A comparative study between investigator safety data and a pharmacovigilance database: a key role of the pharmacovigilant in the relevance of clinical trial publications

V. Pitance1, E. Blanc1, A. El Hachemi Dumas1, D. Bertram1
1 Direction de la Recherche Clinique et de l’Innovation, Hospices Civils de Lyon, 69002 Lyon
Author address: victoire.pitance@chu-lyon.fr

BACKGROUND

Safety assessment of an investigational medicinal product is an essential requirement of a clinical trial, and the Consolidated Standards of Reporting Trials group has produced recommendations to improve the communication of pharmacovigilance (PV) data in scientific publications. However, little data is published as to the quality of reporting.

OBJECTIVES

To compare safety data of a clinical study reported in a published article and in the sponsor’s PV database.

METHODS

Selection of article

- Randomly selected among studies in a PV database
- Compared 2 drugs in term of efficacy (not safety primary outcome)

SAE using are coded using MedDRA® dictionary

Data extraction

Cases of serious adverse events (SAEs) were extracted:
- from the sponsor’s PV database
- from the scientific publication related

SAEs were compared with regards to:
- Frequency
- System Organ Class (SOC)
- Seriousness criteria
- Outcome
- Causality with treatment

RESULTS

<table>
<thead>
<tr>
<th>Article (Number of patients)</th>
<th>PV Database (Number of patients)</th>
<th>PV Database (Number of SAEs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60 patients at least one SAE*</td>
<td>78 patients at least one SAE*</td>
<td>Total of 136 SAE</td>
</tr>
<tr>
<td>MedDRA SOC</td>
<td>Drug A</td>
<td>Drug B</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Infections / infestations</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Injury and poisoning</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Neoplasms</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Surgical and medical procedures</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Eye disorders</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Any other SOC</td>
<td>10</td>
<td>11</td>
</tr>
</tbody>
</table>

General disorders and administration site conditions

Renal / urinary disorders

Respiratory disorders

Vascular disorders

Social Circumstances

Psychiatric disorders

Investigations

Metabolism and nutrition

Reproductive system and breast disorders

Data regarding seriousness criteria, outcome and causality were not displayed in the article (excepted deaths) but available in the PV database:

- A number of SAEs and all characterising data (e.g., seriousness criteria, outcome, causality) were omitted in the restitution of safety data.
- This discrepancy between the data means that more reconciliations should be made between clinical database and sponsor database. A good collaboration between investigator and sponsor is important to improve the quality and the reliability of safety data.
- The presentation of safety elements wasn’t developed according to the same methodology and expertise of the vigilant sponsor.

DISCUSSION- CONCLUSION

Of the 136 SAEs, 32 were related either by the investigator or by the sponsor to the investigational medicinal product of this study (drug A or drug B). These 32 SAEs were related to 24 patients.
- In the Arm « Drug A », 2 deaths were reported in the article, whereas 3 were found in the PV database.
- 4 life-threatening SAEs were reported in PV database.

* A patient may have multiple SAEs

SAE/SOC omitted in publication

In the article the author regroups the other SOCs together but the PV database details the SOC repartition. Of note, 18 SAEs regarding drug administration errors and incorrect storage of drug are flagged with the MedDRA term « no adverse effect » in the PV database which is in the General SOC.

Difference in number of patients between clinical and PV databases

In the SOC injury, there were 3.5 times more patients who presented an SAE in the PV database with Drug A, and 5.5 times more with Drug B. (In PV database, drug administrator errors and incorrect storage of drugs were retained as SAEs).

Difference between number of patients and number of SAEs

A patient may have presented multiple SAEs in the same SOC but bias regarding safety data because the amount of SAEs is important to assess safety of an investigational medicinal product.

* Social Circumstances

* Reproductive system and breast disorders