

## Background

- Pemphigus is a life-threatening autoimmune blistering disease, which is mediated by autoantibodies directed against desmoglein 1 and 3
- Patients often require long-term high-dose corticosteroid therapy which frequently causes adverse effects. Immunosuppressive agents and/or intravenous immunoglobulin (IVIG) are used concomitantly with steroids
- Rituximab, a chimeric murine-human monoclonal antibody that targets the CD20 antigen found on B cells resulting in rapid depletion of B cell population, has been used in various autoimmune diseases
- Although rituximab is not indicated in Canada for the treatment of pemphigus, a single cycle of rituximab (1 cycle of four weekly infusions at a dose of 375 mg/m<sup>2</sup> on days 1, 8, 15, and 22) has been studied in patients with severe pemphigus
- In patients with rheumatoid arthritis, rituximab is administered at a dose of 1000 mg on days 1 and 15
- We hypothesized that the latter protocol would also be effective in pemphigus

## Objective

- To determine whether rituximab at a dose of 1 g on days 1 and 15 is an effective treatment for patients with severe recalcitrant pemphigus

## Methodology

### Treatment

- Rituximab was administered as 1g IV infusion on Days 1 and 15 with 100mg methylprednisolone before each infusion. Corticosteroids and other immunosuppressive agents and IVIG therapy were maintained during the rituximab therapy.

## Patients

- Nine patients with severe pemphigus vulgaris (n=8 or pemphigus foliaceus (n=1) were administered rituximab between January 2008 and August 2008.

## End point

- Each patient was observed for a minimum of six months
- Primary endpoints were dose of corticosteroids (prednisone), whether IVIG therapy was discontinued, the time to partial or complete remission, the number of relapses, and adverse events of treatment

## Statistical analysis

- Basic descriptive statistics were used to characterize the patient population.
- The percentage change in prednisone dose at 1, 3, 6 months after rituximab infusion was calculated. Single-sample paired t-tests were conducted to determine the significance in mean values between treatment time frames.

## Results

Patient Characteristics

Patient No.	Age (yr)	Sex	Diagnosis (ICD-10)	Duration of disease (yr)	Pre-treatment therapy at baseline (mg/d)	Previous immunosuppressive agents	IVIg therapy (subcutaneous/intravenous)	Medication at enrollment	Study treatment
1	43	F	IV	20	MMF	None	Yes	Oral prednisone	No other drugs, azathioprine, azelaic acid
2	42	F	IV	10	MMF	None	Yes	Oral prednisone	None
3	43	F	IV	10	MMF	None	Yes	Oral prednisone	None
4	44	F	IV	22	None	None	None	Oral prednisone	None
5	28	F	IV	10	MMF	None	Yes	Oral prednisone	None
6	48	F	IV	10	MMF	None	Yes	Oral prednisone	None
7	28	F	IV	10	MMF	None	Yes	Oral prednisone	None
8	48	F	IV	11	None	None	None	Oral prednisone	None
9	42	F	IV	22	None	None	None	Oral prednisone	None

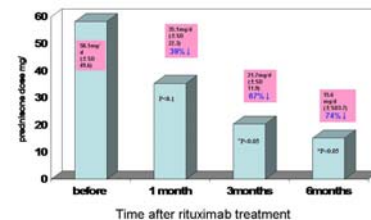
Patients 2 and 4 were admitted to burn unit prior to receiving rituximab.

IV: pemphigus vulgaris, PF: pemphigus foliaceus, MMF: mycophenolate mofetil, HT: hydroxychloroquine

## Response with Rituximab

Response at 6 months	
Complete response (>50% epithelialization)	4 patients
Partial response (>100% epithelialization)	4 patients
Response at 12 months	
Complete response (>50% epithelialization)	3 patients
Partial response (>100% epithelialization)	3 patients
Recurrence	
4 patients had severe recurrence	5 mths (1), 12 mths (2), 13 mths (1)
Second cycle of rituximab	3 patients completed 2 <sup>nd</sup> cycle; 1 pt awaiting approval

## Mean Dose of Prednisone after Rituximab



## Change in circulating pemphigus antibody

	baseline	1 month	3 months	6 months	12 months	Status after 12 months
Case 2	1:160	not done	negative	negative	negative	Flare at 13 months; awaiting second cycle rituximab
Case 3	1:40	not done	negative	negative	not done	Doing well (mild oral lesions only)
Case 9	1:320	1:80	1:80	1:160	not done	Flare on cheek/oral at 6 mths; received second cycle rituximab

## Conclusions and Discussion

- The dose of prednisone was significantly decreased (75% from baseline) following rituximab treatment.
- Of the 6 patients who were receiving IVIG prior to rituximab, 3 patients (50%) stopped IVIG after 6 months. For the 8 patients on mycophenolate, no change in dose was observed at the end of the observation period. Azathioprine was discontinued in one patient.
- All patients had partial response initially between 4-12 weeks. At the end of the observation period (minimum 12 months), 3 out of 9 patients (33%) were in complete remission, 3 were in partial remission (33%) and 4 had recurrence (one patient had recurrence at 5 months and subsequently had complete response).
- Four of the 9 patients (44%) had recurrence requiring a second cycle of rituximab.
- We did not observe any serious adverse effects during the study period. One patient developed pneumonia at 7 months, which resolved with a course of oral antibiotics.
- A single cycle of rituximab 1 g on days 1 and 15 is an effective and safe treatment for patients with recalcitrant pemphigus, although almost half of our patients required a second cycle of rituximab. Most published studies and case reports have used 375 mg/m<sup>2</sup> for four weeks. However, our study provides encouraging results for the use of an alternative regimen that requires only 2 infusions.

## References

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## Disclosures

The authors have no conflicts of interest or competing financial interests with regards to this poster.