Drug Discovery Platform: Cancer Angiogenesis and Tumor Microenvironment

Teicher BA and Ellis LM; Felcht M, et al; Saharinen P and Alitalo K
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
- Advanced and/or metastatic cancer
- Adequate organ function
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Discontinued previous treatments for cancer for at least 28 days or five half-lives prior to study enrollment

Key Exclusion Criteria
- Serious preexisting medical conditions
- Previous treatment with a drug predominantly targeting Ang2 activity
- Symptomatic central nervous system malignancy or metastasis
- Current hematologic malignancies
- Active fungal, bacterial, and/or known viral infection
- Corrected QT interval using Fridericia’s correction of >470 ms on screening electrocardiogram at several consecutive days of assessment
- Known sensitivity to monoclonal antibodies or other therapeutic proteins
- History of hypertensive crisis or hypertensive encephalopathy, or current poorly controlled hypertension despite standard medical management
- Significant bleeding disorder or vasculitis, or a grade ≥3 bleeding episode within 3 months prior to receiving treatment
- Receiving anticoagulation therapy at a therapeutic dose
- Any arterial, venothrombotic, or thromboembolic events within 6 months prior to study treatment
- Liver cirrhosis with Child-Pugh class B or worse, cirrhosis (any degree) and a history of hepatic encephalopathy, or clinically meaningful ascites resulting from cirrhosis
- Pregnant prior to randomization or breast-feeding

Please visit www.clinicaltrials.gov for more information on this clinical trial [NCT02597036].

* This clinical trial is being conducted globally.

Primary endpoint: Establish safety, pharmacokinetic profile, and preliminary efficacy

Part A:
LY3127804 IV Q2W

Part B:
LY3127804 + ramucirumab dose 1 IV Q2W

Part C:
LY3127804 + ramucirumab dose 2 IV Q2W

Part D:
LY3127804 RP2D + ramucirumab dose 1 IV Q2W

Part E:
LY3127804 RP2D IV Q2W + ramucirumab IV Q2W + paclitaxel 80 mg/m² IV days 1, 8, 15 (28-day cycle)
**Target**
Angiogenesis, the growth of new blood vessels, plays a pivotal role in tumor growth, propagation, and metastasis. Angiopoietin2 (Ang2) promotes tumor angiogenesis and growth by destabilizing the Tie2-expressing vasculature, enhancing the endothelial cells’ response to angiogenic stimuli such as vascular endothelial growth factor (VEGF), and inducing Tie2-independent integrin-mediated sprouting tip cell migration.²⁻⁴

**Molecule**
LY3127804 is a humanized and engineered IgG4 isotype antibody designed to bind to Ang2 with high affinity and neutralize Ang2 induced phospho-Tie2.⁵

**Clinical Development**
LY3127804 is being investigated in a phase I clinical trial.

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**References:**