HBM1047, A NOVEL FULLY HUMAN ANTI-CD200R1 ANTAGONIST ANTIBODY WITH POTENT ANTI-TUMOR EFFICACY IN PRECLINICAL MODEL

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Background Immune checkpoint inhibitors have revolutionized cancer immunotherapy, however, only a small subset of patients respond to the treatment. There is still a high unmet medical need, especially for those who are resistant to immune checkpoint inhibitors. Developing new therapeutic targets are urgently needed. CD200-CD200R1 signaling pathway has been shown to inhibit the functions of T cells and myeloid cells, and represents a promising therapeutic target for cancer treatment. In a PD1-resistant mouse tumor model, CD200R1 expression is highly upregulated in tumor infiltrating T cells from PD1-resistant group. Thus, blocking CD200-mediated CD200R1 inhibitory signaling pathway offers promising therapeutic potential for PD1-resistant patients. Moreover, CD200 is highly expressed in many human cancers such as non-small cell lung cancer, pancreatic cancer and brain cancer, which are potential indications for anti-CD200R1 antagonist antibody.

Methods Utilizing the unique Harbour Mice® antibody discovery platform, we generated fully human anti-CD200R1 antibodies that efficiently blocked CD200-CD200R1 interaction. After further characterization and functional screening, we identified a novel fully human anti-CD200R1 antagonistic antibody – HBM1047.

Results HBM1047 demonstrated high binding affinity to both human and cyno CD200R1. It efficiently blocked CD200-CD200R1 interaction and inhibited CD200-induced CD200R1 reporter activity. In human primary cell assays, HBM1047 enhanced T cell activation when combined with anti-PD1 antibody. Furthermore, HBM1047 selectively bound to CD8+ T cells and myeloid cells in human tumor infiltrating lymphocytes from a variety of cancer types. More importantly, when used as monotherapy in preclinical models, HBM1047 showed potent anti-tumor efficacy in both CD200+ and CD200-humanized CDX models. In addition, HBM1047 had a favorable PK profile in mice and exhibited good developability properties.

Conclusions In conclusion, HBM1047 represents a novel fully human anti-CD200R1 antagonistic antibody with promising therapeutic potential for the treatment of cancer.

REFERENCES

Ethics Approval This study obtained ethics approval and all participants gave informed consent before taking part. IRB NO: 3764. IRB protocol: MTG-015