27th ECCMID Vienna, Austria 22 – 25 April 2017
The congress of ESCMID

Session: P083 Antifungal drugs and treatment I

**Category: 6c. Antifungal drugs & treatment**

25 April 2017, 12:30 - 13:30
P1710

# Multiple dose pharmacokinetics of an immediate-release tablet formulation of F901318 in healthy male and female subjects

Tony Kennedy*[1], Graham Allen[2], Jan Steiner[3], Markus Heep[4], Jason Oliver[1], Graham Sibley[5], Derek Law[1]

[1]*F2g Ltd*

[2]*Gamms Consultancy*

[3]*Oxford Therapeutics Consulting*

[4]*F2g Ltd; Development*

[5]*F2g ltd*

**Background:** F901318 is a novel orotomide antifungal agent being developed for the treatment of invasive aspergillosis and scedosporiosis. An oral immediate release tablet developed to support long term treatment in patients has been evaluated in a Phase 1 repeat dose study.

**Material/methods:** F901318 tablets (120 mg active) were made with a hypromellose acetate succinate-based formulation. The tablets were tested in a double-blind placebo-controlled, randomised, parallel group study in 10 healthy male and female subjects, 8 taking active compound and 2 taking placebo.

Healthy males or females between 18 and 55 years of age and weighing between 50-100 kg were entered into the study and were dosed for 10 days once daily with three F901318 tablets (360 mg). A validated analytical assay was used to measure F901318.

**Results:** F901318 was well tolerated in the study with only mild or moderate adverse events observed. The key pharmacokinetic parameters $T_{max}$, $C_{max}$, $AUC_{0-12}$, $AUC_{0-24}$ and $AUC_{0-t}$ are summarised in Table 1. Evidence of enterohepatic recirculation was seen in the presence of secondary peaks which precluded estimation of t½. The plasma F901318 profiles were generally

similar between volunteers and exhibited accumulation with $C_{max}$ and $AUC_{0-24}$ values on day 10 about 2.5 fold and 3.9 fold higher than on day 1.
The mean $C_{24}$ h results in Table 1 show that on day 1 the $C_{min}$ level was *ca*. 0.5 µg/mL and by day 10 was 1.8 µg/mL. Inspection of the mean full profile plot shows that from day 3 onwards the mean $C_{min}$ values were consistently in the range of *ca*. 1 to >2 µg/mL, thus surpassing F901318 exposures needed for efficacy in animal models.

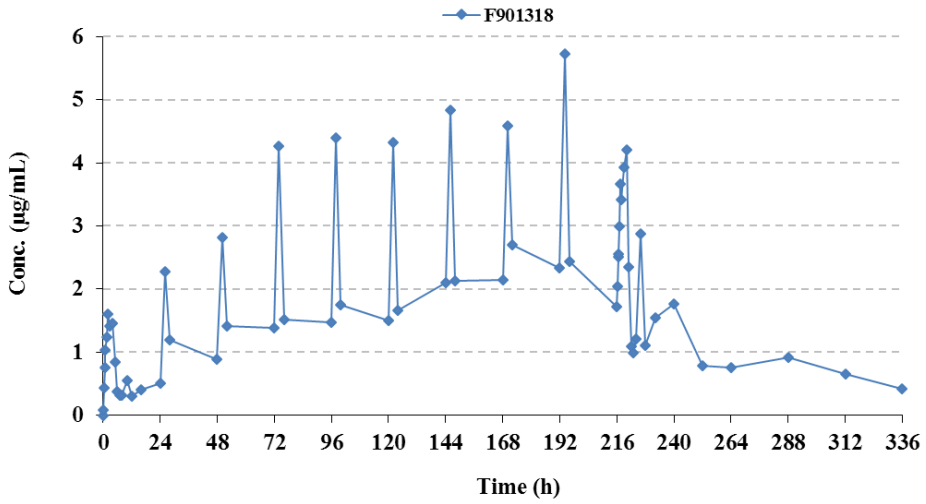


**Table 1. F901318 Plasma exposures on day 1 and day 10**

| | Da | | | | Day 10 | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Param.** | **$C_{max}$** | **$AUC_{0-12}$** | **$AUC_{0-24}$** | **$C_{24}$** | **$C_{max}$** | **$AUC_{0-12}$** | **$AUC_{0-24}$** | **$AUC_{0-t}$** | **$C_{24}$** |
| **Descr.** | **(µg/mL)** | **(µg.h/mL)** | | **(µg/mL)** | **(µg/mL)** | **(µg.h/mL)** | | | **(µg/mL)** |
| Min. | 0.40 | 2.19 | 3.56 | 0.10 | 1.52 | 13.47 | 23.63 | 55.43 | 0.80 |
| Max. | 2.89 | 13.6 | 25.2 | 0.94 | 7.60 | 46.57 | 67.84 | 204.7 | 2.62 |
| Mean | 2.03 | 8.84 | 13.98 | 0.51 | 4.59 | 28.76 | 47.32 | 123.9 | 1.76 |
| % CV | 39.9 | 37.7 | 43.4 | 50.3 | 47.3 | 40.6 | 35.2 | 41.6 | 37.5 |

**Conclusions:** F901318 dosed once daily to healthy volunteers at a dose of 360 mg for ten days was well tolerated. Plasma exposure levels were achieved which exceed the drug exposures required for efficacy in animal models of invasive aspergillosis.