Initial results: Cannabidiol increased exposure of tacrolimus in healthy subjects

PK Interaction between cannabidiol and tacrolimus

PRESENTER:
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BACKGROUND: Presented is an interim feasibility analysis of an open-label, three-period, fixed sequence phase 1 trial (NCT05490511) assessing the safety of co-administering cannabidiol (CBD) and tacrolimus (Tac).

METHODS

Interim Analysis of Tac PK

1. **12 healthy subjects** who completed the study prior to January 1, 2024.
2. Subjects were administered a single-dose Tac 5 mg by mouth in Period 1 (control) and in Period 3 (steady-state CBD).
3. Both periods consist of 10 blood draws, up to 48 hours.

Safety Assessment

1. **15 subjects** who received at least one dose of study drugs prior to January 1, 2024.

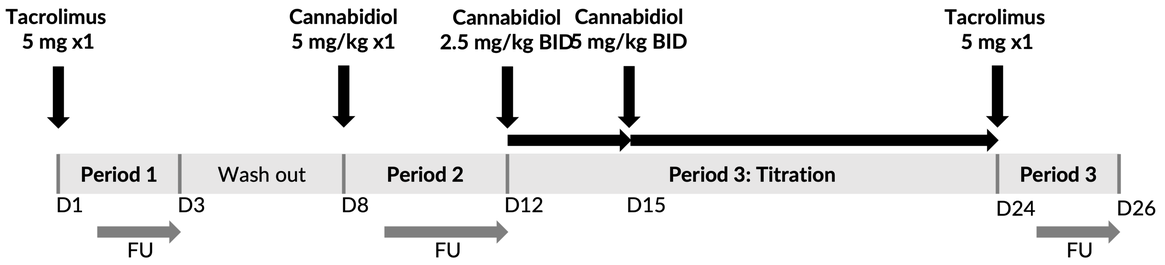
RESULTS

- **CBD increased C_{max} and $AUC_{0-\infty}$ of Tac** by 4.1- and 3.1-fold, respectively.
- All treatment-emergent adverse events (**TEAEs**) were Grade 1 or 2 in severity.

CONCLUSION

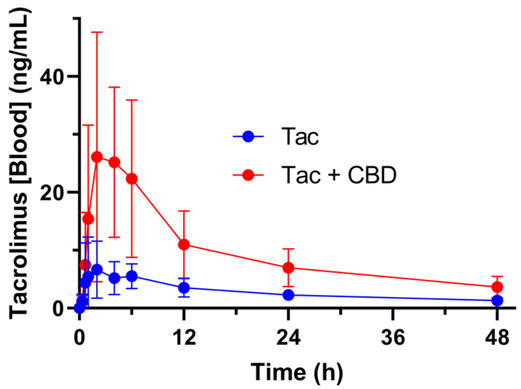
- CBD moderately inhibited Tac metabolism in healthy adults from initial results.
- Results support a strong feasibility of detecting genotype-dependent PK interaction between CBD and tacrolimus

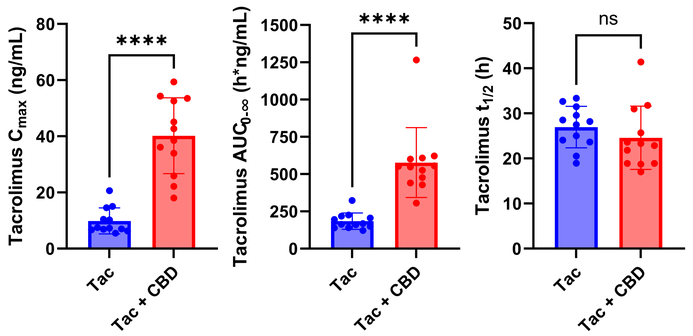
Study Design



FU, follow up

Tacrolimus Pharmacokinetics





****p<0.0001; ns, not significant

	C_{max} (ng/mL)	$AUC_{0-\infty}$ (h*ng/mL)	T_{max} (h)	CL/F (L/h/kg)	Vz/F (L/kg)	$t_{1/2}$ (h)
Period 1	9.9 ± 4.6	184.2 ± 54.7	4.2 ± 3.1	0.4 ± 0.1	14.2 ± 4.7	26.9 ± 4.6
Period 3	40.2 ± 13.5	577.3 ± 234.7	3.9 ± 3.0	0.1 ± 0.1	4.3 ± 1.8	24.6 ± 7.0
Fold change (Period 3/Period 1)	4.1	3.1	0.9	0.3	0.3	0.9

Trial Design: See Poster TIP-002
In Vitro Experiment: See Poster PT-027

Baseline characteristics

Subject Characteristics	All Subjects (n=12)
Age, yr	42.1 ± 15.4
Sex	
Male	2 (16.7%)
Female	10 (83.3%)
Weight, kg	82.2 ± 19.4
BMI, kg/m²	29.0 ± 4.5
Race	
White	11 (91.7%)
Black	1 (8.3%)
Asian	0 (0%)
Ethnicity	
Hispanic	1 (8.3%)
Non-Hispanic	11 (91.7%)
Hct, %	38.8 ± 2.6
Albumin (g/dL)	4.3 ± 0.3
SCr, mg/dL	0.8 ± 0.3
eGFR, mg/mL/1.73 m²	99.8 ± 17.5
> 60 mg/mL/1.73 m²	12 (100%)
< 60 mg/mL/1.73 m²	0 (%)

Adverse events
Individual PK

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