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A phase 2 study of CS2009, a first-in-class PD-1/VEGF/CTLA-4 trispecific antibody, in patients with advanced non-small cell lung cancer (NSCLC)

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Background

CS2009 is a novel PD-1/VEGF/CTLA-4 trispecific antibody. Preclinical and clinical studies demonstrated promising anti-tumor activity in solid tumors. Here, we report the safety and efficacy data from a phase 2 study of CS2009 in advanced NSCLC.

Methods

Patients (pts) with advanced NSCLC were enrolled across different lines of therapy. In the first-line (1L) setting, pts without actionable genomic alterations received either CS2009 monotherapy (mono) or CS2009 + chemotherapy (chemo) (pemetrexed + carboplatin for non-squamous [NSQ] pts; paclitaxel + carboplatin for squamous [SQ] pts.) In the second- or third-line (2/3L) setting, pts who had received prior platinum-based chemo and anti-PD-(L)1 therapy were treated with CS2009 + docetaxel. CS2009 was dosed at 20 or 30 mg/kg Q3W. The primary endpoint was investigator-assessed ORR per RECIST v1.1.

Results

As of April 19, 2026, 86 pts were treated (median age 65.6 [range 38-82]; 77.9% male; 82.6% with ECOG PS 1; 40.7% NSQ; 76.7% PD-L1 TPS $\geq$ 1%). In pts receiving CS2009 mono (n=46), any-grade and grade $\geq$ 3 TRAEs occurred in 67.4% and 6.5% of pts, respectively. The most common TRAEs were AST increased (17.4%), ALT increased (15.2%), hyperthyroidism (13.0%) and rash (13.0%); all grade $\geq$ 3 TRAEs were single-case events. In pts receiving CS2009 + chemo (n=40), any-grade and grade $\geq$ 3 TRAEs occurred in 65.0% and 30.0% of pts, respectively. The most common TRAEs were neutrophil count decreased (35.0%), WBC count decreased (30.0%) and anaemia (30.0%). CS2009 did not appear to increase chemo-associated toxicity. No unexpected safety signals were observed. In preliminary efficacy assessment among evaluable pts, ORR/DCR in 1L mono (PD-L1 TPS $\geq$ 50%) and 1L SQ combination (PD-L1 TPS <50%) cohorts were 81.3%/100% (n=16) and 75.0%/100% (n=8), respectively. Encouraging responses have been observed in other cohorts. Updated data from the 1L mono (n $\approx$ 60, PD-L1 TPS $\geq$ 1%) and combination (n $\approx$ 60, SQ & NSQ) cohorts will be presented at the congress.

Conclusions

CS2009 mono and CS2009 + chemo were both well tolerated and demonstrated promising anti-tumor activity in NSCLC. Phase 3 studies of CS2009 + chemo in advanced NSCLC are planned.

Clinical trial identification

NCT06741644.

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Legal entity responsible for the study

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Disclosure

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