Cirtumzumab, a ROR1 Targeted Mab, Reverses Cancer Stemness, and Its Combination with Ibrutinib Is Safe and Effective: Planned Analysis of the CIRLL Phase 1/2 Trial for CLL and MCL

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Abstract #1755

I. RATIONALE / BACKGROUND

- Receptor tyrosine kinase-like orphan receptor 1 (ROR1) is a cell surface protein expressed primarily during fetal development and is also expressed in adult cancer cells. It is often over-expressed in many different cancers (but not normal cells), including breast, prostate, lung, lymphoma, leukemia, and other NHL.
- Cirtumzumab is a humanized MAb that binds to ROR1 with high affinity and inhibits ROR1 cell signaling. ROR1 is known to be important for the growth of tumor cells in vitro and includes breast, colorectal cancer, and neuroblastoma patients.
- Cirtumzumab is in phase I/II clinical trials in breast cancer and non-small cell lung cancer. In vitro and preclinical studies have shown that it has potential as a monotherapy and in combination with other agents.

II. STUDY DESIGN

- Part 1, Study CIRM-0001: Cirmtuzumab and Ibrutinib Dose Schedule
  - For MCL, N=8 evaluable pts who have received combination therapy and have follow-up data.
  - Receptor tyrosine kinase-like orphan receptor 1 (ROR1) is a cell surface protein expressed primarily during fetal development and is also expressed in adult cancer cells. It is often over-expressed in many different cancers (but not normal cells), including breast, prostate, lung, lymphoma, leukemia, and other NHL.
  - Part 2, Study CIRM-0001: Cirmtuzumab and Ibrutinib Dose Schedule
  - Up to 90 pts who are either R/R or TN will be enrolled and assigned as per the CIRM-0001: Circmtuzumab and Ibrutinib Dose Schedule.
  - The primary objectives are to determine the maximum tolerated dose (MTD) and the recommended phase 2 dose (RP2D) of the combination regimen in a comparative study and is open for enrollment.

III. CLINICAL RESULTS

- Safety of Cirtumzumab and Combination With Ibrutinib
  - Cirtumzumab was very well tolerated and adverse events considered at least possibly related to treatment were grade 1 or 2. No DLT or grade 3 possibly related adverse events occurred.
  - Grade 3 events were only reported as at least possibly related to the combination of cirtumzumab and ibritunib and consisted of adverse events previously reported for ibritunib.
  - A total of 5 SAEs were reported. These were considered potentially related to study agents, in CIRLL, pts 1 and 1. None were considered related to cirtumzumab alone.

- Overall, the addition of ibritunib to cirtumzumab was consistent with the AE profile reported for ibritunib alone.

- The most common events possibly related to cirtumzumab or the combination of cirtumzumab/ibrutinib were neutropenia, rash, fatigue, and anemia.

- Trials were conducted in 4 stages:
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- Overall Conclusions
  - The RDR dose used in Part 2 demonstrates less lymphocytosis and a rapid decrease in lymphocytosis following initiation of ibritunib.

- Cirtumzumab RDR Dose And Clinical Effects
  - Median ALC change over baseline
  - Complete 1 year of planned therapy and did not join Extension. Based on follow-up visits and clinical assessments at 3 and, recently, 6 months post-treatment, 2 pts met criteria for a CR (1 pt each).

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