

Figure S1: Overview of included patients and treatment series in the analysis of blood cell biomarkers

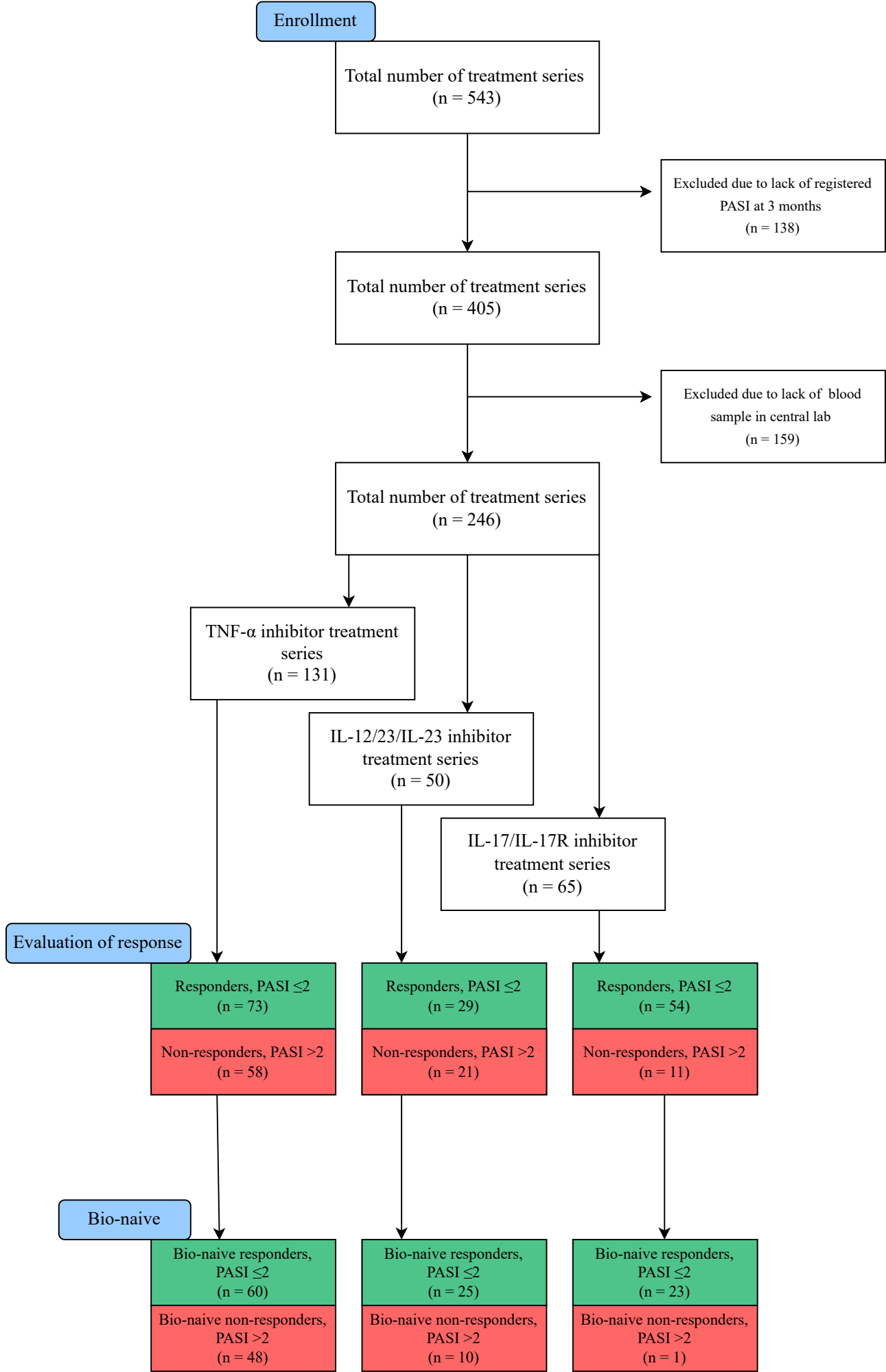


Figure S2: Overview of included patients and treatment series in the analysis of blood cytokines

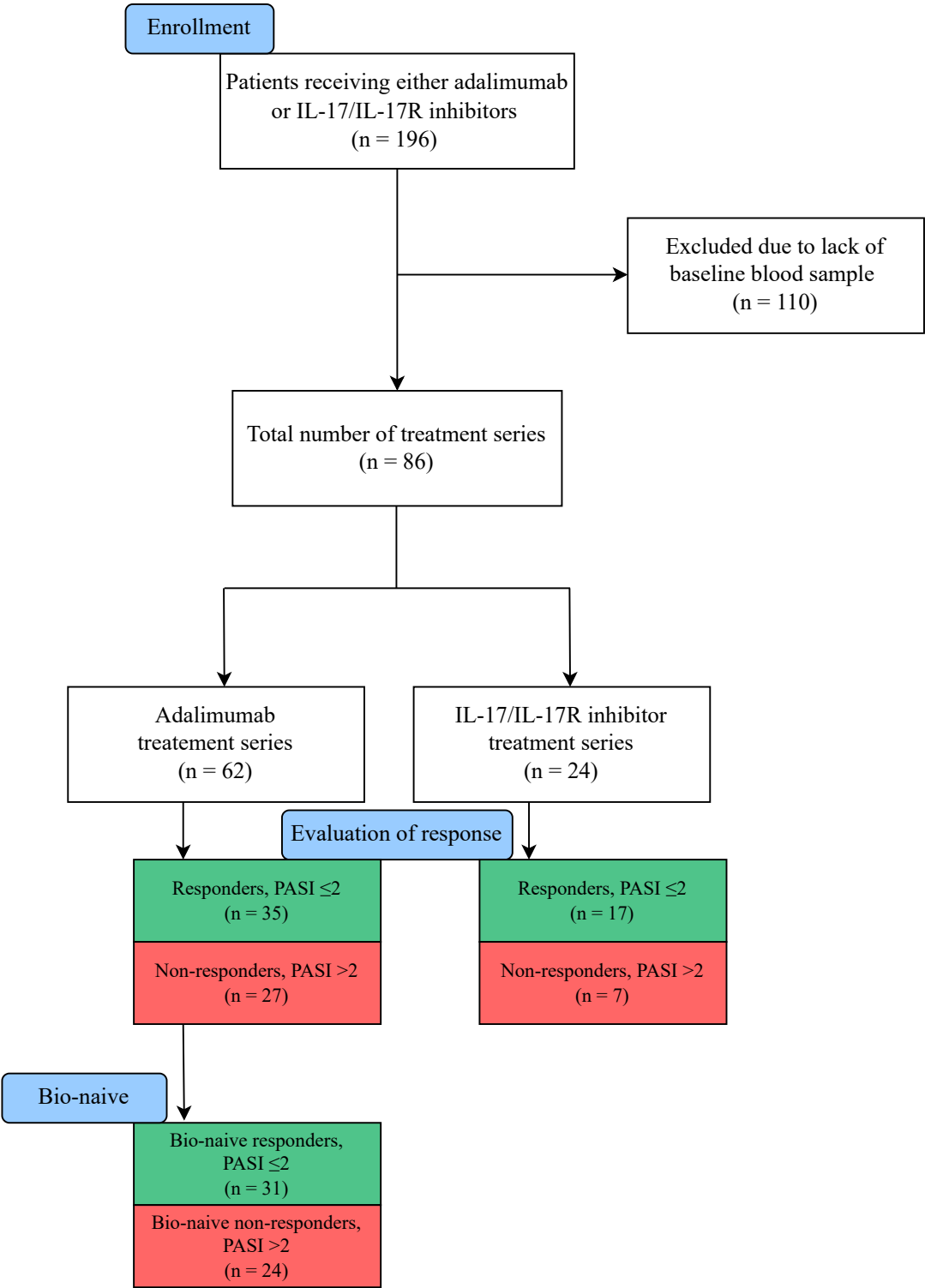


Table S1: Treatments included in the analysis of blood cell biomarkers of inflammation.

	TNF-α inhibitors	IL-17/IL-17R inhibitors	IL-23 inhibitors	IL-12/23 inhibitors
Adalimumab	125			
Certolizumab pegol	2			
Etanercept	1			
Infliximab	3			
Secukinumab		31		
Ixekizumab		21		
Brodalumab		13		
Ustekinumab				37
Guselkumab			10	
Risankizumab			3	
Total	131	65	13	37

Table S2: Treatments included in the analysis of blood cytokines

	TNF- α inhibitors	IL-17/IL-17R inhibitors
Adalimumab	62	
Ixekizumab		11
Brodalumab		12
Secukinumab		1
Total	62	24

Table S3: Blood cell biomarkers of inflammation, numbers of responders and non-responders for different PASI definitions of response to each type of biologics

Response definition	PASI \leq 2		PASI \leq 4	
	Responders	Non-responders	Responders	Non-responders
TNF-α inhibitors				
Adalimumab	71	54	103	22
Infliximab	0	3	2	1
Certolizumab pegol	1	1	1	1
Etanercept	1	0	1	0
<i>Total</i>	<i>73</i>	<i>58</i>	<i>107</i>	<i>24</i>
IL-12/23 inhibitors				
Ustekinumab	25	12	31	6
<i>Total</i>	<i>25</i>	<i>12</i>	<i>31</i>	<i>6</i>
IL-23 inhibitors				
Guselkumab	4	6	5	5
Risankizumab	0	3	1	2
<i>Total</i>	<i>4</i>	<i>9</i>	<i>6</i>	<i>7</i>
IL-17 inhibitors				
Secukinumab	29	2	31	0
Ixekizumab	14	7	19	2
<i>Total</i>	<i>33</i>	<i>9</i>	<i>50</i>	<i>2</i>
IL-17R inhibitors				
Brodalumab	11	2	12	1
<i>Total</i>	<i>11</i>	<i>2</i>	<i>12</i>	<i>1</i>

Table S4: Blood cytokines, numbers of responders and non-responders for different PASI definitions of response to each type of biologics

Response definition	PASI\leq2		PASI\leq4	
	Responders	Non-responders	Responders	Non-responders
TNF-α inhibitors				
Adalimumab	35	27	49	13
IL-17 inhibitors				
Secukinumab	1	0	1	0
Ixekizumab	6	5	10	1
IL-17R inhibitors				
Brodalumab	10	2	11	1

Table S5: Baseline characteristics and levels of blood cell biomarkers of inflammation. Response defined as a PASI ≤4.

	Responders	Bio-naive, responders	Non-responders	Bio-naive, non-responders
TNF-α inhibitors*				
n	107	90	24	18
Age, years, median (IQR)	44 (32-54)	44 (32-56)	45 (33-61)	47 (37-64)
Sex, female, n (%)	31 (29)	26 (29)	8 (33)	5 (28)
BMI, median (IQR)	26.9 (24.3-31.3) ^a	26.9 (34.1-31.1)	31.0 (24.6-34.5)	30.0 (25.1-34.3)
Ever-smokers, n (%)	50 (47) ^a	46 (51)	17 (71)	11 (61)
PsA, n (%)	22 (21) ^b	18 (20) ^c	9 (38) ^d	7 (39) ^e
Baseline PASI, median (IQR)	7.9 (4.8-11.8) ^e	8.1 (5.1-12.3)	10.8 (8.5-12.9)	11.0 (8.8-12.8)
Lymphocytes, 10 ⁹ /L, median (IQR)	1.7 (1.3-2.1) ^f	1.7 (1.3-2.1) ^g	1.7 (1.4-2.5) ^a	1.6 (1.3-2.3)
Neutrophils, 10 ⁹ /L, median (IQR)	3.9 (3.2-5.2) ^f	4.0 (3.2-5.2) ^g	4.2 (3.2-5.9) ^a	4.7 (3.0-5.9)
Platelets, 10 ⁹ /L, median (IQR)	252.0 (210.8-300.8) ^a	253.0 (210.0-301.0) ^a	261.0 (216.0-316.5) ^a	261.0 (218.0-387.0) ^a
NLR, median (IQR)	2.2 (1.8-3.1) ^f	2.2 (1.8-3.1) ^g	2.2 (1.6-3.49) ^a	2.5 (1.7-3.6)
PLR, median (IQR)	149.6 (123.5-176.5) ^f	150.3 (123.5-178.5) ^g	144.8 (95.1-201.3) ^h	185.0 (121.7-221.0) ^a
SII, 10 ⁹ /L, median (IQR)	580.7 (425.1-775.6) ^f	585.2 (436.6-802.6) ^g	524.7 (351.4-1161.5) ^h	742.8 (369.2-1374.7) ^a
IL-23/IL-12/23 inhibitors**	37	30	13	5
n				
Age, years, median (IQR)	38 (25-50)	38 (24-46)	50 (35-56)	50 (36-50)
Sex, female, n (%)	12 (32)	11 (37)	4 (31)	1 (20)
BMI, median (IQR)	25.4 (22.5-30.4)	27.6 (23.4-30.2)	30.0 (27.3-34.9)	28.1 (25.1-30.0)
Ever-smokers, n (%)	18 (49)	14 (47)	9 (69)	3 (60)
PsA, n (%)	3 (8) ⁱ	2 (7) ^j	5 (38)	1 (20)
Baseline PASI, median (IQR)	9.3 (6.8-11.0)	9.0 (7.1-10.5)	12.6 (6.5-13.9)	10.2 (6.5-12.3)
Lymphocytes, 10 ⁹ /L, median (IQR)	1.7 (1.4-2.0) ^h	1.7 (1.4-2.0) ^a	1.5 (1.2-1.9) ^a	1.5 (1.4-1.5)
Neutrophils, 10 ⁹ /L, median (IQR)	4.1 (3.2-5.6) ^h	3.9 (3.0-5.6) ^a	4.3 (3.0-5.6) ^a	3.1 (2.5-3.3)
Platelets, 10 ⁹ /L, median (IQR)	262.0 (232.0-341.0)	253.0 (219.2-278.0)	251.0 (220.0-263.0)	220.0 (220.0-255.0)
NLR, median (IQR)	2.5 (1.9-3.3) ^h	2.4 (1.9-2.9) ^a	2.4 (1.8-3.4) ^a	1.9 (1.6-2.1)
PLR, median (IQR)	159.0 (139.2-206.0) ^h	148.8 (121.4-179.5) ^a	142.8 (98.8-184.1) ^a	143.8 (141.9-175.9)
SII, 10 ⁹ /L, median (IQR)	640.2 (513.1-797.2) ^h	584.3 (492.3-690.0) ^a	514.6 (356.2-1025.9) ^a	363.8 (333.5-545.2)
IL-17/IL-17R inhibitors***	62	24	3	0

n				
Age, years, median (IQR)	44 (32-58)	42 (31-51)	58 (55-67)	-
Sex, female, n (%)	24 (39)	8 (33)	1 (33)	-
BMI, median (IQR)	26.5 (23.1-31.5)	24.0 (21.3-29.1)	40.3 (37.8-45.0)	-
Ever-smokers, n (%)	26 (43)	9 (37)	3 (100)	-
PsA, n (%)	20 (32) ^k	6 (25) ^j	1 (33)	-
Baseline PASI, median (IQR)	9.0 (7.0-11.4) ^a	10.6 (7.5-13.6)	8.4 (6.8-11.7)	-
Lymphocytes, 10 ⁹ /L, median (IQR)	1.8 (1.4-1.9) ^e	1.7 (1.4-1.9)	2.5 (2.4-2.7) ^a	-
Neutrophils, 10 ⁹ /L, median (IQR)	4.0 (3.1-4.8) ^e	4.2 (3.2-4.8)	6.6 (6.4-6.9) ^a	-
Platelets, 10 ⁹ /L, median (IQR)	261.0 (214.0-294.0) ^e	252.5 (215.5-302.2)	259.0 (242.0-275.5)	-
NLR, median (IQR)	2.3 (1.9-2.8) ^e	2.4 (2.0-3.1)	2.7 (2.4-2.9) ^a	-
PLR, median (IQR)	143.3 (114.1-184.9) ^e	147.0 (122.8-196.0)	109.6 (105.5-113.6) ^a	-
SII, 10 ⁹ /L, median (IQR)	562.1 (443.2-721.9) ^e	702.7 (469.7-779.9)	730.7 (678.1-783.3) ^a	-

*TNF- α inhibitors included adalimumab (n=125), infliximab (n= 3), certolizumab pegol (n=2) and etanercept (n=1). **IL-23/IL-12/23 inhibitors included guselkumab (n=10), risankizumab (n=3) and ustekinumab (n=37). ***IL-17/IL-17R inhibitors included secukinumab (n=31), ixekizumab (n=21) and brodalumab (n=13). ^a missing data (n = 1), ^b missing data (n = 23), ^c missing data (n = 20), ^d missing data (n = 5), ^e missing data (n = 3), ^f missing data (n = 7), ^g missing data (n = 6), ^h missing data (n = 2), ⁱ missing data (n = 9), ^j missing data (n=8), ^k missing data (n=11). TNF, tumor necrosis factor; BMI, body mass index; PsA, psoriatic arthritis; PASI, psoriasis area and severity index; IL, interleukin; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII; systemic immune-inflammation index.

Figure S3: Blood cell biomarkers at baseline in responders (PASI ≤ 4) and non-responders (PASI > 4) treated with either tumor necrosis factor (TNF)- α inhibitors, interleukin (IL)-23/IL-12/23 inhibitors, or IL-17/IL-17R inhibitors A) Neutrophil-to-lymphocyte ratio (NLR). B) Platelet-to-lymphocyte ratio (PLR). C) Systemic immune-inflammation index (SII). Responders = psoriasis area and severity index (PASI) ≤ 4 three months after treatment start. Non-responders = PASI > 4 three months after treatment start. Ns = non-significant. * $p < 0.05$.

Figure S4: Blood cell biomarkers at baseline in bio-naive responders (PASI ≤ 4) and non-responders (PASI > 4) treated with either tumor necrosis factor (TNF)- α inhibitors or interleukin (IL)-23/IL-12/23 inhibitors. A) Neutrophil-to-lymphocyte ratio (NLR). B) Platelet-to-lymphocyte ratio (PLR). C) Systemic immune-inflammation index (SII). Responders = psoriasis area and severity index (PASI) ≤ 4 three months after treatment start. Non-responders = PASI > 4 three months after treatment start. Ns = non-significant. * $p < 0.05$.

Figure S3

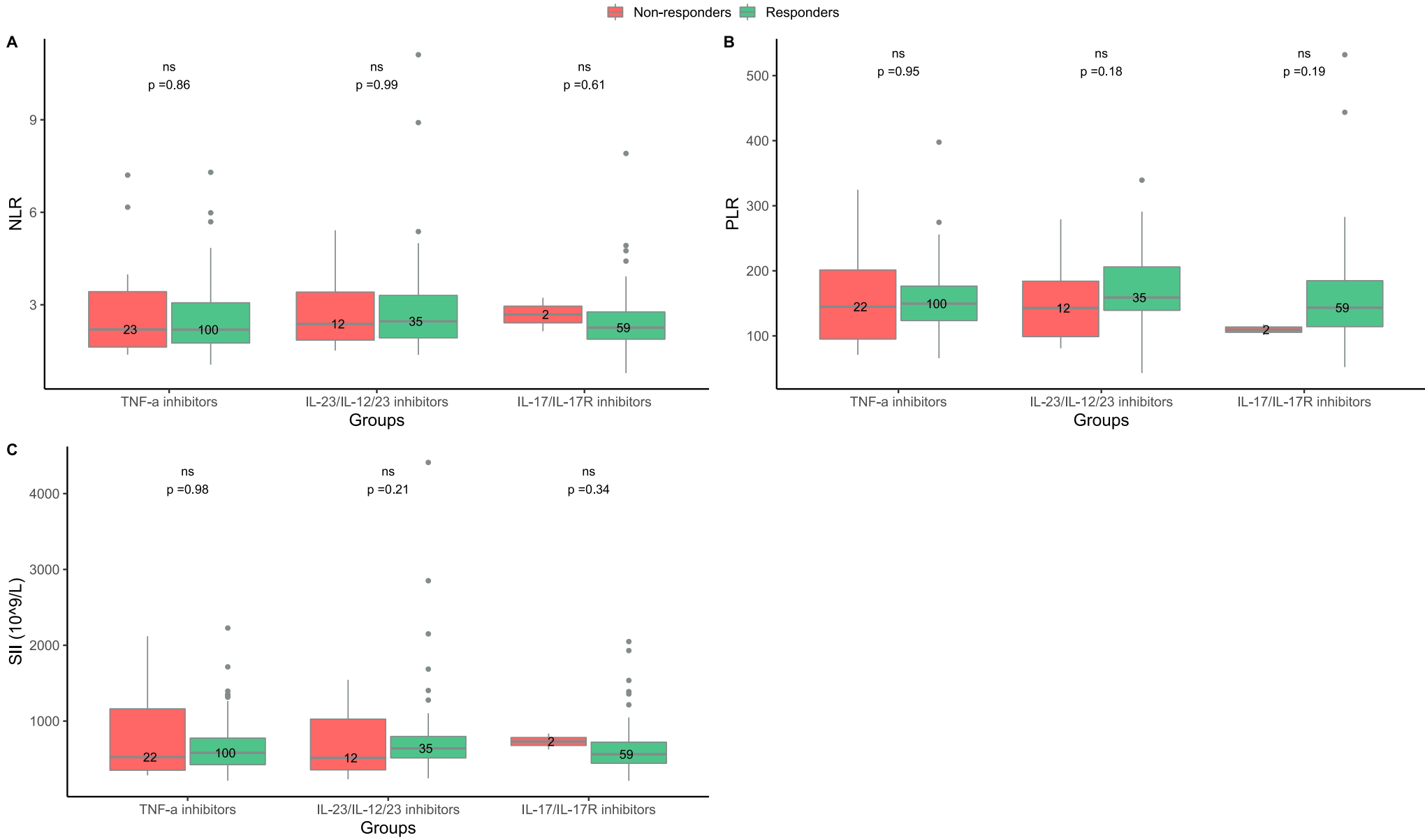


Figure S4

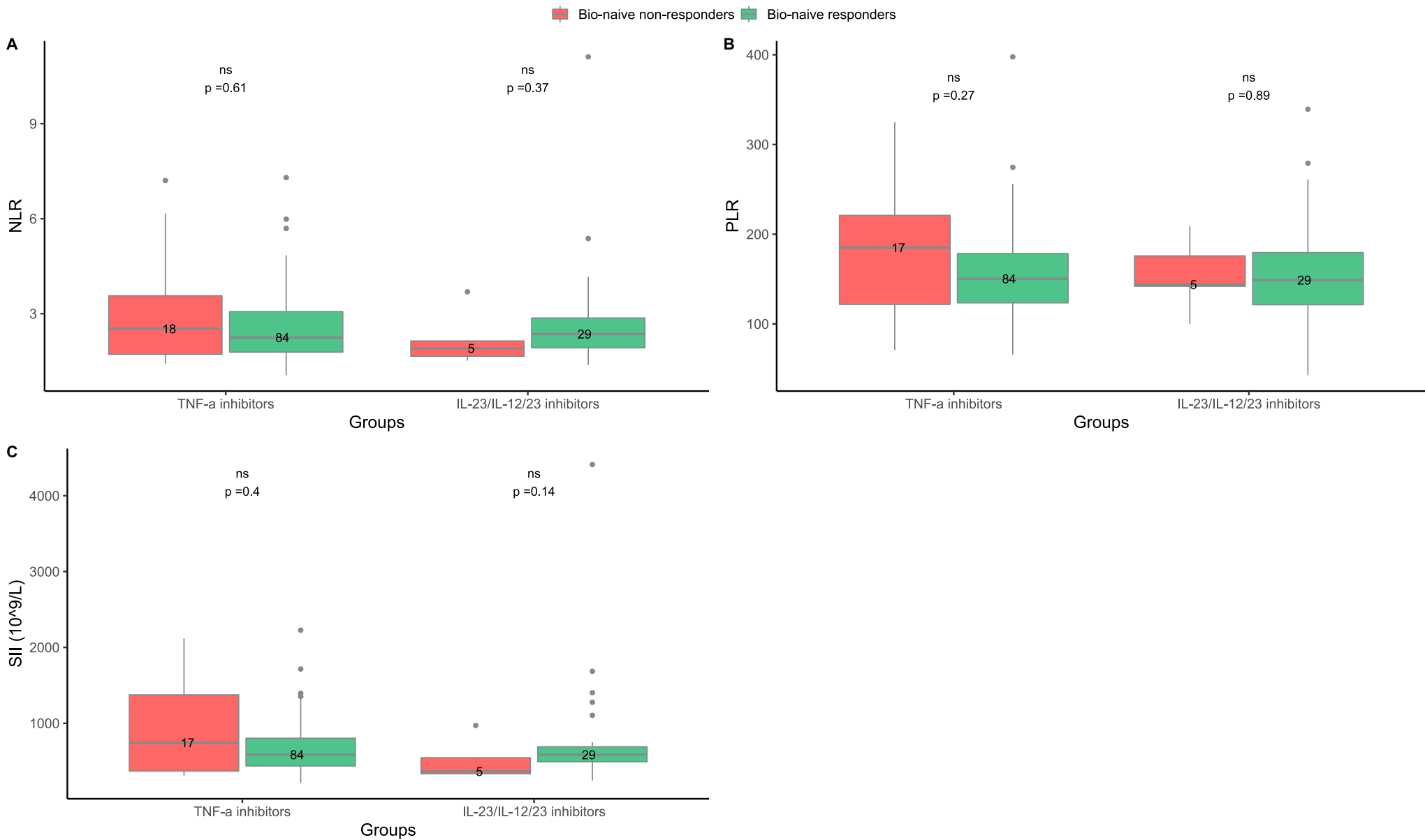


Table S6: Baseline characteristics and cytokine levels. Response defined as an absolute PASI ≤ 4 .

	Responders	Bio-naive, responders	Non-responders	Bio-naive, non-responders
Adalimumab				
n	49	43	13	12
Age, years, median (IQR)	43 (32-55)	42 (32-54)	56 (44-67)	55 (42-68)
Sex, female, n (%)	16 (33)	14 (33)	2 (15)	2 (17)
BMI, median (IQR)	27.7 (24.4-31.6)	28.2 (25.6-32.0)	30.3 (24.4-34.3)	30.0 (24.1-34.7)
Ever-smokers, n (%)	22 (46) ^a	19 (44) ^a	8 (62)	7 (58)
PsA, n (%)	7 (14)	6 (14)	5 (38)	4 (33)
Baseline PASI, median (IQR)	8.2 (4.5-11.9)	9.2 (4.9-13.8)	11.4 (9.4-12.6)	10.7 (9.1-12.4)
TNF- α , pg/mL, median (IQR)	3.89 (2.55-5.20) ^b	3.66 (2.55-5.20) ^c	6.62 (4.97-8.85) ^d	6.43 (4.87-9.35) ^d
IL-6, pg/mL, median (IQR)	1.01 (0.59-1.65) ^d	1.04 (0.63-1.64) ^d	1.86 (1.17-4.09)	1.78 (1.13-2.86)
sIL-6ST, ng/mL, median (IQR)	123.19 (96.36-147.56)	123.34 (96.91-146.86)	137.51 (116.79-152.51)	130.44 (114.78-149.03)
sIL-6R, ng/mL, median (IQR)	31.46 (26.92-43.06)	32.06 (26.31-43.99)	39.63 (32.03-45.64)	38.25 (31.96-42.94)
IL-17/IL-17R inhibitors*				
n	22	0	2	0
Age, years, median (IQR)	53 (42-60)	-	63 (57-69)	-
Sex, female, n (%)	9 (41)	-	0 (0)	-
BMI, median (IQR)	28.5 (24.6-33.3)	-	40.5 (38.5-42.4)	-
Ever-smokers, n (%)	14 (63)	-	2 (100)	-
PsA, n (%)	6 (27)	-	0 (0)	-
Baseline PASI, median (IQR)	7.1 (5.2-9.0)	-	11.8 (10.1-13.4)	-
TNF- α , pg/mL, median (IQR)	4.21 (2.74-9.06) ^e	-	1.88 (1.69-2.06)	-
IL-6, pg/mL, median (IQR)	1.04 (0.73-4.15) ^e	-	2.65 (2.00-3.20)	-
sIL-6ST, ng/mL, median (IQR)	115.50 (105.83-155.81)	-	126.80 (113.60-139.99)	-
sIL-6R, ng/mL, median (IQR)	33.34 (29.19-38.25)	-	27.25 (22.27-32.24)	-

*IL-17/IL-17R inhibitors included secukinumab (n=1), ixekizumab (n=11) and brodalumab (n=12). ^a Missing data (n=1), ^b samples below detection limit (n=4), ^c samples below detection limit (n=2), ^d samples below detection limit (n=3), ^e samples below detection limit (n=1). TNF, tumor-necrosis factor; BMI, body mass index; PsA, psoriatic arthritis; PASI, psoriasis area and severity index; IL, interleukin; sIL-6ST, interleukin-6 signal transducer; sIL-6R, interleukin-6 receptor.

Figure S5: Blood cytokine levels at baseline in responders (PASI ≤ 4) and non-responders (PASI > 4) to treatment with adalimumab or interleukin (IL)-17/IL-17R inhibitors. A) Tumor necrosis factor-alpha (TNF)- α . B) Soluble interleukin-6 signal transducer (sIL-6ST). C) Interleukin-6 (IL-6). D) Soluble interleukin-6 receptor (sIL-6R). Responders = psoriasis area and severity index (PASI) ≤ 4 three months after treatment start. Non-responders = PASI > 4 three months after treatment start. Ns = non-significant. * $p < 0.05$.

Figure S6: Blood cytokine levels at baseline in bio-naïve responders (PASI ≤ 4) and non-responders (PASI > 4) to treatment with adalimumab. A) Tumor necrosis factor-alpha (TNF)- α . B) Soluble interleukin-6 signal transducer (sIL-6ST). C) Interleukin-6 (IL-6). D) Soluble interleukin-6 receptor (sIL-6R). Responders = psoriasis area and severity index (PASI) ≤ 4 three months after treatment start. Non-responders = PASI > 4 three months after treatment start. Ns = non-significant. * $p < 0.05$.

Figure S5

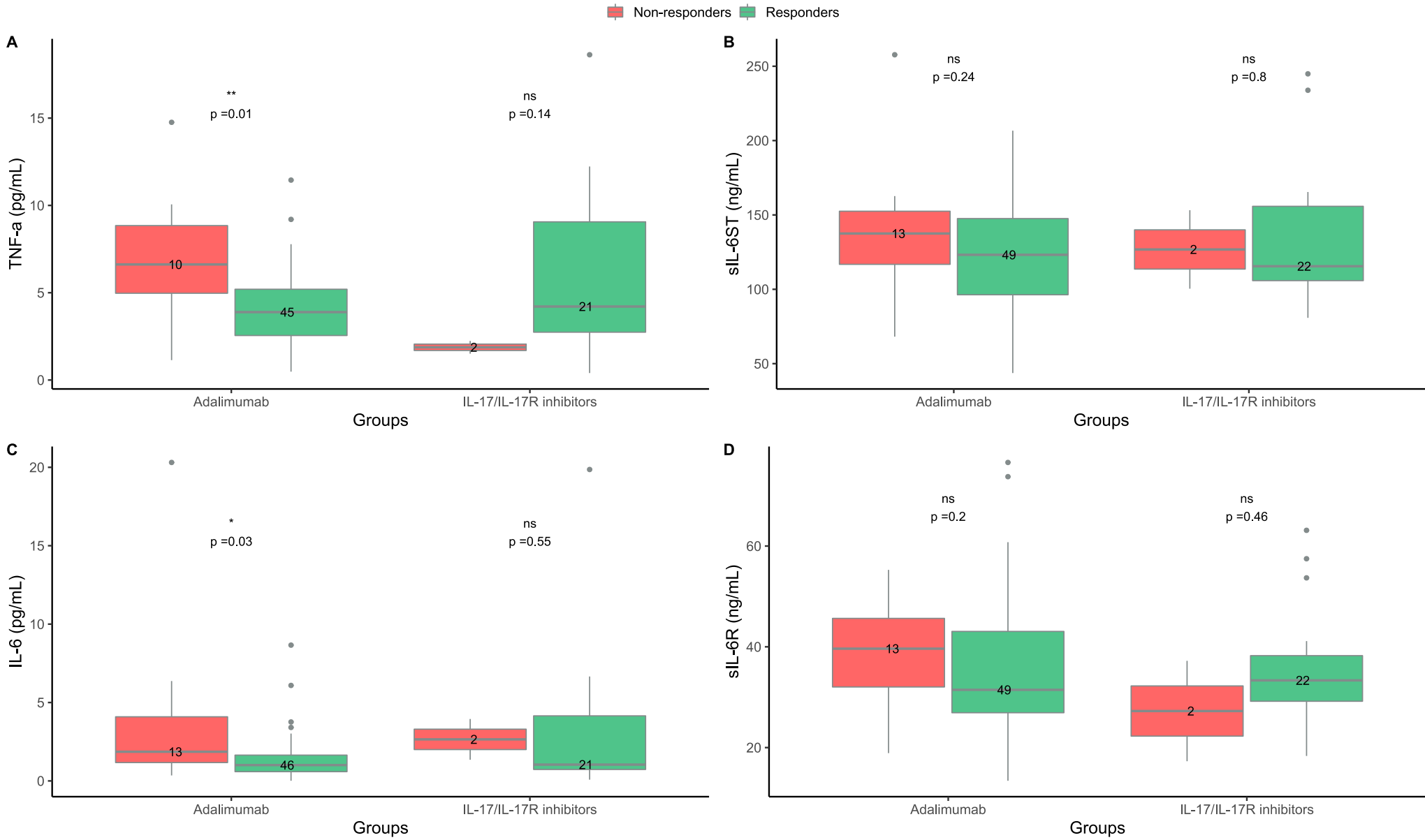


Figure S6

