Exclusion:

- Any previous histological or cytological evidence of small cell OR combined small cell/non-small cell disease in the archival tumor tissue or pretreatment tumor biopsy, or squamous NSCLC histology
- Any history of ILD (including pulmonary fibrosis or radiation pneumonitis), has current ILD, or is suspected to have such disease by imaging during screening
- Clinically severe respiratory compromise (based on investigator's assessment) resulting from intercurrent pulmonary illnesses including, but not limited to:
- Any underlying pulmonary disorder (eg, pulmonary emboli within 3 months prior to study randomization, severe asthma, severe chronic obstructive pulmonary disease, restrictive lung disease, pleural effusion)
- Any autoimmune, connective tissue, or inflammatory disorders for which there is documented or a suspicion of pulmonary involvement at the time of screening (eg, rheumatoid arthritis, Sjogren syndrome, sarcoidosis)
- OR prior complete pneumonectomy
- Is receiving chronic systemic corticosteroids dosed at >10 mg prednisone or equivalent anti-inflammatory activity or any form of immunosuppressive therapy prior to randomization. Patients who require use of bronchodilators, inhaled or topical steroids, or local steroid injections may be included in the study
- Evidence of any leptomeningeal disease
- Has evidence of clinically active spinal cord compression or brain metastases, defined as being symptomatic and untreated, or requiring therapy with corticosteroids or anticonvulsants to control associated symptoms. Patients with clinically inactive or treated brain metastases who are asymptomatic (ie, without neurological signs or symptoms and not requiring treatment with corticosteroids or anticonvulsants) may be included in the study but must have a stable neurological status for ≥2 weeks prior to randomization
- Inadequate washout period prior to randomization, defined as
- Whole-brain radiation therapy <14 days or stereotactic brain radiation therapy <7 days
- Major surgery (excluding placement of vascular access) <28 days
- Radiotherapy treatment to >30% of the bone marrow or with a wide field of radiation <28 days or palliative radiation therapy <14 days or
- Chloroquine/hydroxychloroquine ≤14 days
- Prior treatment with
- Any agent including an ADC containing a chemotherapeutic agent targeting topoisomerase I
- HER3 antibody
- Any systemic therapies (other than EGFR TKIs) in the metastatic or locally advanced setting, including chemotherapy or any other systemic therapy in combination with an EGFR TKI
- Has unresolved toxicities from previous anticancer therapy, defined as toxicities (other than alopecia) not yet resolved by NCI-CTCAE v5.0, grade ≤1 or baseline. Subjects with chronic grade 2 toxicities (defined as no worsening to grade >2 for ≥3 months prior to randomization and managed with standard-of-care treatment)

that the investigator deems related to previous anticancer therapy may be randomized

- Has history of other active malignancy within 3 years prior to randomization, except:
- Adequately resected non-melanoma skin cancer
- Adequately treated intraepithelial carcinoma of the cervix
- Any other curatively treated in situ disease