

534P

Larotrectinib in non-CNS TRK fusion cancer patients: Outcomes by prior therapy and performance status

A. Drilon¹, L. Shen², C.M. van Tilburg³, D.S.W. Tan⁴, S. Kummar⁵, J.J. Lin⁶, F. Doz⁷, R. McDermott⁸, C.M. Albert⁹, J. Berlin¹⁰, S. Bielack¹¹, U.N. Lassen¹², M. Tahara¹³, R. Norenberg¹⁴, M. Fellous¹⁵, H. Nogai¹⁶, R. Xu¹⁷, T.W. Laetsch¹⁸, D.S. Hong¹⁹

¹ Early Drug Development Service, Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY, USA, ² Department of GI Oncology, Peking University Cancer Hospital & Institute, Beijing, China, ³ Department of Pediatric Oncology, Hematology, Immunology and Pulmonology, Hopp Children's Cancer Center Heidelberg (KiTZ), Heidelberg University Hospital and German Cancer Research Center (DKFZ), Heidelberg, Germany, ⁴ Division of Medical Oncology, National Cancer Centre Singapore, Singapore, ⁵ Department of Medicine, Stanford Cancer Center, Stanford University, Palo Alto, CA, USA, ⁶ Department of Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA, ⁷ Department of Pediatric Oncology, Adolescents and Young Adults, Institut Curie and University of Paris, Paris, France, ⁸ Oncology (Medical Oncology), St Vincent's University Hospital and Cancer Trials Ireland, Dublin, Ireland, ⁹ Pediatric Hematology/Oncology, Seattle Children's Hospital and University of Washington School of Medicine, Seattle, WA, USA, ¹⁰ Division of Hematology/Oncology, Vanderbilt University Medical Center, Nashville, TN, USA, ¹¹ Department of Pediatric Oncology, Hematology, Immunology, Klinikum Stuttgart - Olgahospital, Stuttgart, Germany, ¹² Department of Oncology, Rigshospitalet, Copenhagen, Denmark, ¹³ Department of Head and Neck Medical Oncology, National Cancer Center Hospital East, Kashiwa, Japan, ¹⁴ Chrestos Institut, Chrestos Concept GmbH & Co. KG, Essen, Germany, ¹⁵ Global Medical Affairs, Bayer HealthCare Pharmaceuticals, Inc., Basel, Switzerland, ¹⁶ SBU Oncology, Bayer HealthCare Pharmaceuticals, Inc., Basel, Switzerland, ¹⁷ Department of Medical Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China, ¹⁸ Cancer Center, The Children's Hospital of Philadelphia / University of Pennsylvania, Philadelphia, PA, USA, ¹⁹ Department of Investigational Cancer Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Background

Larotrectinib is a first-in-class, highly selective, central nervous system (CNS)-active tropomyosin receptor kinase (TRK) inhibitor approved in over 40 countries, and by the European Medicines Agency, for the treatment of adult and paediatric patients with TRK fusion cancer. In a previous analysis, larotrectinib demonstrated clinical benefit across varying degrees of pre-treatment or performance status in 159 patients with TRK fusion cancer. Here, we report updated data on larotrectinib outcomes stratified by prior lines of systemic therapy and baseline performance status.

Methods

Data were pooled from three clinical trials of patients with non-CNS TRK fusion cancer treated with larotrectinib (NCT02122913, NCT02576431 and NCT02637687). Patients were stratified based on the number of lines of prior systemic therapy (0, 1, 2 or ≥3) or baseline Eastern Cooperative Oncology Group performance status (ECOG PS) (0, 1, 2 or 3), or the equivalent Lansky/Karnofsky performance status for children. A *post-hoc* analysis of objective response rate (ORR; as assessed by investigators using Response Evaluation Criteria in Solid Tumors v1.1), duration of response (DoR), progression-free survival (PFS) and overall survival (OS) was performed. The updated data cut-off was 20 July 2020.

Results

A total of 218 patients were enrolled. Across all patients, the ORR was 75% (95% confidence interval [CI] 68–81), median DoR (mDoR) was 49.3 months (95% CI 27.3–not estimable [NE]), median PFS (mPFS) was 35.4 months (95% CI 23.4–55.7) and the 36-month OS rate was 77% (95% CI 69–84). Stratified efficacy outcomes are shown in the table. The incidence of treatment-related Grade 3–4 adverse events for patients with 0, 1, 2 or ≥3 prior lines of systemic therapy was 19%, 24%, 14% and 14%, respectively. Table: 534P

	Prior lines of systemic therapy N=216†			
	0 n=58	1 n=59	2 n=42	≥3 n=57
ORR %95% CI	8169–91	7360–84	6953–82	7562–86
mDoR	NRNE–NE	NR21.6–NE	54.77.6–54.7	33.914.8–49.3
mPFS	NR25.8–NE	27.515.7–NE	29.47.0–55.7	28.312.2–51.1
36-month OS %94	71	73	71	
	Baseline ECOG PS N=218			
	0 n=114	1 n=78	2 n=23	3 n=3
ORR %95% CI	8577–91	6654–77	6139–80	331–91

	Prior lines of systemic therapyN=216 [†]			
	0 n=58	1 n=59	2 n=42	≥3 n=57
mDoR	NR35.2–NE 33.9	21.2–54.7	21.67.2–NE	5.6NE–NE
mPFS	NR27.5–NE 25.8	9.2–51.1	10.93.6–NE	4.21.1–7.2
36-month OS % 93	66	48	NE	

[†]Two patients were excluded from analysis by prior lines of systemic therapy due to data entry ambiguity. Data show median and 95% CI unless otherwise stated. NR, not reached.

Conclusions

Although the response rates were highest in patients who were treatment-naïve or with an ECOG PS of 0, larotrectinib benefitted patients across varying degrees of pre-treatment and baseline ECOG PS.

Clinical trial identification

NCT02122913, first posted April 25, 2014; NCT02637687, first posted 22 December 2015; NCT02576431: first posted 15 October 2015.

Editorial acknowledgement

Medical writing assistance was provided by Francesca Murphy, Scion (London, UK), supported by Bayer HealthCare Pharmaceuticals, Inc.

Legal entity responsible for the study

Bayer and Loxo Oncology (a subsidiary of Lilly).

Funding

Bayer and Loxo Oncology (a subsidiary of Lilly).

Disclosure

A. Drilon: Financial Interests, Institutional, Advisory Board, Honoraria/advisory boards: Ignyta/Genentech/Roche, Loxo/Bayer/Lilly, Takeda/Ariad/Millennium, TP Therapeutics, AstraZeneca, Pfizer, Blueprint Medicines, Helsinn, Beigene, BergenBio, Hengrui Therapeutics, Exelixis, Tyra Biosciences, Verastem, MORE Health, Abbvie, 14ner/Elevation Onco; Financial Interests, Institutional, Other, Associated research paid to institution: Pfizer, Exelixis, GlaxoSmithKlein, Teva, Taiho, PharmaMar; Financial Interests, Institutional, Other, Research: Foundation Medicine; Financial Interests, Institutional, Royalties: Wolters Kluwer; Financial Interests, Personal, Other, Food/Beverage: Merck, Puma, Merus, Boehringer Ingelheim; Financial Interests, Institutional, Other, CME Honoraria: Medscape, OncLive, PeerVoice, Physicians Education Resources, Targeted Oncology, Research to Practice, Axis, Peerview Institute, Paradigm Medical Communications, WebMD, MJH Life Sciences, Med Learning, Imedex, Answers in CME, Medscape, Clinical Care Optio. L. Shen: Financial Interests, Institutional, Funding, Grants: Beijing Xiantong Biomedical Technology Co., Ltd, Qilu Pharmaceutical Co., Ltd, Zaiding Pharmaceutical (Shanghai) Co., Ltd, Jacobio Pharmaceuticals Co., Ltd., Beihai Kangcheng(Beijing)Medical Technology Co., Ltd.; Financial Interests, Institutional, Other, Consulting: MSD, Merck, BI, Harbour; Financial Interests, Institutional, Invited Speaker: Hutchison Whampoa, Hengrui, ZaiLab, CStone. C.M. van Tilburg: Financial Interests, Institutional, Advisory Role, Advisory boards: Bayer, Novartis. D.S.W. Tan: Financial Interests, Institutional, Other, Consulting: Novartis, Merck, Loxo, AstraZeneca, Roche, Pfizer; Financial Interests, Institutional, Other, Travel: Pfizer, Boehringer Ingelheim, Roche; Financial Interests, Institutional, Other, Honoraria: BMS, Takeda, Novartis, Roche, Pfizer; Financial Interests, Institutional, Funding, Research: Novartis, GSK, AstraZeneca. S. Kummar: Financial Interests, Personal, Full or part-time Employment, Editor in Chief of Current Problems in Cancer: Elsevier; Financial Interests, Institutional, Other, Consulting: Boehringer Ingelheim, Springworks Therapeutics, Varian, Bayer, Genome & Company, HarbourBiomed, Seagen, MundibioPharma; Financial Interests, Institutional, Advisory Role, Advisory board member: Bayer, Genome & Company, HarbourBiomed, Gilead; Financial Interests, Personal, Other, Travel: Bayer; Financial Interests, Personal, Full or part-time Employment, Co-founder: PathomIQ; Financial Interests, Personal, Other, Spouse advisor/founder: Cadila Pharmaceutical Ltd., Arxeon Inc. J.J. Lin: Financial Interests, Personal, Other, Personal Fees/Other: Pfizer, Genentech, C4 Therapeutics, Nuvalent, Blueprint Medicines, Turning Point Therapeutics, Hengrui Therapeutics, Neon Therapeutics, Relay Therapeutics, Novartis, Bayer, Elevation Oncology, Roche. F. Doz: Financial Interests, Institutional, Advisory Board: Bayer, BMS, Roche, Celgene, LOXO Oncology, Servier, Tesaro; Financial Interests, Institutional, Other, Travel: Bayer, BMS, Roche; Financial Interests, Institutional, Other, Consulting: Servier. R. McDermott: Financial Interests, Personal, Advisory Board: Amgen, Bayer, BMS, Clovis, Janssen, Pfizer.; Financial Interests, Personal, Invited Speaker: Astellas, Ipsen, MSD; Financial Interests, Institutional, Principal Investigator, Local PI: Astellas, Bayer, BMS, Clovis, Regeneron; Financial Interests, Institutional, Principal Investigator, Coordinating PI: MSD. J. Berlin: Financial Interests, Institutional, Research Grant, Funding: Bayer; Financial Interests, Institutional, Advisory Board: Bayer. S. Bielack: Financial Interests, Institutional, Advisory Role, Advisory/Consulting: Bayer, Boehringer Ingelheim, Eli Lilly, Ipsen, Roche, and Sensorion. U.N. Lassen: Financial Interests, Institutional, Advisory Board: Bayer, Pfizer, Novartis; Financial Interests, Institutional, Research

Grant, Funding: BMS, GSK, Pfizer and Roche. M. Tahara: Financial Interests, Institutional, Advisory Role, Advisory/Consulting: Bayer, Merck Serono, MSD Ono Pharmaceutica, Rakuten Medical, Pfizer, Lilly, AstraZeneca, LOXO; Financial Interests, Institutional, Other, Honoraria: Eisai, MSD, Ono Pharmaceutica, Bristol-Myers Squibb; Financial Interests, Institutional, Research Grant, Funding: Bayer, Ono Pharmaceutica. R. Norenberg: Financial Interests, Personal, Full or part-time Employment, External employee: Bayer; Financial Interests, Personal, Full or part-time Employment: Contract research organization (CRO). M. Fellous: Financial Interests, Personal, Full or part-time Employment: Bayer. H. Nogai: Financial Interests, Personal, Full or part-time Employment: Bayer. T.W. Laetsch: Financial Interests, Personal, Advisory Role, Consulting: Novartis, Cellectis, Bayer, Loxo, Lilly, Deciphera, Jumo Health, Y-mAbs Therapeutics; Financial Interests, Institutional, Research Grant, Funding: Pfizer, Novartis, Bayer, Loxo, AbbVie, Amgen, Atara, Biotherapeutics, BMS, Lilly, Epizyme, GSK, Janssen, Jubilant Pharmaceuticals, Novella Clinical, Servier.. D.S. Hong: Financial Interests, Institutional, Research Grant, Funding: AbbVie, Adaptimmune, Amgen, AstraZeneca, Bayer, BMS, Daiichi-Sankyo, Eisai, Fate Therapeutics, Genentech, Genmab, Ignyta, Infinity, Kite, Kyowa, Lilly, Loxo Oncology, Merck, MedImmune, Mirati, MiRNA, Molecular Templates, Mologen, NCI-CTEP, Novartis, Pfizer; Financial Interests, Institutional, Other, Travel: Loxo Oncology, MiRNA, ASCO, AACR, SITC, Genmab; Financial Interests, Institutional, Advisory Role, Consulting: Alpha Insights, Axiom, Adaptimmune, Baxter, Bayer, Genentech, GLG, Group H, Guidepoint Global, Infinity, Janssen, Merrimack, Medscape, Numab, Pfizer, Seattle Genetics, Takeda, and Trieza Therapeutics; Financial Interests, Personal, Ownership Interest, Molecular Match (advisor), OncoResponse (founder), and Presagia Inc (advisor): Molecular Match, OncoResponse, Presagia Inc. All other authors have declared no conflicts of interest.

© *European Society for Medical Oncology*