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Centro Internacional de Estudios en Genética Humana

Rearrangements NTRK1, 2, 3

Data obtained from three clinical trials (phase II STARTRK-2, phase I STARTRK-1 and phase I ALKA 372-001, data presented at THE ASCO annual meeting June 2019) given the drug **entrectinib** (Roche) values of objective response, response time, tolerability and safety in patients with rearrangements in the ***NTRK*1, 2 and 3** genes and different types of pediatric and adult tumors: cholangiocarcinoma and **breast, colon/rectum**, gynecological, neuroendocrine, **Non-small-cell lung**, salivary glands, pancreatic, thyroid and sarcoma.

NTRK gen fusion is deffined as a common biomarker across different types of tumors rather than the location where the tumor is originated. There is an unmet medical need for patients with tumors positive to fusion with *NTRK.*

Entrectinib (Roche) is a potent tyrosine inhibitor TrkA (encoded by the *NTRK1*), TrkB (encoded by the *NTRK2* gene) and TrkC (encoded by the *NTRK3* gene). Rearrangements in these genes have been identified in different types of locally advanced or metastatic solid tumors, and the antitumor activity of entrectinib has been proven in these tumors. Entrectinib has been designated 'Breakthrough Therapy'; by the FDA as well as priority drug (PRIME) by the European Medicines Agency (EMA) and designation Sakigake by Japanese health authorities for the treatment of locally advanced or metastatic solid tumors with positive NTRK fusion, in adult and pediatric patients who have progressed after previous therapies or do not have adequate standard therapies.

STUDIES OFFERED BY CIDEGEN

REARRANGEMENTS OF GENES *NTRK1, NTRK2 NTRK3,*

Method: Fluorescence *in situ* hibridization (FISH)

Sample requirements: FFPE tumor block or tumor tissue slides (3-4µm).

Processing time: 5-8 working days after sample receipt. Unless the sample is poor, deteriorated or has characteristics that do not allow the study to be carried out.

DIAGNOSTIC PANEL (50 genes)

Method: Next-Generation Sequencing (NGS). Inside the panel are the genes *NTRK1, 2 y 3*.

Sample requirements: FFPE tumor block or vials with cuts of tumor tissue.

Processing time: 3-4 weeks after sample receipt. Unless the sample is poor, deteriorated or has characteristics that do not allow the study to be carried out.

References:

1. Drilon A, De Braud FG, Siena S, et al. CT007: Entrectinib, an oral pan-Trk, ROS1, and ALK inhibitor in TKI-naïve patients with advanced solid tumors harboring gene rearrangements - updated phase I results. AACR 2016.
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3. Thiele, C.J., Z. Li, and A.E. McKee, On Trk--the TrkB signal transduction pathway is an increasingly important target in cancer biology. Clinical Cancer Research, 2009. 15(19): p. 5962-7.
4. FDA Approves Third Oncology Drug That Targets a Key Genetic Driver of Cancer, Rather Than a Specific Type of Tumor. August 16, 2019. https://www.fda.gov/news-events/press-announcements/fda-approves-third-oncology-drug-targets-key-genetic-driver-cancer-rather-specific-type-tumor.