



WITS RHI

Project Brief: KK-1439-066

Full Title of Study/Programme	A Phase 2 Clinical Study to Evaluate the Pharmacokinetics, Safety, and Efficacy of Doravirine and Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate in Participants With HIV-1, who are 4 Weeks to less than 12 Years of Age and Weigh less than 45 kg
Technical Focus Area/Key Words	Research in Children living with HIV
Rationale	As in adults, the objective of ART in the pediatric population is to achieve and/or maintain suppression of HIV-1 RNA. Sustained virologic suppression preserves/restores immunologic function, inhibits the emergence of drug resistance, and ultimately decreases morbidity and mortality [Panel on Antiretroviral Guidelines for Adults and Adolescents 2018]. Virologic suppression of HIV-1 RNA is even more important in infants and young children because, if left untreated, progression to AIDS and death occurs more rapidly than in adults [Tovo, P. A., et al 1992] [Diaz, C., et al 1998] [HIV Paediatric Prognostic Markers Collaborative Study Group 2003] [Newell, M. L., et al 2004]. Additionally, the advent of cART has dramatically improved neurocognitive development in infants and children with HIV-1, and virtually eliminated HIV encephalopathy among perinatally-infected children [Laughton, B., et al 2018] [Patel, K., et al 2009]. First-line therapy with NNRTIs or switching to NNRTIs while suppressed on ART has proven to be effective for infants, children, and adolescents infected with HIV-1 [Food and Drug Administration 2019]. As infants and children with HIV represent a particularly vulnerable population, development of antiretrovirals that are well tolerated, potent, with a simple once-daily dose regimen continues to be a priority [Food and Drug Administration 2019] [AIDS Free Working Group 2018]. This protocol will assess the PK, safety, and efficacy of an age-appropriate formulation of DOR used in combination with 2 NRTIs or as an FDC of DOR/3TC/TDF in pediatric participants with HIV-1 aged 4 weeks to
Primary Objectives	- To evaluate the steady state pharmacokinetics of DOR when given with 2 NRTIs or as part of the FDC of DOR/3TC/TDF (in participants ≥ 6 to <12 years and weighing ≥ 14 to <45 kg). - To evaluate the safety and tolerability of DOR when given with 2 NRTIs or as part of the FDC of DOR/3TC/TDF (in participants ≥ 6 to <12 years and weighing ≥ 14 to <45 kg) through Week 24.

Secondary Objectives	- To evaluate the pharmacokinetics of DOR as assessed by sparse pharmacokinetic sampling through Week 24. - To evaluate the pharmacokinetics of 3TC and TFV in participants receiving the FDC of DOR/3TC/TDF (in participants ≥ 6 to < 12 years and weighing ≥ 14 to < 45 kg), as assessed by intensive and/or sparse pharmacokinetic sampling through Week 24. - To evaluate the safety and tolerability of DOR when given with 2 NRTIs or as part of the FDC of DOR/3TC/TDF (in participants ≥ 6 to < 12 years and weighing ≥ 14 to < 45 kg) through Weeks 48 and 96. - To evaluate the antiretroviral activity of DOR when given with 2 NRTIs or as part of the FDC of DOR/3TC/TDF (in participants ≥ 6 to < 12 years and weighing ≥ 14 to < 45 kg) separately in treatment-naïve and virologically-suppressed (at baseline) participants as assessed by the proportion of participants with the following at Weeks 24, 48, and 96: - HIV-1 RNA < 50 copies/mL - HIV-1 RNA < 200 copies/mL - HIV-1 RNA ≥ 50 copies/mL (virologically-suppressed [at baseline] participants only) - Log₁₀ drop from baseline in plasma HIV-1 RNA (treatment-naïve participants only)- - To evaluate the immunologic effect of DOR when given with 2 NRTIs or as part of the FDC of DOR/3TC/TDF (in participants ≥ 6 to < 12 years and weighing ≥ 14 to < 45 kg) separately in treatment-naïve and virologically-suppressed (at baseline) participants as measured by change from baseline in CD4+ T-cell count at Weeks 24, 48, and 96.- To evaluate the emergence of genotypic or phenotypic resistance to DOR or other components of the regimen in the resistance analysis subset. - To evaluate adherence to DOR or the FDC of DOR/3TC/TDF (in participants ≥ 6 to < 12 years and weighing ≥ 14 to < 45 kg) at Weeks 24, 48, and 96 - To evaluate the acceptability and palatability of oral pellets/granules of DOR or the FDC of DOR/3TC/TDF (in participants ≥ 6 to < 12 years and weighing ≥ 14 to < 45 kg).
Exploratory Objectives	-None
Primary Endpoint/Outcome	- Steady-state AUC₀₋₂₄, C_{max}, C₂₄, and T_{max} - Adverse events - Grade 3 or 4 adverse events - Deaths - Discontinuation of study intervention due to an adverse event - Discontinuation of study intervention due to a drug-related adverse event

Secondary Endpoint/Outcome	- Plasma concentration of DOR - Plasma concentration of 3TC and TFV - AUC₀₋₂₄ and C_{max} of 3TC and TFV (intensive sampling only). - Adverse events - Grade 3 or 4 adverse events - Deaths - Discontinuation of study intervention due to an adverse event - Discontinuation of study intervention due to a drug-related adverse event - HIV-1 RNA - CD4+ T-cell count and percentage - Viral resistance-associated substitutions - Study intervention compliance - 5-point facial hedonic scale
Study Design (R)	This is a nonrandomized, noncomparative, multi-site, open-label study to evaluate the PK, safety, tolerability, and efficacy of DOR used in combination with 2 NRTIs, and when administered as an FDC of DOR/3TC/TDF (in participants aged 6 to <12 years and weighing at least 14 kg to <45 kg). Pediatric participants with HIV-1 who are treatment-naïve or virologically suppressed on stable cART for ≥3 months with no history of treatment failure will be enrolled. Approximately 84 evaluable participants, 4 weeks to <12 years of age and weighing <45 kg, will be enrolled into the study. Participants will be allocated to 1 of the 3 groups based on weight band (and by extension, age) (Table 1). Weight bands will be opened sequentially based on PK and safety data.
Study arms (R)	100 mg dose of DOR or the 100 mg/300 mg/300 mg dose of the FDC of DOR/3TC/TDF to participants whose body weight is <35 kg at baseline and increases to ≥35 kg during the study.
Study population (R)	Participants With HIV-1, who are 4 Weeks to less than 12 Years of Age and Weigh less than 45 kg
Study sample size (R)	Approximately 84 evaluable participants,
Follow up/duration	Each participant will be in the study for approximately 102 weeks from the time the participant's legally acceptable representative provides documented informed consent through the final contact.
Study/Programme sites	Wits RHI Shandukani Research Centre (SRC)
Study/Programme duration	The Sponsor estimates that the study will require approximately 7 years from the time the first participant (or their legally acceptable representative) provides documented informed consent/assent until the last participant's last study-related contact.
Intervention (R)	Participant of a lower weight band weighing less than 35 kgs will receive DOR in combination with 2 NRTI of the investigator's

	choosing, and participants weighing more than 35kg will receive the fixed dose combination of DOR/3TC/TDF .
Operations	Study specific
Investigators	• Prof Lee Fairlie, Principal Investigator • Dr Faezah Patel. Sub investigator • Dr Elizea Horne. Sub Investigator. • Dr Mrinmayee Dhar • Tiffany Seef • Dr Jeanne Coetzee
Other Partners & Collaborators	None
Sponsors/Donors	Merck Sharp & Dohme Corp, a subsidiary of Merck & Co, Inc. (hereafter referred to as the Sponsor or MSD)
Publications/key presentations to date	None as yet
Progress Update as at Jun 2025	• Protocol amendment 5 • Screened: 16 • Enrolled: 9 • Screening failure: 5 • Discontinued: 2 • Current open weight bands(C 10 to less than 14kgs)
Frequency of donor narrative report	Monthly
Overall Study/Project Contact	Prof Lee Fairlie Hermien Gous
Briefing owner and date	Kabelo Mashaba 18 Mar 2026