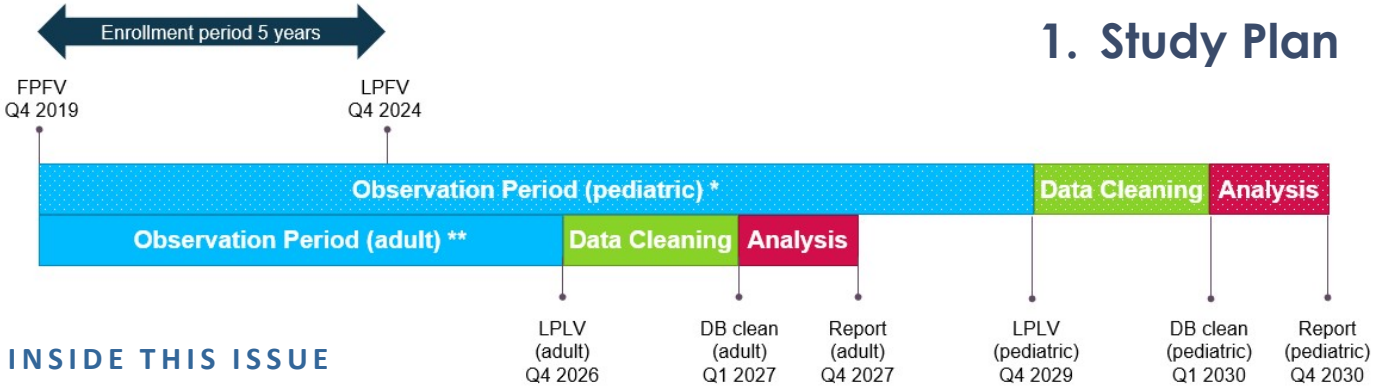
Newsletter

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

Volume 3 – 31 Sep 2022

1. Study Plan



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2. Message from the Steering Committee

"The importance of observational real-world data is escalating in the era of Precision Oncology, so medical community is strongly investing time and resources into implementing characterizing and interpreting of biomarkers predictive of response to treatment with targeted drugs, as well as into gathering RWD of patient efficacy and safety data.
The continued growth of ON-TRK is important, not only for patients with TRK fusion cancer, but also for all with a vision for a future of personalised cancer care."

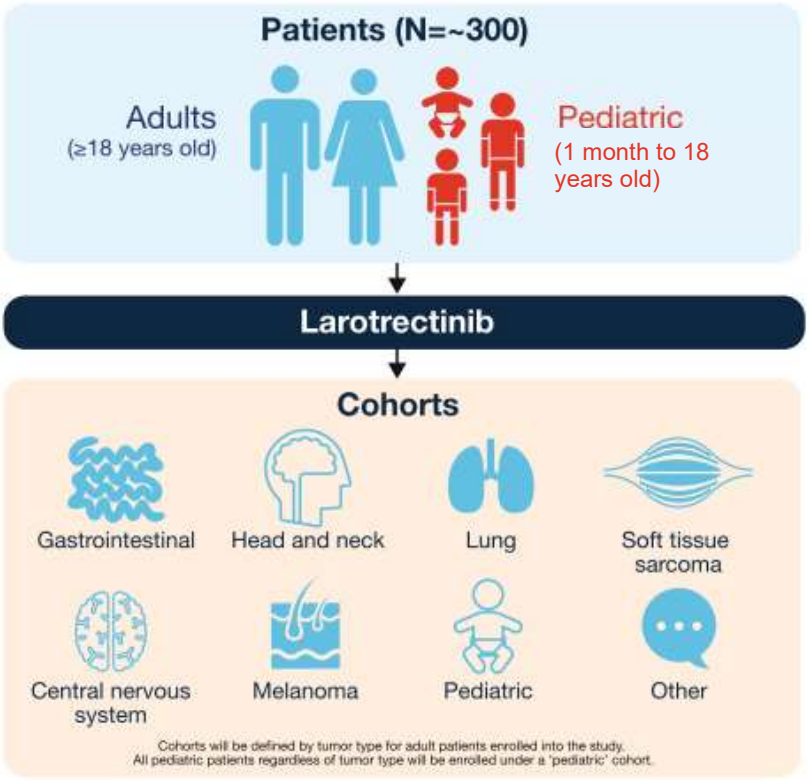
"ON-TRK study is crucial to generate further safety data in real-life setting and address post-approval commitments."

Silvia Novello
Professor of Medical Oncology
Oncology Department
AOU San Luigi
University of Turin
Italy
President of WALCE Onlus (www.womenagainstlungcancer.eu)

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

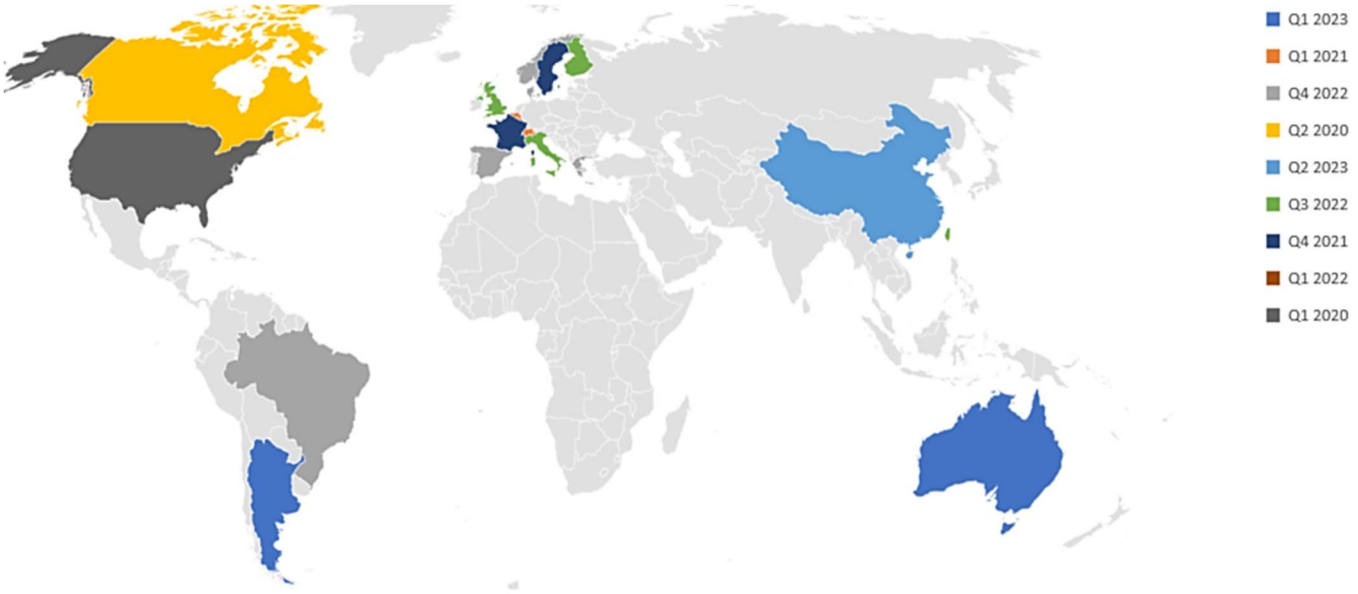
Inclusion

- 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

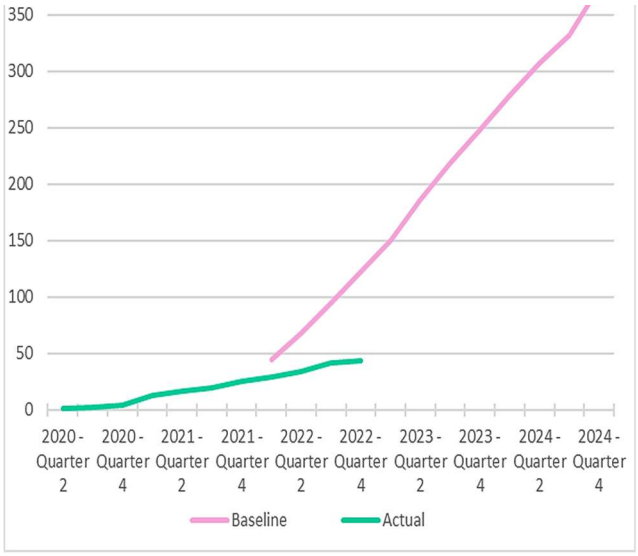
5. Patient enrolment



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	0
Australia	Tiziana Zingali	Q1 2023		3	0	2	0
Belgium	Sander Volon	Q1 2021	09/03/2021	14	3	11	10
Brazil	Sofia Motegi	Q4 2022		10	0	10	0
Canada	Bahiyyih Schmalenberg	Q2 2020	05/08/2020	6	3	6	7
China	Fiona Wu	Q2 2023		30	0	8	0
Denmark	Anni Gansvik	Q4 2022		3	0	2	0
Finland	Paula Lahtinen	Q3 2022		2	0	1	0
France	Pauline Obled	Q4 2021	23/11/2021	15	2	13	12
Germany/Austria	Andreas Nellen	Q4 2021	01/11/2021	15	4	15	10
Greece	Vasileios Markos	Q4 2022		10	0	7	0
Italy	Elena Gandini	Q3 2022		25	0	14	3
Korea	HyunCheol Lee	Q3 2022	19/07/2022	13	1	10	7
Luxembourg	Sander Volon	Q1 2022	05/04/2022	3	1	2	2
Norway	Anni Gansvik	Q4 2022		5	0	2	0
Spain	Anna Maria Vallverdú Salto	Q4 2022		20	0	18	0
Sweden	Anni Gansvik	Q4 2021	21/10/2021	6	1	4	3
Switzerland	Tina Breithaupt	Q1 2021	22/03/2021	16	8	14	10
Taiwan	Lulu Lee	Q3 2022		10	0	7	0
United Kingdom	Anni Gansvik	Q3 2022		10	0	6	2
United States	SuQuay Conaway	Q1 2020	03/04/2020	135	19	55	43
				361	**42**	**217**	**109**

In Q3 2022 we did see an encouraging enrollment rate (3months enrolment average) of 2,67 patients per months.

Enrolment actuals (green) and projection (pink)



Top 5 Enrolling Sites

Site Number	Site name	Enrolled patients
58007 (Switzerland)	University Hospital Basel – **Dr Rothschild**	3
10004 (Germany)	Interdisciplinary Division of Neuro-Oncology – Tübingen - **Dr Tabatabai**	2
26014 (Canada)	Cape Breton Cancer Center – Sydney – **Dr Khodadad**	2
14055 (USA)	Providence Health System - Southern California – **Dr Wagle**	2
58004 (Switzerland)	University Hospital Zurich – **Dr Weller**	2

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 studys 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 Belgium site 28001 which had FPFV on 9 Mar 2021

The medical oncology team at UZ Brussels takes the lead for conducting high quality trials in targeted therapies and tackles the challenge in doing molecular research for many solid tumors such as melanoma, brain tumors, lung- and breast cancer.

We were very excited to participate in the ON-TRK study trial in locally advanced and metastatic TRK fusion cancers.

Our medical oncology staff consists of 7 medical oncologists, a dedicated nursing team, 3 social workers, 2 dieticians, 2 pharmacists, 3 onco-coaches, 6 research coordinators and 5 administrative workers.

The ON-TRK trial was initiated at UZ Brussel in November 2020. Thanks to the tremendous teamwork between the pathology department and our medical oncology center we could include 1 patient within a few months from initiation. The important message that we want to spread is to be alert in requesting NTRK testing, because of the low frequency of NTRK positivity medical oncologists could forget to ask the test.

Therefore, the interchange between both departments is of utmost importance as well as promotion towards the adjacent hospitals.

Regular e-mail reminders from our research coordinators and weekly education of the medical oncology staff reinforced the visibility of the ON-TRK study.

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