P250

P250 -Design of a Randomized, Double-Blind, Placebo-Controlled Phase 3 Trial to Examine the Efficacy and Safety of SNF472 for Treating Calcific Uremic Arteriolopathy (Calciphylaxis)

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Calciphylaxis or calcific uremic arteriolopathy (CUA) in patients with end-stage renal disease is a severe form of vascular calcification characterized by painful necrotic skin ulcers and very high mortality. No approved agents are available for therapeutic use. SNF472, an intravenous formulation of myo-inositol hexaphosphate, inhibits formation and growth of hydroxyapatite crystals, the final common step in the pathophysiology of vascular calcification. In a previous open-label Phase 2 CUA study, improvements in wound healing, pain, and wound-related quality of life were observed following 12 weeks of treatment with SNF472. The objective of this phase 3 randomized, double-blind, placebo-controlled trial is to evaluate the efficacy and safety of SNF472 for treatment of CUA.

The planned enrollment is approximately 66 male and female adult patients on maintenance hemodialysis with a clinical diagnosis of CUA with wound ulceration and wound-related pain. Patients will be randomized 1:1 to receive SNF472 (7 mg/kg) or placebo 3x/week for 12 weeks via infusion through the dialysis circuit during regularly scheduled hemodialysis sessions. In a subsequent 12-week open-label period all patients will receive SNF472. Patients should also receive background care in accordance with the practices of each site (ie, standard care). Wound healing will be assessed with the Bates-Jensen Wound Assessment Tool (BWAT), BWAT-CUA, and qualitative review of wound images. All 13 items comprising the BWAT will be assessed: size, depth, edges, undermining, necrotic tissue type, necrotic tissue amount, exudate type, exudate amount, surrounding skin color, peripheral tissue edema, peripheral tissue induration, granulation tissue, epithelialization. BWAT-CUA is an 8-item targeted modification of BWAT focused on prototypical features of CUA lesions including necrotic tissue type and amount, exudate type and amount, skin color surrounding wound, peripheral tissue edema and induration, and granulation tissue. Pain will be assessed on a 100-mm visual analog scale (VAS) and quality of life (QoL) will be assessed with the Wound-QoL Questionnaire. Standard safety assessments will include adverse events, ECGs, and laboratory parameters.

Planned analyses include mixed model repeated measures analyses of absolute change from baseline to Week 12 to estimate the difference between randomized treatment groups in efficacy endpoints (eg, BWAT-CUA, BWAT, Pain VAS). The models will include fixed effect terms for randomized treatment group, visit, and visit by randomized treatment group interaction. The models will be stratified for sodium thiosulfate use at baseline and baseline scores (BWAT-CUA, BWAT, Pain VAS) will be included as covariates. Safety data will be analyzed descriptively with no formal statistical comparisons of safety data planned.

This study will evaluate whether SNF472 compared to placebo improves wound healing, pain, and quality of life in patients with CUA. Standard safety assessments will be conducted.