29th ECCMID Amsterdam, Netherlands 13 – 16 April 2019

The congress of ESCMID

O0738 Safety, tolerability and pharmacokinetics of posaconazole intravenous solution and oral powder for suspension in children with neutropenia

Andreas H. Groll[1], Hisham Abdel-Azim[2], Thomas Lehrnbecher[3], William Steinbach[4], Amanda Paschke[5], Eric Mangin[5], Gregory A. Winchell[5], Christopher J. Bruno[5]

[1] University Children's Hospital Münster, Münster, Münster, Germany, [2] Children's Hospital Los Angeles, University of Southern California Keck School of Medicine, Los Angeles, Los Angeles, United States, [3] Hospital for Children and Adolescents, University of Frankfurt, Frankfurt, Frankfurt, Germany, [4] Duke University, Durham, Durham, United States, [5] Merck & Co., Inc., Kenilworth, Kenilworth, United States

Background: For adults, posaconazole is approved as an intravenous (IV) solution and 2 different oral formulations (a suspension and an improved bioavailability tablet [both approved for age ≥13 years]). A novel powder for oral suspension (PFS) has been developed to offer the bioavailability of the tablet formulated for weight-based dosing in children.

Materials/methods: This nonrandomized, open-label, sequential dose-escalation trial evaluated the safety, tolerability, and pharmacokinetics (PK) of posaconazole IV and PFS and enrolled children aged 2-17 years with documented or expected neutropenia (NCT02452034). Participants were grouped by age, 2-<7 years and 7-17 years, and received posaconazole IV (3.5, 4.5, or 6.0 mg/kg/d for 10 days); after 10 days, participants could switch to posaconazole PFS at the same dose for ≤18 days. PK sampling was done after 7-10 days on each formulation. Target PK exposure was ~90% of participants with average steady state plasma concentration (C_{avg}) >500 ng/mL.

Results: Table 1 shows geometric mean C_{avg} and proportion of participants with C_{avg} ≥500 ng/mL by dose cohort and age group. Posaconazole IV and PFS were well tolerated in study participants and had a safety profile similar to that for adults.

Table 1.							
Posaconazole dose, mg/kg	**Age group, years**	**IV**	**PFS**				
		n	**Mean C_{avg}, ng/mL**	**C_{avg} ≥500 ng/mL, n (%)**	**n**	**Mean C_{avg}, ng/mL**	**C_{avg} ≥500 ng/mL, n (%)**
3.5	2-<7	11	743	9 (82)	5	510	2 (40)
	7-17	19	1140	19 (100)	10	861	9 (90)
4.5	2-<7	14	1070	14 (100)	8	901	8 (100)
	7-17	15	1240	15 (100)	8	1200	8 (100)
6	2-<7	17	1300	17 (100)	7	960	7 (100)
	7-17	24	1840	24 (100)	12	1040	10 (83)

Conclusions: PFS resulted in lower posaconazole exposures than IV across age groups at all dose levels. Although posaconazole exposure was lower in children aged 2-<7 years for both IV and PFS formulations at all dose levels, both 4.5 and 6 mg/kg/d generally achieved the PK target of ~90% of subjects with a C_{avg} ≥500. Overall, at 6.0 mg/kg/d, mean C_{avg} values were generally closer to systemic posaconazole exposures in adults administered posaconazole IV or tablet.