A Phase 1, Open-label, Dose-escalation Study of SNX-5422 plus Carboplatin and Paclitaxel in Subjects with Advanced Lung Cancers

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Background: SNX-5422 is an orally bioavailable pro-drug of SNX-2112, a highly potent and selective Hsp90 inhibitor with preclinical anti-tumor activity in lung cancer models and synergy with platinum and taxane compounds. Carboplatin/paclitaxel is a commonly used treatment for advanced lung cancer. This phase 1 study examined SNX-5422 plus carboplatin/paclitaxel followed by SNX-5422 maintenance therapy in pts with advanced lung cancers.

Methods: Eligible pts had advanced NSCLC (EGFR wild-type or non-sensitizing mutation, ALK wild-type) or extensive stage SCLC and up to one prior line of chemotherapy. Pts received paclitaxel (175 mg/m^2) and carboplatin (AUC 5) q3w up to 4 courses and SNX-5422 qod (starting at 50 mg/m^2), 21 of 28 days, with a standard 3+3 dose escalation rule during the combination followed by SNX-5422 (100 mg/m^2 qod) monotherapy for maintenance until disease progression. Safety and tolerability were evaluated to determine the maximum tolerated dose (MTD) and pharmacokinetics of SNX-2112.

Results: Since August 2013, 15 pts have been enrolled. No dose-limiting toxicities (DLTs) for the combination were reported for SNX-5422 up to 75 mg/m^2. The SNX-5422 Maximum Tolerated Dose was determined at 100 mg/m^2 for the combination with one grade 3 DLT of diarrhea. Adverse events possibly related to the combination in ≥ 2 pts were diarrhea, nausea, fatigue, neutropenia, alopecia, mostly graded 1 or 2, except for grade 3 neutropenia (2), diarrhea (2), and nausea (1). Of 8 NSCLC pts evaluable for objective response 4 had partial response, 3 stable disease and 1 disease progression as best response during the combination part. Six of 8 NSCLC patients completing the maximum of 4 courses of carboplatin/paclitaxel/ SNX-5422 went onto maintenance. Of 3 SCLC, pts 2 had stable disease and 1 disease progression as best response. Five NSCLC pts are ongoing and with the dose escalation phase completed, the study continues to enroll new NSCLC pts in the expansion cohort.

Conclusion: The addition of SNX-5422 to carboplatin (AUC 5)/paclitaxel (175 mg/m^2) was well-tolerated at doses up to 100 mg/m^2. Preliminary efficacy of this triplet combination in NSCLC is encouraging.

Clinical trial information: NCT01892046.