Abstract C004

The CXCR4 inhibitor X4-136 enhances the in vivo efficacy of established drugs against preclinical models of aggressive pediatric acute lymphoblastic leukemia

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1. Introduction

Acute lymphoblastic leukemia (ALL) is the most common cancer in children; survival has improved dramatically over the past 50 years and new approaches are needed. The Pediatric Preclinical Testing Consortium (PPTC) panel is an in vivo study using the COLLABORATIVE calibration set and represented as specific antbody coating (SABC).

2. Study Methods

Cell surface CXCR4 quantification: PDX cell lines were established from co-culture of mononuclear and red cell specific antibody binding capacity (SABC). Levels of CXCR4 expression were quantified by flow cytometry (BD FACSCanto II; BD Biosciences, NJ).

3. Results

3.1 Expression of CXCR4 on the cell surface of pediatric ALL PDXs and cell lines. Cell surface CXCR4 expression was assessed using the COLLABORATIVE calibration set and represented as specific antibody coating (SABC).

Figure 1. Expression of CXCR4 on the cell-surface of pediatric ALL PDXs and cell lines. Cell surface CXCR4 expression was assessed using the COLLABORATIVE calibration set and represented as specific antibody coating (SABC).

Figure 2. Responses of ALL PDXs to X4-136 alone or in combination with VXL in vivo. Engraftment plots of ALL-4, ALL-7 and ALL-31 (top) and their corresponding Kaplan-Meier survival curves (bottom).

Summary of in vivo efficacy study:

X4-136 in combination with VXL significantly reduced leukemic infiltration. In ALL-31, the X4-136/VXL combination significantly decreased leukemic infiltration in the spleen compared with VXL alone.

Table 1. In vivo responses of pediatric ALL PDXs to X4-136 alone and in combination with VXL.

4. Discussion and Conclusions

In conclusion, the CXCR4 inhibitor X4-136 significantly enhanced the in vivo efficacy of established drugs against pediatric ALL PDX models. X4-136 in combination with VXL elicited remissions in 3/3 PDXs (2 Complete Responses, CRs; 1 Partial Response, PR) in a preclinical model of pediatric ALL.

5. References


More Information

Past Presentations:
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References: