BACKGROUND

VAL-083 is a bi-functional alkylating agent with proven activity against NSCLC in historical anti-PGDS-sponsoring clinical studies. VAL-083 is approved for the treatment of lung cancer in China; however, clinical adoption is limited by lack of modern data related to mechanism-of-action and MoA and utility in the context of standard-of-care in NSCLC. We have previously demonstrated that VAL-083 circumvents cisplatin-resistance in ovarian cancer cells, in vitro and, further, that VAL-083 exhibits superior activity to cisplatin in both in vitro and in vivo NSCLC models, including TKI-resistant NSCLC. Here we aim to further differentiate VAL-083 from current standard-of-care in NSCLC by investigating its MoA in NSCLC, in vitro and in vivo.

Table 2. Historical clinical results with VAL-083 between the platinum drugs and VAL-083 T790M (Zhunzi KRAS mutations. Cisplatin new mutations, demonstrated that VAL-083 has an effective dose that kills 75% of cells. (1-2) Coeval single agent chemotherapeutic, demonstrating that VAL-083 can be used as a single agent in a combination therapy.

ABSTRACT # B42

The preclinical data presented here strongly support VAL-083 as a potential treatment for platinum- and TKI-resistant/refractory NSCLC as a single agent or as part of a combination therapy.

Table 3. ICSO values for VAL-083 in nine human NSCLC cell lines and their p53 status: 3 wild-type (H460, A549, H226), 4 mutant (H1975, SKLU1, H221, H157) and 2 null (H938, H1199) for p53.

Table 4. PC3 cells and the effect of VAL-083 on cell cycle arrest and apoptosis.

CONCLUSIONS & FUTURE DIRECTIONS

Historical clinical activity combined with a new understanding of the MoA supports the potential of VAL-083 as a possible solution for the treatment of chemo-refractory NSCLC.

VAL-083 has a distinct MoA from other chemotherapeutics used in the treatment of NSCLC.

VAL-083 overcomes TKI-resistance in NSCLC cell lines, including cells with the EGFR mutation T790M and KRAS mutations.

VAL-083 displays super-additivity and synergy with both cisplatin and oxaliplatin in NSCLC cell lines, including TKI-resistant cells with T790M or KRAS mutations.

VAL-083 activity is independent of p53 status in a panel of NSCLC cell lines.

An open-label post-market clinical trial in China will investigate the activity of VAL-083 in relapsed/refractory NSCLC. Results will provide guidance to physicians under the context of VAL-083’s current approval in China, and serve as proof-of-concept for expanded clinical development worldwide.

References: