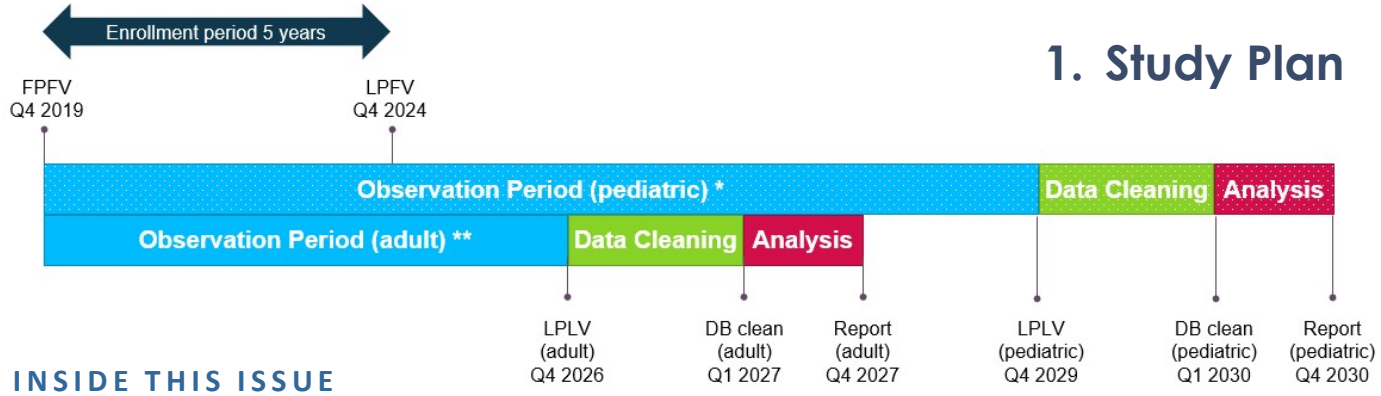
Newsletter

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

Volume 4 – 31 Mar 2023

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. Message from the Steering Committee

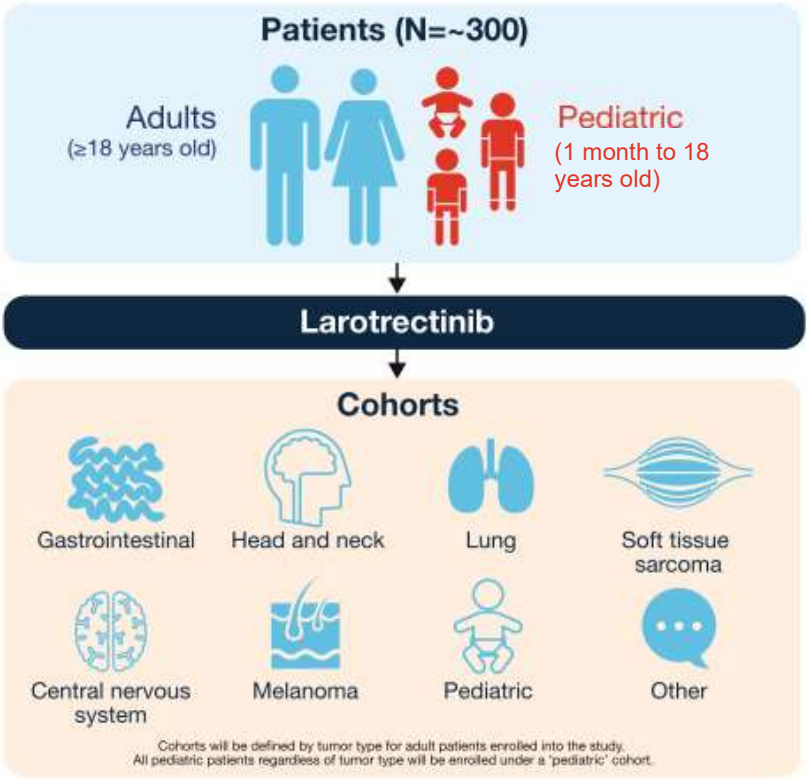
"Understanding the use of precision medicines in the real-life setting by enrolling patients on registries and observational studies is critical. In the era of Precision Oncology, the increasing number of rare biomarker defined cohorts make traditional randomized controlled trials impractical. Increasingly, both the health authorities and medical community are investing time and resources into evaluating real world data on the efficacy and safety of precision biomarker-based treatments. Enrolling patients to the ON-TRK Study, an FDA and EMA post-marketing requirement for the approval of larotrectinib, is critical to continue to gain knowledge about the treatment of patients with TRK fusion cancer, and will contribute to the broader understanding of personalized cancer care."

Theodore W. Laetsch, MD
Associate Professor at
University of Pennsylvania
School of Medicine

3. Study Design

International, prospective, open-label, multicenter, multi-cohort, non-interventional study.

Specific cohorts: gastrointestinal (GI), head and neck (H&N), lung, soft tissue sarcoma (STS), primary central nervous system (CNS), melanoma, pediatrics, and others.



4. Inclusion/Exclusion criteria

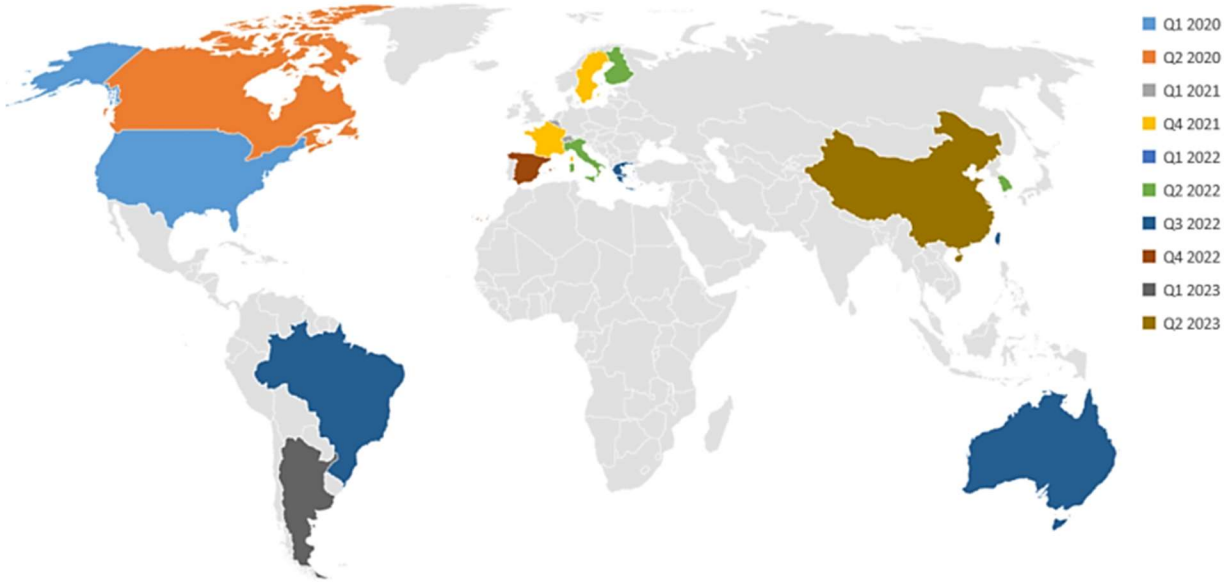
Inclusion

- Adult and pediatric (**from 1 month 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
- **Patients can also be enrolled if the initial visit (larotrectinib start date) occurred within 2 months ±3 days prior to informed consent signed date.**
- 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

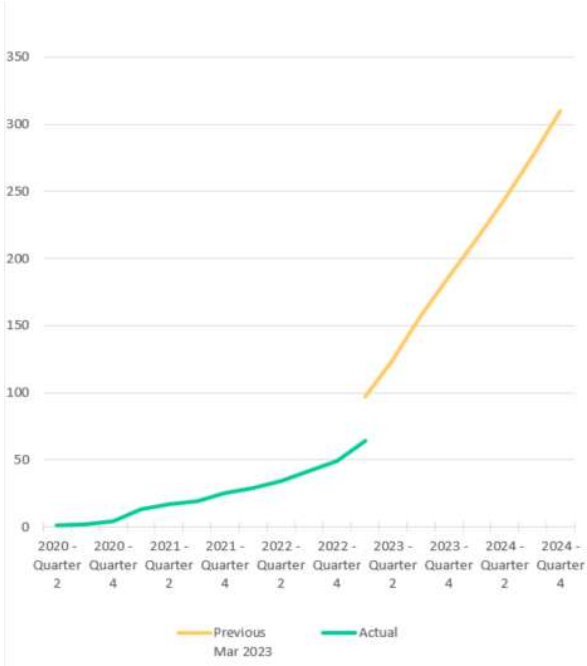
5. Patient enrolment



Achievement since last newsletter: First patient first visit in Italy and Finland. First sites opened in Argentina, Brazil and Greece.

Country	Local Project Manager	Planned FPFV Quarter	Actual FPFV Date	Planned Total Patients	Actual Enrolled Patients	Planned Total Sites	Actual Active Sites
Argentina	Marcel Etchart	Q1 2023		10	0	10	1
Australia	Tiziana Zingali	Q1 2023		3	0	2	0
Belgium	Sander Volon	Q1 2021	09/03/2021	14	6	12	11
Brazil	Sofia Motegi	Q4 2022		3	0	10	7
Canada	Bahiyyih Schmalenberg	Q2 2020	05/08/2020	6	4	8	7
China	Fiona Wu	Q2 2023		30	0	9	1
Finland	Anni Gansvik	Q3 2022	03/02/2023	2	1	1	1
France	Pauline Obled	Q4 2021	23/11/2021	12	4	13	12
Germany/Austria	Andreas Nellen	Q4 2021	01/11/2021	15	5	15	10
Greece	Vasileios Markos	Q4 2022		10	0	7	7
Italy	Elena Gandini	Q3 2022	12/12/2022	25	3	14	11
Korea	HyunCheol Lee	Q3 2022	19/07/2022	13	3	10	8
Luxembourg	Sander Volon	Q1 2022	05/04/2022	3	2	2	2
Spain	Anna Maria Vallverdú Salto	Q4 2022		20	0	18	0
Sweden	Anni Gansvik	Q4 2021	21/10/2021	11	1	8	3
Switzerland	Tina Breithaupt	Q1 2021	22/03/2021	16	9	14	10
Taiwan	Lulu Lee	Q3 2022		10	0	7	0
United States	SuQuay Conaway	Q1 2020	03/04/2020	135	26	55	44
				338	**64**	**215**	**135**

In Q1 2023 we had our most successful quarter regarding patient enrolment - 12 patients enrolled. Compared to all previous quarters. This is the highest enrolment rate ever seen in ON-TRK.



Top 5 Enrolling Sites

Site Number	Site name	Enrolled patients
58007 (Switzerland)	University Hospital Basel – **Dr Rothschild**	3
10003 (Germany)	Onkologische Gemeinschaftspraxis Westerstede - **D. Reichert & J. Janssen**	3
14002 (USA)	UT Southwestern Medical Center / Children's Health – **Dr Tanya Watt**	3
14056 (USA)	Memorial Sloan Kettering Children's Cancer Center – **Dr Tara O'Donohue**	3
58009 (Switzerland)	Luzerner Kantonsspital – **Dr Freimut Schilling**	3

6. Data Privacy

By Global Data Management

In the recent months, it has been detected, that patient data in Radiological Reports and Tumor Resection Reports has been insufficiently redacted.
Since a full birth date is still critical to allow potential identification of the patient's identity, this will be considered a data incident according to data management rules and regulations applied to this study the files will not be processed any further and will be deleted from the EDC upload section.

Therefore, it is crucial to consider data privacy at any time and only upload properly redacted document to the study's EDC system.

7. 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 days after occurrence.

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)

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

8. Safety related information

By Global Safety Leader – Oncology

Safety monitoring of marketed products is a priority at Bayer. Please continue to document and forward all adverse events, non-serious and serious, within the required timelines.

All non-serious AEs must be documented on the AE Report Form or in the CRF/EDC system and forwarded within 7 calendar days of awareness. All SAEs must be documented and forwarded immediately within one business day of awareness.

For patients enrolled retrospectively who started Larotrectinib before signing the ICF within the defined time period, all AEs/SAEs that occurred after starting Larotrectinib treatment should be reported.

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

9. ON-TRK Faces

By Switzerland site 58009 - Luzerner Kantonsspital

ON-TRK Study Center Lucerne. Successful recruitment for both children and adults in one center.

The Lucerne Cantonal Hospital (LUKS) is the largest non-university hospital in Switzerland. We work in specialized, multidisciplinary teams and offer innovative quality medicine. Networking and communication between pediatric oncology and medical oncology is easy and excellent because we work on the same campus. This is significant because NTRK positive patients are rare.

We first opened the ON-TRK study at Lucerne Children's Hospital on 07/28/2021. Thanks to the excellent networking with the adult oncology department of LUKS, we were able to recruit a medical oncologist as SI and integrate him into the study team. The study team consists of 4 pediatric oncologists, one medical oncologist and 2 research coordinators (CRC) of the pediatric oncology department. The entire ON-TRK documentation is done by the CRCs of the pediatric oncology department.

Through the cooperation of the two oncology departments, 4 patients were screened and 3 of these patients have been successfully enrolled in the ON-TRK study. The first enrolled patient was a child with an NTRK positive brain tumor.

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