The growing interest in NTRK oncogenic aberrations in the latest years has its rationale in the recent development of several selective and non-selective Trk inhibitors whose activity and tolerability are being tested in ongoing clinical trials with encouraging results. Among the most promising agents, entrectinib is a multi-kinase inhibitor that targets TrkA, TrkB, TrkC, ROS1, and ALK1, while larotrectinib is a selective inhibitor of Trk receptors. They are orally available, can cross the brain–blood barrier, and have shown remarkable efficacy and acceptable toxicity profiles in the treatment of metastatic or locally advanced NTRK-fusion malignancies, independently of the histotype, fusion type, and patient age.

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