ORIGINAL REPORT

Identification of Risk Factors for Gliptin-associated Bullous Pemphigoid among Diabetic Patients

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Drug-associated bullous pemphigoid has been shown to follow long-term gliptin (dipeptidyl-peptidase 4 inhibitors) intake. This study aimed at identifying risk factors for gliptin-associated bullous pemphigoid among patients with type 2 diabetes. A retrospective study was conducted in a tertiary centre among diabetic patients exposed to gliptins between the years 2008–2021. Data including demographics, comorbidities, medications, and laboratory results were collected using the MDClone platform. Seventy-six patients with type 2 diabetes treated with dipeptidyl-peptidase 4 inhibitors who subsequently developed bullous pemphigoid were compared with a cohort of 8,060 diabetic patients exposed to dipeptidyl-peptidase 4 inhibitors who did not develop bullous pemphigoid. Based on a multivariable analysis adjusted for age and other covariates, Alzheimer's disease and other dementias were significantly more prevalent in patients with bullous pemphigoid ($p = 0.0013$). Concomitant use of either thiazide or loop diuretics and gliptin therapy was associated with drug-associated bullous pemphigoid ($p < 0.0001$ for both). While compared with sitagliptin, exposure to linagliptin and vildagliptin were associated with bullous pemphigoid with an odds ratio of 5.68 and 6.61 ($p < 0.0001$ for both), respectively. These results suggest gliptins should be prescribed with caution to patients with type 2 diabetes with coexisting Alzheimer's and other dementias, or patients receiving long-term use of thiazides and loop diuretics. The use of sitagliptin over linagliptin and vildagliptin should be preferred in these patients.

Key words: autoimmune blistering disease; bullous pemphigoid; bullous drug reaction; drug reaction; dipeptidyl peptidase 4 inhibitor; gliptin.

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SIGNIFICANCE

Bullous pemphigoid has been shown to follow intake of dipeptidyl-peptidase 4 inhibitors. This study identifies additional risk factors for drug-associated bullous pemphigoid among patients with type 2 diabetes receiving gliptins: Alzheimer's disease and other dementias or chronic treatment with thiazide or loop diuretics.

Bullous pemphigoid (BP) is the most prevalent blistering autoimmune disease among elderly individuals (1), typically characterized by pruritus followed by tense blisters involving the skin (2). Mucosal membrane involvement is observed in 20% of patients (3). BP is defined immunologically by the presence of autoantibodies against collagen XVII (BP180, BPAg2) and dystonin (BP230, BPAg1), which serve as hemi-desmosomal structural proteins, located at the dermal–epidermal junction (4).

Dipeptidyl-peptidase 4 inhibitors (DPP-4i), also known as gliptins, are widely used drugs in the treatment of type 2 diabetes mellitus (DM2). As gliptins increase the level of the hormone incretin, they enhance glycaemic control by increasing insulin secretion and decreasing glucagon secretion (5). The first FDA-approved gliptin was sitagliptin in 2006. Currently, more than 10 gliptins have been endorsed and are available for clinical use (6).

Several reasons have been credited for the rise in the incidence of BP over the past decades, one being the increasing use of medications associated with the eruption of this cutaneous disease (6, 7). The most common drugs that induce BP are gliptins, PD-1/PD-L1 inhibitors, loop diuretics, and antibiotics, especially penicillin (6). In recent years, the emergence of DPP-4i as a significant contributor to drug-induced BP has been reported (7–12). The association between DPP-4i intake and development of BP was initially described in 2012 (13). A recent meta-analysis by Kridin and Cohen (14) reported a 3.2-fold increased risk of developing BP following DPP-4i administration, of which vildagliptin was found to have the highest association with BP among the DPP-4i.

Several common comorbidities (15–17) and medications have been shown to be associated with BP. It has yet to be determined whether gliptin intake alone might induce BP or whether additional factors such as concomitant drug therapy and comorbidities are required. The aim of this study is to define the patient population at risk of developing BP secondary to DPP-4i treatment.

MATERIALS AND METHODS

Design and study population

We conducted a single-centre retrospective study among DM2 patients who were treated with gliptins from 1 January 2008 to 31 March 2021 at the Tel Aviv Sourasky Medical Center. Identification of cases and data collection were performed using MDClone software version 6.1 (https://www.mdclone.com/), which enables obtaining big data using our hospital's digital patient database.

This study protocol was approved by the institutional Helsinki research ethics committee in Tel Aviv Sourasky Medical Center, approval number 09-36-20-TLV. The study group included patients with a new diagnosis of BP and history of diabetes and gliptin therapy. BP patients included in the study were all diagnosed by a dermatologist based on clinical, histological, and direct immunofluorescence (DIF) parameters as previously described by Kershenovich et al. (18). All BP patients included in the study had a DIF microscopy of perilesional, uninvolved skin with linear, continuous deposits of IgG and/or C3 along the epidermal basement membrane. Manual revision of all BP patients' medical files was performed. The control group consisted of DM2 patients with a history of gliptin intake, but without BP, admitted to our hospital. The specific gliptin used for each patient was recorded, and if a patient consumed more than one gliptin only the last medication was analysed.

Statistical analysis

Categorical variables were presented with frequencies and percentages, continuous variables were presented with mean (SD) (median, IQR). Association between categorical variables and the binary endpoint (i.e. BP yes/no) was performed using a χ^2 test (or Fisher's exact test). For continuous variables, *t*-test (or Wilcoxon two-sample test) was implemented. Univariate and multivariable logistic regression was performed presenting odds ratios (OR) and adjusted OR (aOR) with 95% confidence intervals (95% CI). The statistical analysis and data management were performed using SAS 9.4 software (SAS Institute Inc, Cary, NC, USA). *P*-value <0.05 was considered statistically significant.

RESULTS

Demographic and clinical characteristics of the study participants

The study group included 76 BP patients with a history of gliptin intake (research group) and 8,060 DM2 patients who received gliptins and did not develop BP (control group). The mean age at the time of data extraction for BP patients and control group was 81.9 and 77.2 years, respectively. Additional demographic characteristics, HbA1c values, and target organ damage are summarized in **Table I**.

Risk factors for developing bullous pemphigoid secondary to DPP-4i

Table II depicts the prevalence of comorbid conditions in the study and control groups (19). A statistically significant higher rate of Alzheimer's disease and other dementias, essential hypertension, and kidney failure was observed in BP patients who received DPP-4i, compared

Table I. Demographic and clinical characteristics of the study participants

	BP (*n* = 76)	No BP (*n* = 8,060)	*p*-value
Demographic characteristics			
Age, years, mean (SD)	81.9 (8.7)	77.2 (11.3)	**< 0.0001**
Median [IQR]	83.1 [75.3–88.7]	[77, 69.9–85.7]	
Female gender, *n* (%)	37 (48.68)	3285 (40.76)	0.1617
BMI, kg/m^2,* mean (SD)	28.7 (5.1)	30.7 (50.2)	0.7605
Median [IQR]	[27.4, 25.4–30.5]	[27.6, 24.6–31.2]	
Weight, kg,* mean (SD)	77.3 (15.8)	80.1 (18)	0.1792
Median [IQR]	[72.5, 66–85]	[79, 68–90]	
Height,* mean (SD)	163.1 (8.3)	166.4 (15.8)	0.0038
Median [IQR]	[164, 160–167]	[168, 160–174]	
Smoking (current/past),* *n* (%)	11 (18.64)	748 (27.38)	0.1357
Smoking years,* mean (SD)	27.5 (16)	34.6 (14.4)	0.2710
Median [IQR]	[25, 20–40]	[37, 25–45]	
Mortality, *n* (%)	23 (30.26)	2588 (32.11)	0.7315
Diabetes characteristics			
Retinopathy, *n* (%)	3 (3.95)	338 (4.19)	
Nephropathy, *n* (%)	1 (1.32)	133 (1.65)	
Neuropathy, *n* (%)	3 (3.95)	224 (2.78)	0.4717
HbA1C,* mean (SD)	7.4 (1.3)	7.7 (1.8)	0.5382
Median [IQR]	[7.3, 6.4–8.1]	[7.3, 6.6–8.3]	
Chronic medications			
Antihypertensives, *n* (%)	22 (28.95)	2569 (31.87)	0.5858
Thiazides, n (%)	21 (27.63)	694 (8.61)	**< 0.0001**
PD1/PD-L1, n (%)	0 (0)	1 (0.01)	
Loop diuretics, n (%)	18 (23.68)	627 (7.78)	**< 0.0001**
NSAIDS, *n* (%)	0 (0)	23 (0.29)	
Penicillins, *n* (%)	0 (0)	16 (0.2)	

*Missing data for percentage of study participants: body mass index (BMI) – 25%, weight – 22%, height – 27%, smoking status – 66%, smoking years – 47%, HbA1C–63%. Statistically significant values are shown in bold.

Table II. Comorbidities of study participants

Comorbidity	BP (*n* = 76) *n* (%)	No BP (*n* = 8,060) *n* (%)	*p*-value
Lupus	0 (0)	17 (0.21)	
Celiac	0 (0)	5 (0.06)	
Rheumatoid arthritis	2 (2.63)	108 (1.34)	0.2745
Inflammatory bowel disease	1 (1.32)	48 (0.60)	0.3695
Hypothyroidism	7 (9.21)	856 (10.62)	0.6912
Graves' disease	0 (0)	3 (0.04)	
Autoimmune thrombocytopenia	0 (0)	19 (0.24)	
Psoriasis	2 (2.63)	118 (1.46)	0.3091
Lichen planus	0 (0)	4 (0.05)	
Dermatomyositis	0 (0)	2 (0.02)	
Vitiligo	0 (0)	17 (0.21)	
Hidradenitis suppurative	0 (0)	11 (0.14)	
Multiple sclerosis	0 (0)	8 (0.1)	
Parkinson's disease	5 (6.58)	218 (2.70)	0.0570
Dementia/Alzheimer's disease	13 (17.11)	418 (5.19)	**0.0002**
Epilepsy	1 (1.32)	166 (2.06)	
Psychosis	0 (0)	16 (0.2)	
Diabetes mellitus	76 (100)	8,060 (100)	
Cushing disease	0 (0)	3 (0.04)	
Ischemic heart disease/myocardial infarction	27 (35.53)	3,308 (41.04)	0.3305
Arrhythmias	3 (3.95)	182 (2.26)	0.2490
Congestive heart failure	16 (21.05)	1,548 (19.21)	0.6843
Primary essential hypertension	67 (88.16)	6,027 (74.78)	**0.0074**
Dyslipidaemia	47 (61.84)	4936 (61.24)	0.9147
Cerebrovascular accident without transient ischaemic attack	15 (19.74)	1,157 (14.35)	0.1835
Myocarditis	0 (0)	7 (0.09)	
Kidney failure	26 (34.21)	1,869 (23.19)	**0.0237**
Nephrotic syndrome	0 (0)	40 (0.50)	
COPD	7 (9.21)	623 (7.73)	0.6307
Restrictive lung disease	1 (1.32)	28 (0.35)	0.2386
Pneumonia	16 (21.05)	1,353 (16.79)	0.3324

Statistically significant values are shown in bold.

Table III. Univariate versus multivariable analysis

	Univariate analysis				Multivariable analysis			
		95% CI				95% CI		
	OR	Low	Up	*p*-value	Adj. OR	Low	Up	*p*-value
Age	1.07	1.05	1.10	**<0.0001**	1.06	1.03	1.08	**0.0001**
Male gender	0.73	0.46	1.14	0.1633	0.98	0.59	1.60	0.9217
Medications								
Chronic thiazides	4.05	2.44	6.74	**<0.0001**	3.69	2.14	6.37	**<0.0001**
Chronic loop diuretics	3.68	2.16	6.28	**<0.0001**	2.95	1.65	5.28	**0.0003**
Comorbidities								
Hypertension	2.51	1.25	5.04	**0.0097**	2.02	0.91	4.48	0.0845
Dementia/Alzheimer's	3.77	2.06	6.91	**<0.0001**	2.92	1.52	5.60	**0.0013**
Chronic renal failure	1.72	1.07	2.78	**0.0254**	1.08	0.64	1.85	0.7708
Type of gliptin								
Sitagliptin	1				1			
Linagliptin	5.68	3.19	10.10	**<0.0001**	5.25	2.83	9.73	**<0.0001**
Vildagliptin	6.61	3.79	11.55	**<0.0001**	6.55	3.64	11.81	**<0.0001**

OR: odds ratio; Adj. OR: adjusted odds ratio; multivariable C-statistics 84%. Statistically significant values are shown in bold.

with DM2 patients treated with gliptins but who did not develop BP. In a multivariable analysis after adjusting for age and other covariates, only Alzheimer's disease and other dementias remained statistically significant for BP development (**Table III**). We did not observe a significant difference for other conditions, including autoimmune diseases, between the two groups.

Additionally, our results showed that the chronic intake of loop diuretics and thiazides was significantly more prevalent among research group when compared with the control group (Table I). Upon performing a multivariable analysis adjusted for covariates (Table III), the association of these drugs with BP was still significant ($p < 0.0001$ for thiazides and $p = 0.0003$ for loop diuretics).

Duration of gliptin intake prior to bullous pemphigoid onset and gliptin characteristics

Twenty-two patients (32.35%) developed BP within one year of gliptin intake, 26 patients (38.24%) within one year to 2 years, and 20 patients above 2 years (29.41%). For the remaining 8 patients, there was no information regarding the time period between intake of gliptin and the development of BP in their medical records. The relative proportion of specific gliptin medication varied between the study and control groups (**Table IV**). Linagliptin and vildagliptin were more prevalent among BP patients than in the control group (32.89% vs 14.31% and 38.16% vs 14.24%, respectively), while sitagliptin had a reduced relative proportion in BP patients (28.95% to 71.45%); these results were all statistically significant.

Table IV. Gliptins characteristics of the study participants

	BP ($n = 76$) *n* (%)	No BP ($n = 8,060$) *n* (%)	*p*-value
Type of gliptin			**<0.0001**
Sitagliptin	22 (28.95)	5,758 (71.45)	
Linagliptin	25 (32.89)	1,153 (14.31)	
Vildagliptin	29 (38.16)	1,148 (14.24)	

Statistically significant values are shown in bold.

Using sitagliptin as a reference for comparison, the three different gliptins were also compared using univariate and multivariable logistic regression models (Table III). For the BP group, linagliptin and vildagliptin had statistically significant higher odds than sitagliptin with aORs of 5.25 ($p < 0.0001$, 95% CI 2.83–9.73) and 6.55 ($p < 0.0001$, 95% CI 3.64–11.81) respectively.

DISCUSSION

BP is a severe blistering autoimmune disease that mainly affects elderly patients with significant morbidity and potential mortality. The rise in BP incidence worldwide has been attributed to the increase in life expectancy, as well as improved diagnostic tests and increased usage of specific medications (20, 21). More than 89 drugs have been reported to induce BP, yet robust evidence suggests that DPP-4i carries the greatest risk for BP induction (22–24).Our study examined comorbidities and concomitant medications that might predispose DM2 patients to develop gliptin-associated BP. Delineating the specific risk factors for gliptin-associated BP in DM2 patients can guide the physician when choosing gliptin therapy in susceptible patients and thus help to decrease gliptin-associated BP incidence.

Because adverse effects of DPP-4i are rare, they are used extensively in elderly DM2 patients (25).

Univariate analysis showed that BP patients were significantly older than the control group and had higher prevalence of chronic renal failure, hypertension, and Alzheimer's disease and other dementias. Upon performing a multivariable analysis with adjustment for age and other covariates only the association of Alzheimer's disease and other dementias with gliptin-associated BP remained significant. Neurological diseases are known to be intertwined with BP onset (26). Studies have credited this to epitope spreading secondary to a cross-reaction between the neuronal and cutaneous isoforms of BPAg1 (27). The results of our study highlight the increased risk for patients with Alzheimer's disease and other demen-

tias to develop BP after exposure to gliptins. Despite BP being linked with other autoimmune disorders and skin diseases (15), the results of our study did not find these comorbidities to increase the risk for BP onset among gliptin-treated DM2 patients.

In previous studies, gliptin has been implicated as a predisposing factor for BP even several years after its onset (28).We confirm these findings, with more than 65% of patients developing BP more than 1 year after gliptin initiation.

Chronic intake of thiazides or loop diuretics was found to be an independent risk factor for developing BP among DM2 patients receiving gliptins. This is not surprising as diuretics have long been associated with drug-induced BP (20, 21). However, the additive risk of gliptin consumption when taken concurrently with thiazides or loop diuretics has not been examined. The pathogenesis of drug-induced BP secondary to thiazides and loop diuretics has been linked to the fact that these medications are thiol-based and may disrupt the integrity of the basement membrane through either immunologic or non-immunologic mechanisms (21). Gliptins can elicit BP in patients with underlying susceptibility by modifying the immune response and altering the antigenic properties of the epidermal basement membrane zone. Therefore, gliptins and sulphur-containing drugs may have an additive effect on BP induction (13). In a recent case-control study by Gravani et al. (29), anticoagulants, proton pump inhibitors, and selective serotonin reuptake inhibitors were associated with a significantly higher risk of drug-associated BP. In light of these results, we suggest that patients' prescribed medications should be thoroughly reviewed. Caution should be advised when prescribing gliptins with thiazides or loop diuretics. Future prospective studies are needed to clarify whether the combination of these drugs has an additive effect on BP induction. Several epidemiological studies have confirmed the link between DPP-4i, particularly vildagliptin, and drug-associated BP risk (10). However, data comparing the risk of BP development among different DPP4i have just begun to emerge. In a study published in 2021 by Jedlowski et al. (30) anagliptin, vildagliptin, and teneligliptin had a higher reporting odds ratio than alogliptin, linagliptin, saxagliptin, and sitagliptin to develop BP. A systematic review and meta-analysis published in 2020 by Phan et al. (31) demonstrated a strong association between vildagliptin and BP. BP has also been linked to linagliptin; however, the association was weaker than with vildagliptin. There was no association between sitagliptin administration and BP. Similar results were also observed in an analysis of cases published by Sun et al. in 2022 (32). Our results are in accordance with previous studies showing linagliptin and vildagliptin had a stronger association with drug-associated BP than sitagliptin. Accordingly, sitagliptin may be a safer option for DM2 patients at risk of developing BP.

The results of our study emphasize the importance of physician vigilance in the treatment of DM2 patients. When considering gliptins for diabetics, attention to patient comorbidities and chronic medications could aid in identifying patients who may be at risk, preventing drug-associated BP and the development of additional unnecessary comorbidities associated with long-term corticosteroid treatment. Our study's limitations arise from its design being a single-centre retrospective study. The study's strength lies in its large cohort size of BP patients with previous exposure to gliptins and comparison of different gliptin subtypes.

In conclusion, our study highlights the need for caution when prescribing gliptins in DM2 patients receiving thiazides or loop diuretics and in those suffering from Alzheimer's disease and other dementias. Sitagliptin should be preferred in these patients over linagliptin and vildagliptin.

The authors have no conflicts of interest to declare.

REFERENCES

1. Joly P, Baricault S, Sparsa A, Bernard P, Bedane C, Duvert-Lehembre S, et al. Incidence and mortality of bullous pemphigoid in France. J Invest Dermatol 2012; 132: 1998–2004.
2. Schmidt E, Zillikens D. Pemphigoid diseases. Lancet 2013; 381: 320–332.
3. Clape A, Muller C, Gatouillat G, Le Jan S, Barbe C, Pham BN, et al. Mucosal involvement in bullous pemphigoid is mostly associated with disease severity and to absence of anti-BP230 autoantibody. Front Immunol 2018; 9: 479.
4. Kasperkiewicz M, Zillikens D. The pathophysiology of bullous pemphigoid. Clin Rev Allergy Immunol 2007; 33: 67–77.
5. Muscelli E, Casolaro A, Gastaldelli A, Mari A, Seghieri G, Astiarraga B, et al. Mechanisms for the antihyperglycemic effect of sitagliptin in patients with type 2 diabetes. J Clin Endocrinol Metab 2012; 97: 2818–2826.
6. Kang SM, Park JH. Pleiotropic benefits of DPP-4 inhibitors beyond glycemic control. Clin Med Insights Endocrinol Diabetes 2021; 14: 11795514211051698.
7. Benzaquen M, Borradori L, Berbis P, Cazzaniga S, Valero R, Richard MA, et al. Dipeptidyl peptidase IV inhibitors, a risk factor for bullous pemphigoid: retrospective multicenter case-control study from France and Switzerland. J Am Acad Dermatol 2018; 78: 1090–1096.
8. Kawaguchi Y, Shimauchi R, Nishibori N, Kawashima K, Oshitani S, Fujiya A, et al. Dipeptidyl peptidase-4 inhibitors-associated bullous pemphigoid: a retrospective study of 168 pemphigoid and 9,304 diabetes mellitus patients. J Diabetes Investig 2019; 10: 392–398.
9. Kridin K, Bergman R. Association of bullous pemphigoid with dipeptidyl-peptidase 4 inhibitors in patients with diabetes: estimating the risk of the new agents and characterizing the patients. JAMA Dermatol 2018; 154: 1152–1158.
10. Lee SG, Lee HJ, Yoon MS, Kim DH. Association of dipeptidyl peptidase 4 inhibitor use with risk of bullous pemphigoid in patients with diabetes. JAMA Dermatol 2019; 155: 172–177.
11. Plaquevent M, Tetart F, Fardet L, Ingen-Housz-Oro S, Valeyrie-Allanore L, Bernard P, et al. Higher frequency of dipeptidyl peptidase-4 inhibitor intake in bullous pemphigoid patients than in the French general population. J Invest Dermatol 2019; 139: 835–841.
12. Varpuluoma O, Forsti AK, Jokelainen J, Turpeinen M, Timonen M, Huilaja L, et al. Vildagliptin significantly increases the risk of bullous pemphigoid: a Finnish nationwide registry study. J Invest Dermatol 2018; 138: 1659–1661.
13. Skandalis K, Spirova M, Gaitanis G, Tsartsarakis A, Bassukas

ID. Drug-induced bullous pemphigoid in diabetes mellitus patients receiving dipeptidyl peptidase-IV inhibitors plus metformin. J Eur Acad Dermatol Venereol 2012; 26: 249–253.
14. Kridin K, Cohen AD. Dipeptidyl-peptidase IV inhibitor-associated bullous pemphigoid: a systematic review and meta-analysis. J Am Acad Dermatol 2021; 85: 501–503.
15. Chen YJ, Wu CY, Lin MW, Chen TJ, Liao KK, Chen YC, et al. Comorbidity profiles among patients with bullous pemphigoid: a nationwide population-based study. Br J Dermatol 2011; 165: 593–599.
16. Di Zenzo G, Della Torre R, Zambruno G, Borradori L. Bullous pemphigoid: from the clinic to the bench. Clin Dermatol 2012; 30: 3–16.
17. Forsti AK, Jokelainen J, Timonen M, Tasanen K. Risk of death in bullous pemphigoid: a retrospective database study in Finland. Acta Derm Venereol 2016; 96: 758–761.
18. Kershenovich R, Hodak E, Mimouni D. Diagnosis and classification of pemphigus and bullous pemphigoid. Autoimmun Rev 2014; 13: 477–481.
19. Huttelmaier J, Benoit S, Goebeler M. Comorbidity in bullous pemphigoid: up-date and clinical implications. Front Immunol 2023; 14: 1196999.
20. Stavropoulos PG, Soura E, Antoniou C. Drug-induced pemphigoid: a review of the literature. J Eur Acad Dermatol Venereol 2014; 28: 1133–1140.
21. Verheyden MJ, Bilgic A, Murrell DF. A systematic review of drug-induced pemphigoid. Acta Derm Venereol 2020; 100: adv00224.
22. Tasanen K, Varpuluoma O, Nishie W. Dipeptidyl peptidase-4 inhibitor-associated bullous pemphigoid. Front Immunol 2019; 10: 1238.
23. Kridin K, Ludwig RJ. The growing incidence of bullous pemphigoid: overview and potential explanations. Front Med (Lausanne) 2018; 5: 220.
24. Persson MSM, Harman KE, Vinogradova Y, Langan SM, Hippisley-Cox J, Thomas KS, Gran S. Incidence, prevalence and mortality of bullous pemphigoid in England 1998–2017: a population-based cohort study. Br J Dermatol 2021; 184: 68–77.
25. Leiter LA, Teoh H, Braunwald E, Mosenzon O, Cahn A, Kumar KM, et al. Efficacy and safety of saxagliptin in older participants in the SAVOR-TIMI 53 trial. Diabetes Care 2015; 38: 1145–1153.
26. Langan SM, Groves RW, West J. The relationship between neurological disease and bullous pemphigoid: a population-based case-control study. J Invest Dermatol 2011; 131: 631–636.
27. Li L, Chen J, Wang B, Yao Y, Zuo Y. Sera from patients with bullous pemphigoid (BP) associated with neurological diseases recognized BP antigen 1 in the skin and brain. Br J Dermatol 2009; 160: 1343–1345.
28. Kridin K, Avni O, Damiani G, Tzur Bitan D, Onn E, Weinstein O, Cohen AD. Dipeptidyl-peptidase IV inhibitor (DPP4i) confers increased odds of bullous pemphigoid even years after drug initiation. Arch Dermatol Res 2023; 315: 33–39.
29. Gravani A, Christou P, Tigas S, Bassukas ID. Co-medications and dipeptidyl peptidase-4 inhibitors associated bullous pemphigoid. An Bras Dermatol 2021; 96: 782–784.
30. Jedlowski PM, Jedlowski MF, Fazel MT. DPP-4 inhibitors and increased reporting odds of bullous pemphigoid: a pharmacovigilance study of the FDA Adverse Event Reporting System (FAERS) from 2006 to 2020. Am J Clin Dermatol 2021; 22: 891–900.
31. Phan K, Charlton O, Smith SD. Dipeptidyl peptidase-4 inhibitors and bullous pemphigoid: a systematic review and adjusted meta-analysis. Australas J Dermatol 2020; 61: e15–e21.
32. Sun L, Wang C, Wu C, Zhou Y, Wang C. Analysis of the clinical characteristics of dipeptidyl peptidase-4 inhibitor-induced bullous pemphigoid. Ann Pharmacother 2022; 56: 205–212.