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INFECTIOUS RISK OF RELAPSED/ REFRACTORY MULTIPLE MYELOMA PATIENTS TREATED WITH BISPECIFIC ANTIBODIES

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Background

Background: T cell engaging therapies are an alternative for multiple myeloma patients (pts) with refractory disease. CD3/BCMA and CD3/GPRC5D Bispecific Antibodies (BsAb) represent promising off-the-shelf options. However, the infectious toxicity related to prolonged cytopenias, hypogammaglobulinemia and T-cell exhaustion is high. Real world data over infectious risk in this population is scarce.

Purpose

To evaluate incidence and severity of infections in multiple myeloma pts treated with commercially available BsAb in a heavily pretreated population.

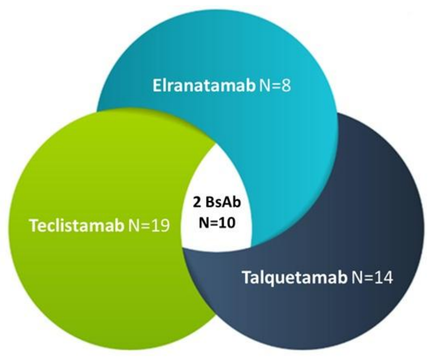
Methods

Unicentric, retrospective analysis of pts receiving CD3/BCMA and/or CD3/GPR5CD BsAb in a tertiary Portuguese Hospital, in regard to number and severity of infections, and correlation with length of BsAb exposure, subtype, number of prior lines, prior autologous transplant, prolonged cytopenias and prophylactic measures. Descriptive and statistical analysis were performed using SPSS.

Results

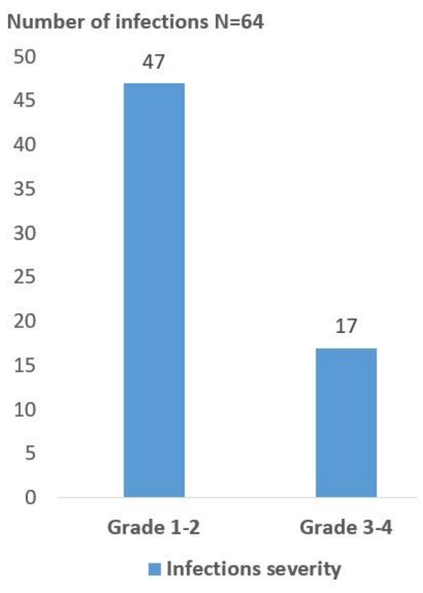
Thirty one pts were included with >3m of exposure to a BsAb, 10 of them treated consecutively with BsAb with two different targets. Median age was 68 [40-84] years, 20 (64%) were male and majority had IgG kappa (17, 55%). Patients received ⩾ 3 prior lines, including autologous transplant (11, 35%), and 9 (30%) received ⩾ 5 lines.

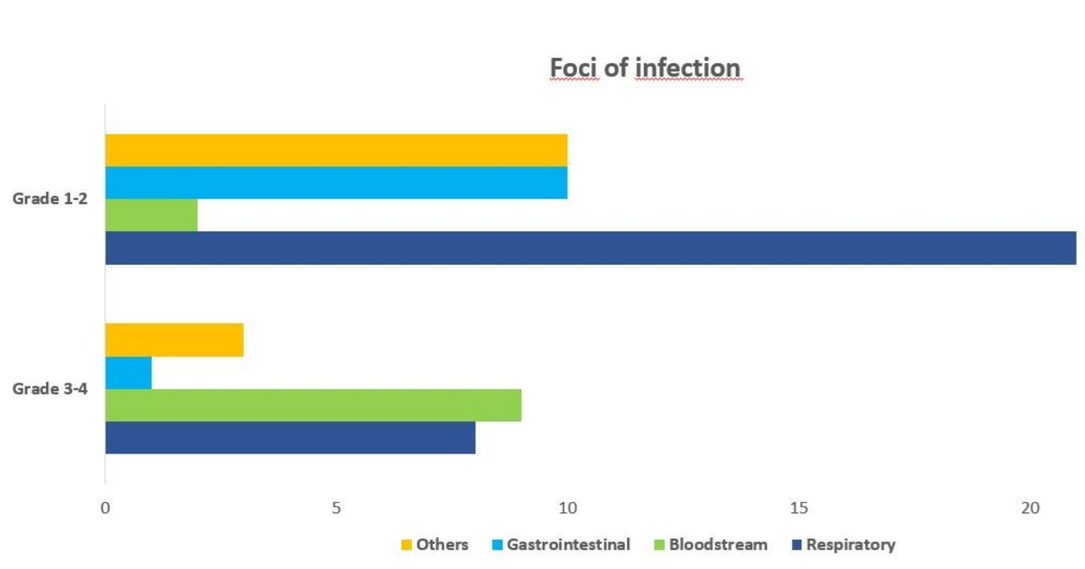
Total of Patients (N)	31 patients
Gender - Male - Female	 N= 20 N= 11
Median age	68 years [40-84]
Multiple Myeloma Subtype	IgG Kappa N=17 CLL Kappa N=6 IgA Lambda N=5 Others N=31
Previous Lines - ≥3 - ≥5	 N=31 N= 9



All received prolonged antiviral and anti-pneumocystis prophylaxis. Antifungal was used in some cases. Immunoglobulin was replaced after first infection (14, 45%) or if serum IgG<400mg/dL (11, 35%). GCS-F support was used in 10 (32%)pts.

During a total exposure time of 389m (median 10.9m per patient), 64 infectious episodes were observed in 26 patients (84%), representing an incidence of 0,19 patient-month. The median number of infections per patient was 2 [0-5] episodes, with 13 (42%) presenting ⩾ 3 episodes or one event G3 or higher. Regarding severity, 47 (74%) were G1-2, 17 (26%) G3-4, no fatal events were recorded. Most common foci of infection were respiratory (47%), followed by bloodstream (17%), gastrointestinal (15%) and others (21%). An etiologic agent was identified in 33 (51%) episodes: 48% bacterial, 45% viral (including *influenzae A* and *B, Sars-Cov2, Syncytial Virus, HHV7, Poxvirus, Cytomegalovirus* and *JC virus*) and 2 pts had a fungal infection. Patients who presented ⩾ 3 infectious episodes or one event ⩾G3 (13) were evaluated for predisposing factors (multiple myeloma subtype, number of previous lines, prior therapy) however none of these parameters were statistically significant in this cohort.





Conclusions

Despite close monitoring and prophylactic measurements, multiple myeloma patients exposed to BsAb are at high risk for infection, that is maintained over exposure time. Sequential T-cell redirecting therapies might increase infectious risk, however alternative options are scarce. The evaluation of larger cohorts and longer follow-up are necessary to identify predisposing factors and allow definition of guidelines for safer application of these newer therapies.

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