

Rituximab in the Treatment of Pemphigus: Outcome in 38 Patients Treated in Texas

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Pemphigus: Background

- Current treatment unsatisfactory
- Oral corticosteroids often fail to produce long term remission
- Oral corticosteroids have many adverse effects
- Rituximab successful for refractory pemphigus in several small reports
- Long term data on rituximab is lacking

Background

- Indications for rituximab therapy from previous studies
 - Patients who have **failed treatment with high-dose prednisone** (1- 1.5 mg/kg/d) for > 3 weeks **with or without adjuvant therapies** (mycophenolate mofetil, azathioprine)
 - **Severe contraindications** to corticosteroid or immunosuppressive therapy

Background

- Dosing of rituximab for autoimmune blistering disorders:
 - Initial cycle:
 - Rheumatoid Arthritis dosing: **Two 1000mg IV given 2 weeks apart**
 - Chronic Lymphocytic Leukemia Dosage: **4 weekly doses of 375 mg/m² IV**
 - Subsequent cycles given if disease activity persists or if unable to discontinue systemic therapy
 - **500 mg IV every 6 months**

Definitions/Outcome Measures

- **Complete Remission (CR):** Absence of new or established lesions while off all therapy for > 2 months
- **CR on minimal therapy:** Absence of lesions on prednisone < 10mg/d and/or minimal adjuvant therapy (half the standard dose) for at least 2 months

Murrell DF, Dick S, Ahmed AR, Pandya AG et al. Consensus statement on definitions of disease, end points, and therapeutic response for pemphigus. JAAD 2008; 58:1043-1046.

Definitions/Outcome Measures

- **Partial Remission (PR):** Clear of lesions off all therapy except for transient new lesions that resolve within 1 week
- **PR on minimal therapy:** Clear except for transient new lesions that resolve within 1 week and on prednisone < 10mg/d and/or minimal adjuvant therapy (half the standard dose) for at least 2 months
- **Relapse/Flare:** Appearance of >3 lesions/month after patient achieves disease control that do not heal spontaneously within 1 week

Murrell DF, Dick S, Ahmed AR, Pandya AG et al. Consensus statement on definitions of disease, end points, and therapeutic response for pemphigus. JAAD 2008; 58:1043-1046.

Study Design

- Aim
 - To determine the efficacy of Rituximab for the treatment of pemphigus vulgaris and foliaceus
- Methods
 - Retrospective chart review of patients with PV or PF who have received rituximab at UT Southwestern and have had at least 9 months follow-up
 - 45 Patients screened
 - **38 patients qualified**
 - **7 disqualified because of lack of sufficient follow-up**

Results- Demographics

- Mean age at infusion: 50 years (range 19 - 77 years)
- 20 Females, 18 Males
- 30 PV, 8 PF
- Median duration of disease before first rituximab infusion
 - 33 months (range 2-187 months)
- Median follow-up time after 1st Infusion
 - 22 months

Results: Cycle 1

- 23 received RA dosing, 15 received CLL dosing
- **26/38 (68%) patients achieved remission**
 - CR in 16 (42%) patients (13 off all therapy, 3 on minimal therapy)
 - PR in 10 (26%) patients (4 off all therapy, 6 on minimal therapy)
 - Time to remission: **3 months** (1 - 7.5 months)
- No response in 12 patients (continued disease or unable to reduce all systemic therapies)
- 28/38 (73%) on adjuvant therapy at time of infusion
- **Mean prednisone dose**
 - **34 mg (4-100mg) at time of infusion → 5 mg at 3-6 months follow-up (75% decrease)**

Results: Cycle 2

- n=29, 25 analyzed (4 lost to follow-up)
- **18/25 (72%) patients achieved remission**
 - CR in 10 (40%) patients (8 off all therapy, 2 on minimal therapy)
 - PR in 8 (32%) patients (4 off all therapy, 4 on minimal therapy)
 - Time to remission: 3 months (1-5)
- No response in 7 patients
- Mean prednisone dose at time of infusion
 - 12 mg (0-60mg)
- 16/25 (64%) on adjuvant therapy at time of infusion

Results: Cycle 3

- **8/10 (80%) patients achieved remission**
 - CR in 2 (20%) patients (1 off therapy, 1 minimal therapy)
 - PR in 6 (60%) patients (4 off therapy, 2 minimal therapy)
 - Time to remission mean: 3 months (2-4 range)
- No response in 2 patients
- Mean prednisone dose at time of infusion
 - 5 mg (0-25)
- 5/10 (50%) on adjuvant therapy at time of infusion

Results: Cycle 4

- **6/6 (100%) patients in remission**
 - CR in 2 patients (1 off therapy, 1 on minimal therapy)
 - PR in 4 patients (2 off therapy, 2 on minimal therapy)
- 3/6 (50%) on adjuvant therapy at time infusion
- Mean daily dose of prednisone at time of infusion
 - 0 mg

Relapse Rates

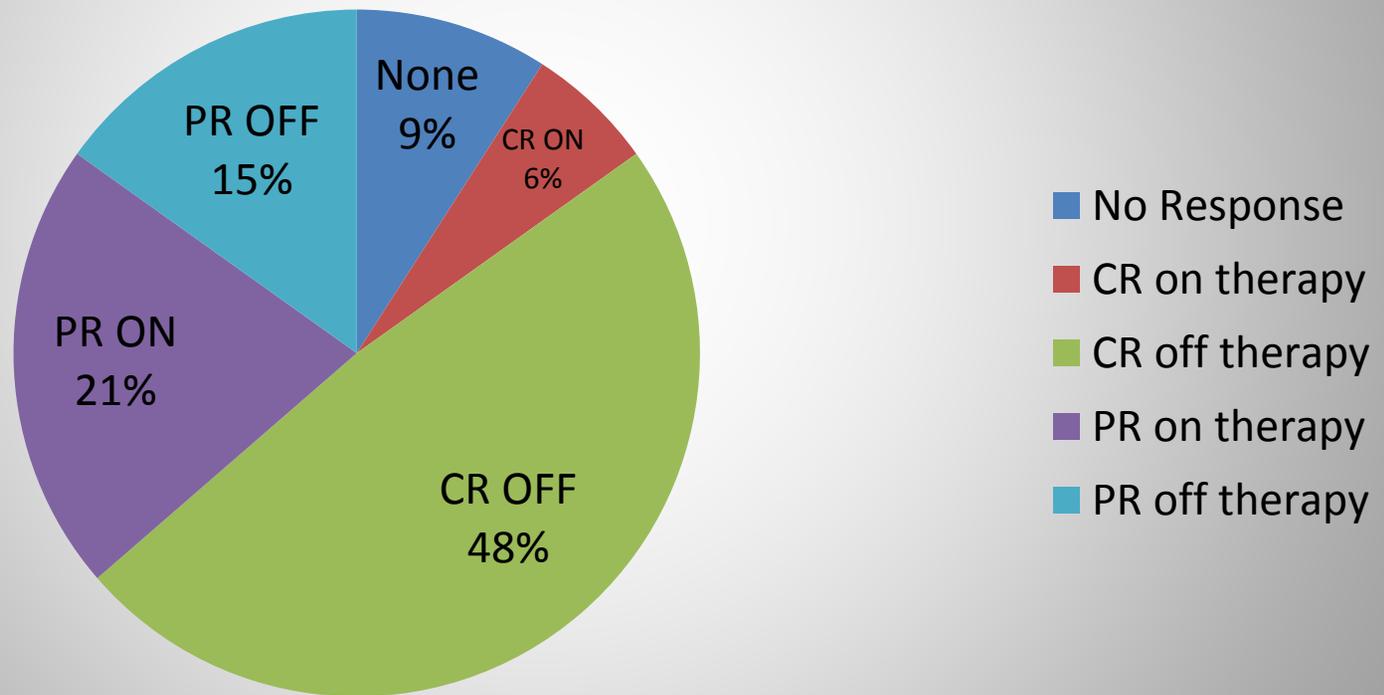
- After cycle 1: 17/26 (65%), mean 11 months
- Cycle 2: 3/18 (18%), mean 12 months
- Cycle 3: 2/8 (20%), mean 12 months
- Cycle 4: 0/5

Patients Receiving additional cycles

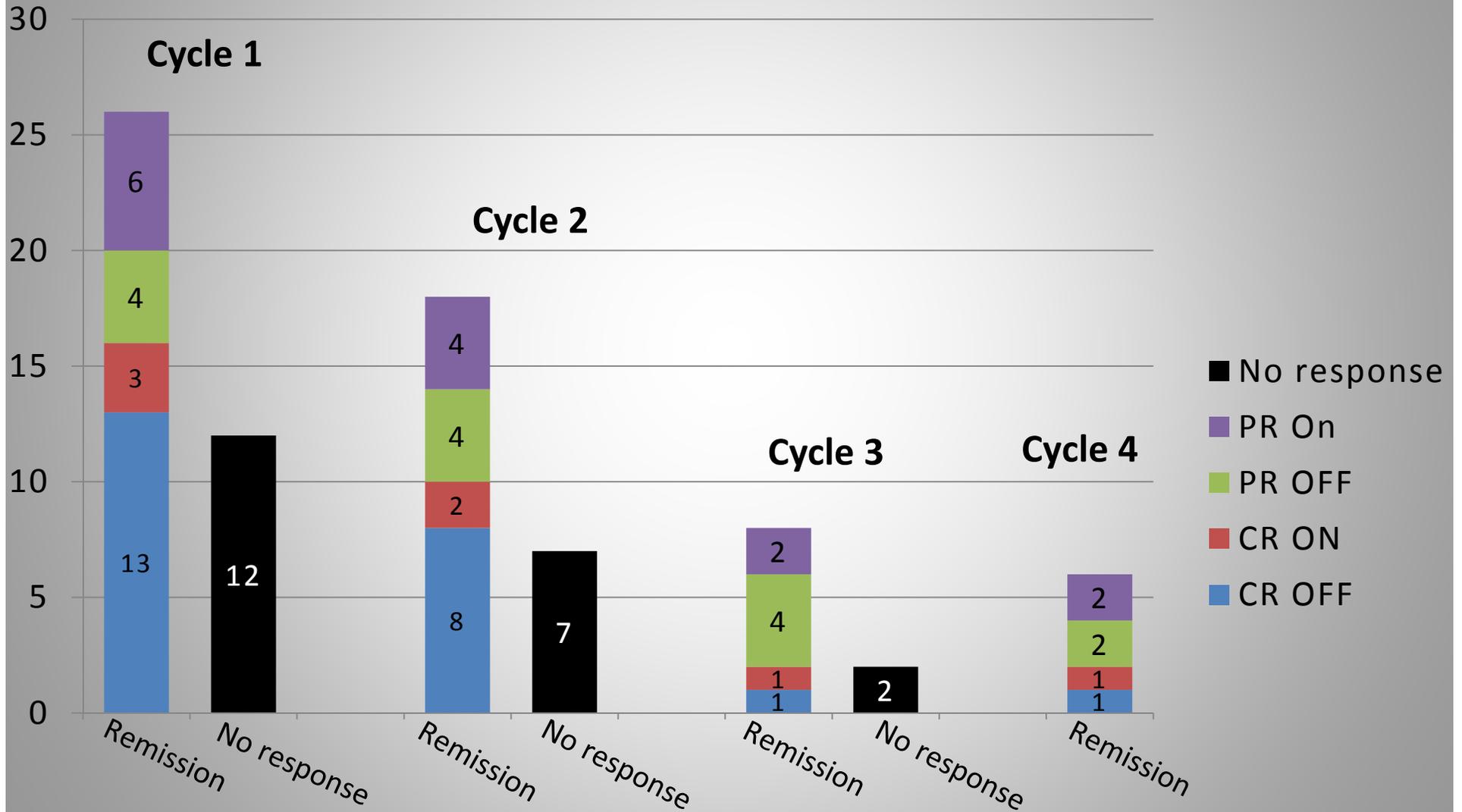
Reason for additional dose	Cycle	Remission	Remission type
No remission in previous cycle	Second (N = 11)	6/11 (54%)	CR= 4 PR= 2
	Third (N = 5)	4/5 (80%)	CR=1 PR=4
	Fourth (N = 2)	2 (100%)	PR=1 CR=1
Relapse after previous cycle	Second (N = 12)	10/12 (83%)	CR=5 PR=5
	Third (N = 3)	2/3 (67%)	CR=1 PR=1
	Fourth (N = 2)	2/2 (100%)	CR=1 PR=1

Remission Rates Overall

Remission Rates (per protocol, n=33)

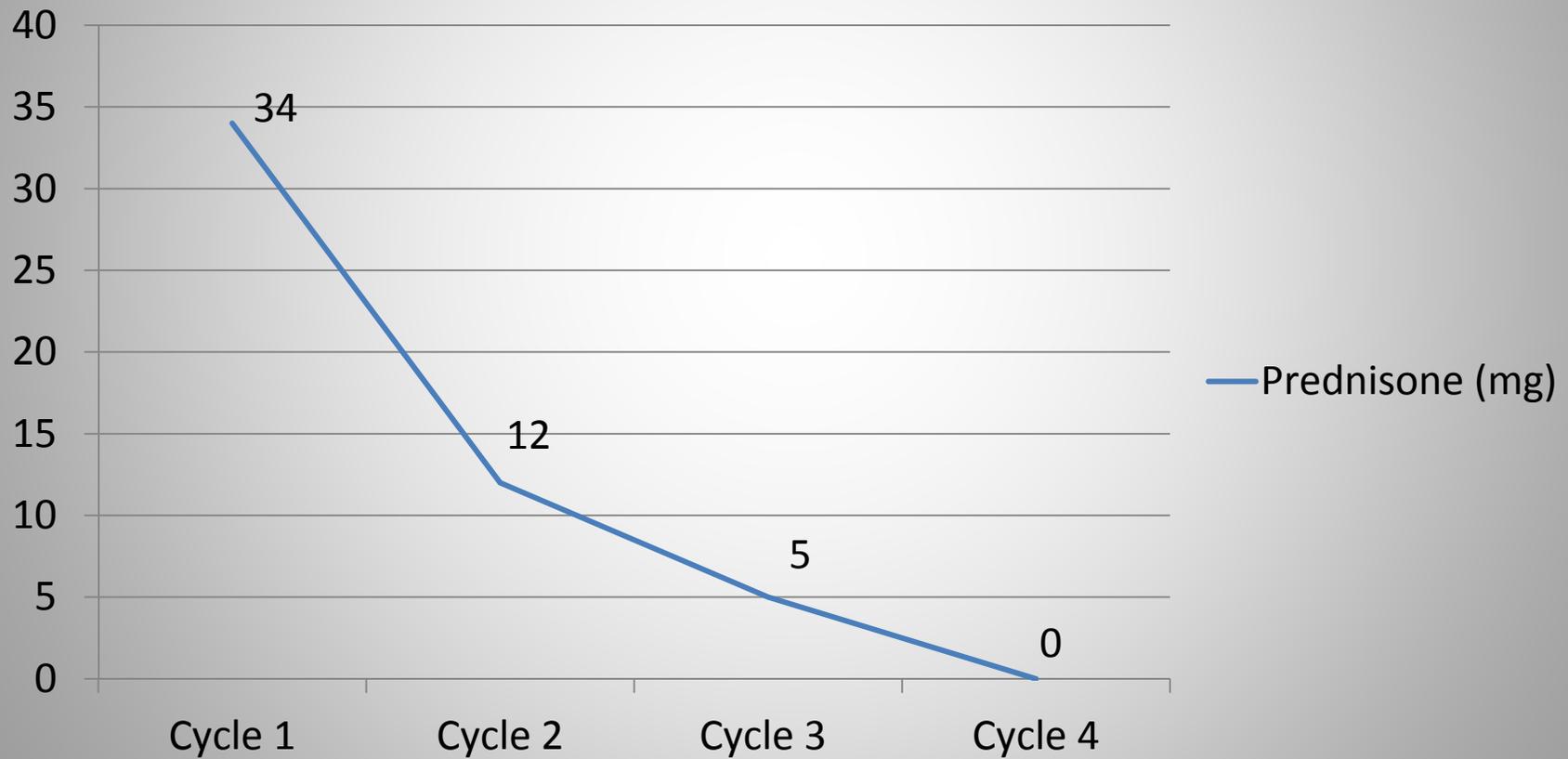


Remission Rates



Mean oral Prednisone Dose

Prednisone (mg), $P < 0.05$





Baseline



2 months



6 months

Summary

- 38 patients treated, 5 lost to follow up
- **Overall remission rate: 90% (30/33)**
- 3 patients with pemphigus foliaceus never achieved remission
 - All 3 patients had substantial improvement of lesions
- Rituximab side effects
 - 2 patients developed Herpes Zoster
 - 6 others with fatigue, myalgias, arthralgias, nausea that resolved shortly after infusion

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