FG2216, A NOVEL ORAL HIF-PHI, STIMULATES ERYTHROPOIESIS AND INCREASES HEMOGLOBIN CONCENTRATION IN PATIENTS WITH NON-DIALYSIS CKD

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In this phase 2 single blind, placebo-controlled, dose-ranging study, we examined the ability of FG-2216 to correct anemia in ESA-naïve patients with CKD. 142 patients with CKD Stages 3 & 4 and Hb < 10.8 g/dL were randomized and treated for up to 15 wks. Initial doses included 375mg (n=26), 625mg (n=52), or 1250mg (n=50), dosed twice weekly and placebo (n=14). After 4 wks of stable dosing, elective titration was employed to achieve a target Hb response. The proportion of treated subjects with Hb response, defined as 1 g/dL increase, was 13 (50.0%), 31 (59.6%), 38 (76.0%) for the FG-2216 dose groups and none for placebo. Analysis of the ITT completer population (N=96) excluding treatment non-completers due to early study termination by the sponsor reveals responder rates of 58.8%, 60.5%, and 90.6% for the FG-2216 dose arms. Mean baseline Hb levels for the FG-2216 starting doses and placebo were 10.2, 10.1, 9.9 and 10.1 g/dL, respectively; following up to 15 wks of therapy, maximum mean Hb changes from baseline were 1.1, 1.4, 2.4 and 0.2 g/dL, respectively. Assessment of endogenous EPO and VEGF 12 hours after the first dose revealed a mean increase from baseline in EPO of 11.9, 28.9, 141.6 for the FG-2216 groups and 1.1 mIU/mL for placebo; mean change from baseline in VEGF was -7.8, -5.4, -3.9 for the FG-2216 groups and 5.2 pg/mL for placebo. There were 41 SAEs reported in 25 subjects, 2 were assessed as possibly related to FG-2216 including 1 death due to fulminant hepatitis. There were no increases in BP observed with any dose level or correlated with increasing Hb levels; there was no increased use of BP medications over time. Oral administration of FG-2216 in ESA-naïve patients with CKD not on dialysis was well tolerated and may effectively treat CKD anemia as evidenced by increasing erythropoietic effect with modest EPO elevation, no VEGF increase and no adverse BP changes.