ALK inhibitor

ALK tyrosine kinase inhibitors (TKIs) such as crizotinib, alectinib and ceritinib showed efficiency in patients with primary NSCLC harboring ALK gene rearrangement. Moreover, response to ALK TKIs was observed in central nervous system (CNS) metastatic lesions of NSCLC. However, there are no reports concerning the frequency of ALK rearrangement in CNS metastases.

ALK inhibitors are potential anti-cancer drugs that act on tumours with variations of anaplastic lymphoma kinase (ALK) such as an EML4-ALK translocation.

About 4-7% of non-small cell lung carcinomas (NSCLC) have EML4-ALK translocations.

ALK inhibitors may provide a new treatment option for brain metastases and could improve overall survival (OS). Even in patients with crizotinib-resistant disease, second generation ALK inhibitors display prominent clinical activity. There is rapidly emerging preclinical and clinical data showing improvement in this issue ¹.

Approved inhibitors

crizotinib (Xalkori) (also a ROS1 inhibitor) approved in Aug 2011 by the US FDA for ALK-positive NSCLC.

Clinical trials

Additional ALK inhibitors currently (or soon to be) undergoing clinical trials include:

Dalantercept, ACE-041 (Acceleron)

Brigatinib (AP26113) (by Ariad) (breakthrough status in U.S.) (also an EGFR inhibitor)

Entrectinib (Nerviano's NMS-E628, licensed by Ignyta and renamed RXDX-101, in the U.S. orphan drug designation and rare pediatric disease designation for the treatment of neuroblastoma and orphan drug designation for treatment of TrkA-, TrkB-, TrkC-, ROS1- and ALK-positive NSCLC)

PF-06463922 (Pfizer)

TSR-011 (Tesaro)

CEP-37440 (Teva)

X-396 (Xcovery)

Discontinued

ASP-3026 (Astellas)

NPM-ALK

NPM-ALK is a different variation/fusion of ALK that drives anaplastic large-cell lymphomas (ALCLs) and is the target of other ALK inhibitors.

Alectinib

Alectinib.

Ceritinib

Ceritinib.

ALK inhibitor for Glioblastoma

ALK inhibitor for Glioblastoma.

1)

Muhammet Hacioglu B, Kostek O, Erdogan B, Uzunoglu S, Cicin I. Targeted therapy with anaplastic lymphoma kinase inhibitors in non-Small-cell lung cancer even with brain metastases. J BUON. 2017 May-Jun;22(3):586-591. PubMed PMID: 28730760.

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