First-in-human study of the CD40 agonist monoclonal antibody (mAb) CDX-1140 alone and in combination with CDX-301 (rFLT3L) in patients with advanced cancers: Interim results

Vonderheide

Consistent with our preclinical studies, the clinical data support that CDX-1140 activates CD40 in tumor cells and dendritic cells, thereby reducing tumor burden and enhancing immune responses.

Monotherapy (n=22)

- CDX-1140 (0.09 mg/kg): Patients achieved clinical activity, with 2/22 (9%) patients achieving a partial response.

Combination (n=8)

- CDX-1140 (0.09 mg/kg) + CDX-301 (1.5 mg/kg): Further clinical activity was observed with 3/8 (38%) patients achieving a partial response.

Incidence of Treatment Related AEs (≥ Grade of Patient or Grade 3)

- Grade 3 adverse events included fatigue, nausea, and hypoxia.

Safety

- All patients experienced at least one AE, with grade 3 adverse events occurring in 11% of patients.

Liver Function Tests & Platelets (up to Cycle 3)

- CDX-1140 alone and in combination with CDX-301 maintained acceptable liver function and platelet counts.

Pharmacokinetic and Antidrug Antibody Analysis

- CDX-1140 shows a dose-dependent increase in systemic exposure and tumor pharmacokinetic levels, with peak levels occurring at the 0.72 mg/kg dose level.

CONCLUSIONS AND FUTURE DIRECTIONS

- Consistent with our preclinical studies, the clinical data support that CDX-1140 is a CD40 agonist that is generally well tolerated at systemic drug concentrations expected to engage CD40-expressing cells in the tumor microenvironment.

- Addition of CDX-301 has not affected the tolerability of the dose levels of CDX-1140 tested to date (0.18 mg/kg) and enhances the clinical activity observed in patients on subsequent cycles.

- Future combination opportunities being considered include varililumab, PD-1/PD-L1 inhibitors and radiation therapy.

Compelling rationale: CDX-1140 and CDX-301 activate 1. CD40 engages classic TLR signaling, 2. CD40 engages TLR signaling in dendritic cells, 3. CD40 engages TLR signaling in tumors, 4. CD40 engages TLR signaling in regulatory T cells, 5. CD40 engages TLR signaling in macrophages, 6. CD40 engages TLR signaling in fibroblasts, 7. CD40 engages TLR signaling in endothelial cells, 8. CD40 engages TLR signaling in cancer cells.