A Phase 2 Trial of SNS-595 in Women with Platinum Resistant Epithelial Ovarian Cancer

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ABSTRACT (Updated October 2007)

Background: SNS-595 is under clinical investigation in adult leukemia and ovarian cancer. Clinical responses have been observed in these indications, as well as in non-small cell (NSCLC) and small cell lung cancers. SNS-595 is a replication-dependent DNA damaging agent that causes irreversible G2 arrest, and rapid apoptosis. A secondary mechanism for SNS-595 is a unique inhibition of topoisomerase IIβ that causes highly selective DNA damage with low dependence on topoisomerase IIα for its potent antitumor activity. A Phase 2 study of single agent SNS-595 in ovarian cancer was initiated based on clinical activity observed in patients (pts) with ovarian cancer in phase I, including one partial response (PR), and supported by preclinical studies in several human ovarian cancer xenograft mouse models. A translational medicine study of SNS-595 activity in ovarian tumor biopsies was undertaken in parallel. Methods: SNS-595 was administered to pts with advanced platinum resistant epithelial ovarian cancer who had progressive disease after 1 or 2 prior platinum containing regimens. Pts could have received an additional biologic or non-platinum therapy after becoming platinum-resistant. Pts remaining on study at 3 months were defined as nonclinical studies that showed additivity or synergy in combination with other chemotherapeutic agents.

RESULTS

SNS-595 is generally well tolerated with a clinically manageable adverse event profile and few (4/19) dose reductions.

- Most common AEs were nausea and fatigue with an incidence of 32% (6/19).
- Incidence of neutropenia and febrile neutropenia were both 11% (2/19).

SAFETY

Table 3: Frequent (≥10%) Adverse Events for all NCI CTCAE Grades

SAFETY

PATIENTS

Table 1: Patient Demographics

Table 2: Patient Baseline Characteristics

CONCLUSIONS AND FUTURE DIRECTIONS

SNS-595 demonstrates a single agent activity in advanced platinum resistant ovarian cancer patients with 88% (15/17) of patients having stable disease or better, including 2 PRs in patients previously resistant to Doxil.

- 38% (5/13) of patients with stable disease have received three or fewer cycles of SNS-595 and remain on study.

- The rate of febrile neutropenia in this study is low (11%, 2/19) indicating that SNS-595 is a generally well-tolerated drug in this population.

- SNS-595 will proceed to Stage 2 of this study having already achieved the pre-specified criterion (2 or more responses) set for Stage 1.

- No resistance to SNS-595 was observed in 17 historical ovarian cancer biopsy specimens tested by EDR® assay for extreme drug resistance.

- Further study of SNS-595 in combination and single agent settings is supported by evidence of clinical activity as well as nonclinical studies that showed additivity or synergies in combination with other chemotherapeutic agents.