Incidence of heart failure following exposure to a Protein Kinase Inhibitor (PKI), a French population-based study.

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Abstract

Aims Protein kinase inhibitors (PKI) have revolutionized the prognosis of several types of cancer, justifying the acceleration of their clinical evaluation before they obtain marketing authorization. Pharmacovigilance signals of heart failure (HF) following exposure to PKIs have been detected in recent years. Our objective was to identify the PKIs most frequently associated with the development of HF. Methods Using the French National Healthcare Database, all patients newly exposed to a PKI between January 2011 and June 2014 were followed up for 18 months. Specific hospitalisation diagnosis and long-term disease codes related to HF were used to identify HF patients. HF Incidence Rate Ratios (IRR) were measured and adjusted Hazard Ratios (aHR) were estimated using a Cox model. Results Thirteen PKIs were studied. Among the 49,714 new PKI users during the study period, the mean IRR of HF was 3.38 per 100 person-years, with a median time to onset of 155 days. We found a significant increase in the incidence of HF for 6 drugs: pazopanib (aHR= 2.42, 95% CI: 1.67-3.52), dasatinib (aHR= 2.22, 95% CI: 1.42-3.44), ruxolitinib (aHR= 2.11, 95% CI: 1.69-2.64), crizotinib (aHR= 1.71, 95% CI: 1.07-2.72), everolimus (aHR= 1.45, 95% CI: 1.26-1.67) and vemurafenib (aHR= 1.37, 95% CI: 1.01-1.86). Conclusions Our study provides knowledge on HF following exposure to a PKI. Additional studies could confirm these results for dasatinib, everolimus, pazopanib and ruxolitinib, and particularly for the two drugs with results slightly above the significance threshold, crizotinib and vemurafenib in our sensitivity analyses.

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