Combination of lemzoparlimab and HER2-ADC elicits enhanced activity against HER2 expressing tumors

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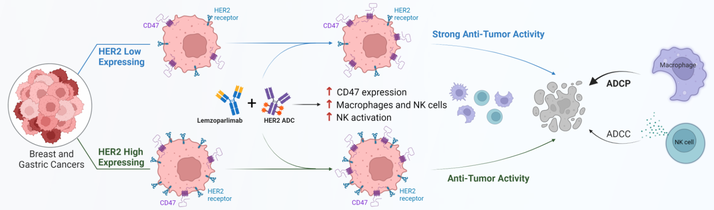
Poster #859

INTRODUCTION

- Lemzoparlimab is a differentiated anti-CD47 antibody with novel epitope and RBC sparing properties.
- CD47 is highly expressed on HER2-expressing tumor cells and dual blockade of CD47 and HER2 pathway was reported to increase the tumor growth inhibition in vitro and in vivo.
- HER2-ADC induced immunogenic cell death of multiple cell lines, providing the scientific rationale to combine with CD47 antibody through the increased surface expression of CD47 and calreticulin.
- Here we evaluated anti-tumor activity of lemzoparlimab in combination with HER2 ADC in cell derived xenograft (CDX) and patient derived xenograft (PDX) breast and gastric cancer models.



RESULTS

Different expression levels of HER2 and CD47 in breast and gastric cancer cell lines

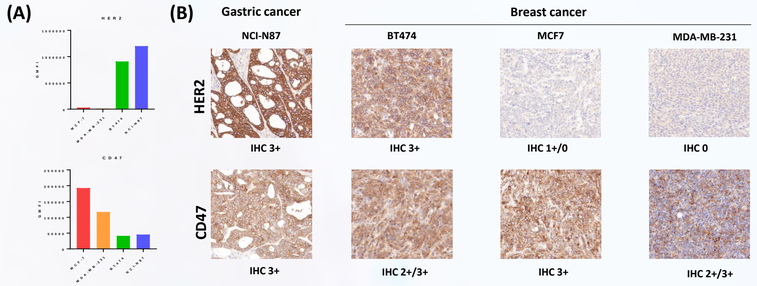


Figure 1. HER2 and CD47 expression were evaluated in various breast and gastric cancer cell lines by flow cytometry (A) or immunohistochemistry (IHC) using HER2 antibody (Gene Tech, EP3) and CD47 antibody (Abcam, EPR21794) (B).

Lemzoparlimab increased *in vitro* cell cytotoxicity or phagocytosis activity in combination with HER2 ADC, especially for HER2 low expressing tumors

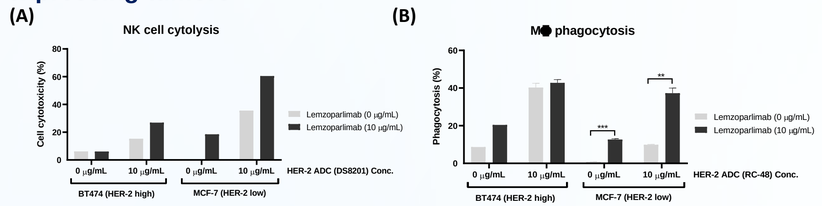


Figure 2. *In vitro* cytolysis or phagocytosis of lemzoparlimab in combination with HER2 ADC was investigated by co-culture of HER2$^+$ tumor cells with PBMCs or macrophages. The activity was measured by CellTiter-Glo (A) or FACS (B).

Lemzoparlimab enhanced *in vivo* anti-tumor activity in combination with HER2 ADC, especially in HER2 low expressing models

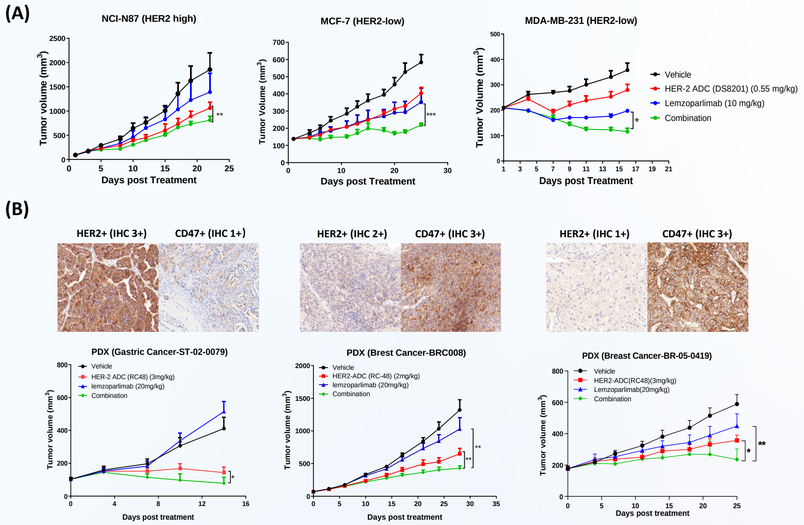


Figure 3. *In vivo* anti-tumor efficacy of lemzoparlimab in combination with HER2 ADC was evaluated in HER2$^+$ CDX (A) or PDX (B) of breast or gastric cancer models (CB17-SCID mice). HER2 or CD47 expression was analyzed by IHC using HER2 antibody (Gene Tech, EP3) or CD47 antibody (Abcam, ERP21794). * and **, p<0.05 and p<0.01 by paired *Student t-test*

Tumor infiltrating immune cell were increased by HER2 ADC in combination with lemzoparlimab

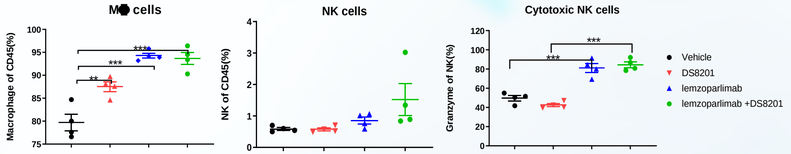


Figure 4. Tumor infiltrating immune cells, in response to treatment of HER2 ADC and lemzoparlimab alone or in combination, were analyzed by flow cytometry for macrophages, total NK and cytotoxic NK cells in MDA-MB-231 CDX model.

CD47 expression and macrophages percentage in tumor areas were increased by HER2 ADC in combination with lemzoparlimab

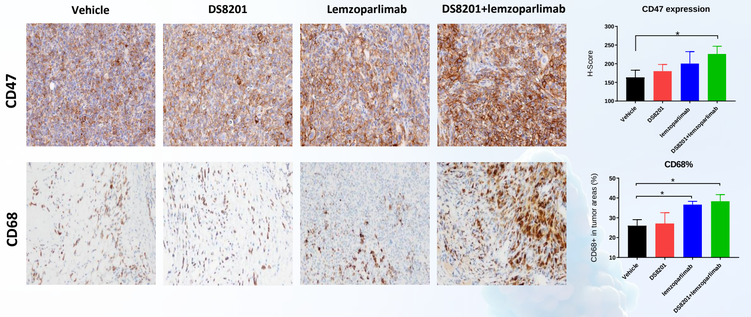


Figure 5. Expression of CD47 and CD68 (macrophages marker) in MDA-MB-231 CDX model, in response to treatment of HER2 ADC and lemzoparlimab alone or in combination, were analyzed by IHC CD47 antibody (Abcam, ERP21794) and CD68 antibody (Abcam, ab125212), respectively.

CONCLUSION

- Lemzoparlimab enhanced HER2 ADC mediated tumor killing by modulating NK cells and macrophage activity to increase cytotoxicity and phagocytosis.
- These data support future clinical investigation of lemzoparlimab and HER2 ADC combination in HER2 positive patients, especially those with HER2-low expressing tumors.