Pharmacokinetics of Envarsus in paediatric kidney transplant recipients – Phase 1 pilot conversion study

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Abstract

Introduction: Tacrolimus is the standard immunosuppressant for paediatric kidney transplants and is routinely administered twice daily (BD-tac). Envarsus (LCP-tac), an extended-release formulation, is approved for adults but not in paediatrics.

Methods: We conducted a pilot open-label phase 1 study in stable paediatric kidney transplant recipients (age <18 at the time of study). Our primary objective was to compare the pharmacokinetics (Pk) of LCP-tac versus BD-tac. We conducted two 24-hour Pk studies: pre-conversion (BD-tac) and four weeks post-conversion to LCP-tac. Patients were followed for six months, with the option to continue LCP-tac.

Results: Five patients completed the study, with no returns to BD-tac. Median age was 15 years (range 11-17). LCP-tac exhibited an extended release profile versus the bimodal profile of BD-tac. Time to maximum concentration was delayed (5 hrs vs. 1 hr), and maximum concentration was lower (9.9 ng/L vs. 14.4 ng/L). Tacrolimus area under the curve (24 hr) was comparable (141 ±46.5 ng/L vs. 164 ±27.8 ng/L). No new safety concerns arose. There was no rejections and no difference in eGFR at the study's end (1.5 ml/min/1.73m^2, range -1.7 to 2.3 ml/min/1.73m2). Concentration/dose ratio was higher in LCP-tac (1.8 ±0.64 vs. 0.8 ±0.39). The final conversion ratio was 0.6 (BD-tac:LCP-tac).

Conclusion: Our pilot study confirms the extended-release Pk profile and improved absorption of LCP-tac compared to BD-tac. A larger study is needed to further evaluate the population Pk characteristics in the children.