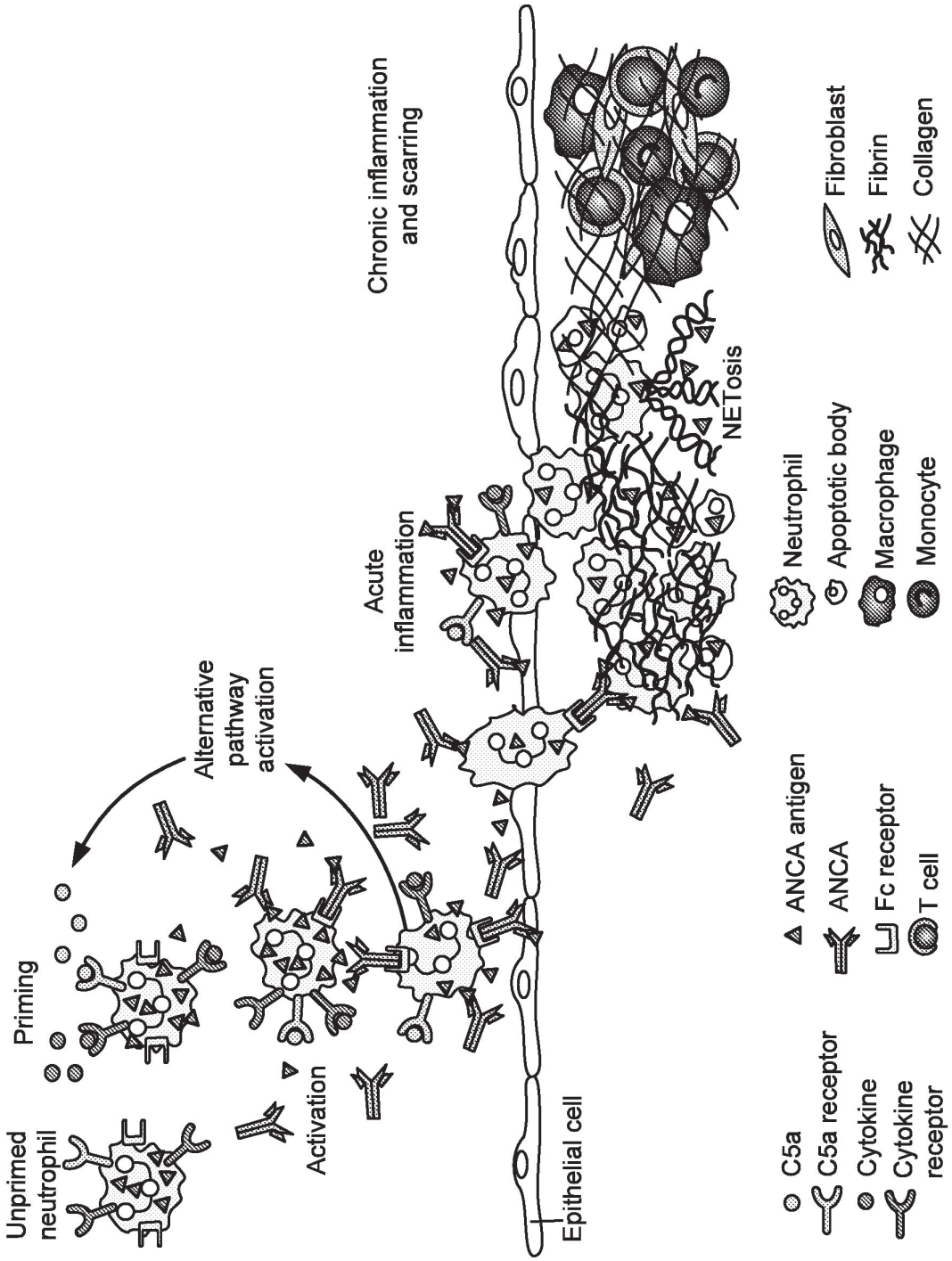
Unprimed neutrophil
Priming
Activation
Alternative pathway activation
Epithelial cell
Acute inflammation
Chronic inflammation and scarring
NETosis
C5a
C5a receptor
Cytokine
Cytokine receptor
ANCA antigen
ANCA
Fc receptor
T cell
Neutrophil
Apoptotic body
Macrophage
Monocyte
Fibroblast
Fibrin
Collagen

FIG. 1

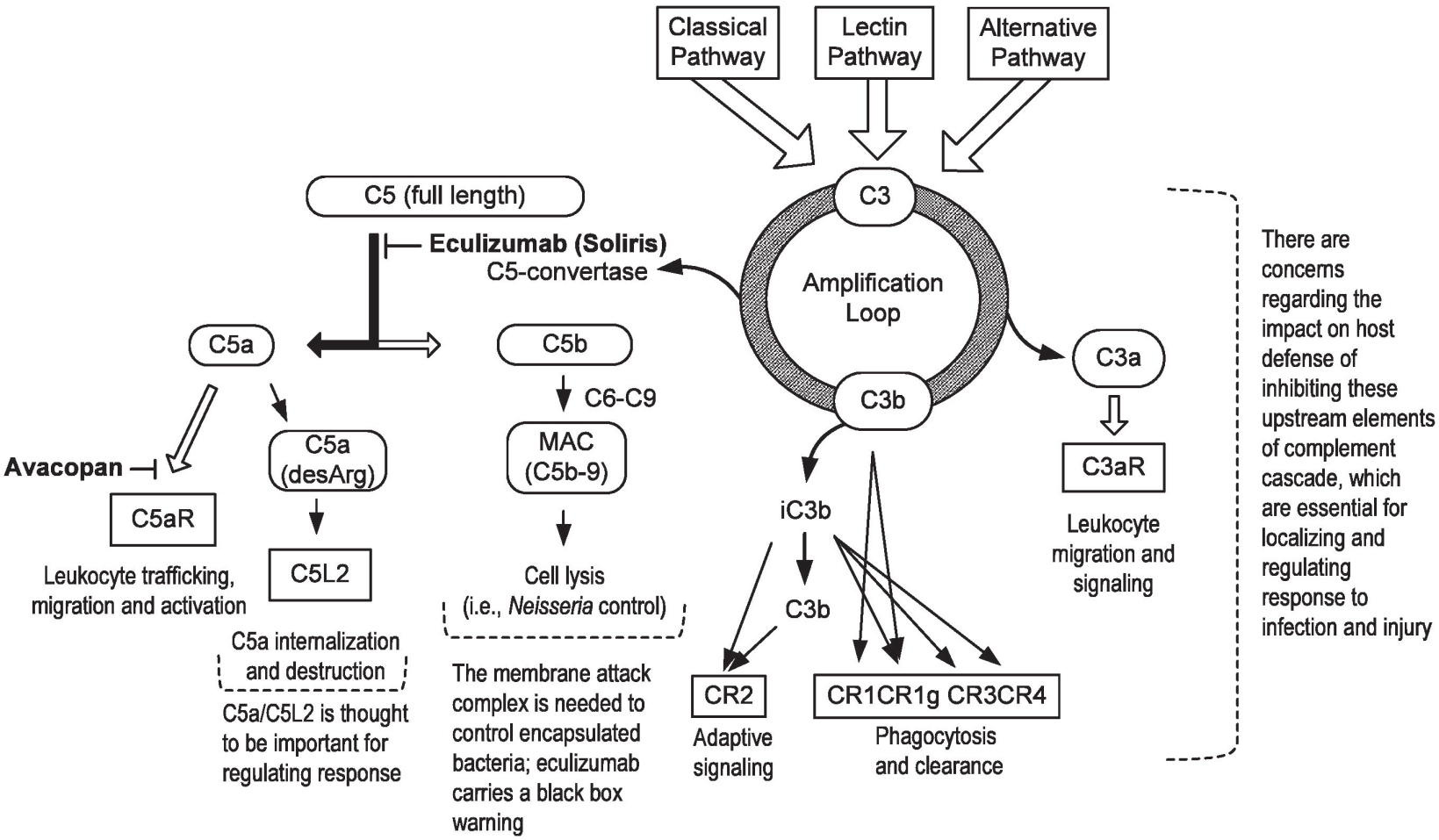
Classical Pathway
Lectin Pathway
Alternative Pathway
C3
Amplification Loop
C3b
C5 (full length)
Eculizumab (Soliris)
C5-convertase
C5a
C5b
C6-C9
MAC (C5b-9)
C5a (desArg)
Avacopan
C5aR
C5L2
Leukocyte trafficking, migration and activation
C5a internalization and destruction
C5a/C5L2 is thought to be important for regulating response
Cell lysis (i.e., Neisseria control)
The membrane attack complex is needed to control encapsulated bacteria; eculizumab carries a black box warning
iC3b
C3b
CR2
Adaptive signaling
CR1CR1g CR3CR4
Phagocytosis and clearance
C3a
C3aR
Leukocyte migration and signaling
There are concerns regarding the impact on host defense of inhibiting these upstream elements of complement cascade, which are essential for localizing and regulating response to infection and injury

FIG. 2

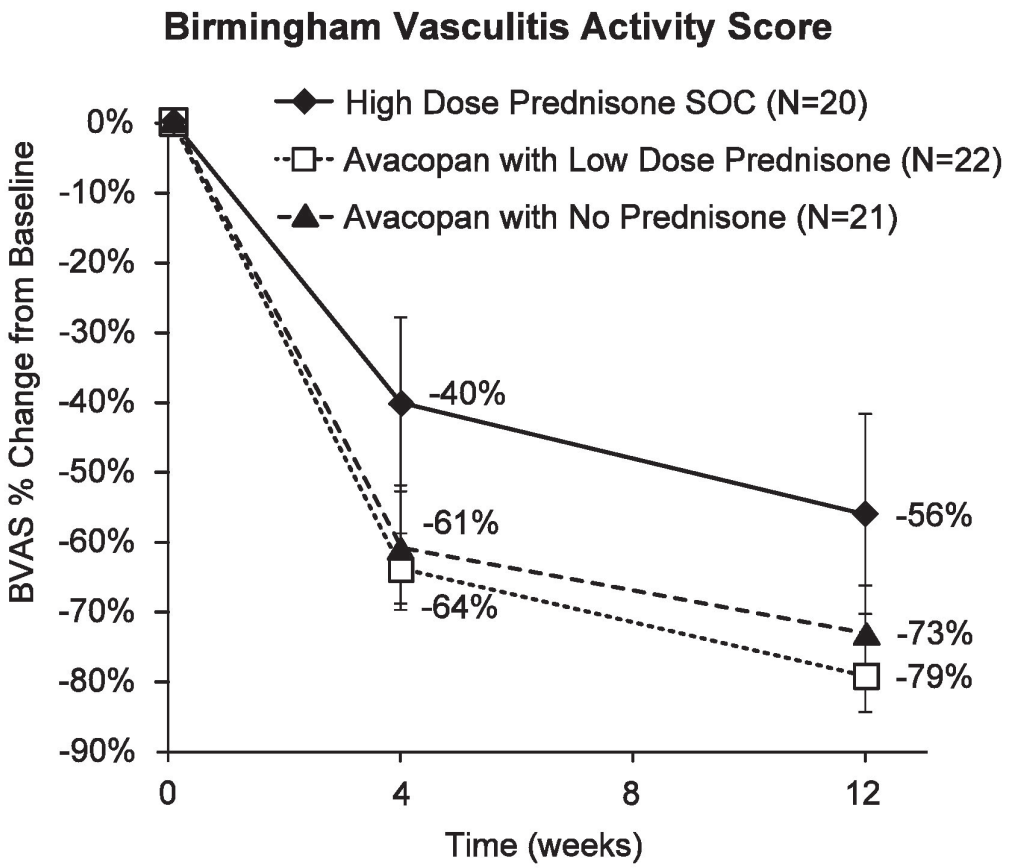
Birmingham Vasculitis Activity Score
High Dose Prednisone SOC (N=20)
Avacopan with Low Dose Prednisone (N=22)
Avacopan with No Prednisone (N=21)
BVAS % Change from Baseline
0%
-10%
-20%
-30%
-40%
-50%
-60%
-70%
-80%
-90%
-40%
-61%
-64%
-56%
-73%
-79%
0
4
8
12
Time (weeks)

FIG. 3A

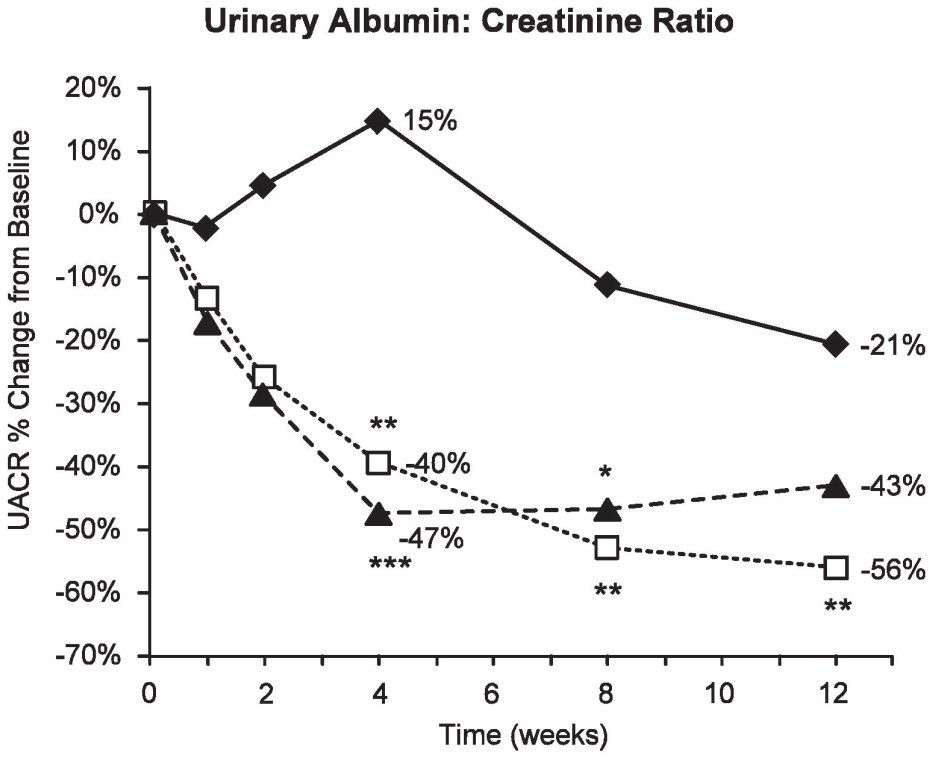
Urinary Albumin: Creatinine Ratio
UACR % Change from Baseline
20%
10%
0%
-10%
-20%
-30%
-40%
-50%
-60%
-70%
0
2
4
6
8
10
12
Time (weeks)
15%
-21%
-40%
-43%
-47%
-56%
*
**
***

FIG. 3B

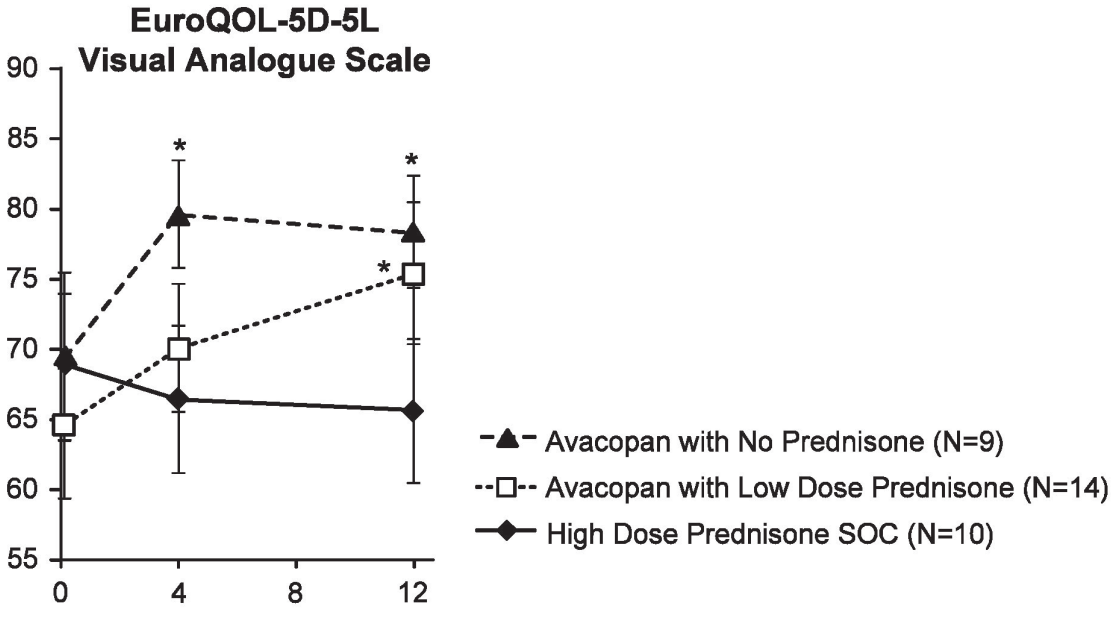
EuroQOL-5D-5L
Visual Analogue Scale
90
85
80
75
70
65
60
55
0
4
8
12
*
Avacopan with No Prednisone (N=9)
Avacopan with Low Dose Prednisone (N=14)
High Dose Prednisone SOC (N=10)

FIG. 3C

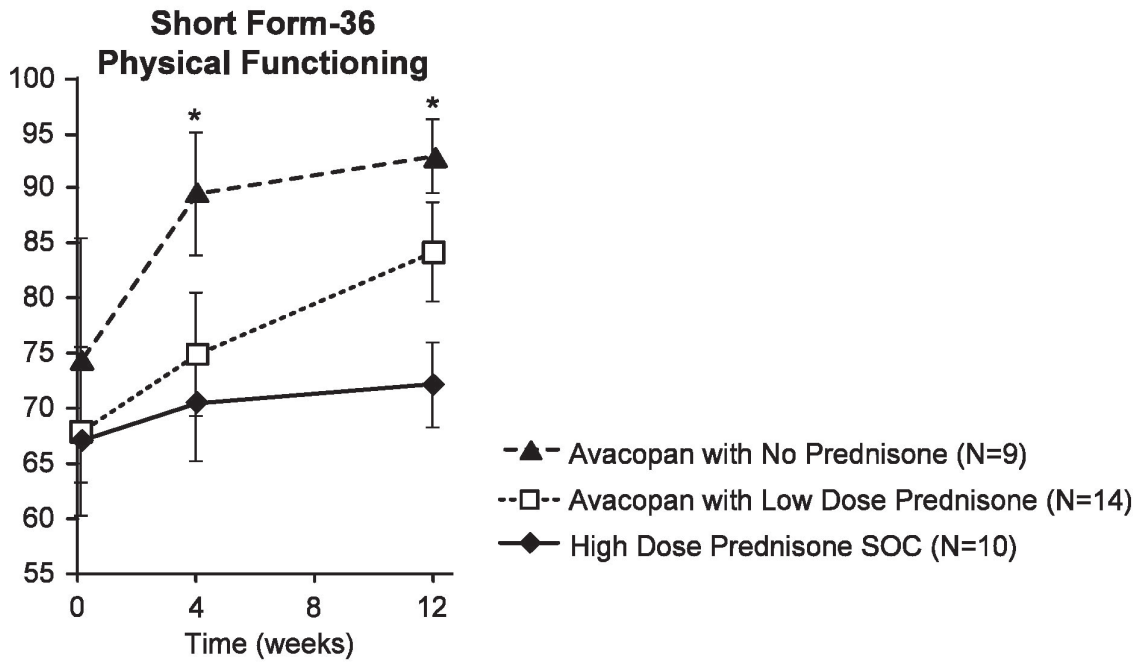
Short Form-36
Physical Functioning
100
95
90
85
80
75
70
65
60
55
0
4
8
12
Time (weeks)
*
*
Avacopan with No Prednisone (N=9)
Avacopan with Low Dose Prednisone (N=14)
High Dose Prednisone SOC (N=10)

FIG. 3D

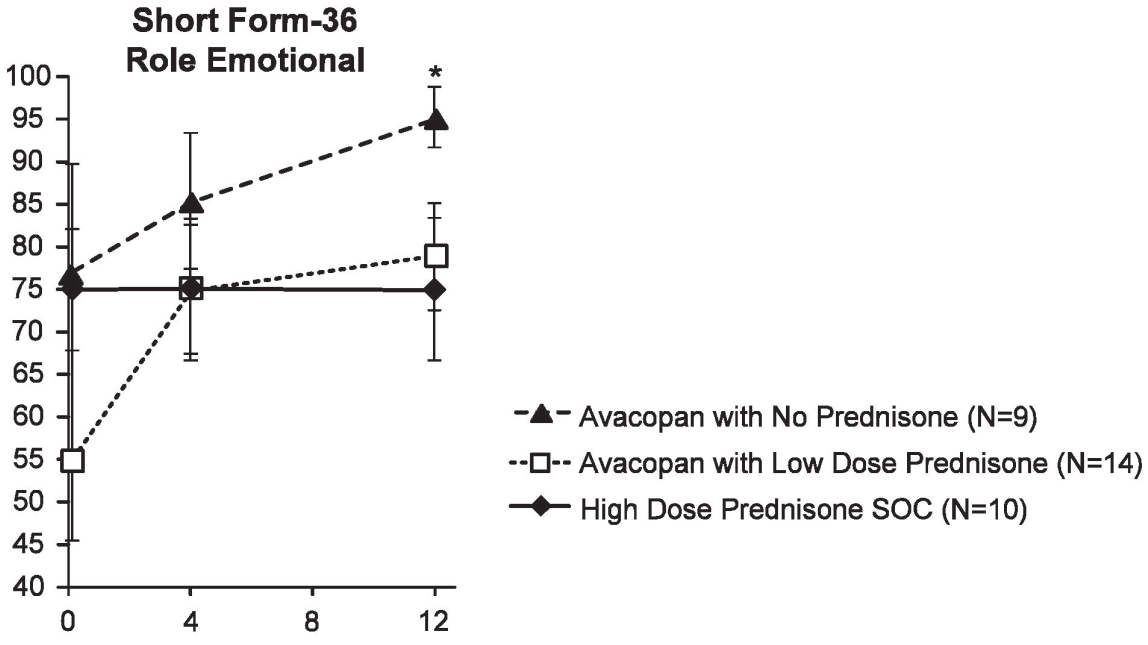
Short Form-36
Role Emotional
100
95
90
85
80
75
70
65
60
55
50
45
40
0
4
8
12
*
Avacopan with No Prednisone (N=9)
Avacopan with Low Dose Prednisone (N=14)
High Dose Prednisone SOC (N=10)

FIG. 3E

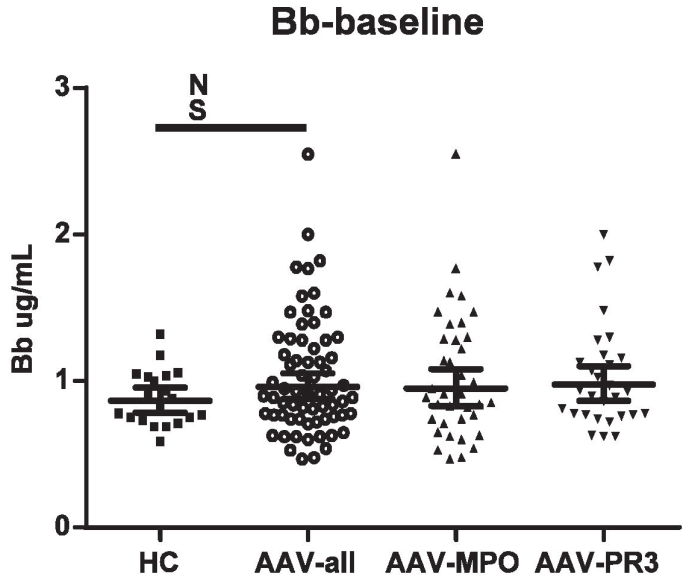
Bb-baseline
N
S
3
2
1
0
Bb ug/mL
HC
AAV-all
AAV-MPO
AAV-PR3

FIG. 4A

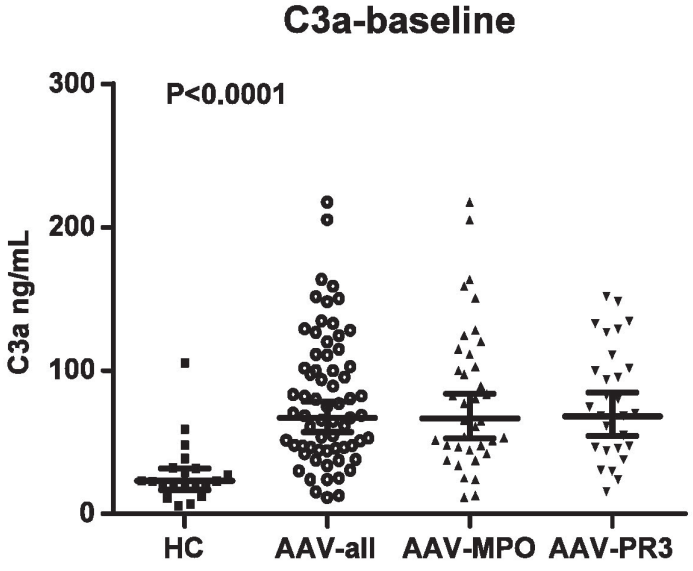
C3a-baseline
P<0.0001
300
200
100
0
C3a ng/mL
HC
AAV-all
AAV-MPO
AAV-PR3

FIG. 4B

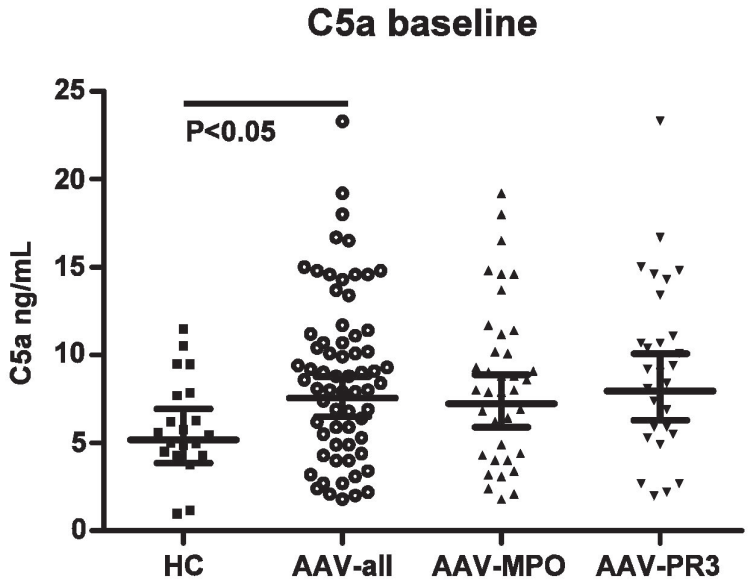
C5a baseline
C5a ng/mL
25
20
15
10
5
0
P<0.05
HC
AAV-all
AAV-MPO
AAV-PR3

FIG. 4C

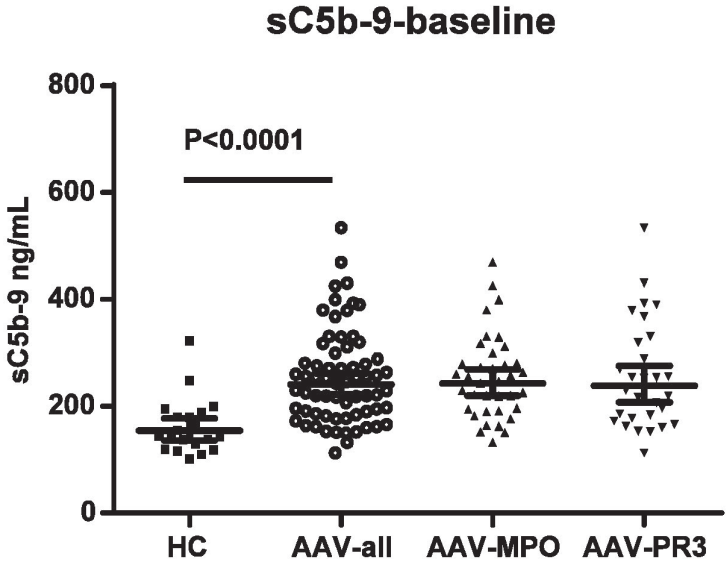
sC5b-9-baseline
sC5b-9 ng/mL
800
600
400
200
0
P<0.0001
HC
AAV-all
AAV-MPO
AAV-PR3

FIG. 4D

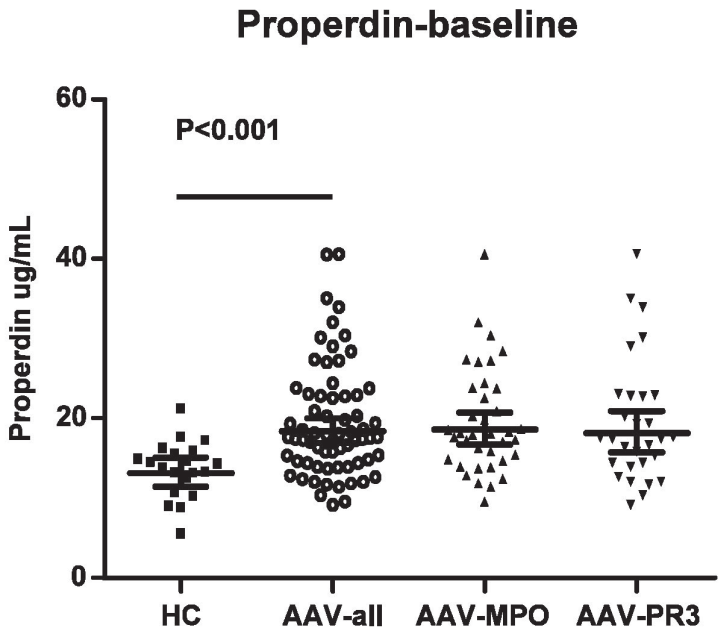
Properdin-baseline
P<0.001
Properdin ug/mL
60
40
20
0
HC
AAV-all
AAV-MPO
AAV-PR3

FIG. 4E

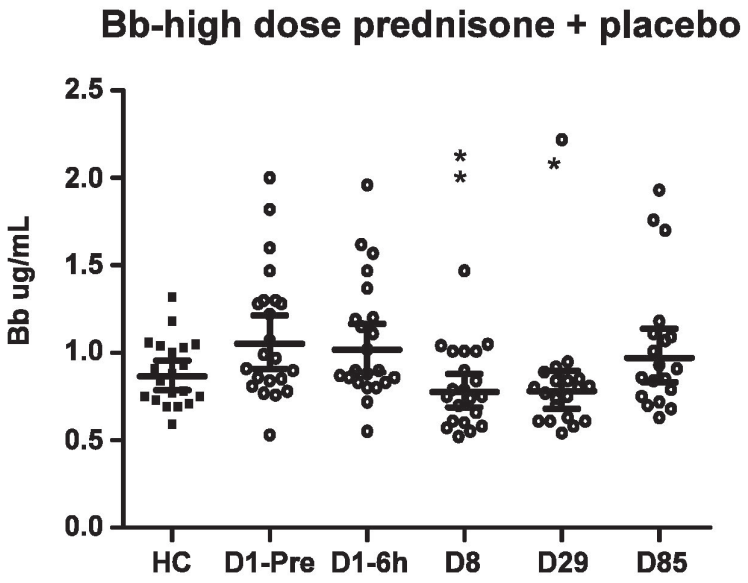
Bb-high dose prednisone + placebo
Bb ug/mL
2.5
2.0
1.5
1.0
0.5
0.0
HC
D1-Pre
D1-6h
D8
D29
D85

FIG. 5A

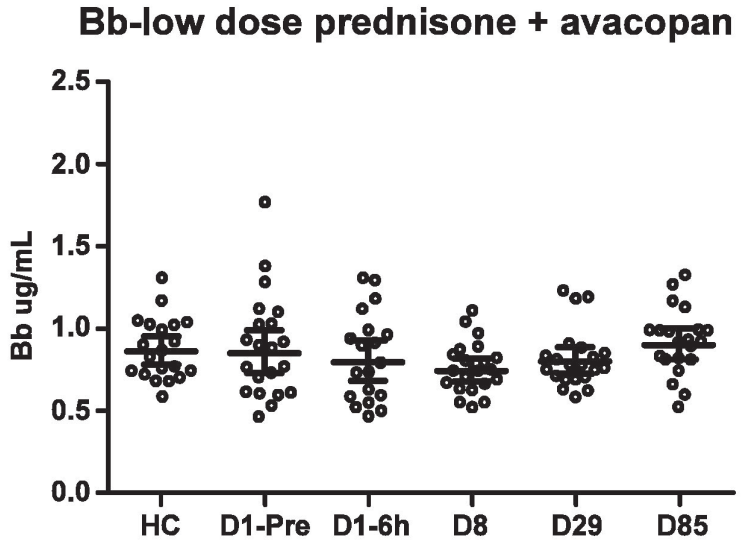
Bb-low dose prednisone + avacopan
Bb ug/mL
2.5
2.0
1.5
1.0
0.5
0.0
HC
D1-Pre
D1-6h
D8
D29
D85

FIG. 5B

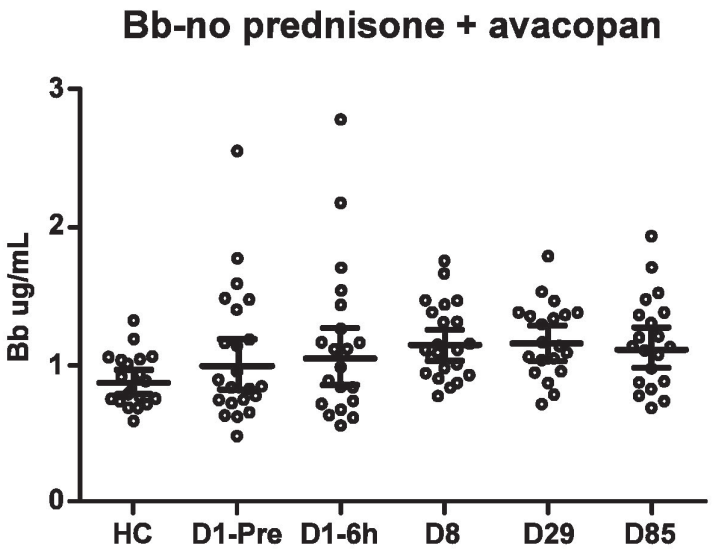
Bb-no prednisone + avacopan
Bb ug/mL
3
2
1
0
HC
D1-Pre
D1-6h
D8
D29
D85

FIG. 5C

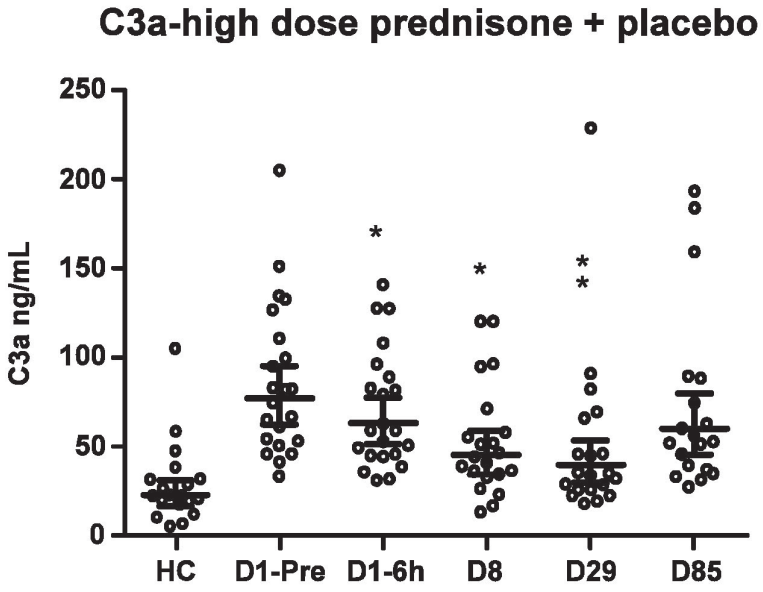
C3a-high dose prednisone + placebo
C3a ng/mL
250
200
150
100
50
0
HC
D1-Pre
D1-6h
D8
D29
D85

FIG. 6A

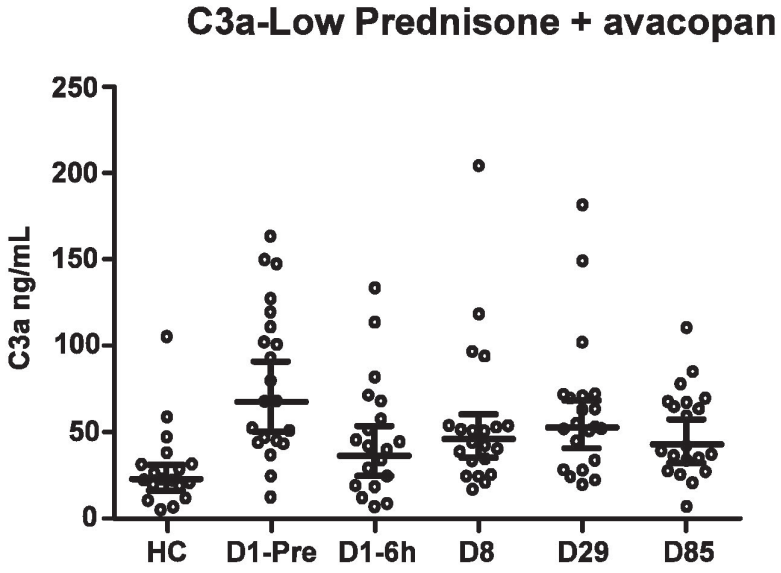
C3a-Low Prednisone + avacopan
C3a ng/mL
250
200
150
100
50
0
HC
D1-Pre
D1-6h
D8
D29
D85

FIG. 6B

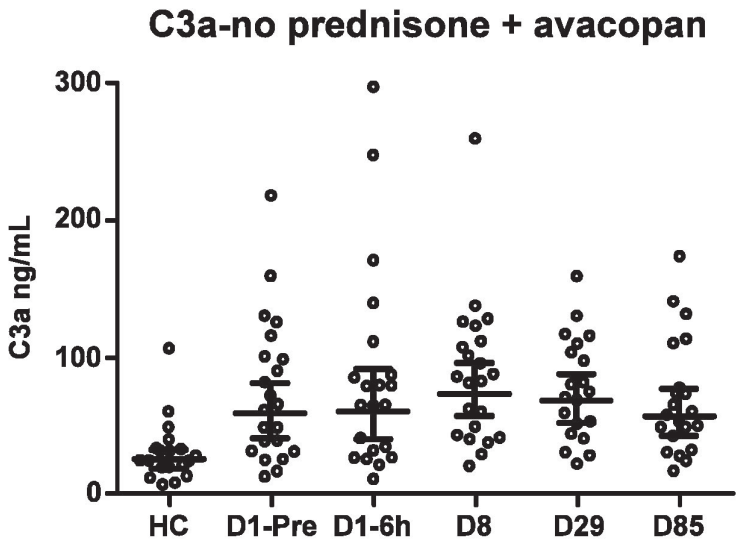
C3a-no prednisone + avacopan
C3a ng/mL
300
200
100
0
HC
D1-Pre
D1-6h
D8
D29
D85

FIG. 6C

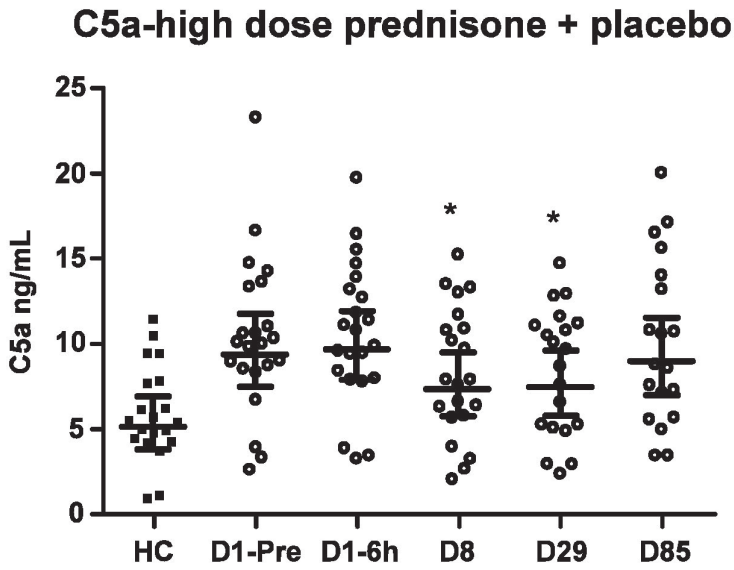
C5a-high dose prednisone + placebo
C5a ng/mL
25
20
15
10
5
0
*
*
HC
D1-Pre
D1-6h
D8
D29
D85

FIG. 7A

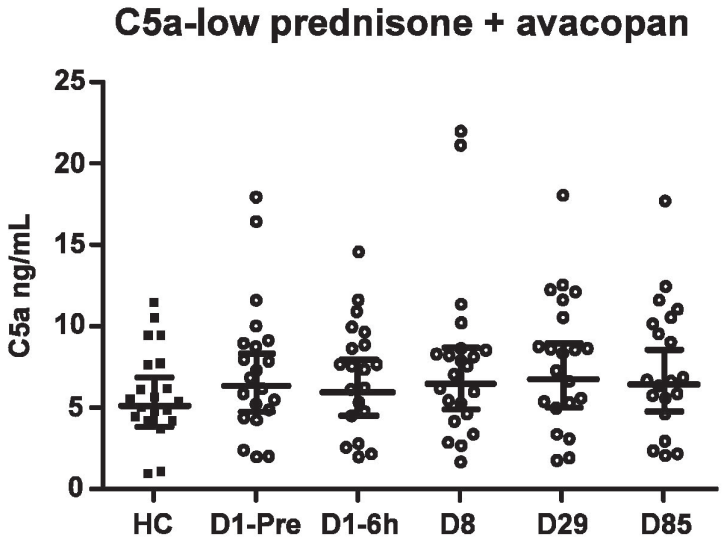
C5a-low prednisone + avacopan
C5a ng/mL
25
20
15
10
5
0
HC
D1-Pre
D1-6h
D8
D29
D85

FIG. 7B

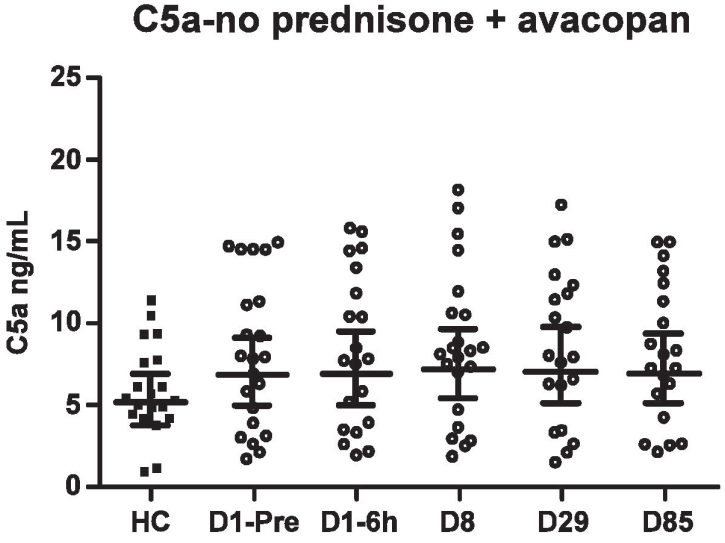
C5a-no prednisone + avacopan
C5a ng/mL
25
20
15
10
5
0
HC
D1-Pre
D1-6h
D8
D29
D85

FIG. 7C

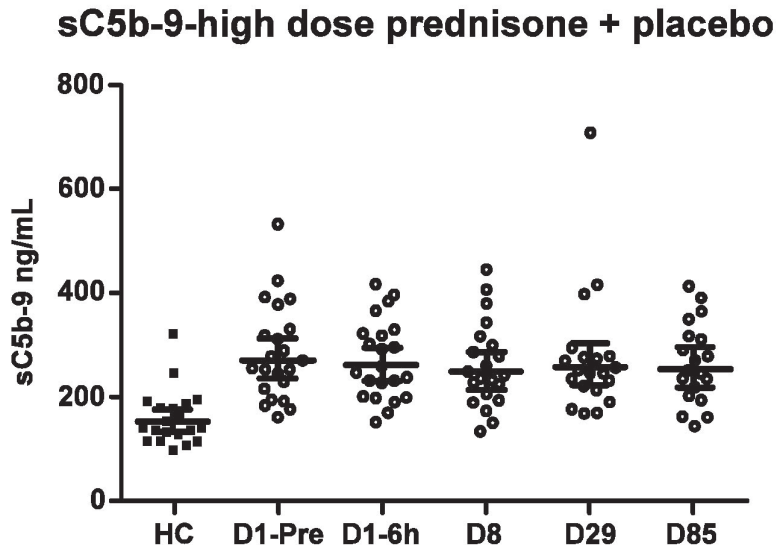
sC5b-9-high dose prednisone + placebo
sC5b-9 ng/mL
800
600
400
200
0
HC
D1-Pre
D1-6h
D8
D29
D85

FIG. 8A

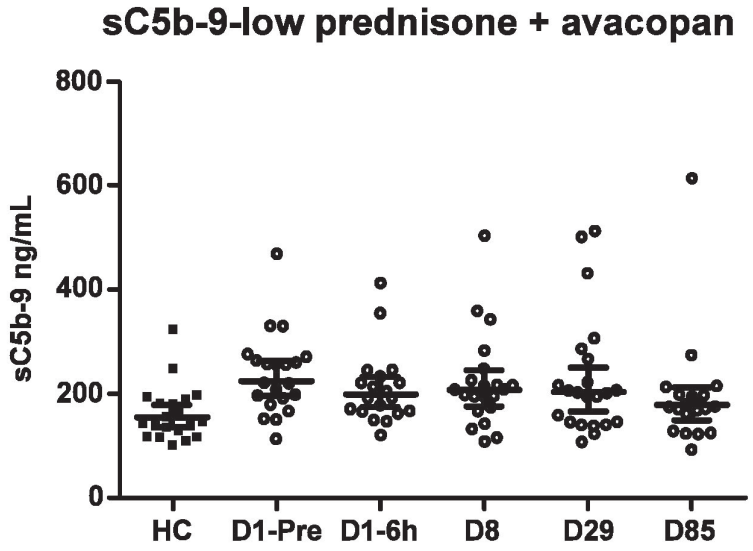
sC5b-9-low prednisone + avacopan
sC5b-9 ng/mL
800
600
400
200
0
HC
D1-Pre
D1-6h
D8
D29
D85

FIG. 8B

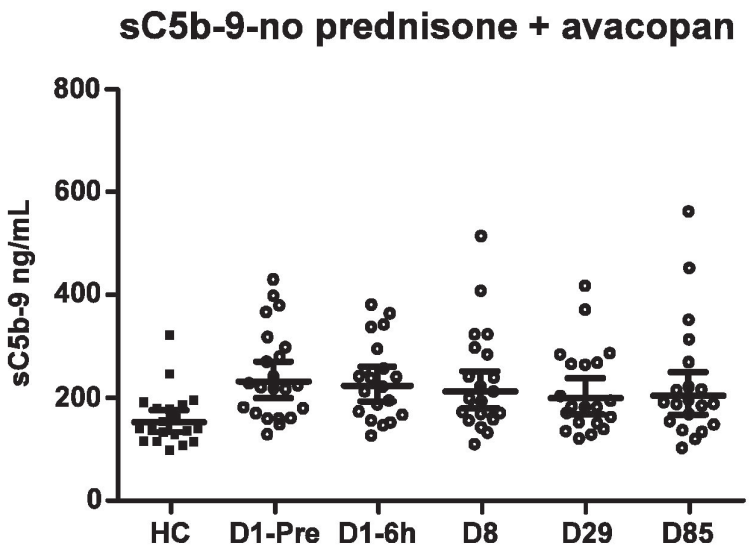
sC5b-9-no prednisone + avacopan
sC5b-9 ng/mL
800
600
400
200
0
HC
D1-Pre
D1-6h
D8
D29
D85

FIG. 8C

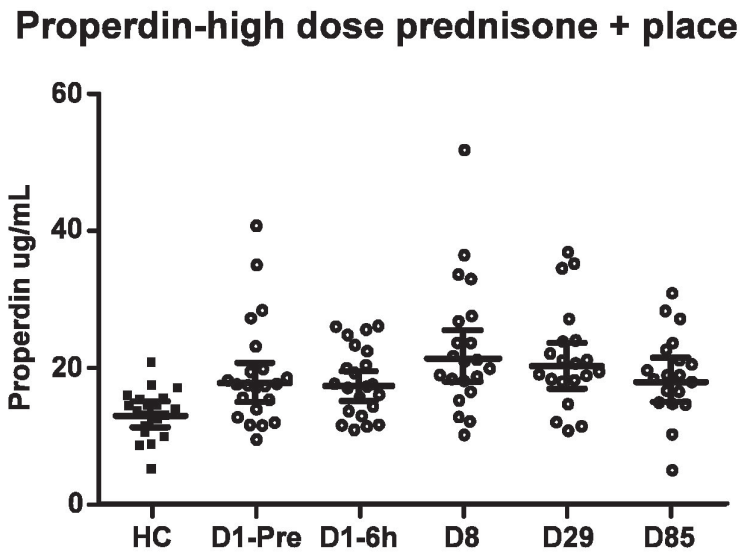
Properdin-high dose prednisone + placebo
Properdin ug/mL
60
40
20
0
HC
D1-Pre
D1-6h
D8
D29
D85

FIG. 9A

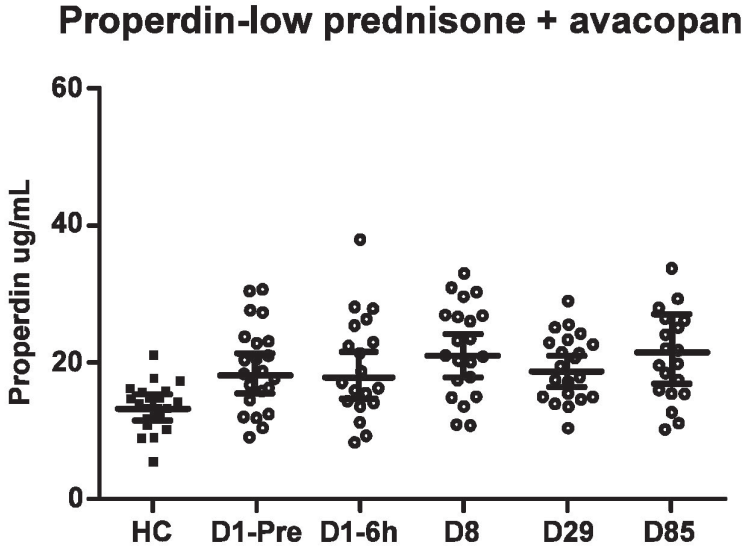
Properdin-low prednisone + avacopan
Properdin ug/mL
60
40
20
0
HC
D1-Pre
D1-6h
D8
D29
D85

FIG. 9B

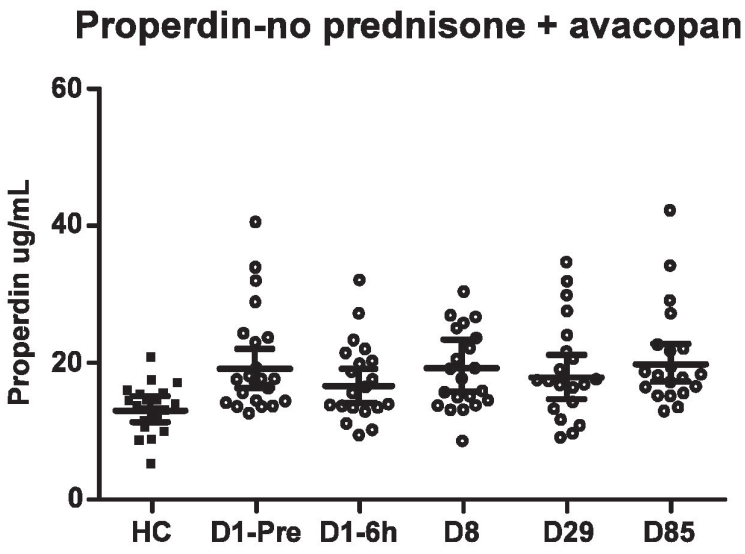
Properdin-no prednisone + avacopan
Properdin ug/mL
60
40
20
0
HC
D1-Pre
D1-6h
D8
D29
D85

FIG. 9C