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

BACKGROUND

- Antitumor tissue-agnostic drugs in oncology are novel therapies with developments based on the presence of at least one oncogenic biomarker alteration (e.g., gene mutations, protein overexpression) as opposed to more traditional drugs, which are indicated according to biologic alteration (e.g., gene mutations, protein overexpression).

- Larotrectinib, a tissue-agnostic drug, is an oral selective tropomyosin receptor kinase (TRK) inhibitor. Old-action 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 or 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.

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

<table>
<thead>
<tr>
<th>Database</th>
<th>Information on disease staging when a new treatment regimen is started to assess the larotrectinib Expected use of larotrectinib (because of the recent approval and the lag time of data sources) assessed</th>
<th>Information on testing for tumor biomarkers and its results, specifically NTRK gene fusion status or testing, but this information can be available through linkage to cancer registries.</th>
<th>Information on intravenous cancer medications</th>
<th>Information on oral cancer medications dispensed by ambulatory pharmacies</th>
<th>Information on site of metastasis and local progression when a new drug is started</th>
<th>Information on Tumor stage</th>
<th>Information on histological morphology</th>
<th>Information on testing for tumor biomarkers and its results, specifically NTRK gene fusion status or testing, but this information can be available through linkage to cancer registries.</th>
</tr>
</thead>
<tbody>
<tr>
<td>GoPharD (Germany)</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>SNDS-France</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>NNHR (Norway)</td>
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<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>SNDS (France)</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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</tr>
<tr>
<td>PHE (England)</td>
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<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

DISCLOSURES

- This study was funded by Bayer AG under a contract granting the research team independent publication rights.

- XGA, NRE, GG, MB, RS, BR, MH, NM, JS, and GT work for entities that perform independent research work for government agencies, private entities, and pharmaceutical companies.

- RSR, WJ, and JZ are employees of Bayer AG.

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 reimbursement settings.

  - Use of other cancer drugs, to identify patients with no satisfactory alternative treatments, as per treatment label indication and contraindications.

  - Tumor diagnosis and disease stage when a new treatment regimen is started to assess the larotrectinib Expected use of larotrectinib (because of the recent approval and the lag time of data sources) assessed.

  - Information on testing for tumor biomarkers and its results, specifically NTRK gene fusion status, 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 (GoPharD)

  2. Sweden: Swedish National Health Registers (SNDS)

  3. Norway: Norwegian National Health Registers (NNHR)

  4. France: Systeme National de Données de la Cancerologie (SNCD)

  5. Italy: Italian Health Database of CancerPharma (IHD)

  6. United Kingdom: Public Health England (PHE)

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 identical markers.

- 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 on biomarkers, characteristics of tumor treatment, and local progression when a new drug is started.

- Future research should focus on assessing the feasibility of conducting a drug utilization study of larotrectinib in these databases.

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CONTACT INFORMATION

Author Service at Alberta, ME PhD, Driscoll, Epidemiology 4171 Medical Sciences, Calgary, AB T2N 4N1, DRDINSBC Institute for Health Data Sciences, 6330.445008, University of British Columbia, Vancouver, BC V6T 2B5, Xabier Garcia de Albeniz, Department of Epidemiology–BIPS GmbH, Bremen, Germany; and Epidemiology–BIPS GmbH, Bremen, Germany; and Epidemiology–BIPS GmbH, Bremen, Germany.

Email: xgarcia@rti.org Phone: +34.93.362.4732