LIBRETTO-431 (Eli Lilly)

A Multicenter, Randomized, Open-Label, Phase 3 Trial Comparing LOXO-292 to Platinum-Based and Pemetrexed Therapy With or Without Pembrolizumab as Initial Treatment of Advanced or **Metastatic** RET Fusion-Positive Non-Small Cell **Lung Cancer**

This is the trial summary as assessed on clinicaltrials.gov on 03/04/2020.

Minor changes in the protocol may occur. You can check this on this direct link:

https://clinicaltrials.gov/ct2/show/NCT04194944?term=LIBRETTO&cond=Lung+Cancer+Metastatic&cntry=BE&draw=2&rank=1

Trial Design:

Arm	Intervention
Selpercatinib	Selpercatinib Administered orally
Pemetrexed plus the investigator's discretion of carboplatin or cisplatin with or without pembrolizumab.	Pemetrexed administered intravenously (IV) plus the investigator's discretion of carboplatin IV or cisplatin IV with or without pembrolizumab IV. Administered intravenously

Inclusion criteria:

- Histologically confirmed, Stage IIIB-IIIC or Stage IV non-squamous NSCLC that is not suitable for radical surgery or radiation therapy.
- A RET gene fusion in tumor and/or blood from a qualified laboratory.
- Tumor tissue in sufficient quantity to allow for retrospective central analysis of RET fusion status.
- Eastern Cooperative Oncology Group (ECOG) performance status of 0-2.
- Adequate hematologic, hepatic and renal function.
- Willingness of men and women of reproductive potential to observe conventional and highly effective birth control for the duration of treatment and for 6 months after.
- Ability to swallow capsules.

Exclusion criteria:

- Additional validated oncogenic drivers in NSCLC if known.
- Prior systemic therapy for metastatic disease. Chemotherapy in the adjuvant/neoadjuvant setting is permitted if it was completed at least 12 months prior to randomization.
- Major surgery within 3 weeks prior to planned start of selpercatinib.
- Radiotherapy for palliation within 1 week of the first dose of study treatment or within 6 months prior to the first dose of study treatment if more than 30 Gy to the lung.
- Symptomatic central nervous system (CNS) metastases, leptomeningeal carcinomatosis, or untreated spinal cord compression.
- Clinically significant active cardiovascular disease or history of myocardial infarction within 6 months prior to planned start of selpercatinib or prolongation of the QT interval corrected for heart rate using Fridericia's formula (QTcF) > 470 milliseconds.

- Active uncontrolled systemic bacterial, viral, or fungal infection or serious ongoing intercurrent illness, such as hypertension or diabetes, despite optimal treatment.
- Clinically significant active malabsorption syndrome or other condition likely to affect gastrointestinal absorption of the study drug.
- Pregnancy or lactation.
- Other malignancy unless nonmelanoma skin cancer, carcinoma in situ of the cervix or malignancy diagnosed ≥2 years previously and not currently active.
- Symptomatic ascites or pleural effusion - requiring chronic treatment with steroids.
- Exclusion Criteria for Participants Receiving Pembrolizumab:
- History of interstitial lung disease or interstitial pneumonitis.
- Active autoimmune disease or any illness or treatment that could compromise the immune system.