Zanidatamab is a promising bispecific antibody for the treatment of HER2-expressing cancers. It binds HER2 in trans and has multiple mechanisms of action that may collectively contribute to its anti-tumor activity. Zanidatamab mediates unique HER2 capping and superior CDC and growth inhibition of HER2-overexpressing tumors compared to trastuzumab, pertuzumab, and trastuzumab + pertuzumab. Zanidatamab is superior to trastuzumab and a combination of trastuzumab + pertuzumab in HER2-overexpressing gastric cancer xenografts. Zanidatamab is actively being evaluated in clinical trials in multiple HER2 overexpressing solid tumors, including in HER2+ BCTC-01, a registration-enabling clinical trial in HER2 gene amplified biliary tract cancer (NCT04466891).

References

Zanidatamab Elicits Superior CDC and Growth Inhibition Compared to Trastuzumab + Pertuzumab

Zanidatamab Mediates Internalization, Receptor Depletion, ADCC and ADCP

Zanidatamab is superior to anti-HER2 mAbs in HER2+ Gastric Cancer Models

Figure 7. A) All test articles administered at 30 mg/kg twice weekly for 5 weeks. B) Two articles administered at indicated equipotent dose levels (efficacy vs. activity) for four weeks. C) + vs. − by fixed mixed-effects model fits to log-transformed tumor volumes over time. Differences in tumor growth rate between treatment groups were assessed using a Wald test.

Figure 10. A) All test articles administered at 30 mg/kg twice weekly for 5 weeks. B) Two articles administered at indicated equipotent dose levels (efficacy vs. activity) for four weeks. C) + vs. − by fixed mixed-effects model fits to log-transformed tumor volumes over time. Differences in tumor growth rate between treatment groups were assessed using a Wald test.

Figure 3. A) Zanidatamab trastuzumab + pertuzumab (24 h), intracellular antibody detected by flow cytometry, B) surface HER2 depletion (24 h) using a Wald test.

Figure 4. A) Zanidatamab treatment results in A) increased antibody internalization relative to trastuzumab (24 h), intracellular antibody detected by flow cytometry, B) surface HER2 depletion (24 h) using a Wald test.

Figure 5. A) Zanidatamab mediates potent CDC with human complement serum in HER2-overexpressing tumor cells; trastuzumab, pertuzumab, and trastuzumab + pertuzumab (1:1) are inactive. B) Zanidatamab mediates potent tumor growth inhibition in HER2-overexpressing tumor cells and is superior to trastuzumab + pertuzumab (1:1) in NCI-N87 and SK-BR-3.

Figure 6. Zanidatamab treatment results in A) increased antibody internalization relative to trastuzumab (24 h), intracellular antibody detected by flow cytometry, B) surface HER2 depletion (24 h) using a Wald test.

Figure 8. A) All test articles administered at 30 mg/kg twice weekly for 5 weeks. B) Two articles administered at indicated equipotent dose levels (efficacy vs. activity) for four weeks. C) + vs. − by fixed mixed-effects model fits to log-transformed tumor volumes over time. Differences in tumor growth rate between treatment groups were assessed using a Wald test.

Figure 9. A) All test articles administered at 30 mg/kg twice weekly for 5 weeks. B) Two articles administered at indicated equipotent dose levels (efficacy vs. activity) for four weeks. C) + vs. − by fixed mixed-effects model fits to log-transformed tumor volumes over time. Differences in tumor growth rate between treatment groups were assessed using a Wald test.