Comparison of parameters collected from clinical trials and registries in severe Hemophilia A patients - a methodological exercise

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Introduction and Objectives

For regulatory purposes data are collected in open-label, industry sponsored studies.[1] With the introduction of several new factor VIII products the number of patients needed for these studies might be a limiting factor to get sufficient data on safety and efficacy in an appropriate timeframe. The data collected in clinical trials are perceived as the most robust and complete source of clinical data to judge the safety and efficacy of new agents. To test the hypothesis whether registry data might complement to clinical trials, we aim to compare data of the PedNet registry with data derived from clinical trials for Marketing Authorization.

Methods

We selected data from 633 severe hemophilia A previously untreated patients (PUPs) enrolled in the PedNet registry (Cohort 1, period 2000-2015)[2] and data from 369 patients (296 PUPs, 73 MTPs) who participated in clinical trials. The data have been retrieved from 8 clinical trials performed in the frame of Marketing Authorization between 1987 and 2009. The data of the study reports for Marketing Authorization was anonymized and consolidated into a confidential database which was established as part of the ABIRISK project and is located in the Paul-Ehrlich-Institut. This database is not public.

References

1. European Medicines Agency. Guideline on the Clinical Investigation of Recombinant and Human Plasma-Derived Factor VIII Products. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2011/08/WC500109692.pdf. Accessed May 30, 2016.
2. Fischer et al., Prospective observational cohort studies for studying rare diseases: the European PedNet Haemophilia Registry. Haemophilia (2014), 20, e280–e286,

Results

Patient distribution to centers and countries

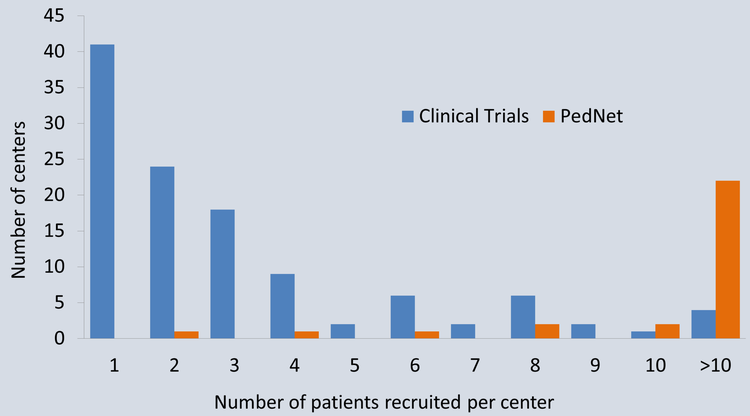

Fig. 1
Number of centers that recruited a particular number of patients. In clinical trials 83 of 115 centers recruit 3 patients or less whereas in PedNet 24 of 29 centers were able to recruit 10 patients or more.

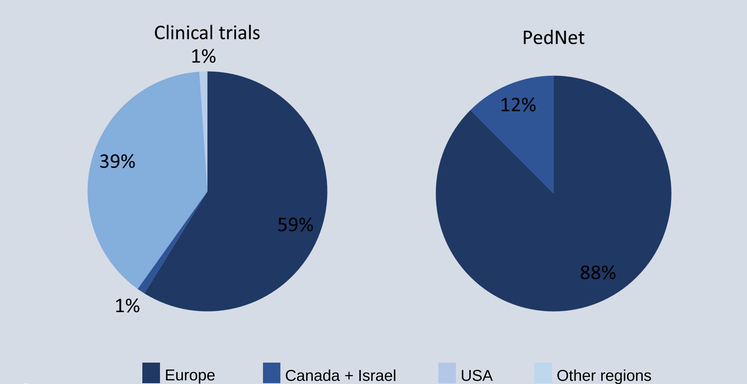

Fig. 2
The distribution of patients to countries shows that within the PedNet registry 88% of patients are treated within one of the centers located in Europe, for the patients recruited in clinical trials 59% of the patients are treated in Europe and 39% in the United States of America.

Patient characteristics

Tab. 1
Comparison of documentation of patient characteristics from both data sources.

Patient characteristics	Clinical trials	PedNet
Total number of patients	369	633
Gender	359 male 1 female 9 not available	630 male 3 female
Family history of hemophilia		
No	36%	54%
Yes	46%	43%
Not available	18%	2%
Age at first treatment		
Available	86%	97%
Not available	14%	3%

Conclusions

- The number of patients recruited per center in clinical trials in 83 of 115 centers is 3 patients or less whereas in PedNet 24 of 29 centers were able to recruit 10 patients or more, implying that more variability could be expected regarding the outcome of the clinical trials.
- The guideline[1] indicate that the study should reflect the population in the countries where the product is intended to be marketed. It seems that more patients from the PedNet are treated in Europe than patients participating in clinical trials (88% versus 59%).
- In PedNet more patients have a negative family history than in clinical trials (54% versus 36%).
- The comparison of selected key parameters derived from clinical trials and PedNet reveals that registries allow for more homogenous data collection.

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