RISK OF MORTALITY BETWEEN BIOSIMILARS AND ORIGINATOR OF EPOETIN ALFA USERS IN ONCOLOGY: AN ANCILLARY COHORT STUDY

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Increased mortality in cancer patients on erythropoiesis-stimulating agents (ESAs) has been showed in a meta-analysis of RCT (Bohlius et al, 2006). However, the risk difference on mortality by different ESAs (whether they are biosimilar or not) was not investigated. A recent comparative observational study highlighted a lower risk on mortality of biosimilars compared to the epoetin alfa originator over a six months follow up, which was on the margin of statistical significance deserving further investigation on potential unmeasured confounding (Trotta et al., 2017). The aim of this ancillary study was to investigate the risk of mortality associated with biosimilars when compared with epoetin alfa originator in naïve patients from the oncology setting. This was an observational, record-linkage multi-database cohort study. Data on ESA use were acquired among patients with cancer from the regional Electronic Therapeutic Plan register between 2012 and 2014. To control for potential residual confounding, information on tumour site and anticancer chemotherapy were retrieved other than previously identified baseline characteristics. Tumour staging was also estimated through an algorithm developed on the basis of health information systems. The outcome was obtained from mortality registry which also include cause of death defined in accordance with the International Classification of Diseases (9th revision). Patients were considered exposed from the first ESA dispensation up to 1 year follow up (intention to treat approach); an as treated analysis was planned as sensitivity analysis. Hazard Ratios of mortality was estimated via a Cox proportional hazards model. Cause-specific mortality was also investigated. A cohort of 2,070 incident users of epoetin alpha was available for the analysis. The use of biosimilars in naïve patients accounted to 21.9% of the cohort. Patients exposed to biosimilars and originators can be considered comparable for baseline characteristics, except for age (68.5 vs 67.1 year), prevalence of lymphatic tumour (22.1% vs 18.1%) and use of targeted antineoplastic drugs (19.9 % vs 15.5%). Replicating the six months analysis and adjusting for new confounders it has been observed a HR of 0.85 (IC95% 0.72-1.00) which was comparable with the previous analysis. When one-year of follow-up was considered this risk estimate became fully balanced between the groups (HR 0.95, (0.80 to 1.13)). Considering cause specific mortality a one-year risk of 0.91 (IC95% 0.79-1.05) for tumour causes and of 1.09 (IC95% 0.35-3.42) for cardiovascular causes were observed. Results of this ancillary study confirm that the risk of mortality is similar between epoetin alpha biosimilars and originator. This study substantiate that information on tumour type and anticancer chemotherapy contribute to residual confounding. These preliminary results should be confirmed through the as treated analysis.

Bohlius et al.(2006). J Natl Cancer Inst. 98: 708-14.

Trotta et al. (2017). BMJ Open. 7.