 0.13 | 0.70 |
| 24 | 39 | 6.0 | (0.4) | 40 | 5.2 | (0.4) | 0.8 | (0.5) | [-0.3, 1.8] | 0.17 | 0.7 | (0.5) | [-0.4, 1.8] | 0.18 | 0.081 |
| 36 | 35 | 8.1 | (0.5) | 39 | 7.1 | (0.4) | 1.0 | (0.6) | [-0.3, 2.3] | 0.11 | 1.0 | (0.6) | [-0.3, 2.3] | 0.13 | 0.16 |
| 48 | 35 | 10.3 | (0.5) | 39 | 9.1 | (0.5) | 1.2 | (0.8) | [-0.3, 2.7] | 0.11 | 1.2 | (0.8) | [-0.3, 2.7] | 0.12 | 0.25 |
| 60 | 33 | 12.1 | (0.6) | 36 | 11.8 | (0.5) | 0.3 | (0.8) | [-1.3, 1.9] | 0.71 | 0.3 | (0.8) | [-1.3, 1.9] | 0.73 | 0.27 |
| 72 | 32 | 13.7 | (0.6) | 33 | 14.2 | (0.6) | -0.5 | (0.9) | [-2.3, 1.2] | 0.54 | -0.5 | (0.9) | [-2.3, 1.3] | 0.56 | 0.46 |
| 84 | 35 | 16.4 | (0.7) | 37 | 15.7 | (0.7) | 0.7 | (1.0) | [-1.3, 2.6] | 0.49 | 0.7 | (1.0) | [-1.3, 2.7] | 0.48 | 0.17 |
| 96 | 32 | 18.8 | (0.7) | 36 | 18.5 | (0.7) | 0.4 | (1.0) | [-1.6, 2.4] | 0.72 | 0.4 | (1.0) | [-1.7, 2.4] | 0.71 | 0.33 |
| Average treatment differences through follow-up+ | | | | | | | 0.5 | (0.6) | [-0.6, 1.7] | 0.37 | 0.5 | (0.6) | [-0.6, 1.7] | 0.38 | 0.12 |

## S14.2 ODYSSEY A - Height (cm) change over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p |
| 12 | 32 | 3.4 | (0.3) | 34 | 2.8 | (0.3) | 0.6 | (0.4) | [-0.2, 1.4] | 0.13 |
| 24 | 32 | 6.5 | (0.4) | 34 | 5.3 | (0.4) | 1.2 | (0.6) | [0.0, 2.3] | 0.050 |
| 36 | 28 | 8.6 | (0.5) | 33 | 7.2 | (0.5) | 1.4 | (0.7) | [-0.0, 2.9] | 0.058 |
| 48 | 28 | 10.9 | (0.6) | 33 | 9.3 | (0.6) | 1.6 | (0.8) | [-0.1, 3.2] | 0.065 |
| 60 | 26 | 12.8 | (0.6) | 30 | 12.1 | (0.6) | 0.7 | (0.9) | [-1.1, 2.5] | 0.44 |
| 72 | 25 | 14.4 | (0.7) | 28 | 14.7 | (0.7) | -0.2 | (1.0) | [-2.2, 1.8] | 0.82 |
| 84 | 28 | 17.3 | (0.8) | 33 | 16.0 | (0.8) | 1.3 | (1.1) | [-1.0, 3.5] | 0.26 |
| 96 | 26 | 19.7 | (0.8) | 32 | 19.0 | (0.8) | 0.8 | (1.1) | [-1.5, 3.1] | 0.50 |
| Average treatment differences through follow-up+ | | | | | | | 0.9 | (0.7) | [-0.4, 2.2] | 0.16 |

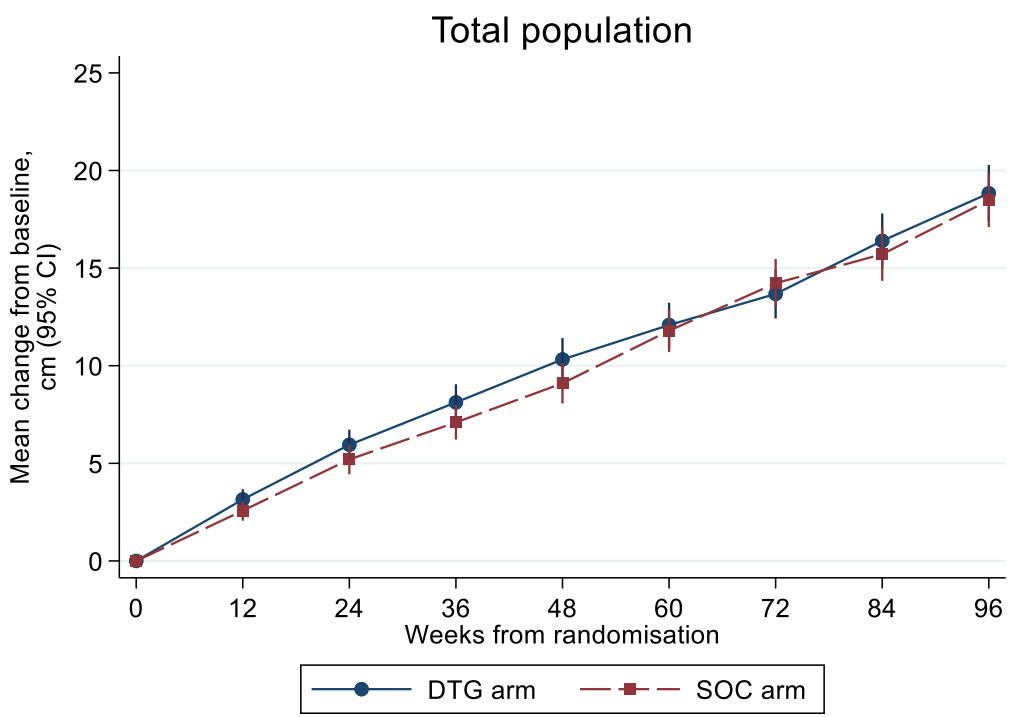
*Change calculated using normal regression adjusting for baseline only. Presenting mean change from a baseline of 71.9 in total and 69.8 in A.

**Normal regression adjusting for baseline and ODYSSEY A/B strata.

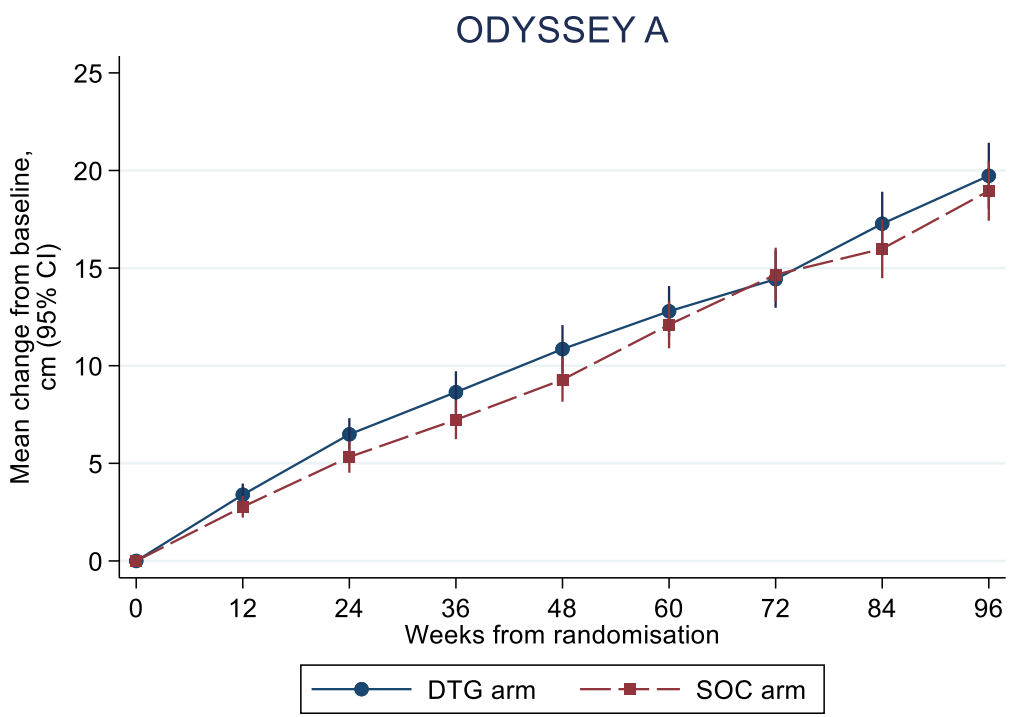
+Linear mixed models fitted with random intercept and fixed effects for treatment group, study visit and adjustment covariates (baseline Height (cm) and ODYSSEY A/B strata (total population only))

++ Test of heterogeneity of treatment effect between ODYSSEY A/B

**S14.3 Total population - Height (cm) change over follow-up**



**S14.4 ODYSSEY A - Height (cm) change over follow-up**



## S14.5 Total population - Weight (kg) change over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | | Adjusted Difference** | | | | Interaction++ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p | mean | (SE) | [95% CI] | p | p |
| 12 | 39 | 0.97 | (0.14) | 40 | 1.12 | (0.14) | -0.15 | (0.19) | [-0.53, 0.24] | 0.45 | -0.14 | (0.20) | [-0.53, 0.25] | 0.47 | 0.75 |
| 24 | 39 | 1.89 | (0.16) | 40 | 1.73 | (0.16) | 0.16 | (0.23) | [-0.29, 0.62] | 0.48 | 0.16 | (0.23) | [-0.30, 0.62] | 0.48 | 0.37 |
| 36 | 36 | 2.43 | (0.20) | 40 | 2.42 | (0.19) | 0.01 | (0.27) | [-0.53, 0.54] | 0.98 | 0.01 | (0.27) | [-0.53, 0.55] | 0.96 | 0.94 |
| 48 | 35 | 3.18 | (0.21) | 40 | 2.95 | (0.20) | 0.23 | (0.29) | [-0.35, 0.82] | 0.42 | 0.26 | (0.29) | [-0.32, 0.85] | 0.37 | 0.98 |
| 60 | 34 | 3.56 | (0.24) | 37 | 3.62 | (0.23) | -0.06 | (0.33) | [-0.71, 0.59] | 0.86 | -0.05 | (0.33) | [-0.70, 0.61] | 0.89 | 0.84 |
| 72 | 33 | 4.19 | (0.27) | 33 | 4.25 | (0.27) | -0.05 | (0.39) | [-0.83, 0.72] | 0.89 | -0.00 | (0.39) | [-0.78, 0.78] | 1 | 0.52 |
| 84 | 36 | 4.57 | (0.24) | 37 | 4.70 | (0.23) | -0.13 | (0.33) | [-0.79, 0.53] | 0.70 | -0.09 | (0.34) | [-0.76, 0.59] | 0.80 | 0.55 |
| 96 | 35 | 4.96 | (0.24) | 36 | 5.14 | (0.24) | -0.18 | (0.34) | [-0.86, 0.49] | 0.60 | -0.15 | (0.34) | [-0.83, 0.54] | 0.67 | 0.71 |
| Average treatment differences through follow-up+ | | | | | | | -0.01 | (0.24) | [-0.48, 0.46] | 0.97 | 0.00 | (0.24) | [-0.47, 0.48] | 0.99 | 0.87 |

## S14.6 ODYSSEY A - Weight (kg) change over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p |
| 12 | 32 | 1.06 | (0.14) | 34 | 1.22 | (0.14) | -0.16 | (0.20) | [-0.57, 0.24] | 0.42 |
| 24 | 32 | 1.95 | (0.17) | 34 | 1.87 | (0.17) | 0.08 | (0.24) | [-0.41, 0.57] | 0.75 |
| 36 | 29 | 2.57 | (0.21) | 34 | 2.54 | (0.19) | 0.03 | (0.28) | [-0.54, 0.60] | 0.91 |
| 48 | 28 | 3.39 | (0.24) | 34 | 3.12 | (0.22) | 0.27 | (0.32) | [-0.37, 0.91] | 0.40 |
| 60 | 27 | 3.75 | (0.26) | 31 | 3.76 | (0.24) | -0.00 | (0.35) | [-0.71, 0.70] | 0.99 |
| 72 | 26 | 4.56 | (0.31) | 28 | 4.43 | (0.30) | 0.13 | (0.43) | [-0.74, 1.00] | 0.76 |
| 84 | 29 | 4.88 | (0.26) | 33 | 4.87 | (0.24) | 0.01 | (0.35) | [-0.70, 0.72] | 0.98 |
| 96 | 29 | 5.24 | (0.27) | 32 | 5.32 | (0.25) | -0.08 | (0.37) | [-0.82, 0.66] | 0.83 |
| Average treatment differences through follow-up+ | | | | | | | 0.03 | (0.25) | [-0.47, 0.53] | 0.90 |

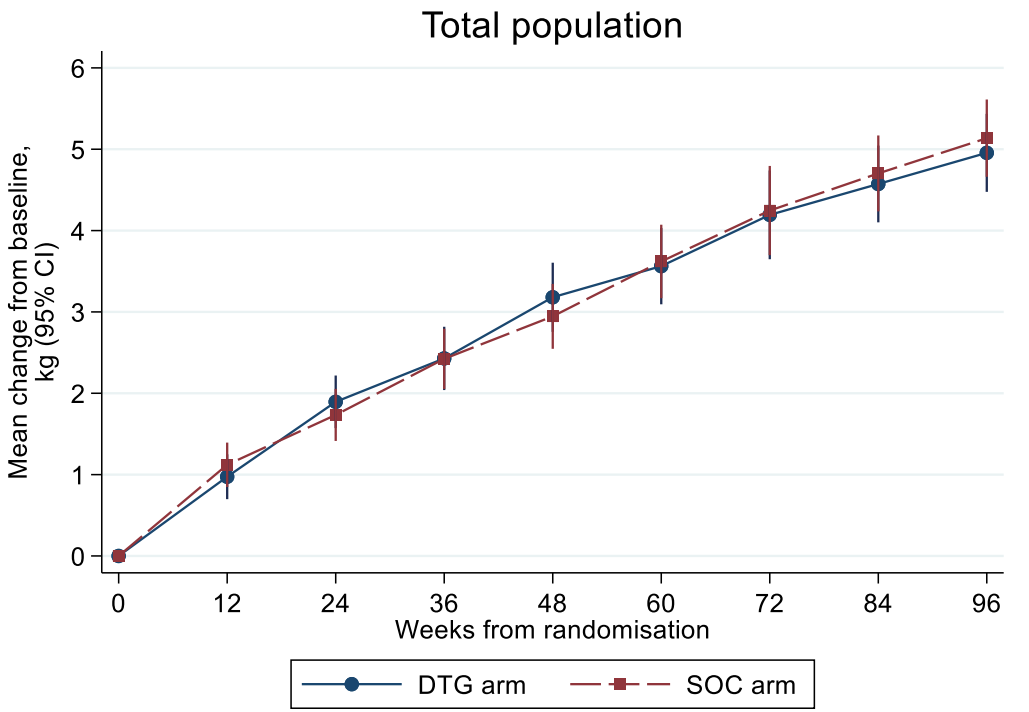
*Change calculated using normal regression adjusting for baseline only. Presenting mean change from a baseline of 8.1 in total and 7.6 in A.

**Normal regression adjusting for baseline and ODYSSEY A/B strata.

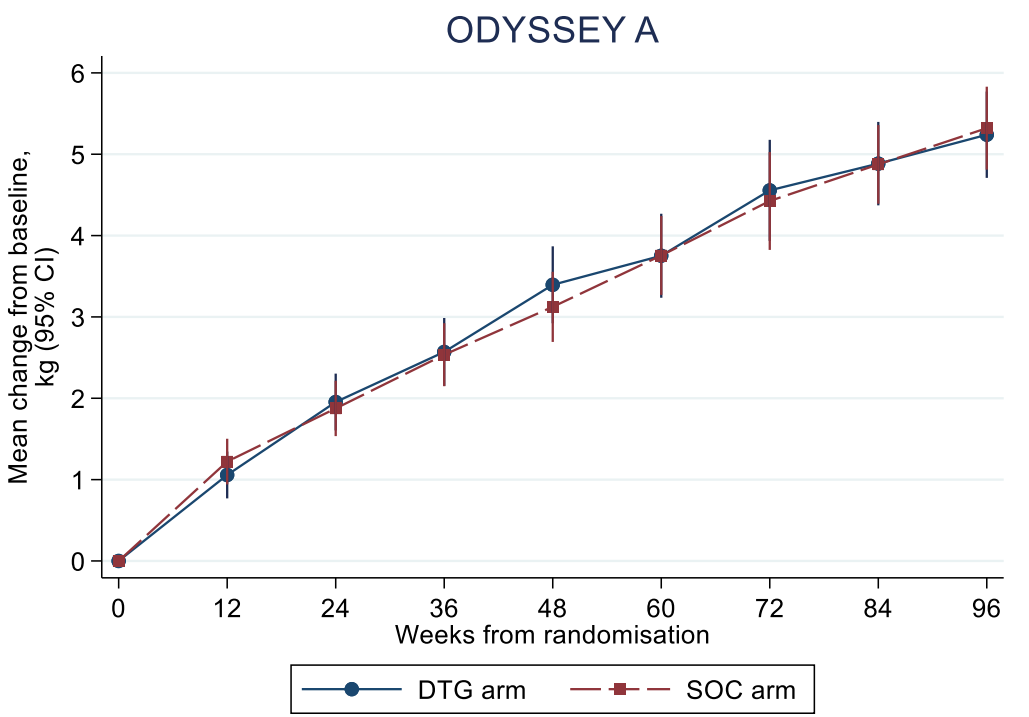
+Linear mixed models fitted with random intercept and fixed effects for treatment group, study visit and adjustment covariates (baseline Weight (kg) and ODYSSEY A/B strata (total population only))

++ Test of heterogeneity of treatment effect between ODYSSEY A/B

**S14.7 Total population - Weight (kg) change over follow-up**



**S14.8 ODYSSEY A - Weight (kg) change over follow-up**



## S14.9 Total population - BMI-for-age change over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | | Adjusted Difference** | | | | Interaction++ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p | mean | (SE) | [95% CI] | p | p |
| 12 | 39 | 0.5 | (0.2) | 40 | 1.0 | (0.2) | -0.5 | (0.3) | [-1.0, 0.1] | 0.097 | -0.4 | (0.3) | [-1.0, 0.1] | 0.10 | 0.42 |
| 24 | 39 | 1.0 | (0.3) | 40 | 1.1 | (0.3) | -0.1 | (0.4) | [-0.8, 0.6] | 0.78 | -0.1 | (0.4) | [-0.8, 0.6] | 0.79 | 0.64 |
| 36 | 35 | 1.0 | (0.3) | 39 | 1.4 | (0.2) | -0.4 | (0.4) | [-1.2, 0.3] | 0.22 | -0.4 | (0.4) | [-1.1, 0.3] | 0.25 | 0.90 |
| 48 | 35 | 1.3 | (0.3) | 39 | 1.6 | (0.3) | -0.2 | (0.4) | [-1.0, 0.5] | 0.55 | -0.2 | (0.4) | [-0.9, 0.6] | 0.64 | 0.81 |
| 60 | 33 | 1.4 | (0.3) | 36 | 1.5 | (0.3) | -0.1 | (0.4) | [-0.9, 0.7] | 0.78 | -0.1 | (0.4) | [-0.8, 0.7] | 0.83 | 0.42 |
| 72 | 32 | 1.7 | (0.3) | 33 | 1.8 | (0.3) | -0.2 | (0.4) | [-1.0, 0.7] | 0.70 | -0.1 | (0.4) | [-0.9, 0.8] | 0.86 | 0.20 |
| 84 | 35 | 1.4 | (0.3) | 37 | 1.8 | (0.3) | -0.4 | (0.4) | [-1.2, 0.4] | 0.30 | -0.3 | (0.4) | [-1.1, 0.5] | 0.42 | 0.33 |
| 96 | 32 | 1.1 | (0.3) | 36 | 1.5 | (0.3) | -0.3 | (0.4) | [-1.2, 0.5] | 0.41 | -0.3 | (0.4) | [-1.1, 0.5] | 0.5 | 0.45 |
| Average treatment differences through follow-up+ | | | | | | | -0.2 | (0.3) | [-0.8, 0.4] | 0.46 | -0.2 | (0.3) | [-0.8, 0.4] | 0.50 | 0.60 |

## S14.10 ODYSSEY A - BMI-for-age change over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p |
| 12 | 32 | 0.70 | (0.22) | 34 | 1.05 | (0.21) | -0.35 | (0.30) | [-0.96, 0.26] | 0.25 |
| 24 | 32 | 1.04 | (0.28) | 34 | 1.20 | (0.28) | -0.17 | (0.40) | [-0.96, 0.62] | 0.67 |
| 36 | 28 | 1.14 | (0.30) | 33 | 1.54 | (0.28) | -0.40 | (0.41) | [-1.22, 0.41] | 0.33 |
| 48 | 28 | 1.63 | (0.31) | 33 | 1.76 | (0.28) | -0.14 | (0.42) | [-0.97, 0.70] | 0.75 |
| 60 | 26 | 1.74 | (0.32) | 30 | 1.67 | (0.30) | 0.07 | (0.44) | [-0.81, 0.95] | 0.87 |
| 72 | 25 | 2.15 | (0.35) | 28 | 1.99 | (0.33) | 0.16 | (0.48) | [-0.80, 1.13] | 0.73 |
| 84 | 28 | 1.80 | (0.33) | 33 | 1.97 | (0.31) | -0.17 | (0.45) | [-1.07, 0.73] | 0.71 |
| 96 | 26 | 1.43 | (0.34) | 32 | 1.59 | (0.31) | -0.15 | (0.46) | [-1.07, 0.76] | 0.74 |
| Average treatment differences through follow-up+ | | | | | | | -0.13 | (0.33) | [-0.78, 0.52] | 0.70 |

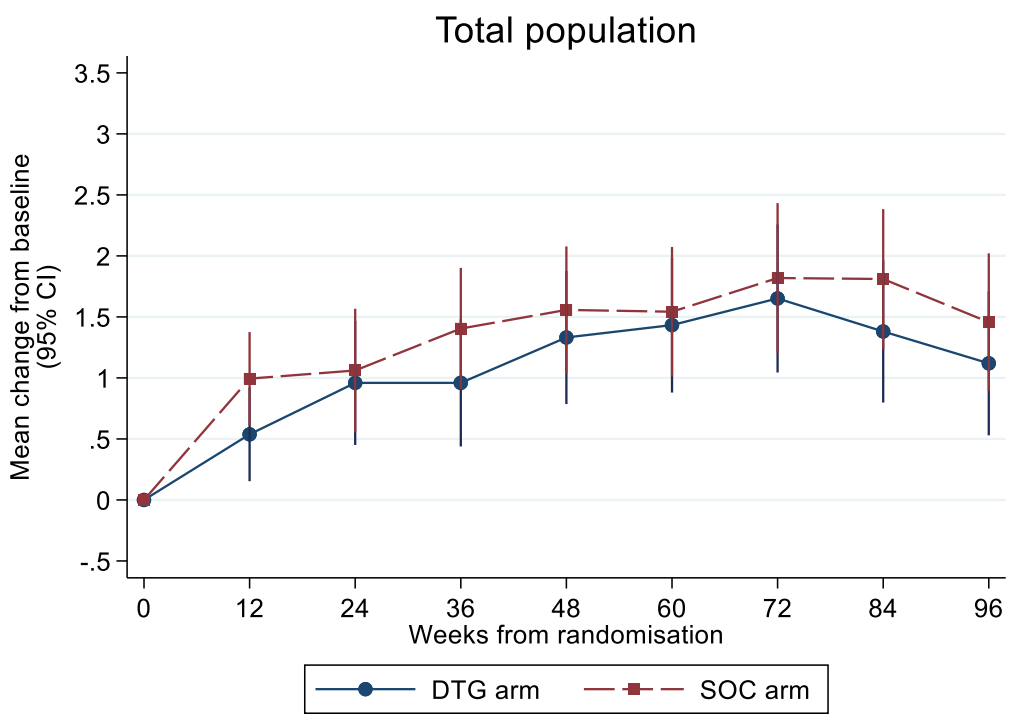
*Change calculated using normal regression adjusting for baseline only. Presenting mean change from a baseline of -0.9 in total and -1.0 in A.

**Normal regression adjusting for baseline and ODYSSEY A/B strata.

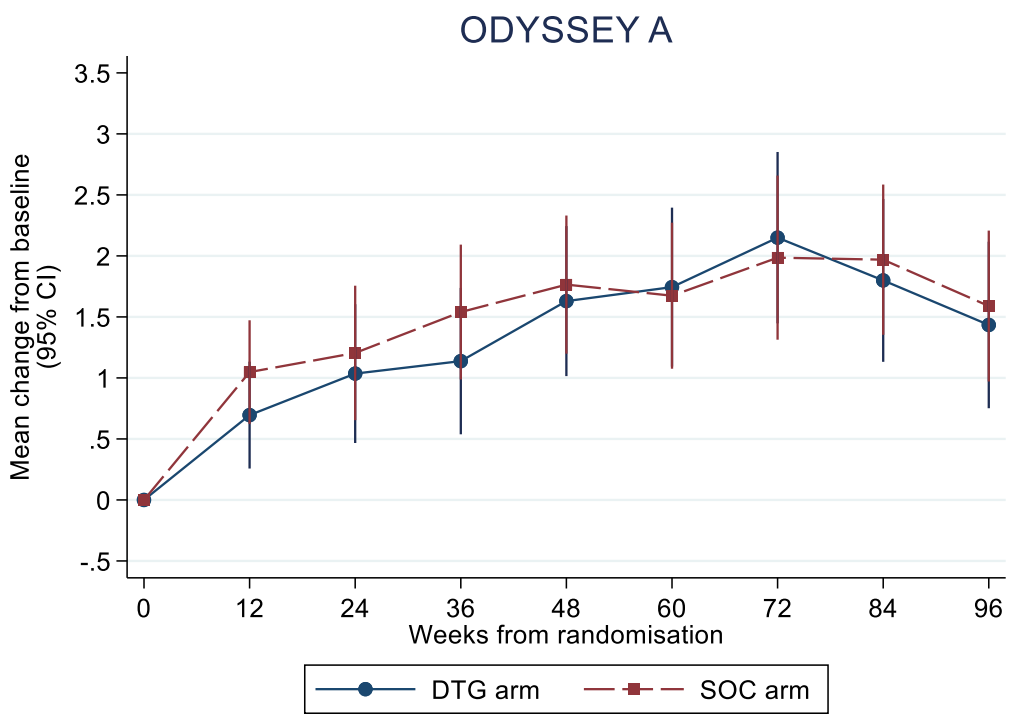
+Linear mixed models fitted with random intercept and fixed effects for treatment group, study visit and adjustment covariates (baseline BMI-for-age and ODYSSEY A/B strata (total population only))

++ Test of heterogeneity of treatment effect between ODYSSEY A/B

**S14.11 Total population - BMI-for-age change over follow-up**



**S14.12 ODYSSEY A - BMI-for-age change over follow-up**



## S14.13 Total population - Weight-for-age change over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | | Adjusted Difference** | | | | Interaction++ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p | mean | (SE) | [95% CI] | p | p |
| 12 | 39 | 0.44 | (0.15) | 40 | 0.54 | (0.15) | -0.10 | (0.21) | [-0.51, 0.31] | 0.64 | -0.09 | (0.21) | [-0.50, 0.33] | 0.68 | 0.82 |
| 24 | 39 | 0.83 | (0.17) | 40 | 0.61 | (0.17) | 0.22 | (0.24) | [-0.25, 0.69] | 0.36 | 0.23 | (0.24) | [-0.25, 0.70] | 0.34 | 0.56 |
| 36 | 36 | 0.88 | (0.17) | 40 | 0.80 | (0.16) | 0.09 | (0.23) | [-0.38, 0.55] | 0.71 | 0.10 | (0.23) | [-0.37, 0.56] | 0.67 | 0.99 |
| 48 | 35 | 1.09 | (0.17) | 40 | 0.87 | (0.17) | 0.23 | (0.24) | [-0.25, 0.71] | 0.35 | 0.25 | (0.24) | [-0.22, 0.73] | 0.29 | 1 |
| 60 | 34 | 1.05 | (0.17) | 37 | 1.03 | (0.16) | 0.02 | (0.24) | [-0.45, 0.49] | 0.93 | 0.04 | (0.24) | [-0.43, 0.51] | 0.87 | 0.85 |
| 72 | 33 | 1.18 | (0.18) | 33 | 1.20 | (0.19) | -0.02 | (0.26) | [-0.55, 0.50] | 0.93 | 0.03 | (0.26) | [-0.49, 0.54] | 0.92 | 0.51 |
| 84 | 36 | 1.17 | (0.16) | 37 | 1.21 | (0.16) | -0.04 | (0.23) | [-0.50, 0.42] | 0.86 | 0.02 | (0.23) | [-0.44, 0.48] | 0.94 | 0.56 |
| 96 | 35 | 1.16 | (0.16) | 36 | 1.20 | (0.16) | -0.03 | (0.23) | [-0.49, 0.42] | 0.88 | 0.00 | (0.23) | [-0.45, 0.45] | 1 | 0.82 |
| Average treatment differences through follow-up+ | | | | | | | 0.06 | (0.19) | [-0.31, 0.44] | 0.74 | 0.08 | (0.19) | [-0.29, 0.45] | 0.67 | 0.96 |

## S14.14 ODYSSEY A - Weight-for-age change over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p |
| 12 | 32 | 0.51 | (0.17) | 34 | 0.61 | (0.16) | -0.11 | (0.23) | [-0.57, 0.36] | 0.66 |
| 24 | 32 | 0.87 | (0.20) | 34 | 0.70 | (0.19) | 0.17 | (0.27) | [-0.38, 0.72] | 0.54 |
| 36 | 29 | 0.97 | (0.20) | 34 | 0.86 | (0.19) | 0.11 | (0.27) | [-0.43, 0.65] | 0.69 |
| 48 | 28 | 1.23 | (0.21) | 34 | 0.97 | (0.19) | 0.26 | (0.28) | [-0.30, 0.82] | 0.35 |
| 60 | 27 | 1.17 | (0.20) | 31 | 1.11 | (0.19) | 0.07 | (0.27) | [-0.48, 0.62] | 0.81 |
| 72 | 26 | 1.40 | (0.21) | 28 | 1.27 | (0.21) | 0.13 | (0.30) | [-0.47, 0.73] | 0.67 |
| 84 | 29 | 1.36 | (0.18) | 33 | 1.27 | (0.18) | 0.09 | (0.26) | [-0.43, 0.60] | 0.73 |
| 96 | 29 | 1.30 | (0.18) | 32 | 1.27 | (0.18) | 0.03 | (0.26) | [-0.48, 0.55] | 0.89 |
| Average treatment differences through follow-up+ | | | | | | | 0.09 | (0.22) | [-0.33, 0.52] | 0.67 |

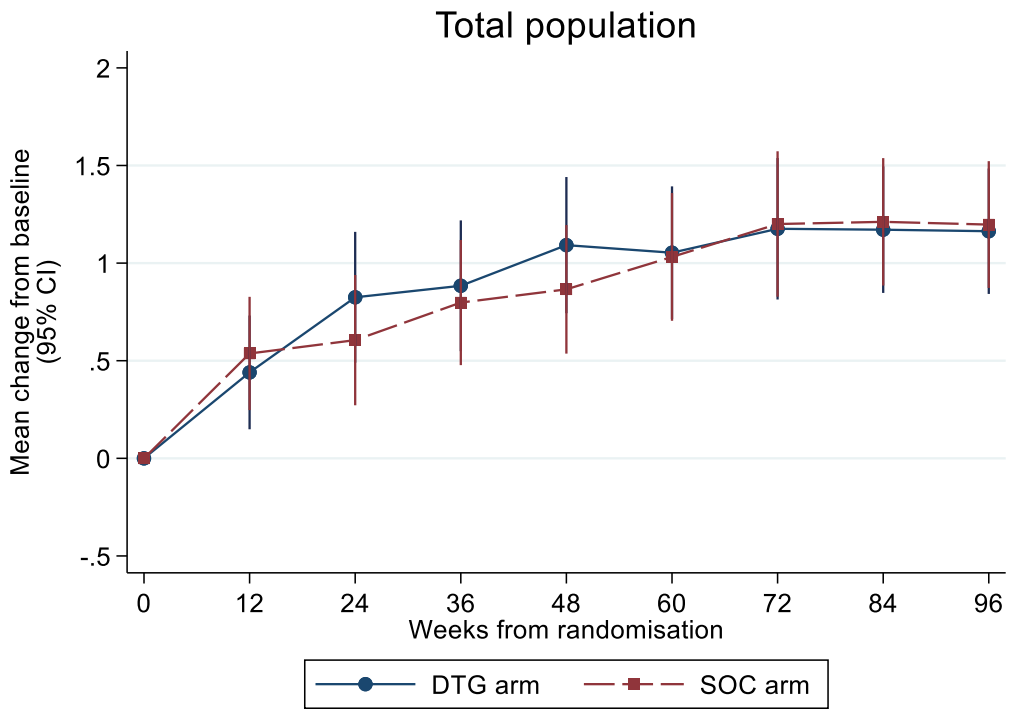
*Change calculated using normal regression adjusting for baseline only. Presenting mean change from a baseline of -2.2 in total and -2.2 in A.

**Normal regression adjusting for baseline and ODYSSEY A/B strata.

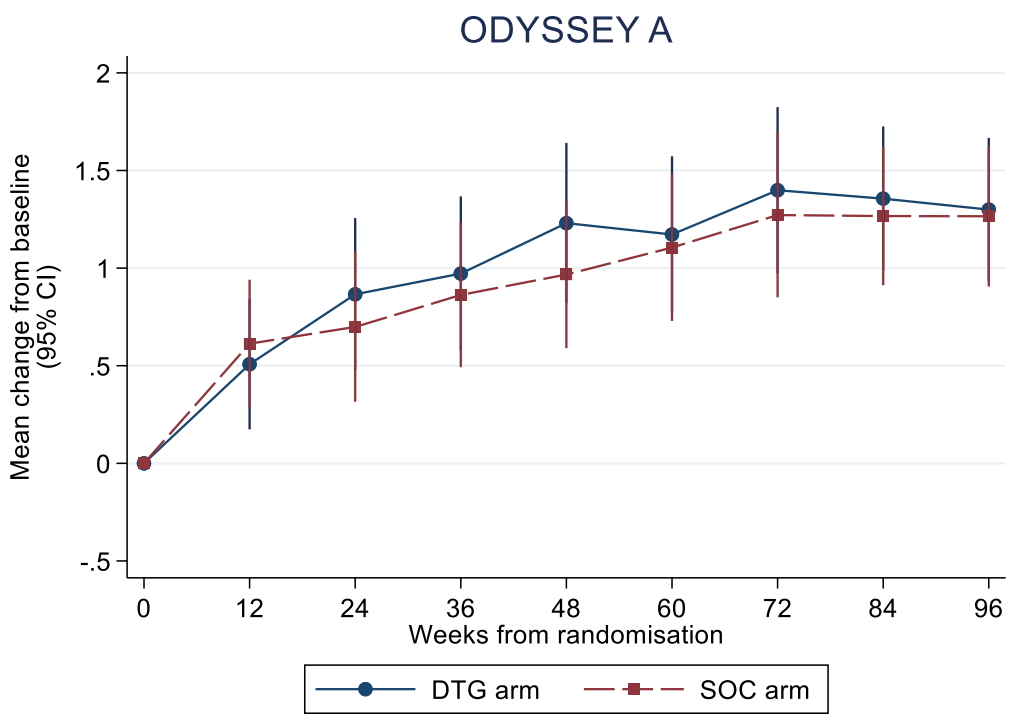
+Linear mixed models fitted with random intercept and fixed effects for treatment group, study visit and adjustment covariates (baseline Weight-for-age and ODYSSEY A/B strata (total population only))

++ Test of heterogeneity of treatment effect between ODYSSEY A/B

**S14.15 Total population - Weight-for-age change over follow-up**



**S14.16 ODYSSEY A - Weight-for-age change over follow-up**



## S14.17 Total population - Weight-for-Height change over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | | Adjusted Difference** | | | | Interaction++ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p | mean | (SE) | [95% CI] | p | p |
| 12 | 38 | 0.4 | (0.2) | 40 | 0.9 | (0.2) | -0.5 | (0.3) | [-1.0, 0.0] | 0.056 | -0.5 | (0.3) | [-1.0, 0.0] | 0.062 | 0.55 |
| 24 | 38 | 0.7 | (0.2) | 40 | 0.9 | (0.2) | -0.1 | (0.3) | [-0.8, 0.5] | 0.71 | -0.1 | (0.3) | [-0.8, 0.6] | 0.72 | 0.60 |
| 36 | 34 | 0.7 | (0.2) | 38 | 1.1 | (0.2) | -0.4 | (0.3) | [-1.1, 0.3] | 0.24 | -0.4 | (0.3) | [-1.1, 0.3] | 0.26 | 0.91 |
| 48 | 34 | 1.0 | (0.3) | 38 | 1.2 | (0.2) | -0.2 | (0.4) | [-0.9, 0.6] | 0.67 | -0.1 | (0.4) | [-0.8, 0.6] | 0.75 | 0.81 |
| 60 | 31 | 1.1 | (0.3) | 35 | 1.2 | (0.3) | -0.1 | (0.4) | [-0.9, 0.6] | 0.73 | -0.1 | (0.4) | [-0.8, 0.6] | 0.78 | 0.45 |
| 72 | 30 | 1.3 | (0.3) | 30 | 1.6 | (0.3) | -0.2 | (0.4) | [-1.1, 0.6] | 0.59 | -0.2 | (0.4) | [-1.0, 0.7] | 0.71 | 0.23 |
| 84 | 33 | 1.2 | (0.3) | 33 | 1.5 | (0.3) | -0.3 | (0.4) | [-1.1, 0.4] | 0.38 | -0.2 | (0.4) | [-0.9, 0.6] | 0.63 | 0.87 |
| 96 | 29 | 1.0 | (0.3) | 31 | 1.2 | (0.3) | -0.2 | (0.4) | [-1.0, 0.6] | 0.56 | -0.2 | (0.4) | [-1.0, 0.6] | 0.67 | 0.88 |
| Average treatment differences through follow-up+ | | | | | | | -0.2 | (0.3) | [-0.8, 0.3] | 0.45 | -0.2 | (0.3) | [-0.7, 0.4] | 0.49 | 0.65 |

## S14.18 ODYSSEY A - Weight-for-Height change over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p |
| 12 | 31 | 0.48 | (0.21) | 34 | 0.90 | (0.20) | -0.42 | (0.29) | [-1.00, 0.16] | 0.15 |
| 24 | 31 | 0.77 | (0.27) | 34 | 0.97 | (0.26) | -0.20 | (0.37) | [-0.94, 0.54] | 0.59 |
| 36 | 27 | 0.81 | (0.29) | 32 | 1.19 | (0.26) | -0.38 | (0.39) | [-1.16, 0.40] | 0.34 |
| 48 | 27 | 1.25 | (0.30) | 32 | 1.33 | (0.27) | -0.08 | (0.40) | [-0.88, 0.73] | 0.85 |
| 60 | 24 | 1.30 | (0.32) | 29 | 1.27 | (0.29) | 0.03 | (0.43) | [-0.82, 0.89] | 0.94 |
| 72 | 23 | 1.75 | (0.34) | 25 | 1.66 | (0.33) | 0.08 | (0.47) | [-0.86, 1.03] | 0.86 |
| 84 | 26 | 1.49 | (0.31) | 30 | 1.65 | (0.29) | -0.16 | (0.42) | [-1.00, 0.69] | 0.71 |
| 96 | 24 | 1.18 | (0.32) | 28 | 1.33 | (0.30) | -0.15 | (0.44) | [-1.03, 0.73] | 0.74 |
| Average treatment differences through follow-up+ | | | | | | | -0.14 | (0.31) | [-0.74, 0.47] | 0.66 |

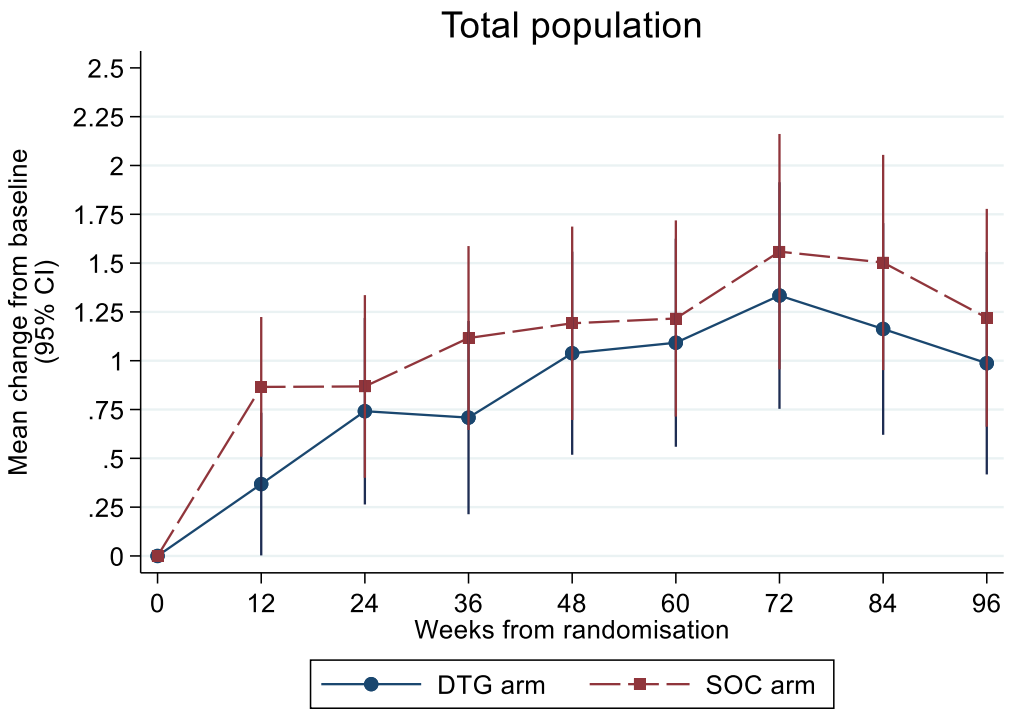
*Change calculated using normal regression adjusting for baseline only. Presenting mean change from a baseline of -0.9 in total and -1.0 in A.

**Normal regression adjusting for baseline and ODYSSEY A/B strata.

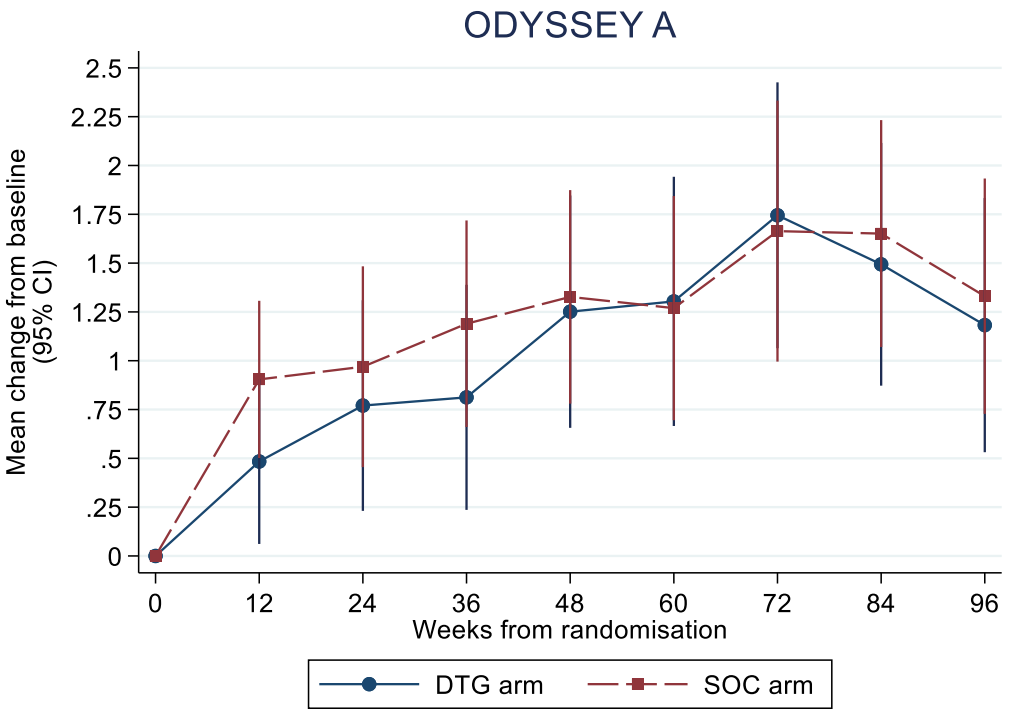
+Linear mixed models fitted with random intercept and fixed effects for treatment group, study visit and adjustment covariates (baseline Weight-for-Height and ODYSSEY A/B strata (total population only))

++ Test of heterogeneity of treatment effect between ODYSSEY A/B

**S14.19 Total population - Weight-for-Height change over follow-up**



**S14.20 ODYSSEY A - Weight-for-Height change over follow-up**



## S14.21 Weight-for-age z-scores over follow-up in participants with weight-for-age z-score <-3 at enrolment*

| | Total | | | A | | |
|---|---|---|---|---|---|---|
| | **DTG** | **SOC** | **Total** | **DTG** | **SOC** | **Total** |
| **Participants <-3 at enrolment** | 14 | 13 | 27 | 14 | 11 | 25 |
| **Week 48** | | | | | | |
| <-3 | 0 ( 0%) | 3 (30%) | 3 (14%) | 0 ( 0%) | 2 (25%) | 2 (11%) |
| -3-<-2 | 4 (36%) | 3 (30%) | 7 (33%) | 4 (36%) | 3 (38%) | 7 (37%) |
| -2-<0 | 7 (64%) | 3 (30%) | 10 (48%) | 7 (64%) | 2 (25%) | 9 (47%) |
| >=0 | 0 ( 0%) | 1 (10%) | 1 ( 5%) | 0 ( 0%) | 1 (13%) | 1 ( 5%) |
| Died/LTFU/Withdrawn | 3 | 3 | 6 | 3 | 3 | 6 |
| **Week 96** | | | | | | |
| <-3 | 0 ( 0%) | 1 (14%) | 1 ( 6%) | 0 ( 0%) | 1 (17%) | 1 ( 6%) |
| -3-<-2 | 3 (30%) | 2 (29%) | 5 (29%) | 3 (30%) | 2 (33%) | 5 (31%) |
| -2-<0 | 7 (70%) | 3 (43%) | 10 (59%) | 7 (70%) | 2 (33%) | 9 (56%) |
| >=0 | 0 ( 0%) | 1 (14%) | 1 ( 6%) | 0 ( 0%) | 1 (17%) | 1 ( 6%) |
| Died/LTFU/Withdrawn | 4 | 6 | 10 | 4 | 5 | 9 |

*Percentages of non-missing

# S15 Biochemistry

Note: ODYSSEY B is not presented here due to having few participants

Throughout this section, n refers to the number of participants with available measurement at each visit week. Numbers in models may be lower where there are missing data at baseline.

## S15.1 Total population - Creatinine changes over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | | Adjusted Difference** | | | | Interaction++ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p | mean | (SE) | [95% CI] | p | p |
| 4 | 38 | -0.01 | (0.02) | 39 | -0.01 | (0.02) | 0.00 | (0.02) | [-0.05, 0.05] | 0.89 | 0.00 | (0.02) | [-0.05, 0.05] | 0.87 | 0.44 |
| 24 | 37 | 0.03 | (0.02) | 39 | -0.01 | (0.02) | 0.03 | (0.03) | [-0.02, 0.09] | 0.25 | 0.03 | (0.03) | [-0.02, 0.09] | 0.27 | 0.16 |
| 48 | 34 | 0.03 | (0.03) | 39 | 0.02 | (0.03) | 0.01 | (0.04) | [-0.06, 0.09] | 0.76 | 0.01 | (0.04) | [-0.07, 0.09] | 0.80 | 0.12 |
| 72 | 35 | 0.03 | (0.02) | 34 | 0.03 | (0.02) | 0.00 | (0.03) | [-0.05, 0.06] | 0.95 | 0.00 | (0.03) | [-0.05, 0.06] | 0.96 | 0.29 |
| 96 | 36 | 0.00 | (0.02) | 36 | 0.02 | (0.02) | -0.02 | (0.03) | [-0.07, 0.03] | 0.47 | -0.02 | (0.03) | [-0.07, 0.03] | 0.47 | 0.59 |
| Average treatment differences through follow-up+ | | | | | | | 0.01 | (0.02) | [-0.03, 0.04] | 0.66 | 0.01 | (0.02) | [-0.03, 0.04] | 0.67 | 0.79 |

## S15.2 ODYSSEY A - Creatinine over follow-up

| Weeks since randomisation | DTG | | | SOC | | | Unadjusted Difference* | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | mean | (SE) | n | mean | (SE) | mean | (SE) | [95% CI] | p |
| 4 | 31 | -0.00 | (0.02) | 33 | 0.00 | (0.02) | -0.01 | (0.03) | [-0.06, 0.05] | 0.85 |
| 24 | 30 | 0.03 | (0.02) | 33 | -0.02 | (0.02) | 0.05 | (0.03) | [-0.01, 0.11] | 0.10 |
| 48 | 27 | 0.01 | (0.03) | 33 | 0.02 | (0.03) | -0.02 | (0.04) | [-0.10, 0.07] | 0.69 |
| 72 | 28 | 0.04 | (0.02) | 29 | 0.03 | (0.02) | 0.01 | (0.03) | [-0.04, 0.06] | 0.58 |
| 96 | 29 | 0.00 | (0.02) | 31 | 0.03 | (0.02) | -0.02 | (0.03) | [-0.08, 0.04] | 0.42 |
| Average treatment differences through follow-up+ | | | | | | | 0.01 | (0.02) | [-0.03, 0.05] | 0.79 |

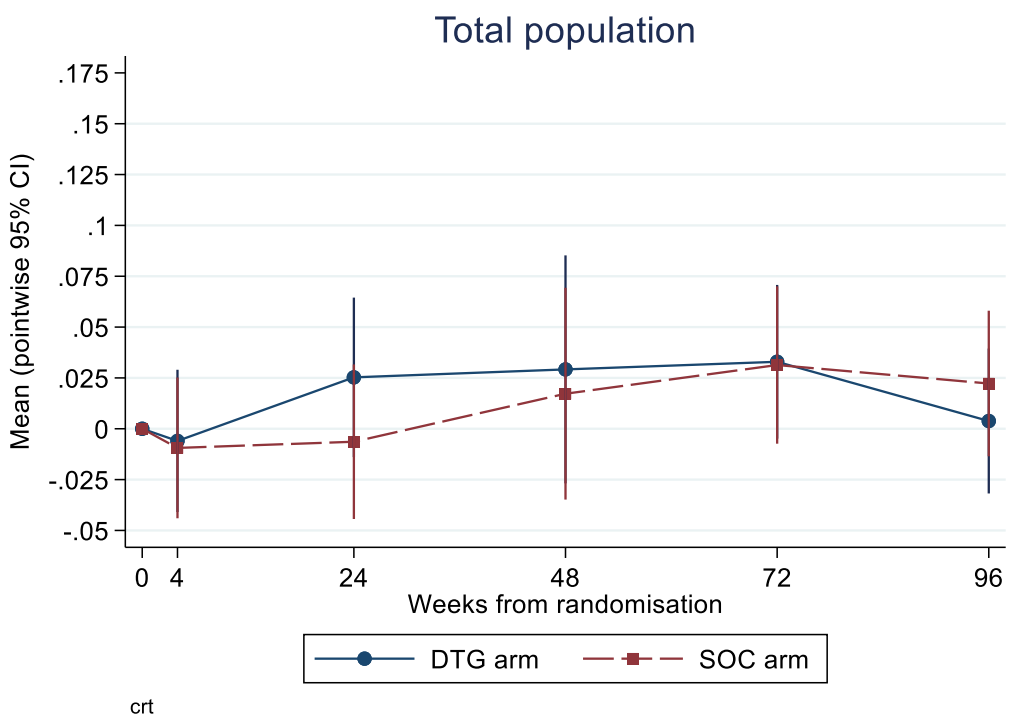
*Change calculated using normal regression adjusting for baseline only. Presenting mean change from a baseline of 0.3 in total and 0.3 in A.

**Normal regression adjusting for baseline and ODYSSEY A/B strata.

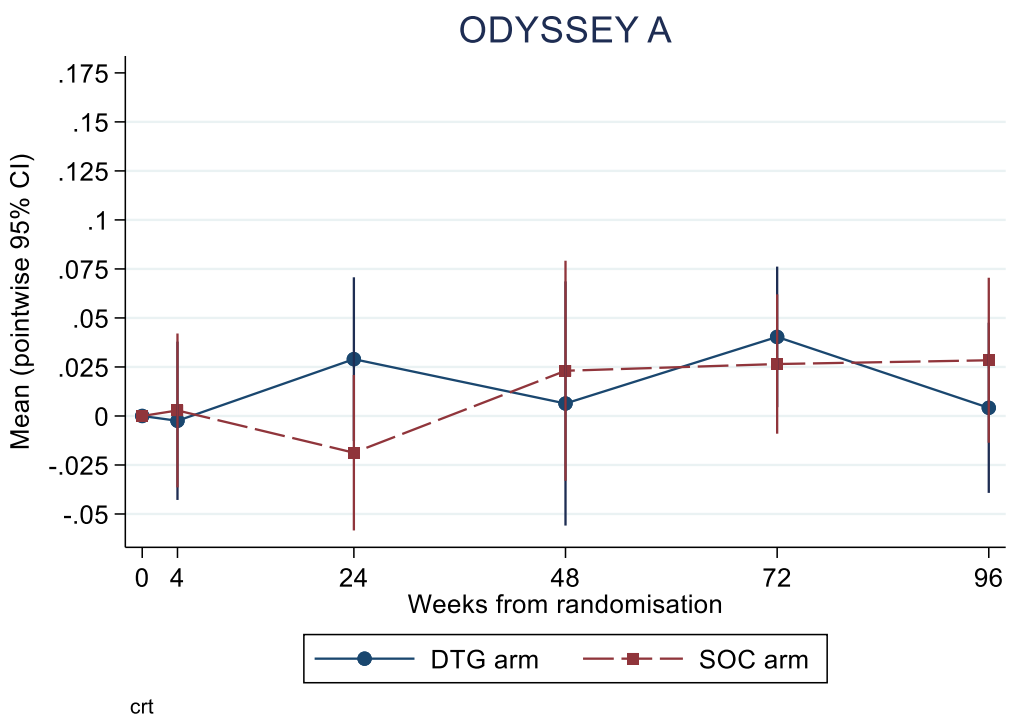
+Linear mixed models fitted with random intercept and fixed effects for treatment group, study visit and adjustment covariates (baseline Creatinine and ODYSSEY A/B strata (total population only))

++ Test of heterogeneity of treatment effect between ODYSSEY A/B

**S15.3 Total population - Creatinine changes over follow-up**



**S15.4 ODYSSEY A - Creatinine changes over follow-up**



**S16 ODYSSEY sites recruiting children to <14kg cohort**

**University of Zimbabwe Clinical Research Centre (UZCRC)**, Box A1578 Avondale, Harare, Zimbabwe

**Joint Clinical Research Centre (JCRC), Lubowa**, Plot 101 Lubowa Estates, off Entebbe road, Kampala, Uganda

**Joint Clinical Research Centre (JCRC), Mbarara**, P.O Box 40, Mbarara Regional referral Hospital, Mbarara, Uganda

**Baylor College of Medicine Bristol Myers Squibb Children's Clinical Centre of Excellence**, Block 5, Mulago Hospital, P.O. Box 72052, Kampala, Uganda

**Chris Hani Baragwanath Hospital: Perinatal HIV Research Unit**, Chris Hani Baragwanath Hospital, P.O. Box 114, Diepkloof, 1864, Soweto, South Africa

**Perinatal HIV Research Unit, Klerksdorp**/Tsepong Hospital Complex, Matlosana, South Africa

**Durban International Clinical Research Site**, Parkhome, Gate 1-King Edward VIII Hospital, Umbilo Road, Congella, Durban, KwaZulu-Natal, 4013, South Africa

## S17 ODYSSEY inclusion and exclusion criteria

### S17.1 Patient Inclusion Criteria

**All patients:**

- Children ≥28 days and <18 years weighing ≥3kg with confirmed HIV-1 infection*
- Parents/carers and children, where applicable, give informed written consent
- Girls who have reached menses must have a negative pregnancy test at screening and randomisation and be willing to adhere to effective methods of contraception if sexually active
- Children with co-infections who need to start ART according to local/national guidelines
- Parents/carers and children, where applicable, willing to adhere to a minimum of 96 weeks' follow-up

*Children weighing 3 to <14kg must be eligible and willing to participate in the Weight band (WB)-PK1 substudy unless direct enrolment for the child's weight band has opened following the WB-PK1 substudy and/or dosing information has become available from the IMPAACT P1093 DTG dose-finding study.

**Additional criteria for ODYSSEY A:**

- Planning to start first-line ART

**Additional criteria for ODYSSEY B:**

- Planning to start second-line ART defined as either: (i) switch of at least 2 ART drugs due to treatment failure; or (ii) switch of only the third agent due to treatment failure where drug sensitivity tests show no mutations conferring NRTI resistance
- Treated with only one previous ART regimen. Single drug substitutions for toxicity, simplification, changes in national guidelines or drug availability are allowed
- At least one NRTI with predicted preserved activity available for a background regimen
- In settings where resistance tests are routinely available, at least one active NRTI from TDF/TAF, ABC or ZDV should have preserved activity based on cumulative results of resistance tests
- In settings where resistance tests are not routinely available, children who are due to switch according to national guidelines should have at least one new NRTI predicted to be available from TDF/TAF, ABC or ZDV
- Viral load ≥500 c/ml at screening visit or within 4 weeks prior to screening

### S17.2 Patient Exclusion Criteria

- History or presence of known allergy or contraindications to DTG
- History or presence of known allergy or contraindications to proposed available NRTI backbone or proposed available SOC third agent.
- Alanine aminotransferase (ALT) ≥5 times the upper limit of normal (ULN), OR ALT ≥3xULN and bilirubin ≥2xULN
- Patients with severe hepatic impairment or unstable liver disease (as defined by the presence of ascites, encephalopathy, coagulopathy, hypoalbuminaemia, oesophageal or gastric varices, or persistent jaundice), known biliary abnormalities (with the exception of Gilbert's syndrome or asymptomatic gallstones)
- Anticipated need for Hepatitis C virus (HCV) therapy during the study
- Pregnancy or breastfeeding
- Evidence of lack of susceptibility to integrase inhibitors or more than a 2-week exposure to antiretrovirals of this class