

Project Brief: SHIELD STUDY

Full Title of Study/Programme	A multicentre, open-label, single-arm trial to evaluate the safety, pharmacokinetics and antiviral activity of fostemsavir in combination with optimized background therapy (OBT) in HIV-1 infected children and adolescents who are failing their current combination antiretroviral therapy (cART) and have dual- or triple-class antiretroviral (ARV) resistance
Technical Focus Area/Key Words	Research in Children and Adolescents
Rationale	The dose selection of FTR for children and adolescents ≥ 20 kg utilized a population pharmacokinetic (POP PK) model-based approach to achieve similar adult TMR exposures following FTR 600mg BID administration with OBT that was demonstrated to be safe and effective in the FTR Phase 3 BRIGHT study in HTE patients.
Primary Objectives	• To evaluate the safety of 24 weeks of treatment with fostemsavir + OBT in HIV-1 infected children and adolescents aged 6 to < 18 years and weighing at least 20kg who are failing their current antiretroviral treatment and have dual- or triple-class ARV resistance. • To evaluate the steady-state pharmacokinetics (PK) of temsavir (the active moiety of fostemsavir) in HIV-1 infected children and adolescents.
Secondary Objectives	• To evaluate the antiviral activity of fostemsavir + OBT at 24 and 48 weeks in HIV1 infected children and adolescents. • To evaluate the safety of 48 and 156 weeks of treatment with fostemsavir + OBT in HIV-1 infected children and adolescents. • To evaluate HIV-1 disease progression while on fostemsavir + OBT in HIV-1 infected children and adolescents. • To evaluate the emergence of ARV resistance among HIV-1 infected children and adolescents with confirmed virologic failure. • To evaluate the efficacy of fostemsavir plus OBT by examining the changes from baseline in CD4+ T cell counts and the percentage of CD4 + T-cells through week 24, 48 and at end of study. • To evaluate the acceptability and swallowability of fostemsavir in HIV-1 infected children and adolescents.
Primary Endpoint/Outcome	• Occurrence of the following events through Week 24: adverse events (AEs), treatment-related AEs, AEs of Grade 3 or higher,

	serious AEs, and AEs leading to premature study treatment discontinuation. • AUC(0-tau), Cmax, Ctau of temsavir across weight bands.
Secondary Endpoint/Outcome	• Proportion of patients with HIV-1 RNA <50 copies/mL at Week 24 and Week 48 using the Food and Drug Administration (FDA) snapshot algorithm. • Change in log10 HIV-1 RNA from baseline to Week 24 and Week 48. • Occurrence of the following events through Week 48 and End of Study: AEs, treatment-related AEs, AEs of Grade 3 or higher, serious AEs, and AEs leading to premature study treatment discontinuation. • Occurrence of new AIDS defining events (Centers for Disease Control Class C events, or WHO 3 or 4 events) or death through end of study visit. • Emergence of genotypic or phenotypic resistance to TMR and components of OBT. • Change in CD4 T-cell count and CD4 percentage from baseline to Week 24, Week 48 and End of Study. • Acceptability and swallowability measures.
Study Design	A multicenter, phase I/II open-label, single-arm trial to evaluate the safety, pharmacokinetics, antiviral activity fostemsavir in combination with optimized background therapy (OBT) in HIV-1 infected children and adolescents who are failing their current combination antiretroviral therapy (cART) and have dual- or triple-class ARV resistance. Dosing of fostemsavir will be administered according to the participant's weight band: 400 mg twice daily if weighing ≥ 20 to <35 kg (given as 2 x 200mg tablets), or 600 mg twice daily if weighing ≥ 35 kg. The study will initially enroll only participants weighing at least 35 kg who will be dosed with the currently available FTR 600 mg formulation twice daily. Enrollment of participants who are at least 6 years of age and weighing at least 20kg to <35 kg will commence once the 200mg formulation becomes available and these participants will be dosed with 400mg twice daily, which will be administered as 2 x 200 mg tablets.
Study population	Children and adolescents from 6 years old and weighing at least 20 kg to less than 18 years of age, who are failing their current combination antiretroviral therapy (cART) and have dual- or triple-class antiretroviral (ARV) resistance.
Study sample size	A minimum of 28 participants will be enrolled into SHIELD: at least 10 evaluable children in the lower weight band (≥ 20 to <35 kg), and at least 50 evaluable participants in the higher weight band (≥ 35 kg).
Follow up/duration	All children are expected to be followed for 36 with the potential or rollover to a continued access study
Study/Programme sites	Wits RHI Shandukani Research Centre (SRC)
Study/Programme duration	Duration of recruitment is estimated to be 156 weeks (36 months) for each weight band.

Study Treatment	Fostemsavir 600mg twice daily (≥ 35 kg) or 400mg (200mg x 2) twice daily (≥ 20 kg to < 35 kg) + optimized background therapy
Operations	Study specific
Investigators	Dr Faezah Patel, Principal Investigator Dr Lee Fairlie, Sub Investigator Dr Elizea Horne, Sub Investigator Dr Mrinmayee Dhar, Sub Investigator Dr Jeanne Coetzee, Sub Investigator
Sponsors/Donors	Fondazione Penta– for the treatment and care of children with HIV (and related diseases) – ONLUS
Funder	ViiV Healthcare
Publications/key presentations to date	- Grasa C, Archary M, Frigati L, Violari A, Patel F, Strehlau R, Camacho-Gonzalez A8, Maboja R9, Rakhmanina N10, Salvadori N, Nardone A, Than-In-At K, Koblansky A, Thakkar N, Tan L, Giaquinto C, Rojo P, Cressey TR Challenges of recruiting children and adolescents living with HIV with multi-drug resistance into a prospective clinical trials. - Archary M, Frigati L, Violari A, Patel F, Strehlau R5, Camacho-Gonzalez A, Maboja R, Rakhmanina N, Grasa C, Salvadori N, Nardone A, Than-In-At K, Parry C, Keegan M13, López Varela E, Giaquinto C, Cressey TR, Rojo P,. Characteristics of antiretroviral resistance in participants from the SHIELD trial: a pharmacokinetic and safety study evaluating fostemsavir in children and adolescents living with multi-drug resistant HIV.
Progress Update as at Jun 2025	- Screened: 6 - Screen failure: 4 - Enrolled: 2 - Currently on protocol amendment 6 - Participants to be rolled over to the PATH access study in 2026
LI participants consented on	3 Monthly
Overall Study/Project Contact	Kabelo Mashaba Faezah Patel
Briefing owner and date	Kabelo Mashaba 10 Mar 2026