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POSTER ABSTRACTS

101.RED CELLS AND ERYTHROPOIESIS, EXCLUDING IRON

Hospitalization for Infection in Patients with Primary Autoimmune Hemolytic Anemia Treated with Rituximab. a Prospective, Nationwide Cohort Study in France

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Introduction

Autoimmune hemolytic anemia (AIHA) is a rare disease caused by the production of autoantibodies directed against red blood cells. Infections are frequent and severe in patients with primary AIHA. Rituximab is the reference second-line treatment for warm AIHA and the basis of the treatment of symptomatic cold agglutinin disease. However, the risk of infection after rituximab is not known in these patients with primary AIHA the real-world. Opportunistic infections had been described and the use of specific prophylaxis is debated. Consequently, this cohort study aimed to: (i) measure the incidence of hospitalization for infection after the exposure to rituximab in adult patients with primary AIHA; (ii) describe the types of these infections; (iii) measure the 30-day overall mortality after the first hospitalization for infection; (iv) determine the factors associated with hospitalization for infection; and (v) assess the effectiveness of pneumocystis prophylaxis.

Methods

Patients were selected from the AHEAD cohort *(Autoimmune HEmolytic Anemia: a population-baseD study)* between January 2012 and July 2018. This cohort consists in all adult patients with incident AIHA, selected in the French National Health Database. This database covers virtually the entire French population (67 million individuals). It links socio-demographic, outpatient, and hospitalization data. Patients with AIHA were identified using the International Classification of Diseases, tenth version (ICD-10) D59.1 code as hospital discharge or long-term disease diagnosis (the latter being coded by general practitioners). Incident cases were selected using a prior observation period of at least 2 years without the D59.1 diagnosis code. This code yielded a positive predictive value of 90.0% (95% CI: 79.5 to 96.2) in a previous validation study. We restricted the study population to adult patients exposed to rituximab. The first infusion of rituximab defined the index date. Patients with causes of secondary AIHA before the index date were excluded. We assessed the cumulative incidence of hospitalizations with a discharge diagnosis of infection during the six months after the index date (median duration of B-cell depletion). The overall mortality was measured during the 30 days after hospitalization for infection. We assessed the association of age, sex, comorbidities, red blood cell transfusions before the index date (as indicator of AIHA severity), exposure to corticosteroids, to other immunosuppressive drugs, splenectomy (time-varying exposures) as well as pneumococcal and influenza vaccinations before the index date on the occurrence of hospitalization for infection using Cox regression models. A sensitivity analysis was performed using Fine and Gray's models with death as competitive risk. Pneumocystis pneumonia was identified using the B48.5 and B59 discharge diagnosis codes. The association with specific prophylaxis was assessed.

Results

Between 2012 and 2018, we identified 959 adult patients with incident primary AIHA who received rituximab. The mean age was 67 years and 61% of the patients were women. The 6-month cumulative incidence of hospitalization with a discharge diagnosis of infection was 18.3% (95% CI: 15.9 to 20.9). The most frequently characterized infections were pulmonary, urogenital, and gastrointestinal. Opportunistic infections were observed in 28 (16.6%) patients. The 30-day overall mortality after the first hospitalization for infection was 12.5% (95% CI: 8.0 to 18.0). The risk factors associated with hospitalization for infection in multivariable analysis were an age ≥70 years (HR: 2.7; 95% CI: 1.6-4.6) and current exposure to corticosteroids (HR: 1.6; IC 95%: 1.2-2.2). The results of the sensitivity analysis were concordant. In total, 189 (19.7%) patients were exposed to pneumocystis prophylaxis and 14 pneumocystis pneumonia occurred. All cases occurred during the exposure to corticosteroids and in patients with no specific prophylaxis. All but 2 were aged ≥70 years.

Conclusion

The incidence of hospitalizations for infection and mortality after hospitalization for infection were high in adult patients with primary AIHA treated with rituximab. Opportunistic infections were not uncommon. Concomitant exposure to corticosteroids and an older age are the main risk factors for infection. Pneumocystis prophylaxis should be discussed for these patients.

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OffLabel Disclosure: Rituximab for the treatment of AIHA

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