Bio Pharma Services Study Design

Tacrolimus ER Tab - FDA – BE Study Design (NTI drug)

Revision tracker

Prepare by	Date	Revision Comments
[redacted]	Jan 2022	New design based on the IR design

Regulatory Body	**FDA**	
Study Drug Information	**Test Product**	**Reference Product**
Strength	Tacrolimus 4mg	ENVARSUS XR 4mg
Formulation	XR tablet	XR tablet
Manufacturer	Any sponsor	Rottendorf Pharma GmbH for Veloxis Pharmaceuticals
Route	Oral	Oral
Therapeutic class/Indication	Immune Diseases Calcineurin-inhibitor immunosuppressant indicated for the prophylaxis of organ rejection in de novo kidney transplant or kidney transplant patients converted from IR formulation to XR	
Study Profile		
Study Phase	Bioequivalence	
Design	4-way fully replicate	
Study Population	Healthy male and non-pregnant female volunteers; 18 years old and above No live vaccines at least 30 days prior to study administration and 30 days post last tacrolimus dose.	
Smoker Use	No	
BMI	18.5 – 30kg/m^2	
Hormonal Contraceptive	No	
Sample Size (# of Subjects)	**Pilot, Fa: 18 subjects (recommended)** **Pivotal: FA and Fe** - Covid-19 buffer: 52 subjects - No covid-19 buffer: 48 subjects (minimum of 38 subjects for power of 80%)	
Study Condition	Fasting and Fed	
In house confinement	-10 to 36 hours post dose	
Washout	At least 14 days	
Dosing Schedule	Single dose (1 x 4 mg)	
PK sampling time points	**FA and Fe:** Pre-dose and at 1, 2, 4, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 24, 28, 32, 36, 48, 60 and 72 hours. (21 time point)	
Clinical Safety Monitoring	• **Vital sign (HR + BP):** pre-dose and at 1, 2, 4, 6, 12, 16, and 24h post dose • **Temperature:** screening, pre-dose and 6-, 12- and 24-hours post dose in every period. • **ECG: Screening,** post study, check-in, 6h, 12h and 24h post dose. (QT prolongation) • **TB skin test:** Screening (*Mandatory for immune suppressant drug class*) • **TB questionnaire:** screening • **Hb and HCT:** period 4 check-in (*common AE includes anemia and study has 4 periods with 21 time point per period)* • **Serum creatinine:** Screening, post study and periods 2, 3 and 4 check-in. (increase creatinine) • **Special Exclusive criteria:** Not received live vaccine from screening to 30 days after study ended	

	[redacted] *confirmed on Jan 04, 2022.*
Hours of PI monitoring	4h
Analytical Details	
Analyte(s)	Tacrolimus
Analytical Method	LC-MS/MS
Matrix	Whole blood
Estimated Analytical Range	**0.1 ng/mL – 100 ng/mL** (validated)