Rituximab intolerance in Waldenström Macroglobulinemia

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Introduction

Rituximab is a chimeric anti-CD20 monoclonal antibody commonly used alone or in combination for the treatment of patients with Waldenström Macroglobulinemia (WM).

Rituximab is an efficacious therapy for WM but has been associated with infusion-related reactions (IRR), especially during the first infusion.

Rituximab has also been associated with an increased risk of infections due to hypogammaglobulinemia.

In this study, we present data on patients who developed intolerance to rituximab defined as the need of stopping rituximab therapy outside of the context of first-cycle IRRs, recurrent infections or severe hypogammaglobulinemia.

Methods

We performed a retrospective chart review within the database of our institution looking for cases with a clinicopathological diagnosis of WM between 1996 and 2013 (n=1,600 records).

Key inclusion criteria were patients >18 years either untreated or previously treated in whom rituximab therapy had to be stopped.

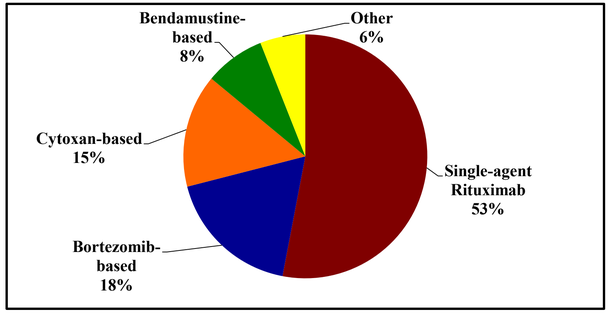
Methods (Continued)

We excluded patients who experienced first-cycle IRRs and patients in whom rituximab was stopped due to severe hypogammaglobulinemia or the onset of recurrent or life-threatening infections.

Sixty-seven patients were identified who met the above criteria. Clinical and laboratory data were collected and tabulated, and are presented using descriptive statistics.

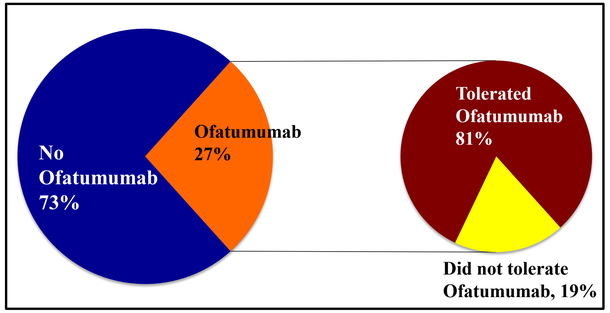
Results

Characteristics (N=67)	Number (%)
Age at WM diagnosis, median (range)	60 (31-85)
Age at intolerance, median (range)	64 (40-86)
Men	42 (63%)
Previous lines, median (range)	1 (0-5)
Previous rituximab	39 (59%)
IgM at intolerance, median (range)	2,736 (549-9,000)
BM involvement at intolerance, median (range)	50% (5-90%)
Hemoglobin at intolerance, median (range)	10.5 (2.9-14.5)
Familial case	6 (11%)
IgM flare	5 (9%)
Intolerance during induction	51 (78%)
Intolerance during maintenance	14 (22%)
Response at intolerance	40 (69%)



Regimens received by WM patients at intolerance

Symptoms related to rituximab intolerance	
Chills	11%
Hypotension	11%
Hives	11%
Shortness of breath	10%
Anaphylactic reaction	8%
Facial swelling	8%
Rash	8%
Chest pain	6%
Fever	4%
Serum sickness	4%
Bronchospasm	3%
Pneumonitis	3%
Back pain	1.4%
EKG changes	1.4%
Stroke-like symptoms	1.4%



WM patients intolerant to rituximab according to subsequent treatment with ofatumumab

Conclusions

•Rituximab intolerance leading to treatment cessation is common in WM patients, and can be prompted by a variety of symptoms.

•Most patients showed response to rituximab at the time of intolerance.

•The use of ofatumumab is feasible and well tolerated in patients intolerant to rituximab.

•Additional research is needed to better understand the pathophysiology behind rituximab intolerance.

Disclosures

The authors have no conflict of interest to disclose.