SUMMARY INFORMATION TYPE	SUMMARY DETAILS
ACRONYM	ODYSSEY (Once daily dolutegravir based ART in young people vs. standard therapy)
Long Title of Trial	A randomised trial of dolutegravir (DTG)-based antiretroviral therapy vs. standard of care (SOC) in children with HIV infection starting first-line or switching to second-line ART (PENTA 20)
Version	2.0
Date	6th March 2015
ISRCTN #	ISRCTN91737921
EudraCT #	2014-002632-14
NCT #	NCT02259127
Study Design	An open-label, multi-centre, randomised (1:1), non-inferiority, Phase II/III, 96-week, 2-arm clinical trial to compare the efficacy and toxicity of DTG plus 2 NRTI vs. standard of care (SOC) in HIV-infected children aged less than 18 years who are starting first-line ART (ODYSSEY A) or switching to second-line ART (ODYSSEY B).
Type of Participants to be Studied	HIV-1 infected children younger than 18 years planning to start first-line or second-line antiretroviral therapy
Interventions to be Compared	DTG + 2 NRTI (DTG arm) vs. SOC (SOC arm) in first-line and second-line antiretroviral regimens
Study Hypothesis	DTG + 2 NRTIs is non-inferior to SOC (NNRTI or PI + 2 or 3 NRTIs) in terms of efficacy and superior in terms of toxicity profile
Primary Outcome Measure(s)	Difference in proportion with failure (clinical or virological) at 96 weeks, estimated using time to the first occurrence of any of the following components: • Insufficient virological response defined as <1 $\log_{10}$ drop at week 24 • Viral load (VL)>400 c/ml at or after 36 weeks confirmed by next visit • Death due to any cause • Any new or recurrent AIDS defining event (WHO 4) or severe WHO 3 event, adjudicated by the Endpoint Review Committee

Secondary Outcome Measure(s)	Secondary efficacy outcomes: • Difference in proportion with clinical or virological failure (as defined above) over 48 weeks • Time to any new or recurrent AIDS defining event (WHO 4) or severe WHO 3 event after 24 weeks from randomisation, adjudicated by the Endpoint Review Committee • Proportion of children with VL suppression <50 c/ml at 48 and 96 weeks • Proportion of children with VL suppression <400 c/ml at 48 and 96 weeks • Rate of clinical events over 96 weeks: WHO 4, severe WHO 3 events and death • Change in CD4 count and percentage from baseline to weeks 48 and 96 • Change in CD4 / CD8 ratio from baseline to weeks 48 and 96 • Proportion developing new resistance mutations in those with viral load >1000 c/ml Secondary safety outcomes: • Change in total cholesterol, triglycerides and lipid fractions (LDL, HDL) from baseline to weeks 48 and 96. These safety outcomes will be used to formally assess superiority of DTG arm vs SOC arm • 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: • Quality of life • Adherence and acceptability
Randomisation	Children starting first- and second-line ART will be randomised separately (both in 1:1 ratio) : ODYSSEY A (first-line ART): • DTG + 2 NRTIs • SOC (defined as PI or NNRTI + 2 or 3 NRTIs) ODYSSEY B (second-line ART): • DTG + 2 NRTI • SOC (defined as PI or NNRTI or raltegravir + 2 NRTIs)
Number of Participants to be Studied	700 HIV-1 infected children, including 310 children starting first-line (ODYSSEY A) and 390 starting second-line ART (ODYSSEY B)
Duration	Participants will be enrolled over 72-96 weeks. All participants will be followed until the last recruited participant reaches week 96
Ancillary Studies/Substudies	The following sub-studies will be performed in selected sites: **Pharmacokinetics (PK) in participants developing TB while on DTG** Full PK curves will be undertaken in at least 10 children receiving DTG and rifampicin; curves will be repeated in the same children after

	completion of TB therapy **Immunology/virology substudy** Mechanisms of CD4 reconstitution, immune activation, HIV reservoir and replication will be compared between DTG vs. SOC arms