Introduction

With the advent of anti-CD20 monoclonal antibodies, the therapeutics of autoimmune bullous disease have taken a leap in the past decade from more global immunosuppression to targeted immunotherapy. Anti CD 20 monoclonal antibody Rituximab revolutionized the therapeutics of autoimmune bullous disease particularly pemphigus. Though it is still being practiced off-label, evidences in the form of RCT and meta analysis are now available. Other novel anti CD 20 monoclonal antibodies like ofatumumab, veltuzumab, and ocrelizumab, tositumomab or obinutuzumab/GA101 may add to the therapeutic options in coming days. Beyond anti CD 20 monoclonal antibodies other options that show promise at least in select scenario are omalizumab, TNF inhibitors plasmapheresis and intravenous immunoglobulin. The present article will discuss the role of rituximab and other newer therapeutics in the treatment of autoimmune blistering disease, especially pemphigus and suggests their positions in the therapeutic ladder.

Pathogenesis

The basic pathology behind these diseases is generation of autoantibodies to target antigens on keratinocytes and dermo-epidermal junctions. Recent researches have given deeper insight into the molecular mechanisms of blister formation in both pemphigus and pemphigoid. Desmoglein 1 and 3 are the prime targets in pemphigus group of patients,[1] whereas antibodies to certain nondesmoglein antigens such as pemphaxin and anti-mitochondrial antibodies are suggested to play an auxiliary role.[2] Epidermal growth factor receptor kinase, other bullous diseases, this molecule too is not free of typical side effects of immunosuppression such as infections. Although resistance to rituximab is quite uncommon, relapse of the autoimmune blistering disease is very commonly encountered. The present article will discuss the role of rituximab and other newer therapeutics in the treatment of autoimmune blistering disease, especially pemphigus and suggests their positions in the therapeutic ladder.

What was known?

- Anti CD 20 monoclonal antibody Rituximab is very effective in the treatment of autoimmune bullous disease especially pemphigus
- Intravenous immunoglobulin and plasmapheresis are also being used in the treatment of pemphigus beyond conventional medications like steroids and immunosuppressives.

Key Words: Biological treatment, immunobullous disease, rituximab, TNF inhibitors
protein kinases A and C, phospholipase C, mechanistic target of rapamycin, etc., are involved in the cell signaling in response to these antibodies, resulting in blistering eventually.\[^3\] Anti-desmocollin-3 has been shown to have a role in atypical pemphigus. Furthermore, the role of various cytokines such as interleukin-1α (IL)-1α and tumor necrosis factor-α (TNF-α) has been emphasized upon recently.\[^4\]

Bullous pemphigoid (BP) patients have autoantibodies against BP230 and BP180 antigen. These are part of the hemidesmosomal adhesion complex, resulting in subepidermal blister formation. IgG antibody to BP antigen activates complement, leads to mast cell degranulation, neutrophil infiltration of the basement membrane, and subsequent blister formation.\[^5\] Even the role of IgE antibodies against some epitope on BP180 antigen has been shown to play a part in blister formation.\[^6-8\] With these discoveries, many newer drugs have been tried in recent times. Some have shown promise, while others are still in the trial phase. However, rarity of the disease and lack of resources, especially in a country like India, have so far prevented us from conducting larger RCTs, which are the need of the hour.

**Principles of Treatment**

Treatment consists of three phases:
1. Control phase - intensive therapy is given until no new lesions appear
2. Consolidation phase - treatment is continued until the lesions completely clear
3. Maintenance phase - lowest dose of the drug is given to prevent the appearance of any new lesions.\[^9\]

Choice of the drug depends on the severity of the symptoms and its side effects. Treatment must be individualized and chosen carefully depending on patient’s profile, i.e., the presence of comorbidities.

**Conventional treatment**

Corticosteroids have perhaps the best evidence so far as initial treatment to induce remission.\[^10\] Used topically for localized disease and oral or intravenous (IV) for extensive involvement. They are given in doses ranging from 1 to 2 mg/kg body weight and continued till remission is achieved. After achieving remission, the doses are gradually tapered and maintained at lowest possible dose for maintenance. When the response is poor, we need to increase the dose of corticosteroids. However, continuous high doses (HDs) of corticosteroids can produce many side effects such as osteoporosis, sepsis, gastrointestinal problems, hyperglycemia, and hypothalamic-pituitary axis suppression. Hence, they are to be combined with steroid-sparing agents. Role of drugs such as azathioprine, mycophenolate mofetil (MMF), methotrexate, cyclophosphamide, cyclosporine, and chlorambucil as steroid-sparing drug is very important to keep the untoward side effects of bullous disease to the minimal level. At present, a combination of steroids and a steroid-sparing agent forms the standard treatment regimen for most of the immunobullous diseases. However, with the advent of targeted therapeutics including monoclonal antibodies, the role of conventional treatment with corticosteroid and immunosuppressive has been put to challenge in the recent past.

**Newer therapies for immunobullous diseases**

Steroids with other steroid-sparing immunosuppressives form the backbone of management of immunobullous diseases. However, the search for newer therapies has continued, for not all the cases respond to the above therapy, and also to avoid side effects associated with the conventional drugs. As the pathogenesis of immunobullous diseases is becoming clearer, some very promising therapies have been tried in recent times.

**Rituximab**

Rituximab is a chimeric murine/human monoclonal antibody against CD20, a surface antigen present on all B lymphocytes. The molecule targets the B-cells specific CD20 to deplete normal and pathogenic B-cells, while sparing terminally differentiated plasma cells. The drug has been conventionally used for lymphomas and rheumatoid arthritis (RA).\[^11\] The antibody is neither internalized by the B-cell nor shed from the plasma membrane, contributing to its persistence on the cell surface.\[^12\]

Its use in immunobullous diseases is new found and off label. From the data available so far, rituximab has shown great promise in the treatment of recalcitrant pemphigus vulgaris (PV), BP, and mucous membrane pemphigoid (MMP).\[^13\] The drug is clinically well tolerated and encountered with adverse events very rarely. The US Food and Drug Administration (US FDA) approved rituximab usage only in refractory low-grade follicular B-cell lymphoma in 1997 and RA refractory to TNF-α inhibitors in 2006.\[^12\] However, the drug is being used increasingly in immunobullous diseases with encouraging results.

Mechanism of action: rituximab acts by depleting CD20+ B-cells. It acts through three possible mechanisms.\[^14\]

1. Complement-dependent cytotoxicity (CDC)
2. antibody-dependent cell-mediated cytotoxicity (ADCC),
3. Inhibition of signaling and apoptosis of antibody-coated B-cells and eventual shift to a normal B-cell repertoire.

The above mechanisms work to deplete CD20+ mature B-cells. However, it spares the hematopoietic stem cells as they do not express CD20 antigen. Therefore, B-cells
do get regenerated in about 6–12 months after stopping the therapy. Beyond these mechanisms, rituximab has also been found to downregulate autoreactive CD4+ T helper cells indirectly through deprivation of antigen presenting signals.[14]

It is also surprising to find that while there is a fall in anti-desmoglein antibody levels; antimicrobial antibodies’ levels in blood are not affected.[15] Studies suggest that protective antimicrobial antibodies are produced by the long-lived CD20+ plasma cells in the bone marrow, whereas autoreactive antibodies are produced by short-lived CD20+ plasma cells in peripheral compartments.[16] This may explain the comparative lower incidence of infection after treatment with rituximab even after causing B-cell depletion.

**Dosage**

The US FDA recommends two regimens for rituximab:[17]

- a. 375 mg/m² IV infusion once a week for 4 weeks, for non-Hodgkin’s lymphoma
- b. 1000 mg at 2-week interval (D1 and D15) for RA.

A relatively new drug for dermatologists, there are still no consensus guidelines. The most common regimen followed by dermatologists at present is 375 mg/m² administered as a slow IV infusion weekly for 4 consecutive weeks as used in non-Hodgkin’s lymphoma.[17] However, even the rheumatologic protocol is also being followed by many dermatologists.

The evidence for rituximab in the treatment of immunobullous diseases has been promising though large RCTs are needed [Table 1].

Rituximab is now regarded an alternative to the long-term use of systemic steroids and immunosuppressives in patients with pemphigus leading to complete sustained remission as shown in five prospective studies[14,28-31] and in two retrospective cohort studies.[12,35] Ahmed and Shetty analyzed the cumulative data on treatment of PV with rituximab and immunosuppressive and found that clinical remission on rituximab therapy was seen in 90%–95% of patients within 6 weeks. Complete resolution was seen in 3–4 months. However, serious adverse effects, including infection and septicemia, were seen in 4.8%–2.1% of patients in the lymphoma and RA protocols, respectively.[16]

**Monitoring and Therapeutic Guidelines**[20]

1. Complete blood count - every 2 weeks during the treatment and 1–3 monthly afterwards
2. CD20+ B-cell count - in patients developing infections
3. HCV and HBV screening - due to increased risk of reactivation
4. Premedication - acetaminophen and diphenhydramine or 100 mg of methylprednisolone to prevent infusion reactions.

**Adverse effects of rituximab**

Serious adverse events are uncommon with rituximab though infusion-related reactions including anaphylaxis, hypotension, fever, headache, and pruritic rash were reported. Moderate-to-severe infusion reactions occur in 10% of patients during the first infusion.[35] Rituximab increases the risk of infection; data suggest that 19% developed bacterial infections, 10% developed viral infections, and 1% developed fungal infections after rituximab therapy.[36] Side effects reported include hypotension during infusion, sepsis, and herpes zoster in various case reports and case series.[37]

**Relapse and resistance with rituximab**

In a study with rituximab, it was found 9 patients out of 21 patients relapsed, requiring retreatment.[17] Hammers et al. found that persistence of anti-desmoglein -3 B-cell clones contributed to rituximab resistance in patients with PV. Destruction of the remaining clones with additional doses of rituximab or another autoantibody-obliterating agent is, therefore, the goal in treating resistance.[38]

**Tumor Necrosis Factor-α Inhibitors**

The earliest use of this group of drugs has been in recalcitrant cases of MMP.[19] The three drugs in this group, i.e., etanercept, adalimumab, and infliximab have been used traditionally in psoriasis and psoriatic arthritis. The new found use in immunobullous diseases has been backed by evidence suggesting the role of TNF-α in the pathogenesis of pemphigus and pemphigoid. Increased levels of TNF-α along with IL-1β, IL-2, 6, and 10 has been shown in skin/serum of patients with pemphigus and pemphigoid.[40] Their levels correlate with disease activity. Early studies showed promise in treating a fair number of treatment-resistant cases in smaller series and case reports, especially those of cicatricial pemphigoid. However, recent studies have failed to live up to the expectations raised by initial success of TNF-α blockers in the treatment of immunobullous diseases [Table 2]. Larger RCTs may be needed before their role in treatment is established.

**Omalizumab**

Omalizumab is a humanized IgG monoclonal antibody that binds to free IgE in the serum and thus decreases the amount of IgE present for binding to high-affinity IgE receptors (FcεRI receptors) on mast cells, basophils, and other inflammatory cells.[47] This prevents the release of inflammatory mediators from these cells and reduces the inflammatory response. The major dermatological indications of omalizumab have been the treatment of IgE-mediated disorders including severe atopic dermatitis and chronic urticaria.[48] As there are circulating IgE antibodies against BP antigen 2 in BP, there is a role of omalizumab in its management.[49] There are many case
### Table 1: Evidence of rituximab in the treatment of immunobullous diseases

| Study                      | Indication                                      | Number of patients | Results                                                                 | Remarks                                                                 |
|----------------------------|-------------------------------------------------|--------------------|------------------------------------------------------------------------|------------------------------------------------------------------------|
| Schmidt et al. [18]        | PV                                              | 103                | Complete remission - 41 (40%)                                         | 14/103 patients suffered side effects, mostly infections               |
|                            |                                                 |                    | Clinical remission - 38 (37%)                                         | Relapse - 13%                                                          |
|                            |                                                 |                    | Partial remission - 21 (21%)                                         |                                                                        |
|                            |                                                 |                    | No improvement - 3 (3%)                                               |                                                                        |
| Eming et al. [14]          | Extensive PV                                    | 11                 | Marked clinical improvement in all patients. Marked decrease in anti-desmoglein antibody level | No serious adverse effects reported                                    |
| Kasperkiewicz et al. [19]  | Autoimmune blistering dermatosis (pemphigus, bullous pemphigoid) | 17                 | 14 - complete clearance                                               | No serious side effects noted                                           |
| Craythorne et al. [20]     | Recalcitrant oral and cutaneous PV              | 6                  | Complete clearance in all at 34 months follow-up                      | No serious adverse effects reported                                    |
| Kim et al. [11]            | Recalcitrant PV                                 | 16                 | Remission and marked clinical improvement                             | No serious adverse effects reported                                    |
| Kanwar et al. [22]         | Resistant and serious pemphigus                 | 10                 | 3 - complete clearance with low dose oral prednisolone                | One patient died of sepsis                                             |
|                            |                                                 |                    | 4 - clinical remission                                                |                                                                        |
|                            |                                                 |                    | 2 - partial remission with low dose prednisolone                      |                                                                        |
|                            |                                                 |                    | 1 - died of sepsis                                                    |                                                                        |
| Schmidt et al. [18]        | Pemphigus foliaceous                            | 20                 | Complete remission - 8 (40%)                                         | One patient - bacterial sepsis                                         |
|                            |                                                 |                    | Clinical remission - 9 (45%)                                         | Relapse - 18%                                                          |
|                            |                                                 |                    | Partial remission - 2 (10%)                                         |                                                                        |
|                            |                                                 |                    | No improvement - 1 (5%)                                              |                                                                        |
| Le Roux-Villet et al. [23] | Mucous membrane pemphigoid                      | 25                 | Clinical remission + partial remission = 88% + 4% after 2nd cycle     | No serious side effects noted                                           |
| Various authors (2007)     | EBA                                             | 7                  | Complete remission - 3                                                | One patient died of pseudomonas pneumonia                               |
|                            |                                                 |                    | Clinical remission - 1                                                | 7 days after 1st infusion                                               |
|                            |                                                 |                    | Partial remission - 2                                                 |                                                                        |
|                            |                                                 |                    | Partial remission - 7                                                 | 3/13 patients developed serious/fatal infections                        |
|                            |                                                 |                    | No improvement - 3                                                    |                                                                        |

EBA: Epidermolysis bullosa acquisita, PV: Pemphigus vulgaris

Reports and case series of omalizumab being used in BP with reasonable success. [50-52]

**Plasmapheresis and Immunoadsorption**

Plasmapheresis is a method of removing circulating autoantibodies present in blood of patients with immunobullous diseases by a filtration process. This modality was used based on the observation that the severity of immunobullous diseases usually correlates with the levels of circulating autoantibodies. [53] It is especially useful in cases which are resistant to steroid therapy. This procedure rapidly reduces the level of pathogenic antibodies in the blood. However, because of the rapid fall in antibody levels, a rebound phenomenon is usually observed. The rebound can be avoided by giving an additional immunosuppressant. The studies conducted mostly have been on plasmapheresis in combination with some other drugs, mostly low-dose steroids or drugs such as azathioprine and cyclophosphamide [Table 3]. Plasmapheresis helps in gaining rapid control of the disease in steroid-resistant patients. Immunoadsorption is claimed to be safer and more efficacious than plasmapheresis.

**Intravenous Immunoglobulins**

Intravenous immunoglobulin (IVIG) has already proved beneficial in the management of many autoimmune
### Table 2: Evidence of TNF inhibitors in the treatment of immunobullous diseases

| Serial number | Study | Drug used       | Indication                     | Number of patients | Results                              | Remarks                                                                 |
|---------------|-------|-----------------|--------------------------------|-------------------|--------------------------------------|-------------------------------------------------------------------------|
| 1             | Sacher et al. [39] | Etanercept | Recalcitrant MMP               | 1                 | Marked and rapid improvement         |                                                                                   |
| 2             | Labrecque and Null [41] | Etanercept 25 mg s/c twice weekly with low-dose steroids | Cicatricial pemphigoid | 1                 | Marked clinical improvement          | Response maintained with etanercept 25 mg thrice weekly with daily dapsone therapy |
| 3             | Canizares et al. [42] | Etanercept 25 mg subcutaneous twice weekly | Cicatricial pemphigoid. Oral mucosal involvement in all and ocular in one | 3                 | Oral lesions improved in all. Ocular disease progression was arrested |                                                                                   |
| 4             | Beroohkim et al. [43] | Etanercept | Given for seronegative arthritis in PV | 1                 | Bulle of PV resolved along with joint pain | First report of efficacy in PV                                                                 |
| 5             | Shetty et al. [44] | Etanercept twice weekly | PV                          | 4                 | Dramatic clinical improvement with steroid-sparing effect |                                                                                   |
| 6             | Fiorentino et al. [45] | Etanercept 50 mg once weekly versus placebo for 16 weeks | PV                          | 8                 | 50% reduction in lesions - 2 placebo, 1 etanercept Dropout - 2 etanercept Failure - 3 etanercept | Limitation: Lack of valid end point Low dose of etanercept used |
| 7             | Hall et al. [46] | Infliximab with prednisolone versus prednisolone alone | PV                          | 10+10             | Infliximab treatment showed no better efficacy clinically | The levels of anti-desmoglein 1 and 3 were lower with infliximab adverse effects same in both group |

MMP: Mucous membrane pemphigoid, PV: Pemphigus vulgaris

### Table 3: Evidence of plasmapheresis and immunoadsorption in the treatment of immunobullous diseases

| Serial number | Study | Indication                     | Number of patients | Results                              | Remarks                                                                 |
|---------------|-------|--------------------------------|-------------------|--------------------------------------|-------------------------------------------------------------------------|
| 1             | Shimanovich et al. [54] | PV                        | 9                 | Clinical remission in all patients at 4 weeks | IA was given with methylprednisolone Azathioprine or MMF used as steroid-sparing agents |
| 2             | Schmidt et al. [55] | Pemphigus                   | PV - 4 PF - 1     | Clinical remission in all patients within 2 weeks | Protein A IA done (staphylococcal protein-A) Methylprednisolone was given initially and later tapered |
| 3             | Eming et al. [56] | Pemphigus                    | PV - 4 PF - 2     | Clinical remission in all patients IA on consecutive days. No relapse at 1 year | Methylprednisolone was given initially and later tapered |
| 4             | Kasperkiewicz et al. [57] | Bullous pemphigoid           | 7                 | 6 patients showed complete remission | Protein A IA done All patients were receiving 0.25 mg/kg prednisolone |
|               |       |                               | 6 - female 1 - male |                                      |                                                                         |
| 5             | Kasperkiewicz et al. [58] | Linear IgA bullous disease  | 1                 | Clinical remission                  | Tryptophan IA used as adjuvant Case report |
| 6             | Westermann et al. [59] | Pemphigoid gestationis      | 1                 | Clinical remission in 4 weeks       | 10 IA over 4 weeks Patient was breastfeeding at the time. Prednisolone 60 mg/day was being given |

PF: Pemphigus foliaceus, PV: Pemphigus vulgaris, MMF: Mycophenolate mofetil, IA: Immunoadsorption
diseases. However, its use in autoimmune blistering diseases does not have much evidence. However, there are small studies, in which IVIG has been shown to be beneficial in steroid-resistant cases of PV, pemphigus foliaceus, BP, and linear IgA bullous dermatosis. IVIG acts by reducing the levels of circulating autoantibodies by increasing their catabolism rate and by preventing apoptosis of keratinocytes. It is usually administered in a dose of 400 mg/kg/day for 5 consecutive days. Total dose in each cycle is 2 g/kg. Four such cycles of IVIG are usually given once every 4 weeks. This dosage usually produces remission in recalcitrant cases of immunobullous disorders. IVIG can be given alone or with conventional immunosuppressives which enhance its effects. In one study, HD-IVIG was combined with rituximab, and rapid resolution of lesions was seen without the usual side effects of rituximab. It has been seen that effect of IVIG is dose-dependent and higher doses of IVIG (400 mg/kg/day) produces a greater effect than lower doses (200 mg/kg/day). In certain studies, IVIG was tapered slowly and continued 6 monthly after inducing clinical remission. IVIG also has steroid-sparing effect and helps in preventing side effects due to long-term administration of immunosuppressives. IVIG is generally well tolerated though there are also a number of potential side effects. Most frequently observed side effects are mild and include nausea, headache, myalgia, flushing, hypertension, and tachycardia. These reactions can be reduced premedication with IV steroids and antihistaminic and by giving a slow infusion over four to five hours.

Serious adverse effects such as renal failure, blood–borne diseases, aseptic meningitis, thromboembolic episodes, and anaphylaxis are rarely seen.

A major benefit of IVIG is that there is no increased risk of infections as seen with other treatment modalities. However, the cost of therapy with IVIG is high.

Recent studies seem to combine newer modalities such as IVIG, immunoadsorption (Table 4), and rituximab. One study combined all three modalities in seven pemphigus patients, and rapid improvement in lesions was observed in all the patients.

### Novel anti-CD20 monoclonal antibodies beyond rituximab

Anti-CD20 antibodies can be categorized as Type I (e.g., rituximab, ofatumumab, veltuzumab, and ocrelizumab) or Type II (e.g., tositumomab or obinutuzumab/GA101), depending on cellular response. Type I antibodies cause a clustering of CD20 that enhances the recruitment and activation of complement for a potent CDC response. On the other hand, Type II antibodies exhibit stronger homotypic adhesion and induction of direct cell death but with a minimal CDC response. Humanized anti-CD20 monoclonal antibodies have the advantage of being less immunogenic than rituximab. Of the next-generation anti-CD20 biologics, only veltuzumab has published literature on the treatment of refractory pemphigus, and only obinutuzumab/GA101 is currently being tested in clinical trials for pemphigus.

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**Table 4: Evidence of intravenous immunoglobulin, in the treatment of immunobullous disease**

| Serial number | Study | Indication | Number of patients | Results | Remarks |
|---------------|-------|------------|--------------------|---------|---------|
| 1             | Amagai et al. [60] | PV and PF | 61 | Disease activity and enzyme-linked immunosorbent assay scores were significantly lower in the 400 mg group than in the other groups | Multicenter, double-blind study, Only single cycle of HD-IVIG was given, No long-term follow-up |
| 2             | Ahmed [65] | PV | 11 | 9 of 11 patients had clinical remission | HD-IVIG was given with rituximab, 2 cycles of rituximab once weekly for 3 weeks and HD-IVIG in 4th week |
| 3             | Ahmed [62] | PV | 21 | Sustained clinical remission in all patients | HD-IVIG used as monotherapy |
| 4             | Sami et al. [64] | PF | 7 | Clinical remission in all patients | Steroid-dependent cases were chosen |
| 5             | Ahmed et al. [29] | Bullous pemphigoid | 7 | All patients achieved clinical remission | Minimum four cycles required for maximum therapeutic effect |
| 6             | Foster and Ahmed [66] | Ocular cicatricial pemphigoid | 10 | Resolution of lesions in all ten patients | |
| 7             | Sami et al. [67] | Cicatricial pemphigoid | 15 | Clinical remission in all patients | |
| 8             | Gourgiotou et al. [68] | Epidermolysis bullosa acquisita | 1 | Clinical remission seen | Case report. HD-IVIG used |
| 9             | Letko et al. [69] | Linear IgA bullous disease | 1 | Clinical remission seen | Case report |

IVIG: Intravenous immunoglobulin, PV: Pemphigus vulgaris, PF: Pemphigus foliaceus, HD: High dose
Veltuzumab
Veltuzumab is a Type I, second-generation humanized anti-CD20 monoclonal antibody. A major advantage of veltuzumab over rituximab is its ability to be administered subcutaneously in low doses (about 20% of the dose of rituximab).[72] Subcutaneous veltuzumab (two 320 mg doses 3 weeks apart) was administered in one patient with pemphigus not responding to rituximab. The patient had complete remission off therapy at 22 months, relapsed at 24 months, and achieved continuous remission after the second administration of veltuzumab. At 35 months of follow-up, the patient experienced no injection site reactions, constitutional symptoms, or adverse events.[73]

Obinutuzumab/GA101
Obinutuzumab/GA101 is a third-generation, Type II humanized anti-CD20 monoclonal antibody with a 50-fold higher binding affinity effector cells and a resultant 10- to 100-fold increase in ADCC against target B-cells.[74] Results from a Phase III, randomized trial of GA101 on patients with chronic lymphocytic leukemia and coexisting conditions demonstrated superior response rates compared to chlorambucil monotherapy or rituximab-chlorambucil therapy. Obinutuzumab/GA101 can be a powerful tool in treating patients with refractory PV in coming days.[75]

Conclusions
Treatment of immunobullous disease has come up a long way from global immunosuppression to more targeted immunotherapy. Rituximab has revolutionized the treatment of immunobullous disease in recent years; however, cost of administration of an intravenous immunotherapy under in-patient basis may limit its uses. Subcutaneous administrable anti-CD20 antibodies, such as veltuzumab, if proven equally or more effective and safer than rituximab, may lead the future of immunotherapy in the field of autoimmune blistering disease.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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