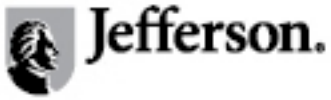

10-2018

Larotrectinib efficacy and safety in TRK fusion cancer: An expanded clinical dataset showing consistency in an age and tumor agnostic approach

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Annals of Oncology 29 (Supplement 8): viii133–viii148, 2018
doi:10.1093/annonc/mdy279

DEVELOPMENTAL THERAPEUTICS

409O Larotrectinib efficacy and safety in TRK fusion cancer: An expanded clinical dataset showing consistency in an age and tumor agnostic approach

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Background: TRK fusion cancer results from gene fusions involving NTRK1, NTRK2 or NTRK3. Larotrectinib, the first selective TRK inhibitor, has demonstrated an overall response rate (ORR) of 75% with a favorable safety profile in the first 55 consecutively enrolled adult and pediatric patients with TRK fusion cancer (Drilon et al.,NEJM2018). Here, we report the clinical activity of larotrectinib in an additional 35 TRK fusion cancer patients and provide updated follow-up of the primary analysis set (PAS) of 55 patients as of 19thFeb 2018.

Methods: Patients with TRK fusion cancer detected by molecular profiling from 3 larotrectinib clinical trials (NCT02122913, NCT02637687, and NCT02576431) were eligible.Larotrectinib was administered until disease progression, withdrawal, or unacceptable toxicity. Disease status was assessed using RECIST version 1.1.

Results: As of Feb 2018, by independent review, 6 PRs in the PAS deepened to CRs. The median duration of response (DoR) and progression-free survival in the PAS had still not been reached, with 12.9 months median follow-up. At 1 year, 69% of responses were ongoing, 58% of patients remained progression-free and 90% of patients were alive. An additional 19 children and 25 adults (age range, 0.1-78 years) with TRK fusion cancer were enrolled after the PAS, and included cancers of the salivary gland, thyroid, lung, colon, melanoma, sarcoma, GIST and congenital mesoblastic nephroma. In 35 evaluable patients, the ORR by investigator assessment was 74% (5 CR, 21 PR, 6 SD, 2 PD, 1 not determined). In these patients, with median follow-up of 5.5 months, median DoR had not yet been reached, and 88% of responses were ongoing at 6 months, consistent with the PAS. Adverse events (AEs) were predominantly grade 1, with dizziness, increased AST/ALT, fatigue, nausea and constipation the most common AEs reported in $\geq$ 10% of patients. No AE of grade 3 or 4 related to larotrectinib occurred in more than 5% of patients.

Conclusions: TRK fusions are detected in a broad range of tumor types. Larotrectinib is an effective age- and tumor-agnostic treatment for TRK fusion cancer with a positive safety profile. Screening patients for NTRK gene fusions in solid- and brain tumors should be actively considered.

Clinical trial identification: NCT02122913, NCT02637687, and NCT02576431.

Legal entity responsible for the study: Loxo Oncology, Inc.

Funding: Loxo Oncology, Inc.

Disclosure: S.G. Dubois: Fees for consulting and advisory board roles: Loxo Oncology. N. Federman: Honoraria from ad boards: Bayer AG and Loxo Oncology. S. Cruickshank: Paid consultant: Loxo Oncology, Inc. N.C. Ku, M.C. Cox: Employee and stockholder: Loxo Oncology, Inc. All other authors have declared no conflicts of interest.