EGRET: A first-in-human study of the novel antibody-drug conjugate AZD9592 as monotherapy or combined with other antitumor agents in patients with advanced solid tumors


TPS3156

Background

- Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) are a standard of care for first-line treatment of EGFR-mutated non-small-cell lung cancer (EGFRm NSCLC).
- However, patients treated with these agents commonly develop resistance. Underlying the need for new therapeutic strategies.
- Alterations of the mesenchymal-epithelial transition tyrosine kinase receptor (cMET), including gene amplification or protein overexpression, are one of the most common mechanisms of resistance to third-generation EGFR TKIs such as osimertinib. cMET is a promising target to overcome resistance to EGFR TKIs in this setting.
- Clinical benefit of bispecific monoclonal antibodies (bsAb) targeting tumor cells expressing both EGFR and cMET has been demonstrated in patients with EGFRm NSCLC, but an antibody-drug conjugate (ADC) targeting both receptors has not been previously developed.

Key inclusion criteria

- Age ≥ 21 years.
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.
- Locally advanced or metastatic HNSCC.
- On the tumor cell surface.
- Recurrent or metastatic HNSCC.
- Untreated or untreated following prior treatment.

Methods

- The first two modules of this Phase 1, multicenter, open-label study are assessing the safety, tolerability and preliminary antitumor activity of AZD9592 monotherapy (Module 1) and AZD9592 in combination with osimertinib (Module 2).
- Each module will include dose-escalation (Part A) and dose-expansion (Part B) cohorts.
- Any dose-escalation cohorts with dose levels not exceeding the maximum tolerated dose (MTD) may be expanded in pharmacodynamic (PD) backfill cohorts.
- Patients in PD backfill cohorts will be required to have a pre- and on-treatment tumor biopsy to evaluate the PD and biological activity of AZD9592.

Key exclusion criteria

- Unresolved toxicities of Grade 3 (NCI CTCAE v5.0) from prior therapy.
- Uncontrolled intercurrent illness within the last 12 months.
- Cardiovascular disorders.
- History of drug-induced interstitial lung disease or pneumonitis that has required oral or intravenous steroids.

Primary objectives

- Assess the safety and tolerability by measuring the incidence of adverse events (AEs), serious AEs, and incidence of DLTs.
- Determine the MTD and/or recommend Phase 3 dose of AZD9592 when administered as monotherapy or in combination with osimertinib.

Secondary objectives

- Assess the antitumor activity of AZD9592 as monotherapy or in combination with osimertinib, by measuring the objective response rate (ORR) according to RECIST v1.1 by investigator assessment.
- Characterize the pharmacokinetics of AZD9592.
- Assess immunogenicity.
- Evaluate the PD and biological activity of AZD9592.

References


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