Side effects of steroid-sparing agents in patients with bullous pemphigoid and pemphigus: A systematic review

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Background: Systemic glucocorticoids are first-line treatment options for autoimmune blistering diseases; however, their long-term use is associated with significant toxicities.

Objective: To evaluate the side effects of steroid-sparing agents and compare them with those of steroids.

Methods: We searched Cochrane Reviews, Embase, MEDLINE, and Scopus between October 1978 and May 2020 using the keywords “bullous pemphigoid,” “pemphigus,” “autoimmune blistering diseases,” and “side effects.” A total of 31 randomized controlled trials and retrospective case series were critically appraised.

Results: This review includes a total of 1685 patients with autoimmune blistering diseases, of whom 781 had bullous pemphigoid and 904 had either pemphigus vulgaris or pemphigus foliaceous.

Limitations: A major limitation is that because adjuvants are generally used in combination with steroids, only 12 of the studies reviewed included a “steroid-only” arm to allow for a direct comparison of side effects. Additionally, there is inadequate literature and lack of standardized grade reporting of specific side effects of each steroid-sparing agent.

Conclusion: In the future, researchers should consider implementing the Common Terminology Criteria for Adverse Events, version 5.0, for reporting of all side effects to allow for consistency and standardization. It would be useful to have an index similar to the Glucocorticoid Toxicity Index to quantify these side effects. (JAAD Int 2022;9:33-43.)

Key words: autoimmune blistering diseases; bullous pemphigoid; CTCAE; glucocorticoids; GTI; immunosuppressants; pemphigus; side effects; steroid-sparing; treatment.

INTRODUCTION

Autoimmune blistering diseases (AIBDs) are a heterogeneous group of skin diseases that are characterized and caused by autoantibodies targeting adhesion molecules on the skin and/or mucous membranes.1 Systemic steroids are the cornerstone of the management of AIBDs and have considerably improved the survival of patients with these diseases.2,3 However, long-term and high-dose treatment with systemic glucocorticoids (GCs) carries the risk of significant side effects, which contribute to morbidity and mortality in patients with AIBDs.4 Therefore, a major goal of the management of AIBDs is to reduce the patient’s cumulative exposure to systemic steroids with the use of adjuvant steroid-sparing agents.1,4,5 This review focuses on the
treatment of bullous pemphigoid (BP) and pemphigus. Given that pharmacologic side effects are crucial limitations while treating diseases, the objective is to assess the side effect profiles of steroid-sparing adjuvant therapies.

**GUIDELINES FOR THERAPEUTIC USE OF STEROID-SPARING ADJUVANT THERAPIES**

The primary treatment option for AIBDs is GCs, as mentioned above. Adjuvant agents are primarily used to reduce a patient's total, cumulative GC dosage and are also considered in circumstances in which monotherapy with GCs is inadequate to induce remission of the disease or when there is relapse during a dose-reduction period of GCs.6,7 The choice of adjuvant treatment is largely dependent on the availability, price, and practical experience of the treating dermatologist as well as the presence of specific contraindications. The use of an immunosuppressive or immunomodulatory agent with potentially GC-sparing ability should be considered, especially when a high, cumulative GC dosage is anticipated or when there are contraindications to oral steroids and comorbidities such as hypertension, diabetes mellitus, osteoporosis, and psychosis.

### Bullous Pemphigoid

The recommendations for the choice of adjuvant drug and its dosage can be classified into 2 groups based on the clinical presentation of BP: extensive BP or localized and mild BP.6 According to the 2015 consensus by the European Dermatology Forum in collaboration with the European Academy of Dermatology and Venereology, steroids are first-line treatment options, followed by steroids in combination with any 1 of the adjuvant agents listed below as second-line treatment options.6

For extensive BP, the adjuvant agents are as follows:

1. Doxycycline alone or in combination with daily oral nicotinamide
2. Azathioprine (AZA) (according to thiopurine methyltransferase [TPMT] activity)5-11
3. Mycophenolate mofetil or mycophenolic acid9,10,11
4. Methotrexate
5. Dapsone13
6. Cyclosporin

For localized and mild BP, the adjuvant agents include doxycycline and nicotinamide, methotrexate, or dapsone in the same dosages as those for extensive BP.

### Pemphigus

An international panel of experts has recommended GCs as a first-line treatment option for pemphigus and anti-CD20 monoclonal antibodies, such as rituximab, as a first-line treatment option for new-onset, moderate-to-severe pemphigus and/or in patients who fail to achieve clinical remission with systemic GCs and/or immunosuppressive agents.15 A course of rituximab is given intravenously, either 1000 mg twice (2 weeks apart) or 375 mg/m² 4 times (1 week apart).15 The first-line, corticosteroid-sparing agents are AZA and mycophenolate mofetil. The recommended AZA dosage varies with TPMT activity: patients with high TPMT activity are given a normal AZA dosage of up to 2.5 mg/kg daily, whereas patients with intermediate or low TPMT activity should receive between 0.5 and 1.5 mg/kg/d (patients with no TPMT activity should not be given AZA). The suggested dosage for mycophenolate mofetil is 30 to 45 mg/kg daily, 1440 mg daily for mycophenolic acid.

The International Blistering Diseases Consensus Group has listed intravenous immunoglobulin (2 g/kg over 2-5 days each month), immunoadsorption, and cyclophosphamide as “other” alternative adjuvant agents, which likely collectively refer to second-line treatment and so forth. The latter 2 do not have recommended dosages. Generally, these agents are not favored either because of their poor side effect profile or associated high costs.

### METHODS

The OVID MEDLINE, OVID Embase, Cochrane Reviews, and Scopus databases were searched between October 1978 and May 2020 for “bullous pemphigoid,” “pemphigus,” “autoimmune blistering diseases,” and “side effects.” Retrospective case series (RCS) with a minimum of 5 cases and randomized controlled trials (RCTs) with a minimum population size of 9 patients were screened by 2
investigators (FAPZ, TS). A single reviewer (FAPZ) independently evaluated each retrieved report. A total of 31 RCTs and RCSs were critically evaluated. The 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist for abstracts and systematic reviews was used (Supplementary Materials 1 and 2, available via Mendeley at https://data.mendeley.com/datasets/hn4hn9yx4g/1). A flowchart outlining the steps taken, according to Preferred Reporting Items for Systematic Reviews.

**Fig 1.** Flowchart illustrating the results of the search strategy. AIBD, Autoimmune blistering disease; BP, bullous pemphigoid.

### Abbreviations used:
- AE: adverse event
- AIBD: autoimmune blistering disease
- AZA: azathioprine
- BP: bullous pemphigoid
- CsA: cyclosporin
- CTCAE: Common Terminology Criteria for Adverse Events
- GC: glucocorticoid
- RCS: retrospective case series
- RCT: randomized controlled trial
- TPMT: thiopurine methyltransferase
Table I. Summary of randomized controlled trials and retrospective case studies evaluating adjuvant therapy in bullous pemphigoid

| Author; year; country | Type | Steroid (GC); adjuvant | Study arms | Study population and indication | CTCAE grading of AEs |
|-----------------------|------|-------------------------|------------|---------------------------------|----------------------|
| Burton et al; 1978; England | RCT, nonblinded | Prednisone; AZA | GC only; GC, AZA | 25 patients with newly diagnosed BP | Grade 2: 2/12 patients (17%) AZA |
| Beissert et al; 2007; Germany | RCT, multicenter, nonblinded | Methylprednisolone; AZA/MMF | GC, AZA; GC, MMF | 73 patients with newly diagnosed mild-to-severe BP | Grade 3: 8/36 patients (22%) MMF Grade 4: 3/36 patients (8%) |
| Sticherling et al; 2017; Germany | RCT, multicenter, nonblinded | Methylprednisolone; AZA/dapsone | GC, AZA; GC, dapsone | 54 patients with newly diagnosed BP | Grade 3: 11/34 patients (32%) MMF Grade 4: 2/34 patients (6%) AZA |
| Gual et al; 2014; Spain | Retrospective case series | Prednisone; CTX | GC, CTX | 20 patients with moderate-to-severe BP, initially treated with STS or systemic GCs and with CsA as first-, second-, or third-line adjuvant | Grade 1: 10/62 patients (16%) Grade 2: 9/62 patients (15%) Grade 5: 5/62 patients (8%) |
| Schmidt et al; 2005; Austria and Germany | Retrospective case series | Methylprednisolone; dapsone | GC, dapsone | 62 patients with untreated or refractory BP | AEs were recorded as the number of events per AE and not all AEs experienced per patient |
| Amagai et al; 2017; Japan | RCT, multicenter, double-blinded | Prednisone; IVIg | GC only; GC, IVIg | 56 patients with BP were on a stable regimen, which included GCs | Grade 1: 10/62 patients (16%) Grade 2: 9/62 patients (15%) Grade 5: 5/62 patients (8%) |
| Kjellman et al; 2008; Sweden | Retrospective case series | Prednisone; MTX | GC, MTX; MTX only | 98 patients with newly diagnosed mild-to-severe BP | Grade 2: 5/98 patients (5%) |
| Du-Thanh et al; 2011; France | Retrospective case series | STS, betamethasone propionate, or clobetasol propionate; MTX | GC, MTX | 70 patients initially treated with short-term STS and low-dose MTX, followed by long-term, low-dose MTX | Grade 1: 2/70 patients (3%) Grade 2: 3/70 patients (4%) Grade 3: 2/70 patients (3%) Grade 4: 8/70 patients (11%) Grade 5: 1/70 patients (3%) |
| Delaumenie et al; 2019; France | Retrospective case series | TPC; MTX | GC, MTX | 51 patients with moderate-to-severe BP, initially treated with TPC as first line | Grade 1 and 2: NA (48%) Grade 3: NA (22%) |
| Polansky et al; 2019; US | Retrospective case series | Prednisone; RTX | GC, RTX | 20 patients with untreated severe or refractory BP | AEs could not be graded because of inadequate information |
| Williams et al; 2017; UK and Germany | RCT, multicenter | Prednisone; tetracycline | GC only; tetracycline only | 234 patients with newly diagnosed BP | Grade 0/1/2: 99/121 patients (81%) Grade 3: 14/121 patients (12%) Grade 4: 5/121 patients (4%) Grade 5: 3/121 patients (3%) |
and Meta-Analyses guidelines, to identify studies for review in this article is shown in Fig 1.

The Common Terminology Criteria for Adverse Events (CTCAE), version 5.0, was used to grade adverse events (AEs) recorded in the studies when possible (Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/hn4hn9xyx4g/1). The common side effects of steroids were referenced using the Glucocorticoid Toxicity Index.17

Tables I8,10,12,18-25 and II26-45 illustrate summarized compilations of the RCTs and RCSs carried out to evaluate the adjuvant therapies used in patients with BP and pemphigus, respectively. The included data are recent and up to date.

RESULTS

A total of 781 participants with BP were included in the selected RCTs and RCSs (Table I).8,10,12,18-25 Of those whose side effects could be assigned a single grade classification according to the CTCAE definitions, 12 participants (1.5%) experienced grade 1 AEs, 24 participants (3.1%) experienced grade 2 AEs, 35 participants (4.5%) experienced grade 3 AEs, 18 participants (2.3%) experienced grade 4 AEs, and 9 participants (1.2%) experienced grade 5 AEs. For pemphigus, there were a total of 904 participants from the selected RCTs and RCSs (Table II).26-45 Of those whose side effects could be assigned a single grade classification according to the CTCAE definitions, 13 participants (1.4%) experienced grade 1 AEs, 155 participants (17%) experienced grade 2 AEs, 17 participants (1.9%) experienced grade 3 AEs, 17 participants (1.9%) experienced grade 4 AEs, and no participant experienced grade 5 AEs.

DISCUSSION

The CTCAE (versions 5.0, 4.0, and 3.0) and its predecessor, the Common Toxicity Criteria (versions 2.0 and 1.0), were developed under the direction of the Cancer Therapy Evaluation Program of the National Cancer Institute in an effort to provide a standard language for reporting AEs that occur in sponsored clinical trials. However, this limits the use of the CTCAE in National Cancer Institute-sponsored trials and creates a disparity between National Cancer Institute-sponsored and nonsponsored trials. The authors recommend that researchers
| Author et al; year; country | Type | Steroid; adjuvant | Study arms | Study population and indication | CTCAE grading of AEs |
|-----------------------------|------|-------------------|-----------|--------------------------------|----------------------|
| Rose et al; 2005; Germany   | RCT, multicenter, nonblinded | Methylprednisolone/ dexamethasone; AZA/CTX | Methylprednisolone, AZA; dexamethasone, CTX | 22 patients with newly diagnosed PV/PF | AEs were recorded as the number of events per AE and not all AEs experienced per patient |
| Kakuta et al; 2018; Japan    | Retrospective case series | None; AZA | AZA only | 8 patients with newly diagnosed PV/PF | Grade 2: 2/8 patients (25%) |
| Dastgheib et al; 2015; Iran  | RCT | Prednisone; AZA/ tacrolimus | GC, AZA; GC, tacrolimus | 41 patients with PV | Grade 1: 3/21 patients (14%) Grade 2: 1/21 patients (5%) Tacrolimus Grade 1: 3/21 patients (14%) Grade 2: 1/21 patients (5%) |
| Chams-Davatchi et al; 2007; Iran | RCT, nonblinded | Prednisone; AZA/ MMF/CsA | GC only; GC, AZA; GC, MMF; GC, CTX | 90 patients with newly diagnosed PV | AEs were not described for each treatment arm; it was noted just that there was no significant difference in AE profiles across the 4 groups |
| Olszewska et al; 2007; Poland | Retrospective case series | Prednisone; AZA/CTX/ CsA | GC only; GC, AZA; GC, MMF; GC, CTX | 101 patients with moderate-to-severe PV | AEs were recorded as the number of events per AE and not all AEs experienced per patient |
| Cummins et al; 2003; US      | RCT, nonblinded | Prednisone; CTX | GC, CTX | A total of 23 with refractory PV/PF | Grade 2: 11/23 patients (47%) Grade 3: 3/23 patients (13%) AEs were recorded as the percentage difference compared with control arm |
| Sharma and Khandpur; 2013; India | RCT, nonblinded | Prednisone; CTX IV pulse therapy | GC only; GC, CTX | 60 patients with mild-to-moderate PV | Grade 2: 23/44 patients (52%) |
| Khandpur et al; 2017; India  | Cross-sectional, prospective, clinical, laboratory investigational | Dexamethasone; CTX IV pulse therapy | GC, CTX | 44 patients with PV/PF who have been on CsA for at least 1 y | |
| Ioannides et al; 2000; Greece | RCT | Prednisone; CsA | GC only; GC, CsA | 33 patients with newly diagnosed PV/PF | AEs were recorded as the number of events per AE and not all AEs experienced per patient |
| Study Authors | Year | Location | Study Design | Steroid-sparing agent | Adjuvant | N | AE | AE Details |
|---------------|------|----------|--------------|----------------------|----------|---|---|-----------------|
| Baum et al<sup>36</sup>; 2016; Israel | Retrospective case series | Prednisone; dapsone | GC, dapsone | 125 patients who received dapsone between 1984 and 2013; for the purpose of this review, excluded patients will be evaluated as they experienced early AEs and, thus, were not included in the study | Grade 2: 99/125 patients (79%) |
| Werth et al<sup>37</sup>; 2008; US | RCT, multicenter, double-blind | Prednisone; dapsone | GC only; GC, dapsone | 19 patients with chronic PV in the maintenance phase<sup>1</sup> | Grade 1: 1/9 patients (11%); Grade 2: 1/9 patients (11%) |
| Svecova; 2016<sup>46</sup>; Slovakia | Retrospective case series | Prednisone; IVIg | GC, IVIg | 10 patients with PV with at least 3 consecutive courses of IVIg | Grade 2: 8/10 patients (80%) |
| Beissert et al<sup>39</sup>; 2010; Canada, Germany, India, Israel, Turkey, Ukraine, UK, US | RCT, nonblinded | Prednisone; MMF | GC only; GC, MMF | A total of 94 with existing mild-to-moderate PV | Grade 3: 3/58 patients (5%) |
| Ioannides et al<sup>40</sup>; 2012; Greece | RCT, nonblinded | Methylprednisolone; MMF | GC only, GC, MMF | 47 patients with newly diagnosed PV/PF | Grade 1: 11/24 patients (46%) |
| Baum et al<sup>41</sup>; 2012; Israel | Retrospective case series | Prednisone; MTX | GC, MTX | 30 patients with untreated or refractory PV | Grade 2: 4/30 patients (13%) |
| Tran et al<sup>42</sup>; 2013; US | Retrospective case series | Prednisone; MTX | GC, MTX | 23 patients with PV with refractory PV and subsequently on MTX for at least 3 consecutive mo | Grade 2: 2/23 patients (9%) |
| Chen et al<sup>43</sup>; 2020; France | RCT, phase 3 open-label | Prednisone; RTX | GC only; GC, RTX | A total of 74 patients with newly diagnosed PV | Grade 1/2: 22/38 patients (58%) all attributed to Infusion-Related Reaction; Grade 3: 10/38 patients (29%) from drug itself; 1/38 patients (3%) from IRR | |
| Kurihara et al<sup>44</sup>; 2019; Japan | Multicenter, phase 1/2 open-label | Prednisolone; RTX | GC, RTX | 9 patients with refractory PV/PF | Grade 4: 2/38 patients (5%); Grade 3/4: 9/9 patients had at least one AE in this grade |
| McCarty and Fivenson<sup>45</sup>, 2014; US | Retrospective case series | Not specified; TCN | GC, TCN | A total of 51 with/without initial GC therapy and at least 3 mo of TCN | Grade 2: 3/51 patients (6%) |

<sup>A</sup>AE, Adverse event; AZA, azathioprine; BP, bullous pemphigoid; CTCAE, Common Terminology Criteria for Adverse Events; CsA, cyclosporin; CTX, cyclophosphamide; GC, glucocorticoid; IV, intravenous; IVIg, intravenous immunoglobulin; MMF, mycophenolate mofetil; MTX, methotrexate; PF, pemphigus foliaceus; PV, pemphigus vulgaris; RTX, rituximab; RCT, randomized control trial; STS, superpotent topical steroids; TCN, tetracycline and nicotinamide; UK, United Kingdom; US, United States.<br><sup>1</sup>Drugs are presented in alphabetical order of steroid-sparing adjuvant agent and the corresponding studies for each drug is arranged in chronological order, ie, most recent to least recent.<br>1The maintenance phase is defined as disease controlled with steroids and/or stable dosages for at least 2 months on cytotoxic agents, including AZA, MMF, or MTX.
### Table III. Common steroid-induced side effects are classified by organ system in alphabetical order

| Organ system                | Side effects                                                                 |
|-----------------------------|------------------------------------------------------------------------------|
| Cardiovascular              | Coronary heart disease, heart failure, hypertension, ischemic heart disease  |
| Dermatologic                | Acne, delayed wound healing, easy bruising, ecchymosis, erosion, hair loss,  |
|                             | hirsutism, purpura, skin atrophy, striae                                       |
| Endocrine and Metabolic     | Adrenal suppression, Cushingoid features, diabetes mellitus, dyslipidemia,    |
| Gastrointestinal            | hyperglycemia, weight gain                                                     |
| Immuneologic                | Gastritis, gastrointestinal bleeding, hepatic steatosis, pancreatitis, peptic |
|                             | ulcer disease, visceral perforation                                            |
| Musculoskeletal             | Predisposition to infections, reactivation of latent infections                |
| Neuropsychiatric            | Akathisia, anxiety, cognitive impairment, depression, euphoria, mood changes, |
|                             | mood lability                                                                  |
| Ophthalmologic              | Cataract, glaucoma                                                             |

### Table IV. Classification of adverse events recorded in the reviewed randomized control trials and randomized case series according to how likely they are due to glucocorticosteroids or steroid-sparing adjuvant therapy for pemphigoid and pemphigus

| Drug | Likely to be true GCAE                                                                                                                                                                                                                                                                                                                                 | Likely to be true AE of adjuvant therapy for pemphigoid and pemphigus | Unable to be distinguished                                                                 |
|------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| AZA  | Amenorrhea, cataract, cerebrovascular accident, Cushingoid features, depression, diabetes mellitus, duodenal ulcer, GI bleeding, GI ulcer, GI discomfort, glaucoma, hot flushes, hyperglycemia, hypertension, hypertrichosis, lumbar stenosis, mood changes, myopathy, edema, osteoporosis, pancreatitis, temporary psychosis, tendonitis, redistribution of fat, weight gain | Diarrhea, liver function test abnormalities, myelosuppression (leukopenia, pancytopenia, thrombocytopenia), pharyngitis, vomiting | Arthralgia/myalgia, dizziness, deep venous thrombosis, drug-related exanthema, effluvium, infection |
| CTX  | Acute myeloid leukemia, bladder symptoms (enuresis, frequency/urgency of urination, hematuria, incontinence, nocturia), myelosuppression (anemia, leukopenia, thrombocytopenia), nausea, vomiting | Acute heart failure, dizziness, infection, headache                   | N/A                                                                                          |
| CsA  | Elevated transaminase, gingival hyperplasia, hyperbilirubinemia, nephrotoxicity (decreased creatinine clearance, increased urea/serum creatinine)                                                                                                                                               | N/A                                                                    | N/A                                                                                          |
| Dapsone | Anemia, cyanosis, fever, liver function abnormalities, methemoglobinemia, paresthesia                                                                                                                                                                                      | Arthralgia/myalgia, dizziness, drug-related exanthema, infection, renal failure | Continued                                                                                                                                 |

Continued
use the CTCAE, version 5.0, while reporting AEs in future clinical studies.

One major limitation of this analysis is that adjuvant interventions are almost always used in combination with steroids and rarely used as monotherapy. Of the 31 selected studies, only 12 included a “steroid-only” arm, which allowed for a direct comparison of the side effects of steroid-sparing agents with those of steroids. This posed a challenge of identifying the true side effects of the adjuvants from those of steroids. To overcome this, commonly accepted steroid-induced side effects were referenced to exclude side effects that are more likely to be caused by steroids than by the adjuvant drugs. These common steroid-induced side effects according to organ system are presented in Table III.

Additionally, the side effects of the adjuvant drugs were extracted from their respective product information, certified by the Food and Drug Administration of the United States, to further guide the distinction between the side effects of the adjuvant drugs and those of steroids (Supplementary Material 3, available via Mendeley at https://data.mendeley.com/datasets/hvihrn9yxy4g/1). The observed AEs for each steroid-sparing agent were then categorized based on how likely they were to be true side effects of the adjuvant drugs by comparing and contrasting data from the aforementioned datasets (Table IV).

Because of lack of available data on specific side effects of each steroid-sparing agent and the lack of standardized grade reporting of such AEs, we were unable to accurately compare the severity of the side effects of steroid-sparing agents with those of the side effects of steroids.

### Table IV. Cont’d

| Drug | Likely to be true GCAE | Likely to be true AEs of adjuvant therapy for pemphigoid and pemphigus | Unable to be distinguished |
|------|-----------------------|-------------------------------------------------|---------------------------|
| IVIg | Chest pain, decreased blood alkaline phosphatase, depressed platelet count, elevated blood lactate dehydrogenase, fever, injection site erythema/pain, liver function test abnormalities, malaise | Arthralgia/myalgia, eye disease, infection | N/A |
| MMF | Fatigue, hypokalemia, liver function test abnormalities, myelosuppression (lymphopenia, neutropenia) | | |
| MTX | Alopecia, anemia, interstitial pneumopathy, liver function test abnormalities, myelosuppression (leukopenia, pancytopenia, thrombocytopenia) | Arthralgia/myalgia, eye disease, infection | |
| RTX | Arthralgia/myalgia, hypogammaglobulinemia, hypergamma glutamyltransferase | Cerebrovascular accident, dental caries, headache, infection, nasal septum perforation, peripheral neuropathy, phlebitis, psoriatic arthropathy, pulmonary embolism, venous thrombosis | |
| TCN | Diarrhea, nausea, vomiting | Decubitus ulcers, deep venous thrombosis, erosive gastritis | |

AE, Adverse event; AZA, azathioprine; CsA, cyclosporin; CTX, cyclophosphamide; GC, glucocorticosteroid; GCAE, glucocorticoid-induced adverse events; IVIg, intravenous immunoglobulin; GI, gastrointestinal; MMF, mycophenolate mofetil; MTX, methotrexate; N/A, not available; RTX, rituximab; RCT, randomized control trial; TCN, tetracycline and nicotinamide.

*The AEs are listed in alphabetical order.

### CONCLUSION

The CTCAE could be used to define terms and could be measured as part of a steroid-sparing agent toxicity index, which could be developed using a similar methodology as that for the Glucocorticoid Toxicity Index. The long-term side effects of medications are otherwise challenging to quantify in patients with chronic autoimmune diseases.
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Conflicts of interest
None disclosed.

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