and groups of events that occurred at disproportionally high frequencies were identified as potential SDRs; p values for the potential SDRs were estimated with Monte-Carlo, permutation-based methods.

Results: For itraconazole, the TBSS identified SDRs for injury and poisoning (7 and 28 day $p = 0.001$) and complications of an implanted or grafted device (7 day $p = 0.001$). Coronary atherosclerosis and other heart disease ($p = 0.002$) and diseases of the circulatory system ($p = 0.01$) were identified at 28 days. Terbinafine use was associated with SDRs for diseases for the circulatory system (7 and 28 day $p = 0.001$) and heart (7 day $p = 0.026$ and 28 day $p = 0.001$), as well as bacterial and viral infection ($p < 0.05$). Use of both drugs was associated with SDRs for diseases of the digestive system ($p < 0.05$).

Conclusions: TBSS identified potential SDRs related to the circulatory system that may reflect the cardiac risk that was described in the itraconazole product label. Two previous signal detection analyses for terbinafine also reported SDRs for diseases of the digestive system (Kulldorff 2013, Brown 2013). Consistency with the known safety profile of these antifungals and with previous analyses supports wider exploration of the TBSS for safety surveillance in longitudinal electronic healthcare data.

751. Does Patient Reporting Lead to Earlier Detection of Drug Safety Signals? *A Retrospective Study in an International Database of Spontaneous Reports*

Leàn Rolfes[1,2], Florence van Hunsel[1,2], Ola Caster[3,4], Henric Taavola[3], Katja Taxis[2] and Eugène van Puijenbroek[1,2]

[1]*Netherlands Pharmacovigilance Centre Lareb's Hertogenbosch, Netherlands;* [2]*University of Groningen, Groningen, Netherlands;* [3]*Uppsala Monitoring Centre, Uppsala, Sweden;* [4]*Stockholm University, Kista, Sweden*

Background: Patient reporting has been suggested to lead to earlier detection of drug safety signals in pharmacovigilance (PV). If patient reporting indeed triggers early signal detection, PV-centres may use this information to prioritize their activities.

Objectives: To assess whether there is a difference in time to reporting between patients and healthcare professionals (HCPs) of adverse drug reactions (ADRs) which have led to drug safety signals.

Methods: This was a retrospective cohort study to compare the difference in time to reporting between patients and HCPs, using the WHO global database of individual case safety reports, VigiBase. Drug-ADR associations were selected by using 60 associations described in comprehensive and well-grounded safety signals disseminated by the Dutch PV centre Lareb between 2011 and 2015. These signals included 18 Important Medical Events (IMEs) and 42 non-IMEs. The primary outcome was the difference in time to reporting between patients and HCPs. The secondary outcome was the difference in time for signals characterized as IMEs, since these may deserve priority over other ADRs. Additionally, given the known differences in the start of patient reporting in PV in the USA (since 1969) and Europe (mainly since 2012), we analysed results from the USA and Europe separately. Since we were primarily interested in the overall difference between the two groups, the date of the first report for each individual signal was used as time zero. Statistical differences in timing were analysed on the corresponding survival curves using the Mann-Whitney U test.

Results: In total 2822 reports were included, of which 52.7% patient reports. The 18 IMEs included 556 reports (31.5% patient reports) and the 42 non-IMEs 2266 reports (57.9% patient reports). Of all included reports, 2124 were from the USA (61.9% patient reports) and 430 from Europe (21.9% patient reports). Overall, HCPs reported significantly earlier than patients: median 7.0 vs 8.3 years ($p < 0.001$). Similar results were found for IMEs, where HCPs and patients took a median time to reporting of 6.9 vs 8.1 years ($p < 0.001$) and for non-IMEs 7.0 vs 8.2 years ($p < 0.001$). For the USA, median time to reporting was 6.0 vs 8.1 years (p value < 0.001) and for Europe 7.8 vs 7.9 years (p 0.03).

Conclusions: ADRs related to drug safety signals were in general reported earlier by HCPs compared to patients. In depth analysis is needed to clarify the practical importance of these findings.

752. Proton Pump Inhibitor Use and Risk of Developing Alzheimer's Disease or Vascular Dementia

Patrick Imfeld[1,2], Michael Bodmer[3], Susan S. Jick[4] and Christoph R. Meier[1,2,4]