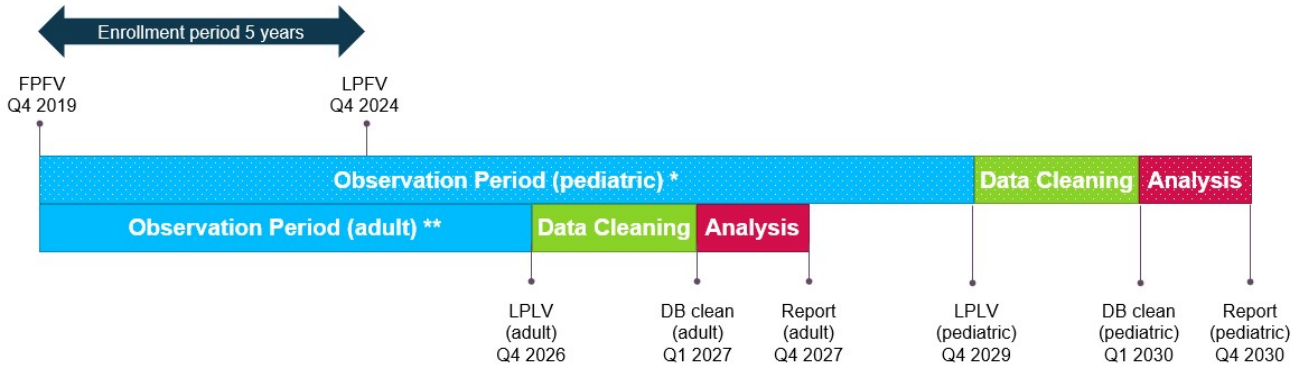
Newsletter

ON-TRK: PrOspective Non-interventional study in patients with locally advanced or metastatic TRK fusion cancer treated with larotrectinib

Volume 2 – 31 Mar 2022

1. Study Plan



INSIDE THIS ISSUE

"ON-TRK study is crucial to generate further safety data in real-life setting and address post-approval commitments."

2. Inclusion/Exclusion criteria

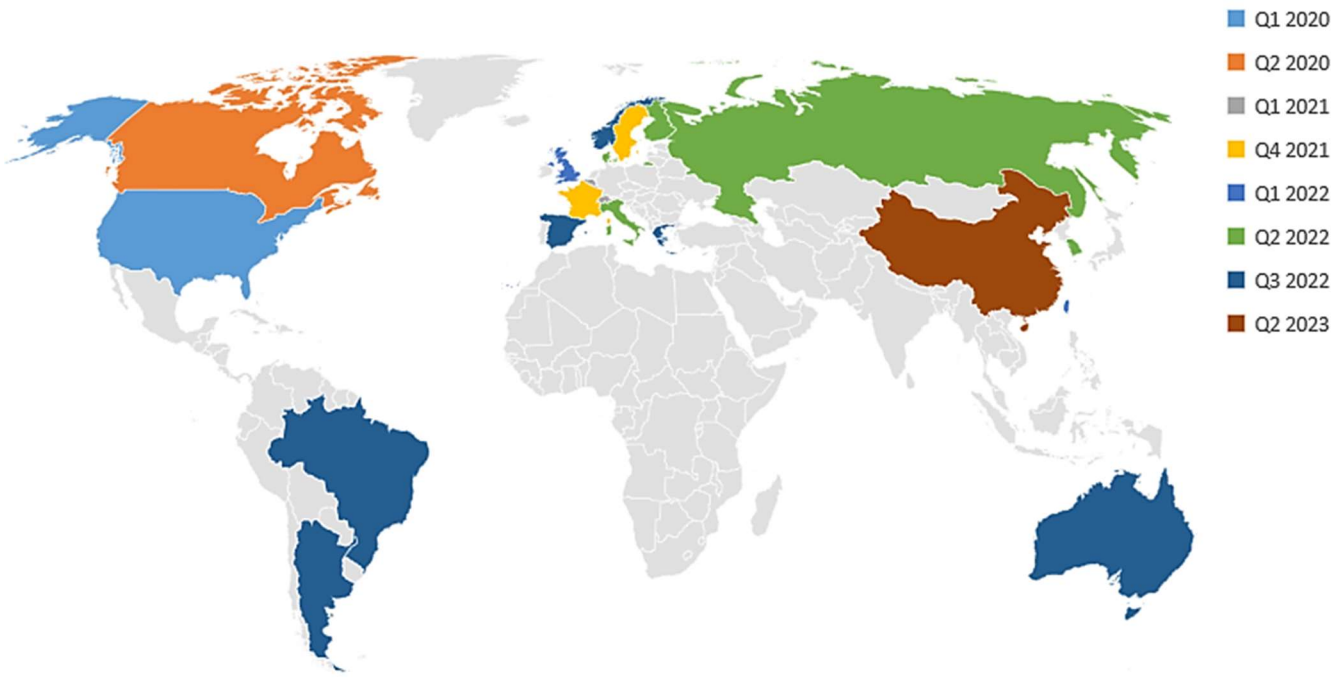
Inclusion

- Adult and pediatric (from birth to 18 year old) patients
- Patients with locally advanced or metastatic solid tumor harboring an *NTRK* gene fusion. *NTRK* (*NTRK1*, *NTRK2*, and *NTRK3*) gene fusions will be identified locally. Acceptable methods of detection of *NTRK* gene fusion include NGS, fluorescence in situ hybridization (FISH), reverse-transcription polymerase chain reaction (rt-PCR) or any other genomic testing able to detect NTRK gene fusion. If a pan-TRK IHC method is used, this result needs to be accompanied with the results using one of the other methods noted above.
- Life expectancy of at least 3 months based on clinical judgement
- Decision to treat with larotrectinib made by the treating physician prior to study enrollment
- Signed informed consent form
- For patients under legal age, signed assent by the patient (where applicable) and parental/legal guardian signed informed consent is required

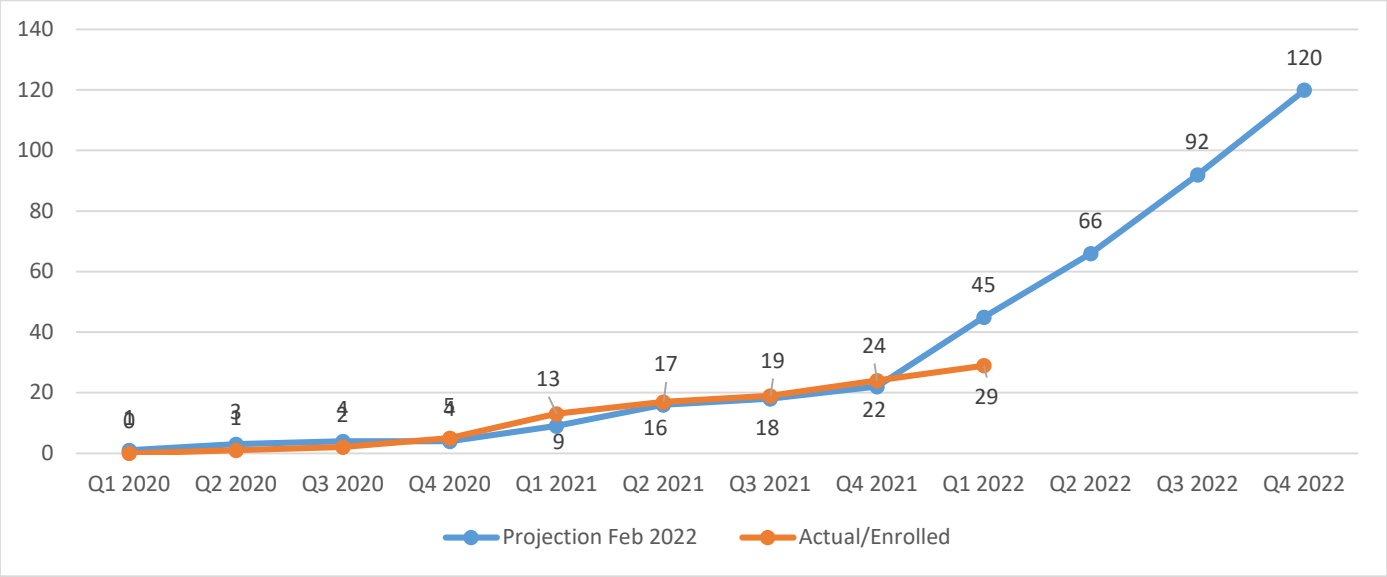
Exclusion

- Any contraindications as listed in the local approved product information
- Pregnancy
- Participation in an investigational program with interventions outside of routine clinical practice
- Prior treatment with larotrectinib or other kinase inhibitor with TRK inhibition
- Patients with NTRK gene amplification or NTRK point mutation

3. Patient enrolment



Country	Local Project Manager	Planned FPFV Quarter	Actual FPFV date	planned # patients	# actual patients	planned # sites	# actual/active sites
USA	SuQuay Conoway	Q1 2020	03. Apr 20	135	14	55	45
Canada	Bahiyyih Schmalenberg	Q2 2020	31. Aug 20	6	2	12	6
Belgium	Caroline Huybrechts	Q1 2021	19. Feb 21	14	2	11	8
Switzerland	Tina Breithaupt	Q1 2021	23. Mar 21	16	6	14	9
Sweden	Anni Gansvik	Q4 2021	14. Oct 22	6	1	4	2
Germany /Austria	Christine Rech, Jasmin Rabe	Q4 2021	01. Nov 22	15	2	15	9
France	Pauline Obled	Q4 2021	23. Nov 22	15	2	12	10
UK	James Horswill	Q1 2022		10		4	1
Luxembourg	Caroline Huybrechts	Q1 2022		3		2	2
Finland	Paula Lahtinen	Q2 2022		2		1	
Taiwan	Caridee Lee	Q1 2022		5		3	
Republic of Korea	HyunCheol Lee	Q2 2022		13		10	
Italy	Nunzia Rizzi	Q3 2022		25		14	
Argentina	Marcel Etchart	Q3 2022		10		15	
Russia	Irina Simakova	Activities on hold until further notice					
Denmark	Anni Gansvik	Q2 2022		6		2	
Brazil	Sofia Mortegi	Q3 2022		20		10	
Greece	Eirini Dalavera	Q3 2022		10		7	
Spain	Anna Maria Vallverdú	Q3 2022		20		18	
Norway	Anni Gansvik	Q3 2022		5		2	
Australia	Swetlana Mactie	Q3 2022		4		3	
China	Sha Wu	Q2 2023		30		8	
Total				341	29	224	92



4. Study extension

By Global Project Management

Due to slow enrolment the study enrolment period was recently extended by 24 months.

Last patient last visit for all cohorts except the pediatric cohort is now planned for Q4 2026 and for the pediatric cohort in Q4 2029.

Data will still be collected from up to 300 patients with NTRK gene fusion globally over a total study period of now 7 instead of 5 years (10 instead of 8 years for pediatric cohort), including 60 instead of 36 months' enrollment and a minimum of 24 months' observation time from study entry for all cohorts but pediatric cohort.

5. Data management

By Bayer study data management

Expectations regarding timelines for documentation:

The time interval between two documented status assessments will be as per routine practice at a site or at the discretion of the treating physician. However, in average, time between visits is expected to be 8 weeks. Please make sure to have these status assessments documented in EDC at a maximum of about 14 day after occurrence.

Query responses:

Automatic queries are directly shown in the EDC after data entry, and manual queries are posted after conduct of data validation activities. Please regularly check the EDC for open queries and resolve them within a maximum of 14 days after query posting.

EDC Upload of NTRK gene fusion reports, tumor resection reports, radiological reports, and images:

- For every enrolled patient: pathological report of the NTRK gene-fusion.
- For every tumor assessment: corresponding radiological report
- If applicable: resection reports (pathological reports and/or molecular testing reports)

6. Safety related information

By Global Safety Leader – Oncology

Larotrectinib demonstrates very good tolerability and positive benefit risk ratio based on clinical trials and post-marketing experience. The safety profile is characterized by adverse events that can be monitored and are manageable and reversible, and comparable across adult and pediatric patients, and tumor types.

Being a priority for Bayer products, safety monitoring of marketed drugs requires engagement of all stakeholders and detailed analysis of the reported safety data.

ON-TRK study targets safety as a primary endpoint which obligates all investigators and participant to be actively engaged in reporting of adverse events during the active study and observation period.

Dear investigators, please pay special attention to detailed collection and timely reporting of safety data during the study and contact pharmacovigilance team if needed with any questions.

With your great help, we will continue to provide safe and effective treatment to our patients.

"Safety Reporting – GCP Definition of AEs and SAE An Adverse Event (AE) is any 'untoward medical occurrence' (unfavourable sign, symptom, laboratory finding, disease) in a patient administered a pharmaceutical product whether related to the product or not. "

7. ON-TRK Faces

By Canadian site 26014 which had FPFV on 5 Aug 2020

The Oncology Team at the Cape Breton Cancer Centre in Nova Scotia, Canada has a keen interest in conducting high-quality research for the purpose of advancing cancer care and providing leading-edge treatment options for patients.

The Centre is home to four Medical Oncologists, two Hematology Oncologists, three Radiation Oncologists, and various support staff including Nurse Practitioners, Registered Nurses, Radiation Therapists, Pharmacists, Social Workers, a Dietician, a Cancer Patient Navigator and Administrative staff. There is also a small sub-team of dedicated research staff, including three Research Coordinators and one Research Administrative Coordinator.

ON-TRK was activated at the site in 2020, and the first two participants in Canada were enrolled within the first 6 months. The team believes that the success of the study at the Cape Breton Cancer Center can be attributed to many factors, including promotion, persistence, and teamwork.
The Centre's promotional strategy included frequent visual and verbal reminders around the Medical Oncology clinics. This was responsible for boosting both ON-TRK awareness and NTRK testing rates. Even though there were numerous negative NTRK results, the Oncologists were persistent in requesting NTRK testing. Because NTRK gene fusions are very rare, it was important to increase the probability of identifying a positive case by amplifying testing rates. The FastTRK program has been able to support these efforts by providing free NTRK testing, and over 50 requests have been sent for testing since the activation of the study.
Although there has been much success, the team did face a few minor challenges. Oncologists wanted the ability to perform more NTRK testing. They reached out to the FastTRK program. FastTRK was quick to provide support by updating their program and providing additional education to the site staff.
The Cape Breton Cancer Centre has the following advice to offer other ON-TRK Investigators be persistent with NTRK testing – increasing testing rates will increase the probability of finding a positive case; work collaboratively with your team—utilizing all team members to their full potential will make workload manageable; be reflective—this helps to identify and resolve challenges; and engage with the Sponsor – they received incredible support from the team at Bayer and FastTRK.

Marcel Schulze
Global Project Manager

Bayer AG
Medical Affairs & Pharmacovigilance, Pharmaceuticals
IEG Study Operations
Building S157, 5/511
Müllerstraße 178
13353 Berlin, Germany

E-mail: marcel.schulze1@bayer.com
Web: http://www.bayer.com