Selinexor in combination with carboplatin and paclitaxel in patients with advanced or metastatic solid tumors: Results of an open label, single-center, multi-arm phase 1b study

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INTRODUCTION
Selinexor is a first-in-class novel, oral potent selective inhibitor of nuclear export (XPO1) that: (1) blocks the transcriptional export of mRNA; and (2) blocks the export of proteins, thereby controlling the cell’s protein expression and output. Preclinical models have suggested that selinexor and CTX exports antimicrobial activity in multiple malignancies.

METHODS
Study design and treatment
The primary objective was to establish the safety and tolerability of Selinexor when administered with standard chemotherapy using a 3+3 dose-escalation design to determine the dose control and progression free survival of selinexor administered with standard chemotherapy treatments were the secondary objectives.

METHODS (Cont’d)
• The primary efficacy parameter was the safety according to NCI CTCAE v 4.03 and the secondary parameters were clinical benefit rate (CBR; percentage of complete response, partial response plus stable disease), disease control rate (DCR; percentage of complete response, partial response plus stable disease for at least 4 months, assessed according to RECIST 1.1 criteria), the objective tumor response rate (partial response). Treatment related adverse events (TRAE) are detailed in Table 1.

RESULTS
The most prevalent grade 3/4 TEAE were neutropenia (69%), hypomagnesemia (88%), anemia (51%), and fatigue (60%).

RESULTS (Cont’d)
• One patient at 60mg once weekly had experienced DLT with grade 4 neutropenia lasting 7 days.
• Partial response was noted in 14 patients (33.3%) in patients with esophageal cancer (n=2), 1 patient each with breast and ovarian cancer. (Figure 2)
• Five patients (41.7%) achieved stable disease and the clinical benefit rate was 75%. Disease control rate (DCR; percentage of CR+PR+SD at 4 months) was 80.8%.
• Majority of patients (84%), including 3 patients who had PR, had prior chemotherapy 7-8 cycles in a “basket type” expansion.

CONCLUSION
One weekly oral selinexor can be safely combined with carboplatin/ paclitaxel and the P2D was 60 mg once weekly in combination with carboplatin and paclitaxel for 7 days.

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Table 1. Patients baseline demographics and disease characteristics

Table 2. Summary of treatment-emergent and -related adverse events in all grades of severity

REFERENCES