P1372 REAL-WORLD RETROSPECTIVE ANALYSIS OF INFECTIOUS COMPLICATIONS AFTER RUXOLITNIB USE IN ACUTE AND CHRONIC GRAFT-VERSUS-HOST DISEASE

Topic: 22. Stem cell transplantation - Clinical

Cátia Sol Reis1, Delfim Duarte1, Inês Brito1, Pedro Silva Coelho1, Luís Leite1, Rosa Branca1, Susana Roncon2, Carlos Pinho Vaz1, António Campos1

1 1. Bone Marrow Transplantation Service, Instituto Português de Oncologia do Porto IPO-Porto, Porto, Portugal; 2. Cellular Therapy Service, Instituto Português de Oncologia do Porto IPO-Porto, Porto, Portugal

Background: Graft-versus-host disease (GvHD) is a major complication of allogenic stem-cell transplantation. Recent randomized trials (REACH2 and REACH3) demonstrated efficacy of the selective JAK1/2 inhibitor ruxolitinib (Ruxo) in steroid-refractory acute (aGvHD) and chronic GvHD (cGvHD) treatment (tr). JAK/STAT signalling is key in the immune response against infection. Therefore there is a putative additional risk of clinically relevant infections in GvHD patients (pts) receiving Ruxo.

Aims: Real life assessment of Ruxo toxicity in GvHD pts, focusing on infection.

Methods: Unicentric retrospective review of GvHD pts who started Ruxo from January 2019 to August 2021.

Results: Included 47pts, median age at Ruxo start 43years [4-66], 7 paediatric, 67%man. Primary disease was haematological malignancy in 90%; even distribution of donor type; myeloablative conditioning in 55%. Ruxo was started for aGvHD in 4pts and for cGvHD in 43pts – these 77% had previous aGvHD. The median follow-up since Ruxo start was 9months [0-37].

Of the 4 pts with aGvHD: 4 had digestive and 3 skin involvement; in 2pts, Ruxo was started after steroid failure, other 2pts as third line. Of the 43pts with cGvHD: 20 had skin, 12 pulmonary, 11 hepatic, 11 ocular, 9 digestive, 8 articular and 3 mucosal involvement with most pts (77%) experienced multiple GvHD involvement. On average, 3 or more treatments per pts [1-5] were attempted before initiating Ruxo.

The median duration of Ruxo exposure was 7months [0-37]. 75%pts (n=35) developed 76 episodes of infectious complications, 58% (n=44) with grade≥3 severity. The median time to first infection grade≥3 was 1,5months. In general, most infections had respiratory origin (37%) followed by urinary tract (16%). In 61% of episodes no infectious agent was identified. A total of 5 episodes resulted in septic shock. Cytomegalovirus (CMV) reactivation occurred in 18pts (38%) and 1pt also had systemic adenovirus infection. None did prophylactic antiviral for CMV reactivation. Invasive fungal infection was observed in 7pts (15%; 2 probable and 5 confirmed) - 3 of these pts did antifungal prophylaxis.

Other toxicities included haematological (n=14, 29%; n=3 grade≥3), increased AST/ALT (n=8, 17%; n=3 grade≥3) and increased GGT (n=4, 8.5%; n=2 grade≥3).

Treatment discontinuation occurred in 17pts (36%) – most commonly due to toxicity (n=8; 17%) and lack of efficacy (n=4; 8.5%). A total of 20pts (43%) died. Most deaths were attributed to GvHD progression (n=10; 21%) followed by infection (n=6; 13%). On multivariate analysis, only infection grade≥3 had statistical impact on mortality (p=0.027; HR 10.037).

Summary/Conclusion:
Infectious complications in our cohort were higher than the incidence reported in REACH2 and REACH3 – particularly severity grade≥3 infections which may reflect Ruxo use in a previously heavily treated population, with higher steroid doses than used in clinical trials. Infections included bacterial, viral and fungal, likely due to Ruxo interference with innate immunity. This subset of pts might benefit from CMV-directed prophylaxis. A careful assessment of infectious risk and antimicrobial prophylaxis could be beneficial in some.

Our study is limited by its retrospective design. Well-designed studies focused on Ruxo-associated infection risk are warranted to correctly evaluate this risk and to define a solid evidence-based infectious prophylactic strategy.