

A study of the drug interaction potential of TBAJ-876 on CYP3A4 and P-gp substrates in healthy adults.

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Background:

- It is important to understand the potential for drug interactions between anti-HIV and anti-TB regimens.
- TBAJ-876, a new diarylquinoline drug candidate, had in vitro signals of possible effects on CYP3A4 and P-gp.
- NC-009 is a planned phase 2 study with TBAJ-876 that will allow participation of patients with TB and HIV coinfection who will receive tenofovir (TFV), a P-gp substrate, and dolutegravir (DTG), a P-gp and CYP3A4 substrate.

Objective

- Evaluate the effects of TBAJ-876 on the probe substrates midazolam of CYP3A4 and digoxin of P-gp.

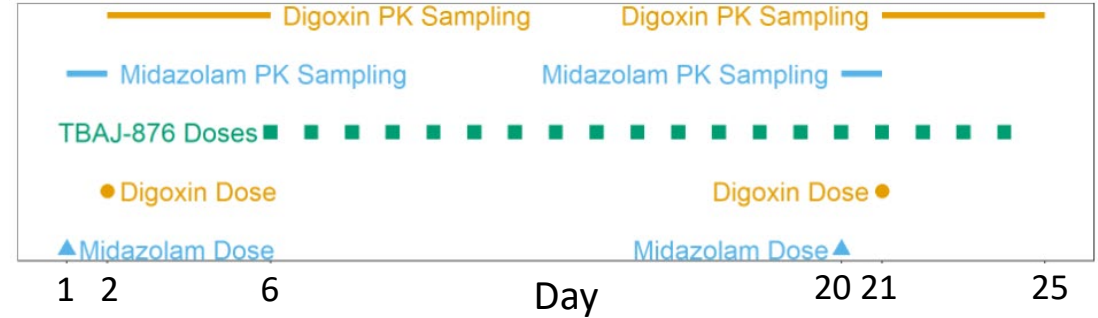
Design:

- One cohort of 26 healthy adults.
- 2 mg midazolam Day 1 and Day 20, 24 hours PK sampling after each.
- 0.25 mg digoxin Day 1 and Day 21, 96 hours PK sampling after each.
- 150 – 200 mg TBAJ-876 Days 6 – 24.

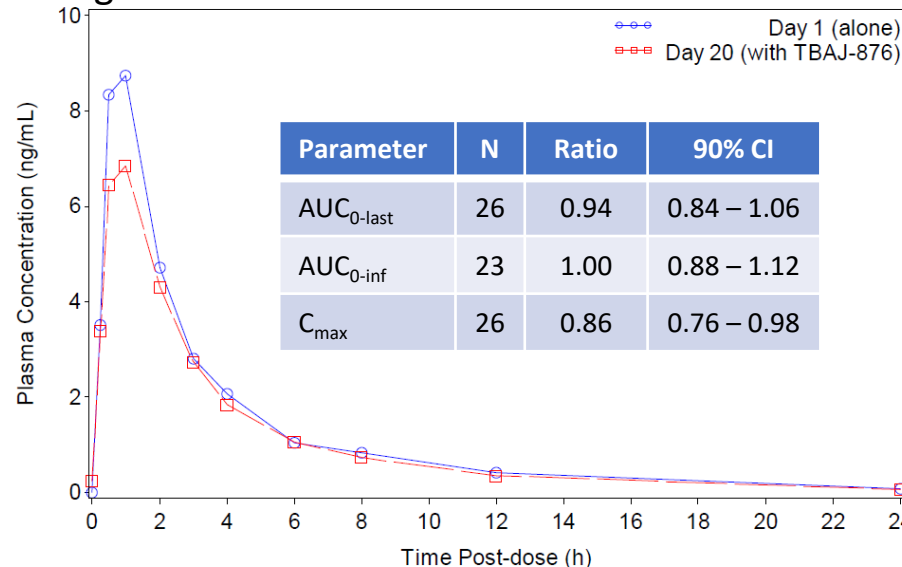
Conclusions:

- No changes may be needed to dosages of substrates of CYP3A4 and P-gp co-administered with TBAJ-876.
- TFV and DTG will be required without dose adjustment as antiretroviral therapy of TB-HIV-coinfected participants in NC-009.
- Confirmation of observations in this study is intended in the NC-009 study.

Study design



Midazolam mean concentration profiles and geometric mean ratios



Digoxin mean concentration profiles and geometric mean ratios

