# JOSHA'S CRITICAL REVIEW OF "Efficacy of Larotrectinib in TRK Fusion– Positive Cancers in Adults and Children"


Authors: Roland Mertelsmann, Gerhard Steinmann


Submitted: 6. May 2018
Published: 10. May 2018
Volume: 5
Issue: 4


Affiliation: Albert-Ludwigs Universität, Freiburg


Languages: English
Keywords: Critical Review, larotrectinib, sarcoma, cancer, oncology, pediatric oncology
DOI: 10.17160/josha.5.4.427

# CRITICAL REVIEW OF: „EFFICACY OF LAROTRECTINIB IN TRK FUSION– POSITIVE CANCERS IN ADULTS AND CHILDREN“

By A. Drilon et al. N Engl J Med 2018;378:731-9.

DOI: 10.1056/NEJMoa1714448

Fusions involving one of three tropomyosin receptor kinases (TRK) occur in diverse cancers in children and adults. *TRK* fusions defined a unique molecular subgroup of advanced solid tumors in children and adults in whom larotrectinib was highly active.

In three Phase 1-2 studies evaluating the efficacy and safety of larotrectinib, in adults and children who had tumors with these fusions remarkable response rates and durable responses were seen. Durable responses were observed without regard to the age of the patient, tumor tissue, and fusion status.

A total of 55 patients, ranging in age from 4 months to 76 years, were enrolled and treated. Patients had 17 unique *TRK* fusion–positive tumor types. The overall response rate was 75% (95% confidence interval [CI], 61 to 85) according to independent review and 80% (95% CI, 67 to 90) according to investigator assessment. At 1 year, 71% of the responses were ongoing and 55% of the patients remained progression-free. The median duration of response and progression-free survival had not been reached. At a median follow-up of 9.4 months, 86% of the patients with a response (38 of 44 patients) were continuing treatment or had undergone surgery that was intended to be curative. No patient discontinued larotrectinib owing to drug-related adverse events.

Larotrectinib had marked and durable antitumor activity in patients with *TRK* fusion–positive cancer, regardless of the age of the patient or of the tumor type.

Salivary-gland tumor (n=19, 37%), Other soft-tissue sarcoma (n=12, 22 %), Infantile fibrosarcoma (n=11, 20%), Thyroid tumor (n=7, 13%), as well as a variety of other malignacies

**JOSHAs Conclusion:** Important Progress, especially for patients with sarcomas for whom very few treatment alternatives exist. TRK-Fusion testing should become routine in patients with sarcoma and selected patients with other refractory malignacies.

## Original Abstract

## Authors

A. Drilon, T.W. Laetsch, S. Kummar, S.G. DuBois, U.N. Lassen, G.D. Demetri, M. Nathenson, R.C. Doebele, A.F. Farago, A.S. Pappo, B. Turpin, A. Dowlati, M.S. Brose, L. Mascarenhas, N. Federman, J. Berlin, W.S. El-Deiry, C. Baik, J. Deeken, V. Boni, R. Nagasubramanian, M. Taylor, E.R. Rudzinski, F. Meric-Bernstam, D.P.S. Sohal, P.C. Ma, L.E. Raez, J.F. Hechtman, R. Benayed, M. Ladanyi, B.B. Tuch, K. Ebata, S. Cruickshank, N.C. Ku, M.C. Cox, D.S. Hawkins, D.S. Hong, and D.M. Hyman

**Background** Fusions involving one of three tropomyosin receptor kinases (TRK) occur in diverse cancers in children and adults. *TRK* fusions defined a unique molecular subgroup of advanced solid tumors in children and adults in whom larotrectinib was highly active.

**Methods** In three Phase 1-2 studies evaluating the efficacy and safety of larotrectinib, in adults and children who had tumors with these fusions remarkable response rates and durable responses were seen. Durable responses were observed without regard to the age of the patient, tumor tissue, and fusion status.

**Results** A total of 55 patients, ranging in age from 4 months to 76 years, were enrolled and treated. Patients had 17 unique *TRK* fusion–positive tumor types. The overall response rate was 75% (95% confidence interval [CI], 61 to 85) according to independent review and 80% (95% CI, 67 to 90) according to investigator assessment. At 1 year, 71% of the responses were ongoing and 55% of the patients remained progression-free. The median duration of response and progression-free survival had not been reached. At a median follow-up of 9.4 months, 86% of the patients with a response (38 of 44 patients) were continuing treatment or had undergone surgery that was intended to be curative. No patient discontinued larotrectinib owing to drug-related adverse events.

**Conclusions** Larotrectinib had marked and durable antitumor activity in patients with *TRK* fusion–positive cancer, regardless of the age of the patient or of the tumor type. Salivary-gland tumor (n=19, 37%), Other soft-tissue sarcoma (n=12, 22 %), Infantile fibrosarcoma (n=11, 20%), Thyroid tumor (n=7, 13%), as well as a variety of other malignacies

**JOSHAs Conclusion: Important Progress, especially for patients with sarcomas for whom very few treatment alternatives exist. TRK-Fusion testing should become routine in patients with sarcoma and selected patients with other refractory malignacies.**

**JOSHA'S Critical Reviews in Oncology and related areas of medicine and science will focus on recently published clinical and non-clinical studies and discoveries. Our editors feel that there is a strong need for expert opinions on studies and discoveries that may potentially impact on patient care. While any judgment will, of course, be a personal and subjective opinion of our editors with all its limitations, we do hope this service will be helpful for our readers and stimulate thoughts and reflections in face of ever more rapid introductions of new drugs and therapeutic strategies in these days. We do encourage comments by our readers!**