FGFR-3 Antibody-Drug Conjugate

LY3076226

Drug Discovery Platform: Cancer Cell Signaling

Derived from Turner N and Grose R.1
The safety and efficacy of the agents under investigation have not been established. There is no guarantee that the agents will receive regulatory approval and become commercially available for the uses being investigated.

Key Inclusion Criteria
- Part A: Advanced or metastatic cancer, including multiple myeloma and lymphoma, and be an appropriate candidate for experimental therapy
- Part B: Locally advanced, unresectable, or metastatic urothelial carcinoma of the bladder, urethra, ureter, or renal pelvis with locally determined overexpression or alterations in FGFR-3
- Part C: Advanced or metastatic cancer, including multiple myeloma and lymphoma, with locally determined overexpression or alterations in FGFR-3
- Adequate organ function

Key Exclusion Criteria
- Prior treatment with an investigational product or nonapproved use of a drug or device (other than the study drug/device used in this study) within 28 days of the initial dose of study drug or concurrently enrolled in any other type of medical research judged not to be scientifically or medically compatible with this study
- Preexisting corneal disease that may interfere with assessment for potential eye toxicity during the study
- Preexisting grade ≥2 skin disorder
- Serious preexisting medical conditions
- Symptomatic central nervous system (CNS) malignancy or metastasis [screening not required]. Participants with treated CNS metastases are eligible for this study if they are not currently receiving corticosteroids and/or anticancer drugs, and their disease is asymptomatic and radiographically stable for at least 28 days
- Current acute or chronic leukemia
- Fridericia-corrected QT interval >480 ms on screening electrocardiogram
- Serious cardiac condition, such as congestive heart failure, New York Heart Association class 3/4 heart disease, unstable angina pectoris, myocardial infarction within the last 3 months, valvulopathy that is severe, moderate, or deemed clinically significant, or arrhythmias that are symptomatic or require treatment (not including participants with rate-controlled atrial fibrillation)

Please visit www.clinicaltrials.gov for more information on this clinical trial [NCT02529553].

* This clinical trial is being conducted in North America.
Target

The fibroblast growth factor receptor (FGFR) family consists of four members—FGFR-1, FGFR-2, FGFR-3, and FGFR-4—which mediate cellular signaling after binding to their high-affinity ligands, the FGFs. The FGF/FGFR signaling pathway has been shown to mediate cell proliferation, migration, motility, and survival. Autophosphorylation of FGFR is required for activation of FGF-induced downstream signaling. The aberrant regulation of this pathway has been implicated in many forms of human malignancies.\(^2\) It has also been determined that activation of the FGF/FGFR pathway may lead to increased tumor angiogenesis and play a role in tumor resistance to antiangiogenic agents and other chemotherapies.\(^1,2\)

Molecule

LY3076226 is an antibody-drug conjugate (ADC) comprised of anti-FGFR-3 antibody conjugated to a microtubule inhibitor, DM4.\(^3\)

Clinical Development

LY3076226 is being investigated in a phase I clinical trial.

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