Feasibility of Studying the Use of Tissue-Agnostic Cancer Drugs in Population-Based European Health Databases

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DISCLOSURES

- This study was funded by Bayer AG under a contract granting the research team independent publication rights.
- XGA, NRG, LG, SB, PB, CD, MH, ML, NM, JS, and GT work for entities that perform independent research work for government agencies, private entities, and pharmaceutical companies.
- RSR, WZ, and JHZ are employees of Bayer AG.

BACKGROUND

- Antitumor, tissue-agnostic drugs in oncology are novel therapies with indications based on the presence of at least one oncogenic biologic alteration (e.g., gene mutations, protein overexpression) as opposed to more traditional drugs, which are indicated according to the anatomical origin of the primary tumor.
- Larotrectinib, a tissue-agnostic drug, is an oral selective tropomyosin receptor kinase (TRK) inhibitor, CNS-active drug that inhibits three TRK proteins: TRKA, TRKB, and TRKC. When chromosomal fusions involving the kinase domain of these genes occur, the resulting chimeric TRK proteins induce downstream ligand-independent signaling, leading to tumor initiation and progression.
- Larotrectinib was approved by the European Medicines Agency in September 2019 as monotherapy in patients with solid tumors that have a neurotrophic tyrosine receptor kinase (*NTRK*) gene fusion; who have a disease that is locally advanced, metastatic, or where surgical resection is likely to result in severe morbidity; and who have no satisfactory treatment options.

OBJECTIVE

- To assess the feasibility of conducting a drug utilization study of larotrectinib in various European data sources

METHODS

- To evaluate the availability of information in each database, we developed a single standardized form sent to each database containing the following topics:
  - Expected use of larotrectinib (because of the recent approval and the lag time of data sources) assessed through the capture of other oral cancer treatments that may share characteristics in terms of reimbursement or drug-dispensing setting.
  - Use of other cancer drugs, to identify patients with no satisfactory alternative treatments, as per larotrectinib label indication specifications.
  - Tumor diagnosis and disease stage when a new treatment regimen is started to assess the larotrectinib label regarding patients with a disease that is locally advanced or metastatic or where surgical resection is likely to result in severe morbidity.
  - Testing for tumor biomarkers and its results, specifically *NTRK* gene fusion, because the label states that patients must have an *NTRK* gene fusion.

Data Sources

- Researchers from seven European databases contributed information; we present results from the six databases that could collaborate in this poster.
  1. Germany: German Pharmacoepidemiological Research Database (GePaRD)
  2. Sweden: Swedish National Health Registers (SNHR)
  3. Norway: Norwegian National Health Registers (NNHR)
  4. France: Système National de Données de Santé (SNDS)
  5. Italy: Italian Health Databases of Caserta/Palermo (IHD)
  6. United Kingdom: Public Health England (PHE)

RESULTS

- Table 1 provides a visual summary of the available information in each investigated database (questionnaires were completed by December 2019).

Table 1. Summary of Information Availability

	GePaRD-Germany	SNHR-Sweden[a]	NNHR- Norway	SNDS-France	IHD- Italy	PHE- England
Information on oral cancer medications dispensed by a hospital pharmacy	🟡	🟢	🟢	🟡	🟢	🟢
Information on oral cancer medications dispensed by ambulatory pharmacies	🟢	🟢	🟢	🟢	🟢	🟢
Information on intravenous cancer medications	🟡	🟡	🟡	🟡	🟢	🟢
Information on rare cancer diagnoses	🟢	🟢	🟡	🟢	🟡	🟢
Tumor stage	🟢	🟢	🟢	🔴	🔴	🟢
Histological morphology	🔴	🟢	🟢	🔴	🔴	🟢
Information on site of metastasis and local progression when a new drug is started	🟢	🔴	🟡	🟡	🟡	🟡
Information on tests (IHC, FISH, RT-PCR, RNA/DNA sequencing) to characterize biomarkers in tumor specimen	🟡	🔴	🔴	🟡	🔴	🟡
Test done to detect *NTRK* gene fusion	🔴	🔴	🔴	🔴	🔴	🟡
Results of the test	🔴	🔴	🔴	🔴	🔴	🟡
Characterization of the *NTRK* fusion	🔴	🔴	🔴	🔴	🔴	🟡
Patient information						
Age, sex, comorbidities, chronic outpatient medication, visits to specialists	🟢	🟢	🟢	🟢	🟢	🟢
Family history of cancer	🟢	🟡	🟡	🔴	🔴	🔴
Body mass index	🔴	🔴	🔴	🔴	🟢	🟢
Smoking status	🟡	🔴	🟡	🔴	🟢	🟢
Alcohol consumption	🟡	🔴	🟡	🔴	🟢	🟢
Socioeconomic status or proxies	🟢	🟢	🟢	🟡	🟢	🟢
Visits to primary care physician	🟢	🔴	🟢	🟢	🟢	🟢
Visits to ambulatory cancer care units	🔴	🟢	🔴	🟢	🟢	🟢
Visits to an emergency room	🟢	🟢	🔴	🟢	🟢	🟢
Cancer screening	🟢	🔴	🔴	🔴	🔴	🟢
Linkage to cancer registry	🟡	🟢	🟢	🟢	🔴	🟢
Linkage to mortality data	🟡	🟢	🟢	🟢	🟢	🟢
Lag-time incorporation of data into the database, months	12	12	6-12	9-15	< 3-12	12-60

DNA = deoxyribonucleic acid; FISH = fluorescence in situ hybridization; ICH = immunohistochemistry; RT-PCR = reverse transcription polymerase chain reaction; RNA = ribonucleic acid.
🟢 indicates that information is available; 🔴 indicates that information is not available; 🟡 indicates that information is partially available (i.e., information was available to some extent, either via unvalidated proxies or directly but with some degree of incompleteness).
[a]Existing National Quality Registers in Sweden, e.g., National Quality Registry for Lung Cancer, likely provide more detailed information on treatment, metastasis, tests to characterize biomarkers in tumor specimen, and smoking.

Evaluation

- The following data sources are assessed in relation to their likelihood/feasibility for the implementation of a drug utilization study of larotrectinib based on the information collected via the questionnaire and via interaction with the research partners.

PHE (England)

Can be a suitable database to evaluate larotrectinib use in the future.

Information on testing for *NTRK* fusion and its result will very likely be available.

The 5-year data lag time should be considered for a larotrectinib drug utilization study.

SNDS (France)

Potentially a suitable database to evaluate larotrectinib use. Most old, common cancer drugs administered in hospital are included in DRG costs and not detailed in the database. However, new, expensive reimbursed drugs are commonly out of the DRG cost and well identified in the database.

SNDS does not capture tumor status nor *NTRK* gene fusion status or testing, but this information could be available through linkage to cancer registries. The "CANCER" national cohort merges most French cancer registries with the SNDS database, and it should be available in the near future.

GePaRD (Germany)

Does not contain all the information to evaluate larotrectinib use because *NTRK* gene fusion status and testing, tumor status, and common cancer drugs are not available.

SNHR (Sweden)

Does not contain all the information to evaluate larotrectinib use because *NTRK* gene fusion status and testing, tumor status (presence and location of metastasis, local progression) when a new drug is initiated, and common intravenous cancer drugs are not available.

NNHR (Norway)

Does not contain all the information to evaluate larotrectinib use because *NTRK* gene fusion status and testing, tumor status, and common cancer drugs are not available.

IHD (Italy)

Does not contain all the information to evaluate larotrectinib use because *NTRK* gene fusion status and testing, tumor status, and common cancer drugs are not available.

CONCLUSIONS

- To date, PHE will very likely contain all elements to evaluate the use of larotrectinib in a drug utilization study. However, PHE has a lag time of up to 5 years for 100% completeness. Additionally, PHE has limited published research on cancers with genomic alterations.
- The custodians of the remaining databases are not aware of plans to add tumour genomic information to the respective databases.
- Studies using real world data on tissue-agnostic drugs bring extra challenges, specifically the lack of availability of relevant information like genomic testing or a comprehensive characterization of tumor status in later stages of the disease. New effort will need to be implemented to be able to deploy these studies successfully.

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