Pharmacokinetics, safety, and efficacy of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) single-tablet regimen in HIV-1-infected children (6 to < 12 years)

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Background: Bictegravir (BIC, B), a novel, unboosted integrase strand transfer inhibitor (INSTI) with a high barrier to resistance and low potential for drug interactions, has been coformulated with the recommended NRTI backbone of emtricitabine (F, FTC) and tenofovir alafenamide (TAF) (B/F/TAF) into a once-daily (QD), single-tablet regimen (STR). We report pharmacokinetics (PK), safety and efficacy in children who switched from a stable antiretroviral regimen to B/F/TAF.

Methods: We conducted a prospective, single-arm, open-label, 2-part, 48-week (W) clinical trial to evaluate switching to the adult formulation of B/F/TAF (50/200/25 mg) QD in virologically suppressed children (6 to <12 years) weighing 25 kg. Intensive PK was evaluated at W2 or W4. PK parameters were compared to B/F/TAF-treated adults to confirm BIC dose. Adverse events (AE), laboratory tests, HIV-1 RNA, were assessed. We report follow up data through W12.

Results: 25 children enrolled; median (range) age 10 (6-11) yrs, median (range) weight 28.4 (25.0-39.0) kg, 52% female, 64% Black, median CD4 count 928 cells/µL. BIC AUC <sub>tau</sub> was similar, C <sub>sub</sub>max <sub>tau</sub> 77% higher, and C <sub>sub</sub>tau <sub>tau</sub> 22% lower in children 25 kg than adults. BIC C <sub>sub</sub>tau <sub>tau</sub> was well above protein-adjusted effective concentration for wild-type virus (162 ng/mL) in all children. FTC and TAF exposures were within safe and efficacious ranges of adults (table). Through median (Q1, Q3) exposure to study drug of 16.1 (15.9, 17.7) weeks, most common AEs were grade 1 diarrhea and upper respiratory tract infection (each 16%, 4/25); no other AE occurred in >2 participants. No participant discontinued for an AE. All (100%) had HIV-1 RNA < 50 c/mL at W12; none met criteria for resistance testing.

Conclusions: B/F/TAF maintained virologic suppression and was well tolerated in children through at least 12 weeks. Similar, but somewhat lower concentrations of all B/F/TAF components of B/F/TAF were achieved. Efficacy and safety in children are consistent with phase 3 B/F/TAF results in adults and adolescents, showing high proportions with viral suppression, excellent tolerability, and no resistance. B/F/TAF may be an important unboosted INSTI, STR option for HIV-infected children due to its small tablet size, high barrier to resistance and lack of food requirement.

| Parameter | Children | Adult | %GLSM Ratio | 90% CI | B/F/TAF | FTC
|-----------|----------|-------|-------------|-------|---------|------|
| Parameter | Children | Adult | Parameter | Children | Adult | Parameter | Children | Adult | %GLSM Ratio | 90% CI | B/F/TAF | FTC
| AUC<sub>tau</sub>, ng*h/mL | 17565 (36.9) | 115034 (36.4) | 121034 (36.4) | 116 (104, 130) | 10201 (26.9) | 116 (104, 130) |
| C<sub>max</sub>, ng/mL | 142 (127, 159) | 2610 (35.2) | 435 (94.9) | 116 (104, 130) | 177 (162, 194) | 185 (162, 210) |
| C<sub>tau</sub>, ng/mL | 177 (162, 194) | 170 (120, 241) | 227 (123, 325) | 177 (162, 194) | 177 (162, 194) | 177 (162, 194) |

Parameters are presented as arithmetic mean (%CV); GLSM, geometric least-squares mean.