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A novel fully human anti-CD47 antibody as a potential therapy for human neoplasms with good safety

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A Novel Fully Human Anti-CD47 Antibody as a Potential Therapy for Human Neoplasms with Good Safety

Abstract

Strategies for targeting CD47 are becoming a hot spot of cancer immunotherapy. However the ubiquitous expression of CD47, especially on the RBC, makes the targeted therapy facing safety risk issues. So, how to balance the safety and efficacy during CD47 inhibition is currently a major question. We had reported an anti-CD47 antibody ZF1 with potent anti-tumor effect. In this study, we further developed and assessed a novel fully human anti-CD47 antibody, AMMS4-G4, derived from ZF1 using affinity maturation. AMMS4-G4 exhibited equivalent anticancer effects with Hu5F9-G4, a humanized anti-CD47 antibody in clinical trial, on the potential of inducing significant phagocytosis of tumor cells *in vitro* and prolonging the survival of leukemia xenografted mice. Additionally, AMMS4-G4 significantly inhibited the growth of grafted solid tumors by enhancing macrophage infiltration and modestly enhanced the anti-tumor activity of opsonizing antibody and antiangiogenic therapy. In cynomolgus monkeys, AMMS4-G4 was safely administered, was well tolerated at doses of 30 and 60 mg/kg, and did not produce serious adverse events, except for the reversible anemia, which was observed after 3 days and started to recover from 9 days later. Remarkably, it was proved by *in vitro* assay that Hu5F9-G4 induced RBC hemagglutination which wasn't observed in AMMS4-G4. On the whole, AMMS4-G4 was demonstrated to be a promising candidate with great potential and safe profile for cancer immunotherapy.

Keywords: anti-CD47 mAb, immunotherapy, safety, leukemia, solid tumor

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