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FIANLIMAB-BASED COMBINATION THERAPIES IN PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER: TRIALS IN PROGRESS UPDATES

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Background: Fianlimab (anti-lymphocyte activation gene 3) and cemiplimab (anti-programmed cell death-1 [PD-1]) are high-affinity, fully human monoclonal antibodies. Cemiplimab has shown promising clinical efficacy in patients with non-small cell lung cancer (NSCLC) and no actionable mutations, alone (PD-ligand 1 [PD-L1] expression ≥50%) and in combination with chemotherapy (regardless of PD-L1 expression). As the standard of care for NSCLC continues to evolve, combination therapy with multiple checkpoint inhibitors ± chemotherapy could improve outcomes. In a study of fianlimab + cemiplimab (NCT03005782), clinically meaningful activity and an acceptable risk–benefit profile were observed in patients with advanced melanoma.

Methods: Two parallel, randomised, multicentre, Phase 2/3 studies are ongoing. In Study 1 (NCT05785767), investigators are evaluating fianlimab + cemiplimab versus cemiplimab monotherapy as first-line treatment in patients with advanced NSCLC and tumours expressing PD-L1 ≥50%. In Study 2 (NCT05800015), investigators are evaluating fianlimab + cemiplimab + platinum-doublet chemotherapy versus cemiplimab + chemotherapy in patients with advanced NSCLC regardless of PD-L1 expression. Eligibility criteria for both studies include: histologically confirmed squamous/non-squamous stage IIIB/C (not candidates for surgical resection or definitive chemoradiation) or stage IV NSCLC (no prior systemic treatment for recurrent/metastatic disease); ≥1 radiographically measurable lesion per RECIST v1.1; ECOG performance status ≤1; adequate organ and bone marrow function.

In the Phase 2 part of Study 1, patients will be randomised 1:1:1 (intravenously every 3 weeks [Q3W]) to receive: fianlimab high dose + cemiplimab 350 mg; fianlimab low dose + cemiplimab 350 mg; or cemiplimab 350 mg + placebo. In the Phase 2 part of Study 2, patients will be randomised 1:1:1 to receive (intravenously Q3W): fianlimab high dose + cemiplimab 350 mg + chemotherapy; fianlimab low dose + cemiplimab 350 mg + chemotherapy; or cemiplimab 350 mg + chemotherapy + placebo. In the Phase 3 part of both studies, patients will be randomised 1:1 into the fianlimab high/low dose group as determined during Phase 2 or the comparator group.

The primary endpoint for Phase 2 of both studies is objective response rate (ORR; BICR). In the Phase 3 part, the primary endpoint is overall survival (OS). Secondary endpoints for both studies include tolerability, safety, ORR (investigator assessment), DCR, TTR, DOR, PFS, OS (Phase 2), PROs, pharmacokinetics and immunogenicity.

Both studies are open for enrolment, along with a third Phase 2 study in which fianlimab + cemiplimab + chemotherapy will be evaluated as perioperative therapy in patients with stage II/III NSCLC (NCT06161441).

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