

**Table S1. IgG, IgE and IgA humoral responses to BP180/BP230 in idiopathic and drug-associated bullous pemphigoid patients.**

AutoAb	Antigen/epitope	ICI-BP	IBP	GABP	ICI-BP vs IBP (p)	ICI-BP vs GABP (p)
		<b>Reactivity, n/N (%)</b>				
<b>IgG</b>	<b>BP180 NC16A<sup>a</sup></b>	41/50 (82.0)	53/59 (89.8)	20/30 (66.7)	NS	NS
	<b>BP230<sup>a</sup></b>	12/50 (24.0)	33/59 (55.9)	5/30 (16.7)	<b>0.001</b>	NS
	<b>ECD-BP180<sup>b</sup></b>	44/47 (93.6)	46/59 (78.0)	29/30 (96.7)	<b>0.044</b>	NS
	<b>BP180 – E-1080<sup>c</sup></b>	26/47 (55.3)	19/59 (32.2)	13/30 (43.3)	<b>0.028</b>	NS
	<b>BP180 – E-1331<sup>d</sup></b>	34/47 (72.3)	24/59 (40.7)	16/30 (53.3)	<b>0.002</b>	NS
<b>IgE</b>	<b>BP180 NC16A<sup>e</sup></b>	24/34 (70.6)	13/28 (46.4)	8/30 (26.7)	NS	<b>&lt;0.001</b>
	<b>BP230<sup>e</sup></b>	21/34 (61.8)	19/28 (67.9)	11/30 (36.7)	NS	NS
<b>IgA</b>	<b>BP180 NC16A<sup>e</sup></b>	26/34 (76.5)	14/28 (50.0)	11/30 (36.7)	0.06	<b>0.003</b>
	<b>BP230<sup>e</sup></b>	20/34 (58.8)	15/28 (53.6)	8/30 (26.7)	NS	<b>0.019</b>
		<b>Titers, mean (SD)</b>				
<b>IgG</b>	<b>BP180 NC16A<sup>a</sup>, U/ml</b>	80.1 (53.2)	110.2 (168.2)	62.8 (56.3)	NS	NS
	<b>BP230<sup>a</sup>, U/ml</b>	25.8 (18.3)	68.2 (57.1)	39.2 (20.2)	<b>&lt;0.001</b>	NS
	<b>ECD-BP180<sup>b</sup>, PIV</b>	104.1 (62.7)	77.0 (42.3)	96.5 (55.8)	<b>0.037</b>	NS
	<b>BP180 – E-1080<sup>c</sup>, PIV</b>	138.0 (122.2)	115.7 (134.2)	124.4 (95.5)	NS	NS
	<b>BP180 – E-1331<sup>d</sup>, PIV</b>	95.1 (84.0)	36.8 (37.3)	36.5 (47.4)	<b>0.006</b>	<b>0.007</b>
<b>IgE</b>	<b>BP180 NC16A<sup>e</sup>, PIV</b>	53.7 (86.7)	15.5 (9.7)	13.1 (6.3)	<b>0.030</b>	0.052
	<b>BP230<sup>e</sup>, PIV</b>	43.9 (50.0)	51.7 (56.5)	38.7 (42.0)	NS	NS
<b>IgA</b>	<b>BP180 NC16A<sup>e</sup>, PIV</b>	52.3 (43.2)	57.0 (58.6)	78.6 (70.3)	NS	NS
	<b>BP230<sup>e</sup>, PIV</b>	60.8 (46.9)	66.7 (65.2)	39.2 (39.2)	NS	NS

*GABP: gliptin-associated bullous pemphigoid; ICI-BP: immune checkpoint inhibitor-associated bullous pemphigoid; IBP: idiopathic bullous pemphigoid; NS: not statistically significant; PIV: pemphigoid index value.*

<sup>a</sup> Commercial ELISA tests (MBL). Cut-off: 9.0 U/ml for both; sensitivity: 82.8% BP180, 57.8 BP230; specificity: 98,9% BP180, 99,0% BP230.

<sup>b</sup>ELISA based on the entire ectodomain of BP180 (amino acid residues 490-1497). Cut-off: 10.02 PIV; sensitivity: 80%; specificity: 100%.

<sup>c</sup>ELISA based on the mid-portion of the extracellular domain of BP180 (amino acid residues 1080-1107). Cut-off: 14.9 PIV; sensitivity: 51%; specificity: 96%.

<sup>d</sup>ELISA based on the C-terminal region of the extracellular domain of BP180 (amino acid residues 1331-1404). Cut-off: 4.5 PIV; sensitivity: 49%; specificity: 100%.

<sup>e</sup>ELISAs based on modified MBL protocols. IgE cut-offs: BP180  $\geq 3.2$  PIV, BP230  $\geq 4.5$  PIV; IgA cut-offs: BP180  $> 13.8$  PIV, BP230  $> 14.5$  PIV. Cut-off values were determined as the mean of optical density measured in 50 healthy donor sera plus 3 standard deviations.

*The variability of totals is due to sera availability for the execution of the different assays. Mean IgG titers were calculated on positive sera only. Statistically significant results are reported in bold and italic.*

Table SII. IgG reactivity and mean titers in different subgroups of ICI-associated bullous pemphigoid patients.

Antigen/epitope	Age			Tumor					Drug			Delay		
	≤75 years	>75 years	<i>p</i> value	Melanoma	Lung	Kidney or urothelial	Other	<i>p</i> value	Nivol.	Pembrol.	<i>p</i> value	≤ 40 w	> 40 w	<i>p</i> value
	<i>Reactivity, n/N (%)</i>													
<b>BP180 NC16A<sup>a</sup></b>	19/24 (79.2)	22/26 (84.6)	NS	13/15 (86.7)	12/16 (75.0)	10/10 (100)	6/9 (66.7)	NS	20/23 (87.0)	19/22 (86.4)	NS	17/25 (68.0)	22/23 (95.7)	<b>0.032</b>
<b>BP230<sup>a</sup></b>	6/24 (25.0)	6/26 (23.1)	NS	5/15 (33.3)	3/16 (18.8)	2/10 (20.0)	2/9 (22.2)	NS	6/23 (26.1)	5/22 (22.7)	NS	4/25 (16.0)	7/23 (30.4)	NS
<b>ECD-BP180<sup>b</sup></b>	22/24 (91.7)	22/24 (91.7)	NS	12/13 (92.3)	15/16 (93.8)	9/10 (90.0)	9/9 (100)	NS	20/21 (95.2)	19/21 (90.5)	NS	21/23 (91.3)	21/22 (95.5)	NS
<b>BP180 E-1080<sup>c</sup></b>	10/24 (41.7)	16/24 (66.7)	NS	8/13 (61.5)	7/16 (43.8)	5/10 (50.0)	6/9 (66.7)	NS	12/21 (57.1)	9/21 (42.9)	NS	14/23 (60.9)	12/22 (54.5)	NS
<b>BP180 E-1331<sup>d</sup></b>	14/24 (58.3)	20/24 (83.3)	NS	10/13 (76.9)	11/16 (68.8)	8/10 (80.0)	5/9 (55.6)	NS	15/21 (71.4)	16/21 (76.2)	NS	15/23 (65.2)	17/22 (77.3)	NS
	<i>Titer, mean (SD)</i>													
<b>BP180 NC16A<sup>a</sup></b>	69.4 (43.5)	89.3 (59.8)	NS	89.7 (66.4)	80.9 (50.1)	57.3 (29.4)	95.4 (58.9)	NS	86.7 (51.3)	65.7 (48.7)	NS	60.7 (45.1)	93.6 (55.4)	<b>0.067</b>
<b>BP230<sup>a</sup></b>	16.4 (5.8)	35.2 (22.1)	0.06	24.6 (17.2)	17.5 (4.2)	22.5 (3.7)	44.5 (38.8)	NS	22.6 (16.9)	20.7 (6.2)	NS	32.8 (26.7)	22.6 (14.3)	NS
<b>ECD-BP180<sup>b</sup></b>	112.3 (70.6)	95.9 (54.2)	NS	97.9 (78.8)	110.6 (66.4)	84.2 (50.6)	117.3 (41.6)	NS	111.0 (70.1)	99.0 (64.5)	NS	70.5 (52.9)	135.0 (58.1)	<b>&lt;0.001</b>
<b>BP180 E-1080<sup>c</sup></b>	114.7 (104.5)	152.5 (133.2)	NS	69.2 (71.3)	194.9 (152.8)	112.3 (85.4)	184.5 (135.3)	NS	157.6 (152.0)	97.6 (74.9)	NS	139.8 (116.6)	135.8 (133.6)	NS

<b>BP180 E-1331<sup>d</sup></b>	72.3 (55.7)	111.2 (97.4)	NS	91.7 (92.3)	103.7 (77.9)	63.5 (73.0)	133.7 (102.4)	NS	88.2 (80.3)	82.0 (80.8)	NS	53.4 (51.5)	129.8 (90.7)	<b><i>0.013</i></b>
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ICI: immune checkpoint inhibitors; NS: not statistically significant; PIV: pemphigoid index value.

<sup>a</sup>Commercial ELISA tests (MBL). Cut-off: 9.0 U/ml for both; sensitivity: 82.8% BP180, 57.8 BP230; specificity: 98.9% BP180, 99.0% BP230.

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The variability of totals is due to the availability of clinical data and/or of sera for the execution of different assays. Mean autoantibody titers were calculated on positive sera only. Statistically significant results are reported in bold and italic.

Table SIII. IgE and IgA reactivity and mean titers in different subgroups of ICI-associated bullous pemphigoid patients.

AutoAb	Antigen/ epitope	Age			Tumor					Drug			Delay			
		≤75 years	>75 years	<i>p</i> value	Melanoma	Lung	Kidney or urothelial	Other	<i>p</i> value	Nivol.	Pembrol.	<i>p</i> value	≤ 40 weeks	> 40 weeks	<i>p</i> value	
<i>IgE</i>	<b>BP180-NC16A</b>	<b>Reactivity, n/N (%)</b>														
		13/19 (68.4)	11/15 (73.3)	NS	9/13 (69.2)	4/9 (44.4)	6/6 (100)	5/6 (83.3)	NS	15/19 (78.9)	7/13 (53.8)	NS	13/18 (72.2)	10/15 (66.7)	NS	
	<b>BP230</b>	12/19 (63.2)	9/15 (60.0)	NS	7/13 (53.8)	5/9 (55.6)	4/6 (66.7)	5/6 (83.3)	NS	13/19 (68.4)	7/13 (53.8)	NS	9/18 (50.0)	11/15 (73.3)	NS	
	<b>BP180 NC16A</b>	15/19 (78.9)	11/15 (73.3)	NS	10/13 (76.9)	7/9 (77.8)	4/6 (66.7)	5/6 (83.3)	NS	14/19 (73.7)	10/13 (76.9)	NS	15/18 (83.3)	10/15 (66.7)	NS	
<i>IgA</i>	<b>BP230</b>	9/19 (47.4)	11/15 (73.3)	NS	8/13 (61.5)	4/9 (44.4)	4/6 (66.7)	4/6 (66.7)	NS	11/19 (57.9)	4/13 (30.8)	NS	13/18 (72.2)	7/15 (46.7)	NS	
<i>IgE</i>	<b>BP180 NC16A</b>	<b>Titer, mean (SD) – PIV</b>														
		60.1 (113.6)	46.2 (40.9)	NS	33.4 (30.8)	20.1 (9.6)	50.2 (48.9)	121.4 (174.5)	NS	68.0 (106.2)	28.5 (31.2)	NS	32.6 (26.7)	81.0 (129.5)	NS	
	<b>BP230</b>	39.0 (43.7)	50.4 (59.6)	NS	29.4 (33.3)	17.0 (12.2)	63.5 (58.6)	75.3 (72.4)	NS	40.5 (41.7)	29.4 (33.5)	NS	53.6 (66.1)	36.1 (36.9)	NS	
	<b>BP180 NC16A</b>	51.6 (51.7)	53.2 (30.3)	NS	66.7 (58.3)	59.0 (37.2)	30.3 (18.0)	31.8 (9.9)	NS	52.2 (53.3)	56.9 (30.3)	NS	38.5 (20.2)	76.3 (59.0)	<i>0.06</i>	
<i>IgA</i>	<b>BP230</b>	47.4 (36.4)	71.7 (53.2)	NS	65.2 (43.2)	33.7 (14.0)	65.9 (43.0)	74.0 (79.1)	NS	46.4 (31.5)	86.0 (53.0)	NS	58.9 (48.5)	64.3 (47.4)	NS	

ICI: immune checkpoint inhibitors; NS: not statistically significant; PIV: pemphigoid index value.

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