How Do Experts Treat Patients with Bullous Pemphigoid around the World? An International Survey

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Many treatments are currently proposed for treating patients with bullous pemphigoid (BP). We assessed treatment modalities of BP depending on the different countries, BP extent, and patients' comorbidities. We surveyed worldwide experts about how they treat patients with BP. A total of 61 experts from 27 countries completed the survey. Severe and moderate BP were treated with oral prednisone (61.4 and 53.7%, respectively) or superpotent topical corticosteroids (CSs) (38.6 and 46.3%, respectively). Conventional immunosuppressants were more frequently combined with oral prednisone (74.5%) than with superpotent topical CS (37.5%) in severe BP. Topical CSs were mainly used in Europe in mild (81.1%), moderate (55.3%), and severe (54.3%) BP. In the United States of America and Asia, systemic CSs were mainly proposed for treating severe (77.8 and 100%, respectively), moderate (70 and 77.8%, respectively), and also mild (47.1 and 33.3%, respectively) BP. Most experts reduced the initial dose of oral CS in patients with diabetes mellitus (48.1%) or cardiac insufficiency (40.2%) but rarely changed BP treatment in patients with neurological disorders or neoplasia. This survey showed major differences in the way patients with BP are treated between AmeriPac countries (United State of America, Latin America, and Australia) and Asia on the one hand and Europe and the Middle East on the other hand.

JID Innovations (2022);**2:**100129 doi:10.1016/j.xjidi.2022.100129

INTRODUCTION

Treatment of bullous pemphigoid (BP) remains challenging because elderly patients with BP have a poor tolerance for many treatments (Bernard et al., 1995; Joly et al., 2002; Jung et al., 1999; Korman, 1998; Langan et al., 2008). The main deleterious prognostic factors of BP include older age; poor general condition; comorbidities, in particular, debilitating neurological disorders; and the use of high doses of systemic corticosteroids (CSs) (Cortés et al., 2011; Joly et al., 2012, 2005, 2002; Rzany et al., 2002). A wide range of treatments is available, the use of which is highly variable and largely depends on dermatologists' experience. High doses of oral

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Abbreviations: BP, bullous pemphigoid; CS, corticosteroid; MMF, mycophenolate mofetil; RCT, randomized controlled trial; US, United States

Received 1 November 2021; revised 2 January 2022; accepted 25 January 2022; accepted manuscript published online XXX; corrected proof published online XXX

Cite this article as: JID Innovations 2022;2:100129

CSs are still considered the mainstay of treatment for patients with BP in some countries, whereas they are no longer recommended in other countries owing to the frequency and severity of their side effects (Fine, 1995; Korman, 1998; Westerhof, 1989). Medium doses of oral prednisone have recently been proposed by a panel of experts in the European Academy of Dermatology and Venereology/European Dermatology Forum guidelines without clear evidence from the literature (Cozzani et al., 2018). Superpotent topical CSs have been shown to be safer and more effective than high doses of oral prednisone in patients with extensive BP, but their use is limited by the poor practicability of this treatment (Joly et al., 2012, 2002; Sobocinski et al., 2016; Terra et al., 2014). The usefulness of immunosuppressants as first-line therapies and CS-sparing agents remains debatable because no randomized controlled trial (RCT) has shown a benefit of this combined treatment over CSs alone (Beissert et al., 2007; Guillaume et al., 1993; Kirtschig et al., 2010). Finally, the use of immunomodulants such as tetracycline, dapsone, or fumarate seems extremely heterogeneous among countries (Bouscarat et al., 1996; Feliciani et al., 2015; Williams et al., 2017). These latter treatment options are mentioned in the European and Japanese guidelines (Ujiie et al., 2019), despite conflicting results from the literature. Tetracyclines have been claimed to be noninferior to medium doses of prednisone in an RCT (Williams et al., 2017), whereas in the real life, 72% of the patients who were started with tetracyclines alone required additional oral prednisolone, and only 12% of patients were able to continue doxycycline alone throughout the study (Micallef and Harman, 2021). Similarly, a CS-sparing effect of dapsone is often claimed, whereas in an RCT comparing dapsone with azathioprine, only 11% of patients treated with dapsone were able to completely taper CS (Sticherling et al., 2017). The purpose of this worldwide survey was to assess the treatment modalities of patients with BP depending on the different countries, BP extent, and patients' comorbidities.

RESULTS

Experts

A survey was sent to 78 experts identified by their publications in the field of BP. They were practicing in 27 countries in Europe, the United States (US), Asia, the Middle East, Australia, and South America. A total of 61 surveys (78.2%) were completed. A total of 54% of the responses came from Europe, 19.7% came from the US, 11.5% came from the Middle Eastern countries, 11.5% came from Asia, 1.6% came from Australia, and 1.6% came from South America (Brazil).

Most treatments were available in different countries except fumarate, which is only available in Germany. In addition, superpotent topical CSs, rituximab, mycophenolate mofetil (MMF), and intravenous Igs were either not reimbursed and/or only available to a small number of patients with BP in some European countries (Hungary and Croatia) as well as in Singapore, Australia, Iran, and Turkey.

Management of patients with BP depending on disease severity

The respective frequencies of the various treatments used depending on the clinical severity of BP are shown in Table 1.

Treatment of severe types of BP. Severe BP was treated with oral prednisone or superpotent topical CSs in 51 of 83 (61.4%) or 32 of 83 (38.6%) cases, respectively. The most frequently used initial dose of prednisone was 0.75 mg/kg/day (51.0% of responses that indicated the use of prednisone), whereas the initial doses of clobetasol propionate were quite variable, ranging from 20 (50.0% of responses) to 30 mg/day (34.4%) and 40 mg/day (34.4%).

Conventional immunosuppressants (MMF, methotrexate, and azathioprine) were more frequently associated with oral prednisone (38 of 51 [74.5% of responses]) than with superpotent topical CSs (12 of 32 [37.5%]). Interestingly, among the 50 responses mentioning the use of an immunosuppressant, azathioprine (17 of 38 [44.7%]) and MMF (13 of 38 [34.2%]) were the main immunosuppressants associated with oral CSs, whereas methotrexate was mainly associated with topical CSs (6 of 12 [50.0%]). Doxycycline and dapsone were associated with (oral or topical) CS in 18 of 83 (21.6%) and 11 of 83 (13.3%) responses, respectively.

Treatment of moderate types of BP. Oral prednisone and topical CSs were used in 43 of 80 (53.7%) and 37 of 80 (46.3%) cases, respectively. Immunosuppressants were less frequently associated with oral CSs than in severe types of BP (21 of 43 [48.8%] vs. 38 of 51 [74.5%] of responses) ($P = 0.02$). The most frequently used initial doses of oral prednisone were 0.5 mg/kg/day in 65.1% of cases, and that of clobetasol propionate was between 20 g/day (23 of 37 [62.2%]) and 30 g/day (11 of 37 [29.7%]). Immunomodulators were associated with oral or topical CSs in proportions quite similar to those proposed in severe BP: doxycycline in 19 of 80 cases (23.8%) and dapsone in 6 of 80 cases (7.5%). Doxycycline and dapsone were associated with oral or topical CSs in 19 of 80 cases (23.8%) and 6 of 80 cases (7.5%), respectively.

Treatment of mild types of BP. Topical CSs were proposed in 50 of 70 (71.4%) cases for treating mild types of BP, mainly at an initial dose of 20 g/day (16 of 50 [32.0%] of responses), whereas oral prednisone was proposed in 20 of 70 (28.6%) cases, mainly at an initial dose of 0.5 mg/kg/day (14 of 20 [70.0%]). Tetracyclines were more frequently used for treating these mild types of BP (24 of 70 [34.3%]) than conventional immunosuppressants (9 of 70 [12.9%]) ($P = 0.005$).

Treatment of localized types of BP. Topical CSs were used in 63 of 65 (96.9%) cases, mainly at an initial dose of 20 g/day in 24 of 63 (39.3%) responses. Doxycycline was associated with topical CS in 9 of 61 (14.8%) cases.

During the consolidation phase, patients with a favorable course were usually treated with the same treatments as those used during the initial phase of treatment. Oral and/or topical CS doses were first tapered in between 71.7 and 87.8% of cases and then stopped before reducing immunosuppressants.

Management of patients with BP by experts from different geographic areas

We then analyzed experts' responses according to the geographic areas, that is, the US, South America, Europe, Middle East, Asia, and Australia. Because treatment modalities of BP were quite similar in the US, Australia, and South

Table 1. Treatment Modalities of Patients with Bullous Pemphigoid Depending on Disease Severity

Treatments	Severe/Extensive n (%)	Moderate n (%)	Mild n (%)	Localized n (%)
Initial treatment	n = 83[1]	n = 80[1]	n = 70[1]	n = 65[1]
Prednisone ± immunosuppressant	51 (61.4)	43 (53.7)	20 (28.6)	2 (3.1)
Dose of prednisone	n = 51	n = 43	n = 20	n = 2
1.0 mg/kg/d	9 (17.6)	5 (11.6)	1 (5.0)	0 (0.0)
0.75 mg/kg/d	26 (51.0)	4 (9.3)	1 (5.0)	0 (0.0)
0.5 mg/kg/d	15 (29.4)	28 (65.1)	14 (70.0)	2 (100)
0.1–0.3 mg/kg/d	0 (0.0)	0 (0.0)	2 (10.0)	0 (0.0)
Immunosuppressant/immunomodulant when associated with prednisone	n = 51	n = 43	n = 20	n = 2
Mycophenolate mofetil	13 (25.5)	9 (20.9)	1 (5.0)	0 (0)
Methotrexate	8 (15.6)	3 (7.0)	2 (10.0)	0 (0)
Azathioprine	17 (33.3)	9 (20.9)	2 (10.0)	0 (0)
Doxycylin ± nicotinamide ± potent topical corticosteroids	15 (29.4)	10 (23.3)	8 (40.0)	1 (50.0)
Dapsone ± potent topical corticosteroids	8 (15.7)	2 (4.7)	3 (15.0)	0 (0)
Rituximab	5 (9.8)	0 (0)	0 (0)	0 (0)
Intravenous Ig	6 (11.7)	1 (2.3)	1 (5.0)	0 (0)
Topical corticosteroid ± immunosuppressant	32 (38.6)	37 (46.3)	50 (71.4)	63 (96.9)
Dose of topical corticosteroid	n = 32	n = 37	n = 50	n = 63
40 g/d	11 (34.4)	6 (16.2)	2 (4.0)	0 (0)
30 g/d	11 (34.4)	11 (29.7)	6 (12.0)	6 (9.8)
20 g/d	16 (50.0)	23 (62.2)	16 (32.0)	24 (39.3)
10 g/d	0 (0)	0 (0)	0 (0)	2 (3.3)
Immunosuppressant/immunomodulant when associated with topical corticosteroid	n = 32	n = 37	n = 50	n = 63
Mycophenolate mofetil	2 (6.3)	4 (10.8)	1 (2.0)	0 (0)
Methotrexate	6 (18.8)	4 (10.8)	1 (2.0)	0 (0)
Azathioprine	4 (12.5)	5 (13.5)	2 (4.0)	2 (3.3)
Doxycyclin ± nicotinamide	3 (9.4)	9 (24.3)	16 (32.0)	9 (14.8)
Dapsone	3 (9.4)	4 (10.8)	6 (12.0)	1 (1.6)
Rituximab	1 (3.1)	0 (0)	0 (0)	0 (0)
Intravenous Ig	1 (3.1)	1 (2.7)	1 (2.0)	0 (0)
Consolidation phase	n = 76	n = 75	n = 65	n = 62
Prednisone ± immunosuppressant	42 (55.3)	32 (42.7)	15 (23.1)	2 (3.2)
Topical corticosteroid ± immunosuppressant	27 (35.5)	31 (41.3)	46 (70.8)	57 (91.9)
Immunosuppressant alone	7 (9.2)	12 (16.0)	4 (6.2)	3 (4.8)
Tapering of treatment	n = 41	n = 35	n = 28	n = 11
Reduction and finally omitting the corticosteroid before reducing the immunosuppressant	36 (87.8)	28 (80.0)	20 (71.4)	9 (81.8)
Reduction of the corticosteroid in parallel with reduction of the immunosuppressant and omitting the corticosteroid first	3 (7.3)	4 (11.4)	2 (7.1)	1 (9.1)
Reduction of the corticosteroid in parallel with reduction of the immunosuppressant and omitting the immunosuppressant first	2 (4.9)	3 (8.6)	6 (21.4)	1 (9.1)

[1]Data are expressed as the number of responses.

America (AmeriPac group), we pooled their responses in the analysis. The main treatments used by experts from Europe, US/Australia/South America, Asia, and the Middle East, depending on the clinical severity of BP, are shown in Table 2.

Severe BP. Oral CSs (usually at an initial dose of 0.5–0.75 mg/kg/day) were mostly used in the AmeriPac group (14 of 18 [77.8%]), Asia (7 of 7 [100%]), and the Middle East (7 of 10 [70%]), whereas both oral CSs (21 of 46 [45.7%]) and topical CSs (25 of 46 [54.3%]) were used in Europe. Conventional immunosuppressants (MMF, methotrexate, and azathioprine) were almost systematically associated with CSs in the AmeriPac group (17 of 18 [94.4%]) and Asia (6 of 7 [85.7%]) and less frequently in Europe (24 of 46 [52.1%]) and the Middle East (3 of 10 [30%]). The immunosuppressants that were most commonly associated with CS in Europe were methotrexate, where 10 of 24 (41.7%) responses mentioned its use, and azathioprine with 12 of 24 (50.0%) responses, whereas MMF and azathioprine were preferentially used in the AmeriPac group (10 of 17 [58.8%] and 5 of 17 [29.4%], respectively) and in Asia (2 of 6 [33.3%] and 4 of 6 [66.7%], respectively).

Moderate BP. As in severe BP, oral CSs (alone or associated with immunosuppressants or immunomodulants) were

Table 2. Treatment Modalities of Patients with Bullous Pemphigoid in Europe, US/Australia/South America, Middle East, and Asia Depending on Disease Severity

Severity of Bullous Pemphigoid	Europe n (%)	US/Australia/ South America n (%)	*P* Value	Asia n (%)	*P* Value	Middle East n (%)	*P* Value
Severe	n = 46	n = 18		n = 7		n = 10	
Prednisone alone or with immunosuppressant	21 (45.7)	14 (77.8)	0.03	7 (100.0)	0.01	7 (70.0)	0.3
Topical corticosteroid alone or with immunosuppressant	25 (54.3)	4 (22.2)	0.03	0 (0)	0.01	3 (30.0)	0.3
Moderate	n = 38	n = 20		n = 9		n = 8	
Prednisone alone or with immunosuppressant	17 (44.7)	14 (70.0)	0.1	7 (77.8)	0.1	4 (50.0)	1
Topical corticosteroid alone or with immunosuppressant	21 (55.3)	6 (30.0)	0.1	2 (22.2)	0.1	4 (50.0)	1
Mild	n = 37	n = 17		n = 6		n = 7	
Prednisone alone or with immunosuppressant	7 (18.9)	8 (47.1)	0.05	4 (66.7)	0.03	1 (14.3)	1
Topical corticosteroid alone or with immunosuppressant	30 (81.1)	9 (52.9)	0.05	2 (33.3)	0.03	6 (85.7)	1
Localized	n = 33	n = 15		n = 7		n = 7	
Prednisone alone or with immunosuppressant	0 (0)	1 (6.7)	0.3	1 (14.3)	0.2	0 (0.0)	1
Topical corticosteroid alone or with immunosuppressant	33 (100)	14 (93.3)	0.3	6 (85.7)	0.2	7 (100.0)	1

Abbreviation: US, United States.

Data are expressed in the number of responses. Comparisons were calculated by exact Fisher's exact test, versus the European group. Severe, >30 new blisters per day or >30 intact recent blisters; moderate, 10–30 new blisters per day or 10–30 intact recent blisters; and mild, <10 new blisters per day or <10 intact recent blisters.

mainly used in the AmeriPac group and Asia (14 of 20 [70.0%] and 7 of 9 [77.8%] responses, respectively), whereas both oral and topical CSs were used in Europe and the Middle East: oral CSs (17 of 38 [44.7% and 4 of 8 [50%], respectively) and topical CS (21 of 38 [55.3%] and 4 of 8 [50.0%], respectively).

Mild BP. Topical CSs were most frequently used in Europe (30 of 37 [81.1%] of responses) and the Middle East (6 of 7 [85.7%] responses), whereas in the AmeriPac group and Asia, both topical (9 of 17 [52.9%] and 2 of 6 [33.3%], respectively) and oral (8 of 17 [47.1%] and 4 of 6 [66.7%], respectively) CSs were used. Conventional immunosuppressants were very rarely used in Europe in mild types of BP (3 of 37 [8.1%]) and a little bit more frequently (5 of 17 [29.4%]) by the AmeriPac dermatologists. Doxycycline (associated with oral or topical CSs) was mostly used in the AmeriPac group (11 of 17 [64.7%]) and Asia (3 of 6 [50%]) and less frequently in Europe (8 of 37 [21.6%]) and the Middle East (2 of 7 [28.6%]). Dapsone was used almost exclusively in Europe in association with topical CSs (6 of 30 [20%]).

Localized BP. Topical CSs were almost exclusively used in these localized types of BP worldwide (60 of 62 [96.8%] of responses), most often alone (55 of 62 [81.6%]) or rarely associated with doxycycline (7 of 62 [11.3%]).

Management of patients with severe associated medical conditions

Treatment modifications according to comorbidities are shown in Table 3. Experts reduced the initial doses of oral CSs or, if possible, did not use any oral CS in patients with severe diabetes mellitus (48.1%) or cardiac insufficiency (40.2%). This was particularly true in patients with severe types of BP, who are usually treated with the highest doses of prednisone. Most experts did not modify the treatment of patients with BP with severe neurological conditions, regardless of the BP severity (45.6, 60.6, and 85.7% of responses in patients with severe, moderate, and mild BP, respectively). Similarly, most experts did not modify the treatment of patients with BP who had associated neoplasia, particularly in those with severe BP (57.9%). They indicated not using immunosuppressants in patients with neoplasia in only 22.8% of cases. Experts avoided methotrexate or any other immunosuppressant in patients with renal insufficiency in only 21.1% or 23.0% of cases, respectively.

DISCUSSION

This survey showed that the two main treatments proposed for patients with BP were oral prednisone and superpotent topical CSs. High doses of oral CSs have been considered the mainstay of treatment for patients with BP for many years (Korman, 1998; Westerhof, 1989). Poor tolerance of high doses of oral CSs in elderly patients with BP has been suspected in many open studies in the literature (Joly et al., 2005; Roujeau et al., 1998; Rzany et al., 2002) and has been definitely shown in an RCT, which showed that superpotent topical CSs were safer and more effective than 1 mg/kg/day of oral prednisone (Joly et al., 2002). Accordingly, a 1.0 mg/kg/day dose of oral prednisone was rarely proposed by experts (17.5%), even in patients with severe BP. The most frequently proposed starting dose of prednisone was 0.5–0.75 mg/day (Morel and Guillaume, 1984). A starting dose of 0.5 mg/kg/day of prednisone has been recommended in the European Guidelines on BP (Feliciani et al., 2015), despite the lack of evidence showing the efficacy of this medium dose in patients with extensive BP (Daniel et al., 2011; Kirtschig et al., 2010; Singh, 2011). An initial dose of 0.5 mg/kg/day was frequently proposed by experts in patients with mild and moderate BP, which is in accordance with the RCT by Joly et al. (2002), which showed a 91% rate of disease control with this dosage in patients with mild/moderate BP.

Clobetasol propionate cream was used at an initial dose of between 20 and 30 g/day, as was done in three large clinical trials that showed a 74–100% rate of clinical remission in both types of BP (Joly et al., 2009, 2002; Terra et al., 2014).

Table 3. Management of Patients with BP According to Associated Disorders

n (%)	Severe/Debilitating Neurological Condition (Severe Dementia, Stroke, Severe Parkinson's Disease, Bed-Ridden Patients…)			Severe Diabetes Mellitus			Cardiac Insufficiency/ Severe Cardiovascular Associated Condition			Renal Insufficiency (Creatinine Clearance <40 ml/min)			Associated Cancer		
No. of responses	**Severe, 79**	**Moderate, 71**	**Mild, 63**	**Severe, 79**	**Moderate, 69**	**Mild, 62**	**Severe, 77**	**Moderate, 73**	**Mild, 66**	**Severe, 74**	**Moderate, 72**	**Mild, 65**	**Severe, 57**	**Moderate, 55**	**Mild, (51)**
No change	36 (45.6)	43 (60.6)	54 (85.7)	19 (24.1)	34 (49.3)	48 (77.4)	26 (33.8)	38 (52.1)	49 (74.2)	32 (43.2)	40 (55.6)	53 (81.5)	33 (57.9)	40 (72.7)	47 (92.1)
No or lower dose of corticosteroids	22 (27.8)	16 (22.5)	3 (4.8)	38 (48.1)	24 (34.8)	8 (12.9)	31 (40.2)	20 (27.4)	5 (7.6)	16 (21.6)	10 (13.9)	5 (7.7)	4 (7.0)	2 (3.6)	1 (2.0)
No/some/any immunosuppressant	7 (8.9)	4 (5.6)	1 (1.6)	1 (1.3)	0 (0.0)	0 (0.0)	7 (9.1)	4 (5.5)	6 (9.1)	17 (23.0)	12 (16.7)	3 (4.6)	13 (22.8)	9 (16.3)	2 (3.9)
Complete change of regimen and use other drugs	14 (17.7)	8 (11.3)	5 (7.9)	21 (26.6)	11 (15.9)	6 (9.7)	13 (16.9)	11 (15.1)	6 (9.1)	9 (12.2)	10 (13.9)	4 (6.2)	7 (12.3)	4 (7.3)	1 (2.0)

Abbreviations: BP, bullous pemphigoid; No., number.

Extensive/severe BP, >30 new blisters/day or >30 intact recent blisters; moderate BP, 10–30 new blisters/day or 10–30 intact recent blisters; and mild but nonlocalized BP, <10 new blisters/day or <10 intact recent blisters.

Despite the fact that no RCT could show any benefit for the association of conventional immunosuppressants with CSs over CS alone (Daniel et al., 2011; Kirtschig et al., 2010), immunosuppressants were widely proposed by experts mainly in association with systemic CSs in the treatment of severe BP. In fact, although several open-label studies evaluating methotrexate, MMF, and azathioprine have suggested their efficacy either alone (Greaves et al., 1971; Grundmann-Kollmann et al., 1999; Paul et al., 1994) or in association with systemic or topical CSs (Beissert et al., 2007; Du Thanh et al., 2011; Guillaume et al., 1993), the only RCT that assessed the safety and efficacy of azathioprine in addition to oral CSs showed no benefit and an increased risk of treatment side effects, particularly, severe infections in patients with the combined treatment relative to infections in those who received oral prednisone alone (Guillaume et al., 1993). In our survey, methotrexate was most commonly proposed in association with topical CSs (mainly in European countries), whereas azathioprine and MMF were preferentially associated with oral prednisone (Beissert et al., 2007).

Dapsone was rarely proposed (from 4.7 up to 15.7%) regardless of BP severity. Its efficacy has been suggested in small retrospective case series and a recent RCT (Bouscarat et al., 1996; Gürcan and Ahmed, 2009; Schmidt et al., 2005). Doxycycline was proposed in a minority of patients with mild and moderate types of BP (23.9 and 34.3%, respectively), whereas a recent RCT suggested that a regimen associating doxycycline with topical CSs would be non-inferior to a medium dose of oral prednisolone (Williams et al., 2017).

Interestingly, the way experts treat the different types of BP was quite different between the AmeriPac countries (US, Latin America, and Australia) and Asia on the one hand and between Europe and the Middle East on the other hand. Topical CSs were mainly used by experts from Europe and the Middle East to treat mild BP (around 80%), moderate BP (around 50%), and severe types of BP (54.3%). These findings are in accordance with the European guidelines, which recommended the use of topical CSs as first-line treatment for both mild, moderate, and severe types of BP (Korman, 1998). Conversely, systemic CSs were mainly proposed by AmeriPac and Asian dermatologists, not only in moderate (70 and 77.8%, respectively) and severe (77.8 and 100%, respectively) types of BP but also quite frequently in mild types of BP (47.1 and 33.3%, respectively). This finding might be explained by the different healthcare systems and the very high price of clobetasol propionate cream in the US, Australia, and some Asian countries. Moreover, the absence of dermatology-specific in-patient hospitalization units in the US and Australia makes the application of topical CSs over large body surface areas difficult.

As expected, many experts suggested not using oral CSs or at least reducing the dose of CSs in patients with BP with diabetes mellitus or cardiac insufficiency and avoiding the use of methotrexate in patients with renal insufficiency. Surprisingly, only 22.8% of experts avoided immunosuppressants in patients with BP with associated cancer.

A limitation of our study is the presence of only one expert from Africa and nine Asian experts. This is related to the fact that the 78 experts who participated in this publication were

first identified by their publications in the field of BP, agreed to complete the survey, and participated in the international meeting on autoimmune bullous diseases during which the relevance of questions in the survey was discussed. However, we aimed to only survey renowned international experts who have published in the field of autoimmune bullous diseases. Because there could be more than one answer to a given question in the survey, the number of responses was higher than the number of experts. This could have led to an over-representation of the responses of experts who completed several questions.

Overall, this study showed a wide heterogeneity in the treatments used in patients with BP, which appears to be at least as much related to physicians' habits and characteristics of the different healthcare systems as to evidence-based medicine.

MATERIALS AND METHODS

A preliminary survey was sent by e-mail to a panel of international experts in the field of autoimmune bullous diseases in March 2017. Survey questions were related to the different options used for the initial and the consolidation phases of treatment of patients with BP, depending on severity and patients' associated disorders.

Disease severity was classified as severe (>30 new blisters per day or >30 intact recent blisters), moderate (10–30 new blisters per day or 10–30 intact recent blisters), mild (>10 new blisters per day or >10 intact recent blisters), and localized BP. The different comorbidities considered were the presence of a severe or debilitating neurological condition (severe dementia, stroke, severe Parkinson's disease, bed-ridden patients), severe diabetes, cardiac insufficiency or severe cardiovascular conditions, renal insufficiency, and associated cancer.

The relevance of questions in the survey and the different ways of treating patients with BP were discussed by the International Bullous Diseases Consensus Group during an international meeting on autoimmune bullous diseases in Lübeck (Germany) in June 2017. On the basis of the comments and discussions, the initial survey was modified and sent to a larger number of international experts to ensure the widest possible representation. The final results were discussed by the International Bullous Diseases Consensus Group in March 2018 during the annual meeting of the American Academy of Dermatology in San Diego.

Responses are expressed in numbers and percentages. Because participants were allowed to tick several responses, the percentages were calculated using the number of responses instead of the number of authors. The frequencies were compared using Fisher's exact test. A value of $P < 0.05$ was considered statistically significant.

Data availability statement

No datasets were generated or analyzed during this study.

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CONFLICT OF INTEREST

DFM is a consultant for Roche, Principia-bio, Lilly, GSK, Novartis, Sanofi, Regeneron, and ArgenX; a coinventor of Bullous Pemphigoid Disease Area Index; and inventor of Autoimmune Bullous Disease Quality of Life and Autoimmune Bullous Disease Quality of Life. MA has received research grants from Maruho, Kose, and JSR. VA conducted a clinical trial for Roche. JB is a consultant for Castle Creek Pharma, KBHB, and TWI. DC is a consultant for Principia Biopharma, Afyx Therapeutics, and Cabaletta Bio. RH is consultant and/or clinical trial investigator for Cabelleta, Argenx, Principia, Regeneron, Akari, and Alexion and an Editor of *JID Innovations*. NJK has served as a consultant, principal investigator, advisory board member, or speaker for AbbVie, Amgen, Celgene, Chemocentryx, Dermira, Eli Lilly, Genentech, GlaxoSmithKline, Immune, Janssen, Kyowa Hakko Kirin Pharma, Leo Pharma, Menlo Therapeutics, Novartis, Pfizer, Principia, Prothena, Regeneron, Rhizen, Sun Pharma, Syntimmune, Trevi, UCB, Valeant, and XBiotech. AP is a consultant for Principia Biopharma, Jannsen, Leo, Novartis, AbbVie, Lilly, UCB, and Genesis Pharma – Greece. ESc is a consultant for UCB, Incyte, Argenx, Roche, Genentech, AstraZeneca, Admirx, Synthon, Imevax, and Thermo Fisher Scientific. In addition, he received honoraria from Novartis, Biotest, and Fresenius. He has research grants with UCB, Incyte, Argenx, Admirx, Synthon, and Biotest. ESp is consultant for Solgel, Pierre Fabre, Kamari, BIOMX, and Bayer. SU is a consultant for Roche. VPW is a consultant for Genentech, Janssen, Lilly, Principia, AstraZeneca, Argenx, and Regeneron and received grants from Genentech, Syntimmune, and Regeneron. DZ has obtained support for research and development work, lecturing, and consulting from AbbVie, Argenx, Biotest, Euroimmun, Fresenius, Janssen, and UCB Pharma within the last 3 years and speaker's honoraria/travel support from Biotest, Fresenius, Miltenyi, Roche, Biogen, AbbVie, UCB, Janssen, and Novartis. PJ is a consultant for Roche, Amgen, Principia Biopharma, Argenx, AstraZeneca, Thermo Fisher Scientific, Sanofi, Akari, Janssen, Novartis, Servier, Chugai, Kezar Life Science, Regeneron, UCB, Lilly, and AbbVie. The remaining authors state no conflict of interest.

ACKNOWLEDGMENTS

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