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Efficacy and safety of AK112 (Ivonescimab), a PD-1/VEGF bispecific antibody, as first-line treatment for patients with IMDC favorable-risk advanced renal cell carcinoma (aRCC): Results from a phase Ib/II study

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Background

A substantial proportion of patients with IMDC favorable-risk aRCC fail to derive benefit from anti-angiogenic tyrosine kinase inhibitors, and the addition of conventional anti-PD-1 monoclonal antibodies confers no further improvement. Ivonescimab is a novel tetravalent bispecific antibody that simultaneously targets PD-1 and VEGF-A, aiming to enhance antitumor immunity while blocking angiogenesis within the tumor microenvironment. We present the results of AK112 monotherapy in treatment-naïve aRCC patients with IMDC favorable-risk.

Methods

This was an open-label, single-arm, phase Ib/II trial (NCT06472895). Patients with untreated IMDC Favorable-Risk advanced ccRCC received AK112 every 3 weeks. The primary endpoint was Objective Response Rate (ORR) by RECIST 1.1. Secondary endpoints included Disease Control Rate (DCR), Duration of Response (DoR), Progression-Free Survival (PFS), Overall Survival (OS), and safety.

Results

As of April 27, 2026, 26 patients were enrolled with a median follow-up of 9.1 months, and tumor assessments were performed in 21 patients. The median age was 56.5 years. 88.5% were male, and 42.3% had metastases at more than two sites. PD-L1 expression was negative in 42.3% of patients, positive in 15.4%, and not tested in the remaining patients. No DLT was observed among the 20 and 30 mg/kg dose cohorts. Accordingly, RP2D of ivonescimab was determined as 30 mg/kg. The ORR was 57.1% with 12 partial responses. Only one patient had PD (classified as PR per iRECIST), yielding an overall DCR of 95.2%. The median PFS was not reached. The 12-month and 18-month PFS rates were both 87.9%. Grade ≥3 Treatment-related adverse events (TRAEs) were reported in 26.9% of patients. The most common ≥20% TRAEs were proteinuria (42.3%), rhinitis (38.5%), pruritus (34.6%), hypertension (26.9%), hypertriglyceridemia (26.9%) and arthralgia (23.1%). No treatment-related deaths occurred.

Conclusions

First-line ivonescimab monotherapy demonstrated promising antitumor activity and a manageable safety profile in patients with IMDC favorable-risk aRCC. Further follow-up for survival endpoints is ongoing.

Clinical trial identification

NCT06472895.

Legal entity responsible for the study

The authors.

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Disclosure

All authors have declared no conflicts of interest.

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