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POSTER ABSTRACTS

637.MYELODYSPLASTIC SYNDROMES - CLINICAL AND EPIDEMIOLOGICAL

AK117 (anti-CD47 monoclonal antibody) in Combination with Azacitidine for Newly Diagnosed Higher Risk Myelodysplastic Syndrome (HR-MDS): AK117-103 Phase 1b Results

Miao Miao[1], *Qingliang Teng*[2], *Depei Wu*[1], *Zhongxing Jiang*[3], *Songfu Jiang*[4], *Fei Li*[5], *Yang Liang, MDPhD*[6], *Zhongmin Maxwell Wang*[7], *Baiyong Li*[7], *Yu Xia*[7], *Hongyan Tong, PhD*[8]

[1] The First Affiliated Hospital of Soochow University, Suzhou, China
[2] Taian City Central Hospital, Taian, China
[3] The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China
[4] The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China
[5] The First Affiliated Hospital of Nanchang University, Nanchang, China
[6] Sun Yat-sen University Cancer Center, Guangzhou, China
[7] Akeso Biopharma Inc., Zhongshan, China
[8] The First Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China

Background: CD47, an immune checkpoint overexpressed by tumor cells, plays a crucial role in evading the antitumor immune response. AK117, an IgG4 monoclonal antibody (mAb) targeting CD47, has emerged as a potential best-in-class therapy with high affinity binding to CD47 and without inducing hemagglutination effects. By blocking CD47, AK117 effectively triggers macrophage-mediated phagocytosis of hematological malignancy cells, and in combination with azacitidine (AZA), it synergistically enhances the activation of "eat me" signals. In this study, we present the Phase 1b data from the AK117-103 study conducted in patients with newly diagnosed higher risk myelodysplastic syndrome (HR-MDS).
Methods: Eligible patients with newly diagnosed intermediate/high/very high-risk MDS, determined by the Revised International Prognostic Scoring System (IPSS-R) prognostic risk score >3, were enrolled to receive combination therapy with AK117 and AZA. AK117 was administered intravenously (IV) following various dosing regimens (20-30 mg/kg once weekly [QW], or 20-45 mg/kg every 2 weeks [Q2W], or 30 mg/kg every 4 weeks [Q4W]), whereas AZA was administered subcutaneously (SC) at the standard dosage (75 mg/m ^{2}, Day 1-7, Q4W). The primary endpoints of this study were safety/tolerability and the complete remission (CR) rate based on the International Working Group (IWG) 2006 response criteria.
Results: As of June 9, 2023, 72 patients were enrolled (median age: 66 years, 69.4% males). Most patients exhibited abnormal hematologic conditions at baseline, including decreased hemoglobin, neutrophil count, and platelet count. Specifically, 69.4% of patients had Grade ≥3 anemia, 61.1% had Grade ≥3 neutrophil count decrease, and 47.2% had Grade ≥3 platelet count decrease. For the recommended phase 2 dose (RP2D) group, treated with a combination of AK117 30 mg/kg Q2W and AZA, 30 patients were enrolled with a median age of 67 years, 80.0% of whom were males. According to IPSS-R risk assessment, 33.3%, 23.3%, and 43.3% of patients had intermediate, high, and very high risk, respectively. 30.0% of patients had poor-risk cytogenetics, with 23.0% of those being complex. After a median follow-up of 6.6 months (ranging from 0.4-17.2 months), anemia (a primary adverse event associated with CD47 blocking antibodies) occurred in 30.6% (22/72) of the patients, of which Grade ≥ 3 anemia accounted for 22.2% (16/72). Other commonly observed treatment-emergent adverse events (TEAEs) (≥30%) included decreased neutrophil count (77.8%), decreased white blood cell count (72.2%), decreased platelet count (69.4%), pyrexia (58.3%), decreased lymphocyte count (41.7%), constipation (41.7%), and vomiting (31.9%). Three patients (4.2%) discontinued treatment due to TEAEs. The efficacy of AK117 was compared at different dosages, and ultimately, 30mg/kg Q2W was chosen as the RP2D. As of June 21, 2023, among 27 evaluable patients, the CR rate was 48.1%. 8 patients achieved marrow CR (5 also with hematologic improvement [HI]), and 2 patients achieved HI alone. Among 24 evaluable patients with ≥ 3 months follow-up, the CR rate further escalated to 54.2%. Of 13 evaluable patients who initially required red blood cells (RBC) transfusions, 8(61.5%) became independent of RBC transfusion.
Conclusions: AK117 in combination with AZA was well tolerated with low incidence of anemia and demonstrated promising efficacy in patients with newly diagnosed HR-MDS.

Disclosures No relevant conflicts of interest to declare.

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