A Phase 1 Study of Selinexor in Combination with Paclitaxel and Carboplatin in Patients with Advanced Ovarian or Endometrial Cancers


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**BACKGROUND**

- XPO1 is a major nuclear export protein for tumor suppressor proteins (TSPs), including p53, p73, FOXO, pRB, BRCA1 and P21.
- Selective Inhibitor of Nuclear Export (SINE) compounds inhibit XPO1, leading to nuclear retention of TSPs and selective tumor cell apoptosis.
- Selinexor (S) is a first-in-class oral, covalent SINE compound.
- In a Phase II clinical trial of its with relapsed ovarian cancer (OC) and endometrial cancer (EC), treatment with single-agent selinexor demonstrated anti-cancer activity.1

**METHODS**

- Preclinical studies have shown that SINE compounds behave synergistically to enhance cancer cell death when combined with different therapeutic agents.
- Paclitaxel and carboplatin (TC) chemotherapy is commonly utilized in the treatment of advanced GYN malignancies.
- Phase IB study (NCT02419945) to evaluate the safety of selinexor in combination with multiple standard chemotherapy agents including TC in advanced malignancies is ongoing.
- Clinical exploratory analysis has demonstrated selinexor target engagement and a relationship between baseline circulating tumor cells and duration of response.

**RESULTS**

This ongoing study has enrolled 16 patients (data cutoff: August 25, 2017) with ≥3 dose escalations shown in Table 2 and tumour shrinkage rates and PFS in Table 3. All patients experienced an adverse event (AE). A summary of AEs is shown in Tables 4 & 5.

**Conclusions**

- Selinexor in combination with TC in advanced OC, EC, and ECs was tolerated.
- Bone marrow toxicity appears to be greater in this study compared to that seen with TC in this patient population. (2-5)

**References and Acknowledgements**

- Investigator-Initiated study supported by Karyopharm Therapeutics.
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