Clinical validation for LOXO-101 against TRK fusion cancer

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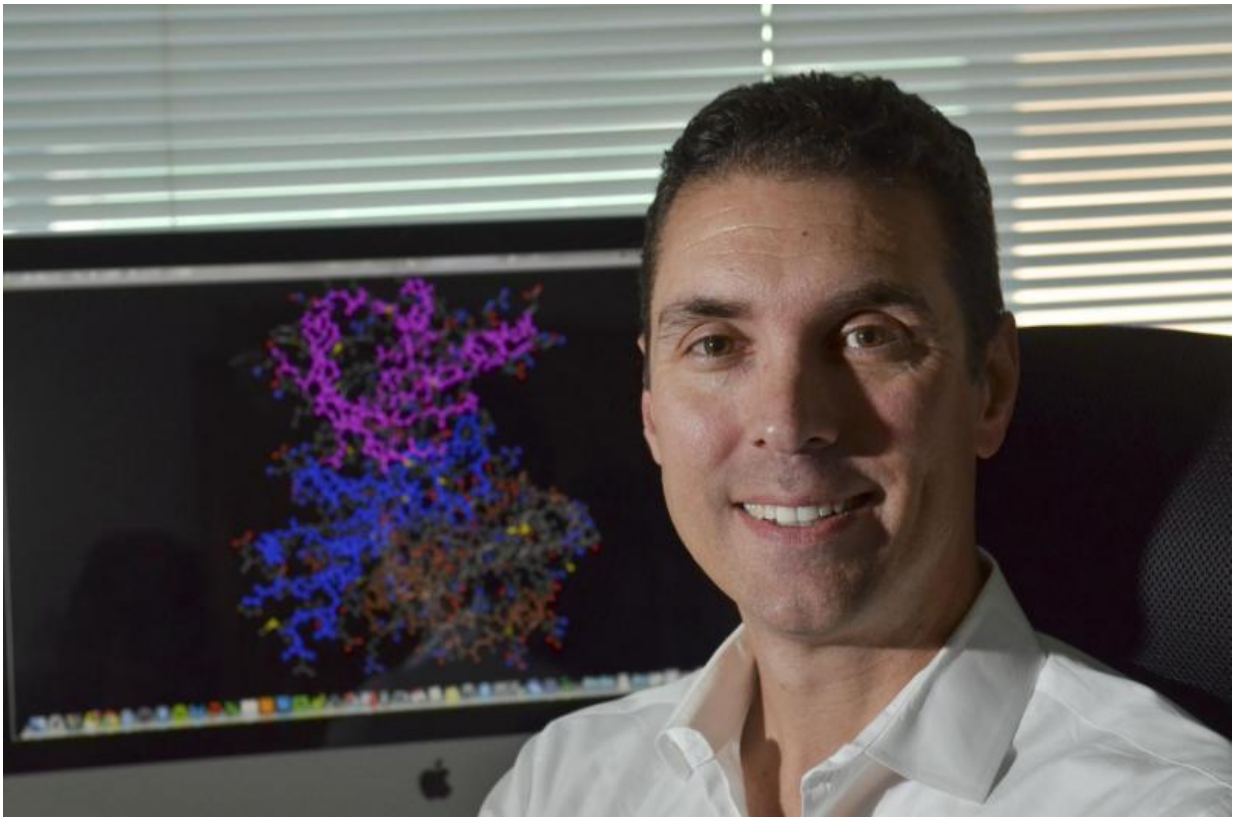

Robert Doebele, M.D., Ph.D., and colleagues report first patient response to new investigational anti-cancer agent, LOXO-101 against TRK cancer. Credit: University of Colorado Cancer Center

The University of Colorado Cancer Center and Loxo Oncology, Inc., a biopharmaceutical company focused on the discovery, development and

commercialization of targeted cancer therapies, today announced the publication of a research brief in the online edition of the journal *Cancer Discovery*, describing the first patient with a tropomyosin receptor kinase (TRK) fusion cancer enrolled in the Phase 1 dose escalation trial of LOXO-101, the only selective TRK inhibitor in clinical development. Additional contributors to the paper include the Knight Cancer Institute at Oregon Health & Science University and Foundation Medicine, Inc.

The peer-reviewed research brief describes a female patient with advanced soft tissue sarcoma widely metastatic to the lungs. The patient's physician submitted a tumor specimen to Foundation Medicine for comprehensive genomic profiling with FoundationOne Heme, where her cancer was demonstrated to harbor a TRK gene fusion. Following multiple unsuccessful courses of treatment, the patient was referred to the University of Colorado for enrollment in the Phase 1 trial of LOXO-101 in March 2015. On study, the patient's shortness of breath rapidly resolved and she was able to discontinue her supplemental oxygen and resume activities of daily living. Imaging studies following one month of treatment, the first imaging studies conducted post-treatment, confirmed that her tumors had substantially regressed, meeting a partial response (PR) definition by standard RECIST 1.1 criteria. As discussed in the publication, with 4 months of treatment, additional CT scans demonstrated almost complete tumor disappearance of the largest tumors. After 4 months of dosing, the patient did not have any adverse events that were attributed to LOXO-101.

"It is exciting to think that TRK fusions may join a relatively short, but growing, list of actionable oncogenic drivers found across human cancer," said lead author Robert C. Doebele, M.D., Ph.D., LOXO-101 clinical investigator, and University of Colorado Cancer Center member. "To see a rapid and unequivocal response in the first TRK fusion patient treated with LOXO-101 provides early but encouraging validation of this target. Of course, it will be important to see repeatable and durable

results as more patients with TRK fusions are treated over time. This case study also illustrates the clinical value of multiplex genetic testing in patients with advanced cancer. Broad testing for all known actionable molecular alterations gives patients the best opportunity to find commercially available or investigational targeted therapies that have been rationally designed to treat their cancers."

The publication also describes novel assays for assessing LOXO-101's impact on TRK signaling, patient-derived TRK fusion models in vitro and in vivo which illustrate LOXO-101's TRK inhibition, and the first-ever description of the molecular epidemiology of TRK fusions in soft tissue sarcoma.

LOXO-101, built specifically to inhibit TRK, is currently being studied in a Phase 1 trial of patients with advanced solid tumors. The trial continues to enroll patients at escalating oral doses of fixed once-daily and twice-daily regimens. As reported at the 2015 American Association for Cancer Research (AACR) meeting, LOXO-101 has been well tolerated with no drug-related adverse event signals reported at doses that consistently achieve systemic drug exposures anticipated to inhibit TRK signaling by over 90 percent. For more information on the Phase 1 trial, including study sites and eligibility criteria, visit clinicaltrials.gov (study identifier NCT02122913), or contact the Loxo Oncology Physician and Patient Clinical Trial Hotline at 1-855-NTRK-123. Loxo Oncology's Policy for Access to Investigational Agents can be found on the Loxo Oncology web site.

"TRK is increasingly recognized for its role in cancer biology, and this first peer-reviewed clinical validation is an important step forward," said Jennifer Low, M.D., Ph.D., chief medical officer of Loxo Oncology. "We continue to be encouraged by the safety and pharmacokinetics we have seen so far in the LOXO-101 Phase 1a trial, and we look forward to sharing more information about our clinical program later this year."

"Our goal is to better understand the genetic drivers of sarcoma to improve treatment options for patients," said Lara E. Davis, M.D., a medical oncologist and sarcoma specialist with the OHSU Knight Cancer Institute. "These early results validate that further study of TRK in the complex field of sarcoma is warranted."

Provided by University of Colorado Denver