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Phase 1 dose expansion of a tetravalent CD137/PD-L1 bispecific antibody (FS222) in PD-1 inhibitor- resistant melanoma patients

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Background

FS222 is a PD-L1/CD137 bispecific antibody designed to promote PD-L1 dependent CD137 agonism. We previously reported results from the dose escalation of the FIH phase 1 study evaluating FS222 monotherapy in patients (pts) with advanced solid tumors. Here we present safety, efficacy and biomarker results from a dose expansion in immunotherapy experienced melanoma pts.

Methods

Pts with unresectable/metastatic cutaneous melanoma and at least one prior PD-1 inhibitor regimen received FS222 1.5 mg/kg every 4 weeks (Q4W). The primary objective was safety. Additional key objectives included evaluation of antitumor activity and immune pharmacodynamics.

Results

As of the DCO on 08/Mar/2026, 42 melanoma pts were treated with FS222, including an exploratory cohort of 8 pts who received prophylactic corticosteroid on day 8 of the first two cycles to test the effect on immune inflammatory reactions. The median number of prior lines of treatment was 2 (1-4) and 79% had also received a CTLA4 inhibitor. The median duration of exposure was 109 days (17 – 283) and 11 pts remained on treatment. The most common ($\geq 20\%$) treatment-related AEs (TRAEs) included transaminase increase (TAI) (43%), thrombocytopenia (36%), anemia (24%) and pyrexia (21%). Grade ≥ 3 TRAEs occurred in 38% of pts, with TAI (19%); hemophagocytic lymphohistiocytosis-like events (HLH-L; 14%), neutropenia (5%) and leukopenia (5%) in ≥ 2 pts. Serious TRAEs occurred in 31% of pts, with HLH-L (14%), TAI (5%) and pyrexia (5%) in ≥ 2 pts. Serious HLH-L events generally improved with corticosteroid treatment. The overall rate of treatment discontinuation was low (7%). Increases in peripheral CD8+ T cell proliferation and immune cytokines were observed in most patients. Analysis of serial biopsies is underway. Investigator-assessed ORR was 36% (n=15/42) and the disease control rate was 52% (n=22). Most responses (10/15) were ongoing as of the DCO (range 8-28 wks).

Conclusions

An FS222 expansion cohort in immunotherapy-resistant melanoma pts showed a manageable safety profile, encouraging anti-tumor activity and evidence of peripheral immune activation despite prior immunotherapy treatment, consistent with results from the dose escalation.

Clinical trial identification

NCT04740424.

Legal entity responsible for the study

invoX Pharma LLC.

Funding

invoX Pharma LLC.

Disclosure

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