**BACKGROUND**

- **Baseline Patient Characteristics**
  - **Monotherapy** vs **Combination**
    - **Age, years**
      - Monotherapy: 64.5 (44-81), Combination: 60.5 (53-83)
    - **Male**
      - Monotherapy: 9 (69%), Combination: 2 (50%)
    - **ECOG**
      - Monotherapy: 5 (38%), Combination: 0
    - **No. prior treatment**
      - Monotherapy: 4 (1-9), Combination: 3 (2-5)
    - **Prior checkpoint inhibitor**
      - Monotherapy: 7 (54%), Combination: 1 (25%)
    - **Prior chemotherapy**
      - Monotherapy: 12 (62%), Combination: 4 (100%)

- **Toxicity**
  - 1 DLT (CDX-1140 monotherapy, 0.18 mg/kg), grade 3 pneumonitis and hypoxia. Patient subsequently died due to Enterobacter pneumonia/bacteremia deemed unrelated to CDX-1140
  - No other treatment related SAEs or treatment related deaths
  - All additional treatment-related toxicity grade 1-2: nausea, fatigue, anorexia, arthralgia, myalgia, fever, chills, generalized muscle weakness, hot flash, dizziness

- **No Significant Drug-related Changes in Liver Function Tests or Platelets**
  - CDX-1140 monotherapy from 0.09 to 3.0 mg/kg IV q4w – 1+5 design for 1st two dose levels, then 3+3 design thereafter
  - CDX-1140 dose escalation from 0.01 to 3.0 mg/kg IV q4w
  - CDX-301 (75 μg/kg sc) x 5 days prior to 1st two CDX-1140 doses
  - DLT evaluation period: 35 days after the 1st CDX-1140 infusion (i.e., 7 days after the 2nd infusion)

**INITIAL RESULTS**

- **Activation of Peripheral Blood Immune Cells**
  - **Up-regulation of B-cell CD86**
  - **Rapid Depletion of Circulating B-cells**
  - **B-Cell Depletion is Transient**

- **Dose-Dependent Induction of Pro-Inflammatory Cytokines and Chemokines**
  - Levels analyzed by Luminex or ELISA (TNF-alpha only)
  - Dashed line: assay lower limit of quantitation

- **Circulating B-Cells**
  - Rapid depletion on Day 1 and Day 2
  - Downregulation on Day 1 and Day 2

- **CD54 Expression on Plasmacytoid DC**
  - Increase on Day 1 and Day 2

- **CD54 Expression on Myeloid DC**
  - Increase on Day 1 and Day 2

- **CD54 Expression on NK Cells**
  - Increase on Day 1 and Day 2

- **CD54 Expression on T Cells**
  - Increase on Day 1 and Day 2

- **Preliminary Evidence of Increased Immune Activity with Combination of CDX-1140 and CDX-301**
  - Enhanced cytokine production
  - Monocytes

**CONCLUSIONS AND FUTURE DIRECTIONS**

- **CDX-1140 monotherapy to date (at doses ≤ 0.18 mg/kg):**
  - Well-tolerated with minimal drug-related toxicity
  - Transient, dose-dependent pharmacodynamic effects
  - Results consistent with CD40-mediated immune cell activation and the hypothesis that CDX-1140 may achieve dose levels optimal for systemic exposure

- **CDX-1140 at 0.09 mg/kg** in combination with CDX-301:
  - No safety concerns to date with patients initiating treatment
  - Preliminary evidence of enhanced immune activation

- **Further dose-escalation will define recommended dose for evaluation of clinical activity in expansion cohorts**
- **Study amended to include non-Hodgkin’s lymphoma (NHL) in monotherapy portion**
- **Further opportunities include combinations with varilumab (in lymphomas), radiation therapy, and/or checkpoint blockade**
  - Several B cell lymphomas including DLBCL and follicular lymphoma express CD40 and CD27
  - Varilumab is a potent anti-CD27 agonist

**References**

2. Viale, et al. CIL 2018
3. Anandabapathy, et al. BMT 2015
4. Breton, et al. JEM 2015
7. Thomas, et al. AACR 2018

**Abbreviations:** CRC, colorectal cancer; RCC, renal cell cancer; NSCLC, non-small cell lung cancer; HNSCC, head and neck squamous cell carcinoma; WBC, white blood count; ALT, alanine aminotransferase; AST, aspartate aminotransferase; PK, pharmacokinetic; PD, pharmacodynamic; SD, standard deviation; DLBCL, diffuse large B-cell lymphoma

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