Elective Discontinuation of Larotrectinib in Pediatric Patients With TRK Fusion Sarcomas and Related Mesenchymal Tumors

Leo Mascarenhas, MD, MS[1]; Steven G. DuBois, MD, MS[2]; Catherine M. Albert, MD[3]; Stefan Bielack, MD[4]; Daniel Orbach, MD[5]; Noah Federman, MD[6]; Birgit Geoerger, MD, PhD[7]; Ramamoorthy Nagasubramanian, MD[8]; Yizhou Zhang, MD[9]; Julia Chisholm, BMBCh, PhD[10]; Soledad Gallego Melcon, MD, PhD[11]; Hiroaki Goto, MD, PhD[12]; Daniel A. Morgenstern, MB, BChir, PhD[13]; Cormac Owens, MD[14]; Alberto S. Pappo, MD[15]; Sébastien Perreault, MD[16]; Johannes H. Schulte, MD[17,18]; Neerav Shukla, MD[19]; Christian Michel Zwaan, MD, PhD[20,21]; Natascha Neu, MS[22]; Vadim Bernard-Gauthier, PhD[23]; Esther De La Cuesta, MD, MBA[24]; Cornelis M. van Tilburg, MD, PhD[25,26,27,28]; and Theodore W. Laetsch, MD[29]

DOI https://doi.org/10.1200/JCO.24.00848

ABSTRACT

Larotrectinib is a highly selective tropomyosin receptor kinase (TRK) inhibitor with efficacy in children with TRK fusion tumors. We evaluated patient outcomes after elective discontinuation of larotrectinib in the absence of disease progression in a protocol-defined wait-and-see subset analysis of eligible patients where treatment resumption with larotrectinib was allowed if disease progressed. We also assessed the safety and efficacy of larotrectinib in all pediatric patients with sarcoma. This cohort included 91 patients (younger than 18 years) from two clinical trials: infantile fibrosarcoma (49), other soft tissue sarcomas or related mesenchymal tumors (41), and bone sarcoma (1). Treatment-related adverse events were of maximum grade 1 or 2 in 25% and 25% of patients, respectively. The overall response rate was 87% (95% CI, 78 to 93). In the wait-and-see analysis, 47 patients discontinued larotrectinib. Median time from discontinuation to disease progression was not reached. Sixteen patients had tumor progression during the wait-and-see period. All 16 patients resumed larotrectinib, and 15 (94%) achieved disease control, with 11 objective responses. Larotrectinib continues to demonstrate durable responses with favorable safety in children with TRK fusion sarcomas. Treatment discontinuation is feasible in select patients with objective response and clinical benefit noted in those who have disease progression after elective treatment discontinuation.

ACCOMPANYING CONTENT

Article, 10.1200/JCO-24-01854

Data Supplement

Protocol

Accepted December 18, 2024

Published January 27, 2025

J Clin Oncol 00:1-8

View Online Article

INTRODUCTION

NTRK gene fusions are oncogenic drivers in infantile fibrosarcoma (IFS) and other sarcomas in pediatric patients.[1-5] Larotrectinib is a first-in-class, highly selective, tumor-agnostic tropomyosin receptor kinase (TRK) inhibitor used to treat patients with TRK fusion cancer.[2,6-8]

The optimal treatment duration and long-term adverse effects of larotrectinib in children are unknown. We evaluated the safety and efficacy of larotrectinib in the cohort of pediatric patients with TRK fusion sarcomas and related mesenchymal tumors from two larotrectinib clinical trials: SCOUT and NAVIGATE. SCOUT allowed the treating investigator to electively discontinue larotrectinib in the absence of on-treatment progressive disease (PD) and permitted the resumption of larotrectinib in patients who experienced disease progression after elective discontinuation in a wait-and-see cohort. To the best of our knowledge, this is the first report of patient outcomes from this wait-and-see analysis.

METHODS

Larotrectinib-treated pediatric patients with sarcoma in the SCOUT (ClinicalTrials.gov identifier: NCT02637687) phase I/II study and NAVIGATE (ClinicalTrials.gov identifier: NCT02576431) phase II basket trial formed the analytic cohort; the trial designs were previously published.[2,9,10] Protocols were approved by the independent review board/ethics committee at each site and complied with the International Ethical Guidelines for Biomedical Research Involving Human Subjects, Good Clinical Practice guidelines, the Declaration of Helsinki, and local laws. Patients and/or their parents signed an informed consent form before inclusion in the trials. Additional details are provided in the Data Supplement (online only).

In SCOUT, patients could stop larotrectinib in the event of on-study surgical resection or ongoing nonsurgical complete response (CR), partial response (PR) ≥1 year, or stable disease (SD) ≥2 years (wait-and-see). Patients who stopped

TABLE 1. Demographic and Clinical Characteristics

Characteristic	All Patients (N = 91)	Patients Who Entered the Wait-and-See Analysis (n = 47)
Age, years, median (range)	2.3 (0-18)	0.9 (0-13)
Sex, No. (%)		
Male	53 (58)	25 (53)
Female	38 (42)	22 (47)
ECOG performance status or equivalent Karnofsky/Lansky, No. (%)		
0	71 (78)	39 (83)
1	13 (14)	6 (13)
2	7 (8)	2 (4)
Disease status at enrollment, No. (%)		
Locally advanced	62 (68)	39 (83)
Metastatic	29 (32)	8 (17)
Years since diagnosis, median (range)	0.4 (0-18)	0.3 (0-6)
Histologic subtype, No. (%)		
IFS	49 (54)	30 (64)
Other STS and related mesenchymal tumors	41 (45)	17 (36)
Spindle cell	19 (21)	9 (19)
NOS	7 (8)	1 (2)
Malignant peripheral nerve sheath tumor	5 (6)	—
Inflammatory myofibroblastic tumor	4 (4)	3 (7)
Lipofibromatosis	1 (1)	1 (2)
Lipofibroma	1 (1)	1 (2)
Malignant mesenchymal tumor	1 (1)	—
Myofibromatosis	1 (1)	1 (2)
Myopericytoma	1 (1)	1 (2)
Small round cell	1 (1)	—
Bone sarcoma	1 (1)	—
Previous therapy, No. (%)[a]		
Surgery	38 (42)	13 (28)
Radiotherapy	6 (7)	1 (2)
Systemic therapy	57 (63)	26 (55)
No. of previous systemic therapies, No. (%)[b]		
Treatment-naïve	34 (37)	21 (45)
1	29 (32)	16 (34)
2	17 (19)	8 (17)
≥3	11 (12)	2 (4)
Best response to most recent previous therapy, No. (%)[c]		
CR	2 (2)	1 (2)
PR	9 (10)	4 (9)
SD	29 (32)	13 (28)
PD	11 (12)	4 (9)
Other[d]	9 (10)	4 (9)

Abbreviations: CR, complete response; ECOG, Eastern Cooperative Oncology Group; IFS, infantile fibrosarcoma; NOS, not otherwise specified; PD, progressive disease; PR, partial response; SD, stable disease; STS, soft tissue sarcoma.

[a]Patients may be counted in more than one row.

[b]Number of previous systemic regimens (excluding previous radioactive iodine) in the metastatic and/or unresectable setting.

[c]Percentages on the basis of the number of patients who received previous systemic therapy.

[d]Other includes unknown and not evaluable.

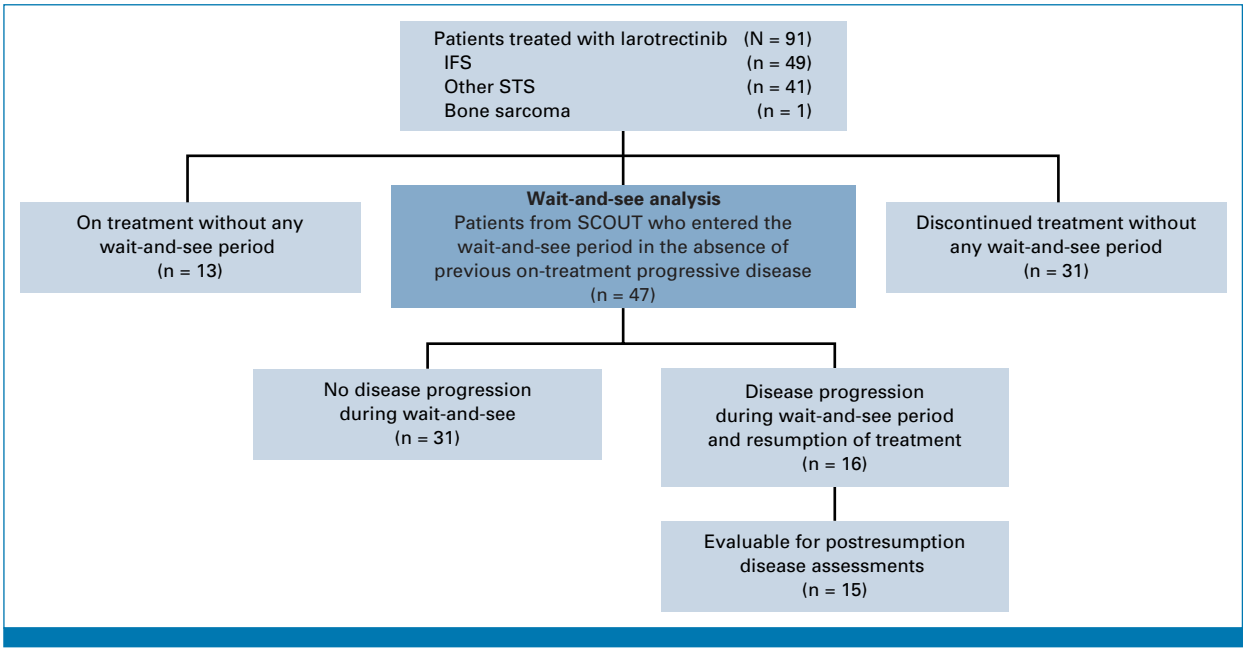

FIG 1. Flow diagram showing patient disposition at data cutoff. IFS, infantile fibrosarcoma; STS, soft tissue sarcoma.

larotrectinib were actively followed for disease progression and were allowed to resume larotrectinib if their tumor progressed (data cutoff: July 20, 2023).

RESULTS

Patient and Tumor Characteristics

The analytic cohort included 91 patients (SCOUT [90] and NAVIGATE [1]). Forty-nine (54%) patients had IFS, 41 (45%) had various other soft tissue sarcomas/related mesenchymal tumors (STS), and 1 (1%) had bone sarcoma (Table 1). Details on *NTRK* gene fusions, fusion partners, and testing methods used to identify *NTRK* gene fusions are provided in the Data Supplement (Tables A1 and A2).

Safety and Tolerability

The treatment duration in the 91 patients ranged from 1 to 87+ months (Data Supplement, Fig S1). Treatment-related adverse events were of maximum grade 1 or 2 in 23 (25%) and 23 (25%) patients, respectively (Data Supplement, Table A3).

Efficacy Outcomes

Ninety-one patients were assessed by the independent review committee for response. The overall response rate was 87% (95% CI, 78 to 93): 47 (52%) CR (including 13 pathologic complete response [pCR]), 32 (35%) PR, seven (8%) SD, three (3%) PD, and two (2%) not evaluable (Data Supplement, Fig S2). Additional efficacy outcomes are reported in the Data Supplement and Figures S3-S6.

Wait-and-See Analysis

Forty-seven patients entered a wait-and-see period; 30 (64%) had IFS and 17 (36%) had other STS (Fig 1). There were eight (17%) and 39 (83%) patients with metastatic and locally advanced disease, respectively. The median time from the start of initial larotrectinib treatment to discontinuation was 14.7 months in all patients (range, 3.0-64.6), 17.2 months in patients with IFS (range, 3.7-58.9), and 9.0 months in patients with other STS (range, 3.0-64.6). Twenty-one (45%) patients discontinued larotrectinib after an on-study tumor resection: 11 R0 resection (negative surgical margins including 10 pCR), 8 R1 resection (microscopic residual tumor), one R2 resection (macroscopic residual tumor), and one unknown surgery outcome. The median time from initial treatment start to discontinuation for these 21 surgical patients was 6.9 months (range, 3.0-25.7). The median time to discontinuation in the 26 (55%) patients without tumor resection after achieving CR (n = 15), PR (n = 10), or SD (n = 1) was 19.8 months (range, 11.1-64.6).

Of the 47 patients in the wait-and-see period, 16 (34%) had documented disease progression after elective discontinuation of larotrectinib (Fig 2). The time from larotrectinib discontinuation to disease progression in these 16 patients was <3 months (nine patients), 3 to <6 months (three patients), 6 to <12 months (two patients), 12 to <18 months (one patient), and ≥24 months (one patient). After a median follow-up of 41.3 months (95% CI, 31.0 to 50.0), the median time to progression in the 47 patients was not reached (range, 0+ to 77.6+). Median time from discontinuation to subsequent progression for the 21 surgical patients and for

Best Response Before or at the Time of Stopping Larotrectinib, No.	Surgical (n = 21)[a] pCR[b] (n = 10)	Unknown (n = 1)	R0 (n = 1)	R1 (n = 8)	R2 (n = 1)	Nonsurgical (n = 26)	Total (N = 47)
Time to stopping larotrectinib, months, median (range)	7 (5-22)	3 (3-3)	22 (22-22)	8 (4-26)	6 (6-6)	20 (11-65)	15 (3-65)
Progressed, No.	2	0	0	1	1	12	16
Time from stopping larotrectinib to progression, months, median (range)[c]	NR (0-76)	NR (50-50)	NR (36-36)	NR (1-78)	1 (1-1)	NR (1-59)	NR (0-78)
Duration of follow-up, months, median[d]	49	50	36	39	NR	41	41

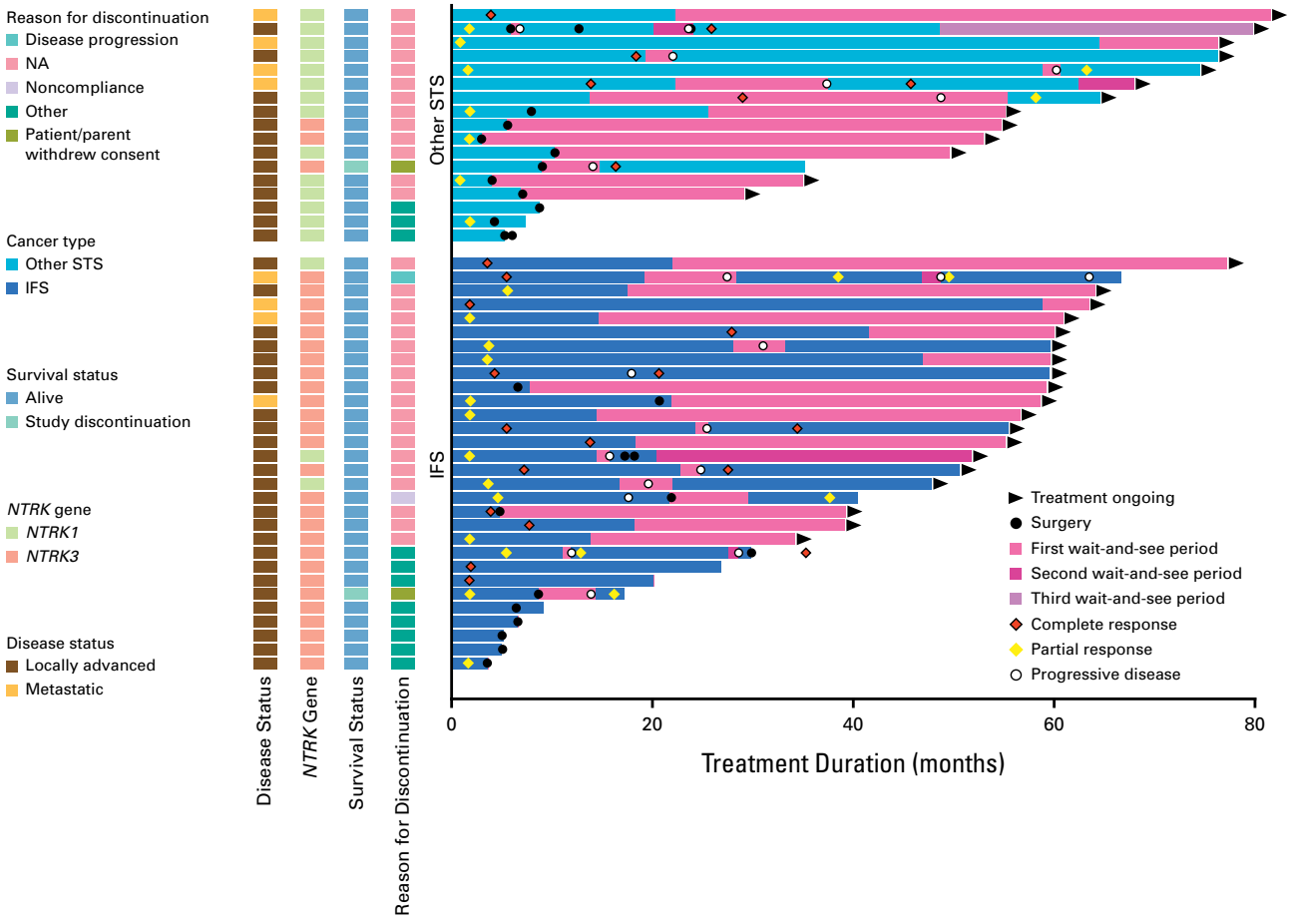

FIG 2. Pediatric patients with TRK fusion sarcoma who entered the wait-and-see analysis. [a]Surgery took place before or ≤1 week after discontinuation. [b]pCR is defined as no pathologic evidence of tumor, negative surgical margins, and no other evidence of disease. [c]Kaplan-Meier estimate. [d]Inverse Kaplan-Meier estimate. IFS, infantile fibrosarcoma; NA, not applicable; NR, not reached; pCR, pathologic complete response; STS, soft tissue sarcoma; TRK, tropomyosin receptor kinase.

the 26 nonsurgical patients was not reached (range, 0+ to 77.6+ and range, 0.9 to 59.2+, respectively) and was similar for patients with IFS or other STS (Figs 3A and 3B).

The 16 patients who progressed/relapsed during wait-and-see period resumed treatment with single-agent larotrectinib. The median time from drug hold to resumption of larotrectinib was 3.9 months (range, 0.9-41.6). Of the 16 patients who resumed larotrectinib, 11 patients (69%) had an objective response to treatment (five CR and six PR [two pending confirmation]) and four had SD. One patient restarted treatment and then had surgery, so the best overall response was undefined. The patient later had a second surgery which led to pCR, entered a second wait-and-see period, and was still in wait-and-see period at the time of the data cutoff. All 47 patients in the wait-and-see cohort were alive at the data cutoff time.

DISCUSSION

In this global multicenter clinical trial data set of, to our knowledge, the largest pediatric TRK fusion sarcoma population treated with a TRK inhibitor to date, larotrectinib

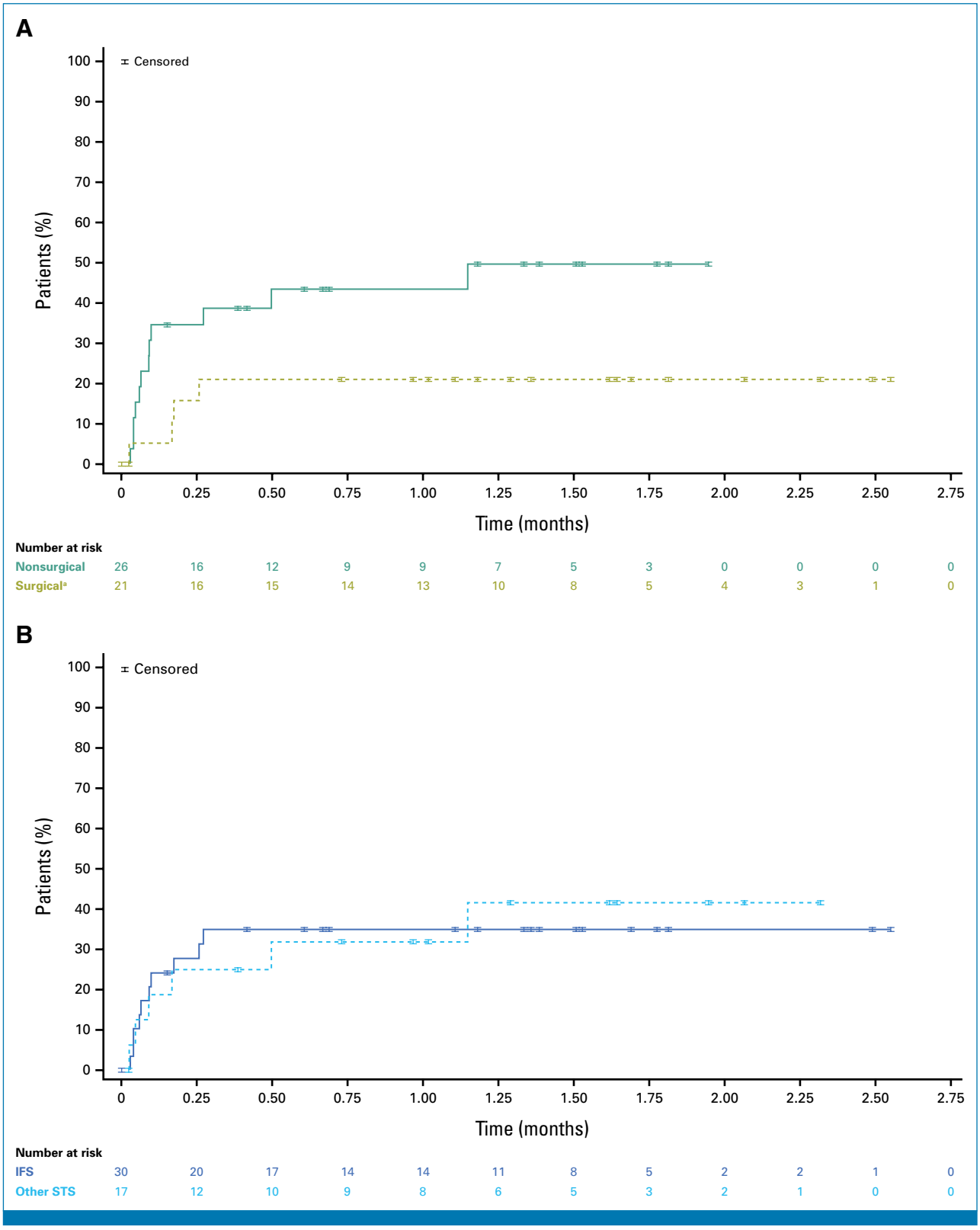

FIG 3. Time from discontinuation to progression by (A) surgery status and (B) histology for the patients in the wait-and-see analysis. [a]Surgery took place before or ≤1 week after discontinuation. IFS, infantile fibrosarcoma; STS, soft tissue sarcoma.

demonstrated long-lasting activity that affected the survival of pediatric patients with IFS or other STS and related mesenchymal tumors. No new safety signals were observed, and adverse events were consistent with the known safety profile of larotrectinib.[2,9] Liver enzyme elevation, mostly grade 1/2, was the most common toxicity.

Approximately a third of the patients who electively discontinued larotrectinib had disease progression. Fifteen of the 16 (94%) patients who progressed or relapsed achieved disease control when larotrectinib was resumed, with 69% (11 of 16) having an objective response. All patients in the wait-and-see cohort were alive at the cutoff. This suggests that patients with localized completely resected tumors can discontinue larotrectinib and surgical local control should be strongly considered as soon as feasible without significant morbidity after response to larotrectinib. Moreover, elective discontinuation with close monitoring after prolonged disease response, even without surgical local control, could potentially be considered in some patients. However, longer follow-up is necessary to determine the optimal length of therapy to allow for larotrectinib discontinuation in this group.

Larotrectinib leads to rapid clinical improvement in patients, allowing for less morbid surgical procedures in responding patients.[11] This rapid response can be especially important when there are life-threatening complications including compression of vital structures or tumoral hemorrhage.[12]

A limitation was that decisions to discontinue treatment in the absence of disease progression and treatment duration before discontinuation varied according to investigator discretion. The Children's Oncology Group conducted a prospective study, ADVL1823 (ClinicalTrials.gov identifier: NCT03834961), which assessed the optimal duration of larotrectinib; follow-up is ongoing to evaluate durability of response after patients stop treatment.[13]

A strength of this analysis is the large sample size for a rare disease and a clinical trial design that permitted the wait-and-see analysis. The EPI-VITRAKVI study (ClinicalTrials.gov identifier: NCT05236257) compared results from the larotrectinib SCOUT trial with external historical controls treated with chemotherapy.[14,15] The findings indicate that in patients with IFS, larotrectinib reduced morbidity and the need for aggressive local therapies compared with chemotherapy and should be considered as first-line therapy.[15]

The larotrectinib wait-and-see analysis results suggest that there is a subset of patients who maintain durable remissions off treatment. For those who had tumor progression after treatment was withheld, the clinical benefit noted on resumption of larotrectinib is encouraging.

AFFILIATIONS

[1]Cedars Sinai Medical Center, Los Angeles, CA
[2]Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, MA
[3]Seattle Children's Hospital, University of Washington, Fred Hutchinson Cancer Center, Seattle, WA
[4]Pädiatrie 5 (Onkologie, Hämatologie, Immunologie), Zentrum für Kinder-, Jugend- und Frauenmedizin, Stuttgart Cancer Center, Klinikum Stuttgart—Olgahospital, Stuttgart, Germany
[5]SIREDO Oncology Center (Care, Innovation and Research for Children, Adolescents and Young Adults with Cancer), Institut Curie, PSL University, Paris, France
[6]David Geffen School of Medicine, University of California, Los Angeles, CA
[7]Gustave Roussy Cancer Center, Department of Pediatric and Adolescent Oncology, INSERM U1015, Université Paris-Saclay, Villejuif, France
[8]Nemours Children's Hospital, Orlando, FL
[9]Sun Yat-sen University Cancer Center, Guangzhou, China
[10]Children and Young Peoples Unit, Royal Marsden Hospital and Institute of Cancer Research, Sutton, United Kingdom
[11]Pediatric Oncology and Hematology, Vall d'Hebron Children's Hospital, Barcelona, Spain
[12]Kanagawa Children's Medical Center, Yokohama, Japan
[13]Hospital for Sick Children and University of Toronto, Toronto, ON, Canada
[14]Department of Haemato-Oncology, Our Lady's Children's Hospital, Dublin, Ireland
[15]St Jude Children's Research Hospital, Memphis, TN
[16]Department of Neurosciences, CHU Sainte Justine, Montreal, QC, Canada
[17]Charité-Universitätsmedizin Berlin, Berlin, Germany
[18]Department of Pediatric Hematology and Oncology, University Children's Hospital, Eberhard Karls University Tuebingen, Tuebingen, Germany
[19]Memorial Sloan Kettering Cancer Center, New York, NY
[20]Princess Máxima Centre, Utrecht, the Netherlands
[21]Erasmus MC, Rotterdam, the Netherlands
[22]Chrestos Concept GmbH & Co, KG, Essen, Germany
[23]Bayer Pharmaceuticals, Inc., Toronto, Canada
[24]Bayer HealthCare Pharmaceuticals, Inc, Whippany, NJ
[25]Hopp Children's Cancer Center Heidelberg (KiTZ), Heidelberg, Germany
[26]Department of Pediatric Oncology, Hematology, Immunology and Pulmonology, Heidelberg University Hospital, Heidelberg, Germany
[27]Clinical Cooperation Unit Pediatric Oncology, German Cancer Consortium (DKTK), German Cancer Research Center (DKFZ), Heidelberg, Germany
[28]National Center für Tumor Disease (NCT), Heidelberg, Germany
[29]Children's Hospital of Philadelphia/University of Pennsylvania, Philadelphia, PA

CORRESPONDING AUTHOR

Leo Mascarenhas, MD, MS; e-mail: Leo.Mascarenhas@cshs.org.

DISCLAIMER

The sponsor was involved in the study design, collection, analysis, and interpretation of data, as well as data checking of information provided in the manuscript. However, ultimate responsibility for opinions, conclusions, and data interpretation lies with the authors. The views expressed are those of the authors and not necessarily those of the

National Institute for Health Research or the Department of Health and Social Care.

EQUAL CONTRIBUTION

L.M., S.G.D., C.M.v.T., and T.W.L. contributed equally to this work.

PRIOR PRESENTATION

Presented at the 56th Annual Congress of the International Society of Paediatric Oncology, Honolulu, HI, October 17-20, 2024; and at the Connective Tissue Oncology Society 2024 Annual Meeting, San Diego, CA, November 13-16, 2024.

SUPPORT

Supported by Bayer Healthcare and Loxo Oncology, Inc, a wholly owned subsidiary of Eli Lilly and Company. S.G.D. was supported by Alex's Lemonade Stand Foundation. J.C. was supported by the Giant Pledge through the Royal Marsden Cancer Charity, and this work represents independent research supported by the National Institute for Health Research Biomedical Research Center at The Royal Marsden NHS Foundation Trust and the Institute of Cancer Research, London.

CLINICAL TRIAL INFORMATION

NCT02637687 and NCT02576431

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI https://doi.org/10.1200/JCO.24.00848.

DATA SHARING STATEMENT

Availability of the data underlying this publication will be determined according to Bayer's commitment to the EFPIA/PhRMA "Principles for responsible clinical trial data sharing." This pertains to scope, time point, and process of data access.

As such, Bayer commits to sharing upon request from qualified scientific and medical researchers patient-level clinical trial data, study-level clinical trial data, and protocols from clinical trials in patients for medicines and indications approved in the United States and European Union (EU) as necessary for conducting legitimate research. This applies to data on new medicines and indications that have been approved by the EU and US regulatory agencies on or after January 1, 2014.

Interested researchers can use www.vivli.org to request access to anonymized patient-level data and supporting documents from clinical studies to conduct further research that can help advance medical science or improve patient care. Information on the Bayer criteria for listing studies and other relevant information is provided in the member section of the portal.

Data access will be granted to anonymized patient-level data, protocols, and clinical study reports after approval by an independent scientific review panel. Bayer is not involved in the decisions made by the independent review panel. Bayer will take all necessary measures to ensure that patient privacy is safeguarded.

AUTHOR CONTRIBUTIONS

Conception and design: Leo Mascarenhas, Steven G. DuBois, Natascha Neu, Vadim Bernard-Gauthier, Esther De La Cuesta, Cornelis M. van Tilburg, Theodore W. Laetsch

Provision of study materials or patients: Leo Mascarenhas, Steven G. DuBois, Catherine M. Albert, Stefan Bielack, Daniel Orbach, Noah Federman, Birgit Geoerger, Ramamoorthy Nagasubramanian, Yizhou Zhang, Julia Chisholm, Soledad Gallego Melcon, Hiroaki Goto, Daniel A. Morgenstern, Cormac Owens, Alberto S. Pappo, Sébastien Perreault, Johannes H. Schulte, Neerav Shukla, Christian Michel Zwaan, Cornelis M. van Tilburg, Theodore W. Laetsch

Collection and assembly of data: Leo Mascarenhas, Steven G. DuBois, Catherine M. Albert, Stefan Bielack, Daniel Orbach, Noah Federman, Birgit Geoerger, Ramamoorthy Nagasubramanian, Yizhou Zhang, Julia Chisholm, Soledad Gallego Melcon, Hiroaki Goto, Daniel A. Morgenstern, Cormac Owens, Alberto S. Pappo, Sébastien Perreault, Johannes H. Schulte, Neerav Shukla, Christian Michel Zwaan, Cornelis M. van Tilburg, Theodore W. Laetsch

Data analysis and interpretation: Leo Mascarenhas, Steven G. DuBois, Natascha Neu, Vadim Bernard-Gauthier, Esther De La Cuesta, Theodore W. Laetsch

Manuscript writing: All authors

Final approval of manuscript: All authors

Accountable for all aspects of the work: All authors

ACKNOWLEDGMENT

The authors would like to thank the patients, their families, and all investigators involved in these studies. The authors would like to thank Pierre Arvis for his review and insightful comments. Statistical analyses were provided by Ricarda Norenberg (Chrestos Concept GmbH & Co KG). Programming was provided by Wenjun Xin (Bayer Healthcare Pharmaceuticals, Inc) and Berit Geiss (Chrestos Concept GmbH & Co KG). Medical writing support was provided by Anastasija Pesevska, PharmD, and Cindy Cheung, MBBS (MD), and editorial support was provided by Melissa Ward, BA, of Scion (a division of Prime, London, UK) supported by Bayer according to Good Publication Practice guidelines.[16]

REFERENCES

1. Davis JL, Lockwood CM, Stohr B, et al: Expanding the spectrum of pediatric NTRK-rearranged mesenchymal tumors. Am J Surg Pathol 43:435-445, 2018
2. Drilon A, Laetsch TW, Kummar S, et al: Efficacy of larotrectinib in TRK fusion-positive cancers in adults and children. N Engl J Med 378:731-739, 2018
3. Amatu A, Sartore-Bianchi A, Bencardino K, et al: Tropomyosin receptor kinase (TRK) biology and the role of *NTRK* gene fusions in cancer. Ann Oncol 30:viii5-viii15, 2019
4. Cocco E, Scaltriti M, Drilon A: *NTRK* fusion-positive cancers and TRK inhibitor therapy. Nat Rev Clin Oncol 15:731-747, 2018
5. Lemelle L, Guillemot D, Hermann AL, et al: Neurotrophic tropomyosin receptor kinase (*NTRK*) fusion positive tumors: A historical cohort analysis. Expert Rev Anticancer Ther 23:865-874, 2023
6. Drilon A: TRK inhibitors in TRK fusion-positive cancers. Ann Oncol 30:viii23-viii30, 2019
7. Bayer HealthCare Pharmaceuticals Inc: VITRAKVI prescribing information, 2022. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/210861s008lbl.pdf
8. Bayer AG: VITRAKVI summary of product characteristics, 2023. https://www.ema.europa.eu/en/documents/product-information/vitrakvi-epar-product-information_en.pdf
9. Hong DS, DuBois SG, Kummar S, et al: Larotrectinib in patients with TRK fusion-positive solid tumours: A pooled analysis of three phase 1/2 clinical trials. Lancet Oncol 21:531-540, 2020
10. Laetsch TW, DuBois SG, Mascarenhas L, et al: Larotrectinib for paediatric solid tumours harbouring *NTRK* gene fusions: Phase 1 results from a multicentre, open-label, phase 1/2 study. Lancet Oncol 19:705-714, 2018
11. DuBois SG, Laetsch TW, Federman N, et al: The use of neoadjuvant larotrectinib in the management of children with locally advanced TRK fusion sarcomas. Cancer 124:4241-4247, 2018
12. Orbach D, Sparber-Sauer M, Laetsch TW, et al: Spotlight on the treatment of infantile fibrosarcoma in the era of neurotrophic tropomyosin receptor kinase inhibitors: International consensus and remaining controversies. Eur J Cancer 137:183-192, 2020

13. Laetsch TW, Voss S, Ludwig K, et al: Larotrectinib for newly diagnosed infantile fibrosarcoma and other pediatric *NTRK* fusion–positive solid tumors (Children's Oncology Group ADVL1823). J Clin Oncol 10.1200/JCO-24-01854 [epub ahead of print on December 9, 2024]
14. Carton M, Del Castillo JP, Colin JB, et al: Larotrectinib versus historical standard of care in patients with infantile fibrosarcoma: protocol of EPI-VITRAKVI. Future Oncol 19:1645-1653, 2023
15. Orbach D, Carton M, Khadir SK, et al: Therapeutic benefit of larotrectinib over the historical standard of care in patients with locally advanced or metastatic infantile fibrosarcoma (EPI VITRAKVI study). ESMO Open 9:103006, 2024
16. DeTora LM, Toroser D, Sykes A, et al: Good Publication Practice (GPP) guidelines for company-sponsored biomedical research: 2022 update. Ann Intern Med 175:1298-1304, 2022

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Elective Discontinuation of Larotrectinib in Pediatric Patients With TRK Fusion Sarcomas and Related Mesenchymal Tumors

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/authors/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

Leo Mascarenhas
Consulting or Advisory Role: Gilead Sciences, Novartis
Research Funding: AstraZeneca/MedImmune (Inst), Lilly (Inst), Bayer (Inst), Salarius Pharmaceuticals (Inst), Turning Point Therapeutics (Inst), Pfizer (Inst), Amgen (Inst), E.R. Squibb Sons, LLC (Inst), Jazz Pharmaceuticals (Inst), Bayer (Inst)
Uncompensated Relationships: Children's Oncology Group Foundation, The Pablove Foundation

Steven G. DuBois
Consulting or Advisory Role: Bayer, Amgen, Jazz Pharmaceuticals, InhibRx
Research Funding: Merck (Inst), Roche/Genentech (Inst), Lilly (Inst), Curis (Inst), Loxo (Inst), BMS (Inst), Eisai (Inst), Pfizer (Inst), Turning Point Therapeutics (Inst), Bayer (Inst), Salarius Pharmaceuticals (Inst)
Travel, Accommodations, Expenses: Roche/Genentech, Salarius Pharmaceuticals
Uncompensated Relationships: Y-mAbs Therapeutics, Inc

Stefan Bielack
Honoraria: SERB Pharmaceuticals
Consulting or Advisory Role: SERB SAS, Atheneum, Medicys Healthcare Fieldwork Experts
Expert Testimony: Zschimmer & Schwarz Mohsdorf GmbH

Daniel Orbach
Honoraria: Bayer Health (Inst), Bayer Health (Inst), Roche (Inst), EUSA Pharma (Inst), Novartis (Inst), Merck
Consulting or Advisory Role: Bayer
Research Funding: Bayer (Inst)

Noah Federman
Stock and Other Ownership Interests: 2seventy bio, Bolt Biotherapeutics, Bluebird Bio
Consulting or Advisory Role: Bayer, SpringWorks Therapeutics
Speakers' Bureau: Bayer, Springworks Therapeutics, Fennec Pharma

Birgit Geoerger
Consulting or Advisory Role: AZD, Novartis, Roche/Genentech

Julia Chisholm
Consulting or Advisory Role: Roche, Bayer, Roche/Genentech, Bayer
Research Funding: Bayer (Inst)
Other Relationship: Children's Oncology Group, National Cancer Institute

Hiroaki Goto
Consulting or Advisory Role: Ohara Pharmaceutical, Ono Yakuhin
Speakers' Bureau: Takeda, Alexion Pharmaceuticals, Amgen, Novartis, Bayer, Nippon Shinyaku, Pfizer/Astellas, CSL Behring
Research Funding: Amgen (Inst)

Daniel A. Morgenstern
Honoraria: Ology Medical Education, HMP, Takeda Israel Ltd
Consulting or Advisory Role: Clarity Pharmaceuticals, Y-mAbs Therapeutics, Inc, US World Meds, RayzeBio, Regeneron, AbbVie
Speakers' Bureau: Y-mAbs Therapeutics, Inc, Takeda Israel Ltd
Research Funding: Bristol Myers Squibb (Inst), AbbVie (Inst), Lilly (Inst), Bayer (Inst), Cellectar (Inst), Roche (Inst), Blueprint Medicines (Inst)
Travel, Accommodations, Expenses: AbbVie
Uncompensated Relationships: Oncoheroes Biosciences

Cormac Owens
Consulting or Advisory Role: Y-mAbs Therapeutics, Inc, Norgine, BMSi
Patents, Royalties, Other Intellectual Property: Board member of SIOPEN which gets royalty payments from EUSA for sales of Qarziba (Inst)

Alberto S. Pappo
Honoraria: Bayer, Roche, Lilly, Pfizer
Consulting or Advisory Role: Merck, Loxo/Bayer, EUSA Pharma, Debbio, Lilly, Pfizer

Sébastien Perreault
Leadership: Bayer
Stock and Other Ownership Interests: novocure, Day One Therapeutics
Honoraria: Bayer
Consulting or Advisory Role: Bayer
Speakers' Bureau: Bayer
Expert Testimony: Bayer

Neerav Shukla
Consulting or Advisory Role: Illumina

Christian Michel Zwaan
Consulting or Advisory Role: Takeda (Inst), Pfizer (Inst), AbbVie (Inst), Jazz Pharmaceuticals (Inst), Incyte (Inst), Novartis (Inst), Kura Oncology (Inst), Gilead Sciences (Inst), Sutro Biopharma (Inst), BeiGene (Inst)
Research Funding: Takeda (Inst), AbbVie/Genentech (Inst), Pfizer (Inst), Jazz Pharmaceuticals (Inst), Kura Oncology (Inst), Daiichi Sankyo (Inst)
Travel, Accommodations, Expenses: Syndax, AbbVie

Natascha Neu
Other Relationship: Bayer

Vadim Bernard-Gauthier
Employment: Bayer

Esther De La Cuesta
Employment: Bayer
Stock and Other Ownership Interests: Bayer
Travel, Accommodations, Expenses: Bayer

Cornelis M. van Tilburg
Consulting or Advisory Role: Novartis, Bayer, Alexion Pharmaceuticals, Roche
Travel, Accommodations, Expenses: Lilly

Theodore W. Laetsch
Stock and Other Ownership Interests: Advanced Microbubbles
Consulting or Advisory Role: Bayer, Massive Bio, AI Therapeutics, Jazz Pharmaceuticals, GentiBio, ITM Oncologics, GlaxoSmithKline
Research Funding: Pfizer (Inst), Bayer (Inst), Turning Point Therapeutics (Inst), Lilly (Inst), Roche/Genentech (Inst), Taiho Oncology (Inst), Advanced Accelerator Applications/Novartis (Inst), BioAtla (Inst), Roche (Inst), Jazz Pharmaceuticals (Inst), Exelixis (Inst), Adaptimmune (Inst), Adaptimmune (Inst)

No other potential conflicts of interest were reported.