A Phase Ib/II Study of Cancer Stemness Inhibitor Napabucasin (BBI-608) Combined with Weekly Paclitaxel in Platinum Resistant Ovarian Cancer

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CLINICAL CONTEXT

Napabucasin inhibits a cancer stemness marker in ovarian cancer models, and in combination with paclitaxel, delays xenograft tumor growth in a human ovarian cancer xenograft model as measured by mean MTV (mm3).

PATIENT CHARACTERISTICS

CANCER STEMNESS & NAPABUCASIN

Matriproteins with advanced epithelial ovarian, fallopian tube, or peritoneal cancer who have progressed on a prior taxane-based regimen and who were platinum resistant or refractory were enrolled. Napabucasin 240–480 mg BID (using 80 mg capsules) and paclitaxel 80 mg/m2 BSA administered IV weekly 3 of every 4 weeks. A sample size of 40 evaluable patients was estimated to be needed to determine an ORR of at least 45% with a 35% Type I error.

NAPABUCASIN MONOTHERAPY IN OVARIAN XENOGRAFT MODELS

Napabucasin reduces pSTAT3 and cancer stem cell marker CD44 in human ovarian cancer xenograft models. In a xenograft model of ovarian cancer (SK-OV-3) and CA-125 is deceased after 4 weeks of Napabucasin administration.

RATIONAL FOR COMBINATION REGIMEN

Napabucasin in combination with Paclitaxel

1. Significant tumor burden in a xenograft model of ovarian cancer

TRIAL DESIGN

Objective:

To evaluate preliminary anti-tumor activity of napabucasin plus weekly paclitaxel with MTD identified.

Key Design Elements:

1. For dose escalation, combinations of napabucasin and paclitaxel were administered BID (using 80 mg capsules) and paclitaxel 80 mg/m2 administered IV weekly 3 of every 4 weeks. A sample size of 40 evaluable patients was estimated to be needed to determine an ORR of at least 45% with a 35% Type I error.

SAFETY PROFILE

Adverse Events Related to Napabucasin (N = 56)

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RESPONSE PER RECIST 1.1 – PLATINUM RESISTANT OVARIAN CANCER

All patient had CR or PR or 50% or more shrinkage during the course of therapy. Average shrinkage was observed by cycle 4 with 63% of patients achieving >50% necrosis.

CONCLUSIONS

Napabucasin was safely combined with full dose weekly paclitaxel (80 mg/m2) in patients with platinum resistant ovarian cancer.

1. Objective response, partial response, prolonged stable disease, and encouraging progression free and overall survival were observed in patients with heavily pre-treated platinum resistant ovarian cancer and a median of 4 prior systemic chemotherapy regimen (range 1 to 10 prior regimens).

2. Significant decreases in CA-125 tumor marker levels were observed.

3. Further clinical evaluation of napabucasin in combination with weekly paclitaxel is warranted in patients with platinum resistant ovarian cancer.