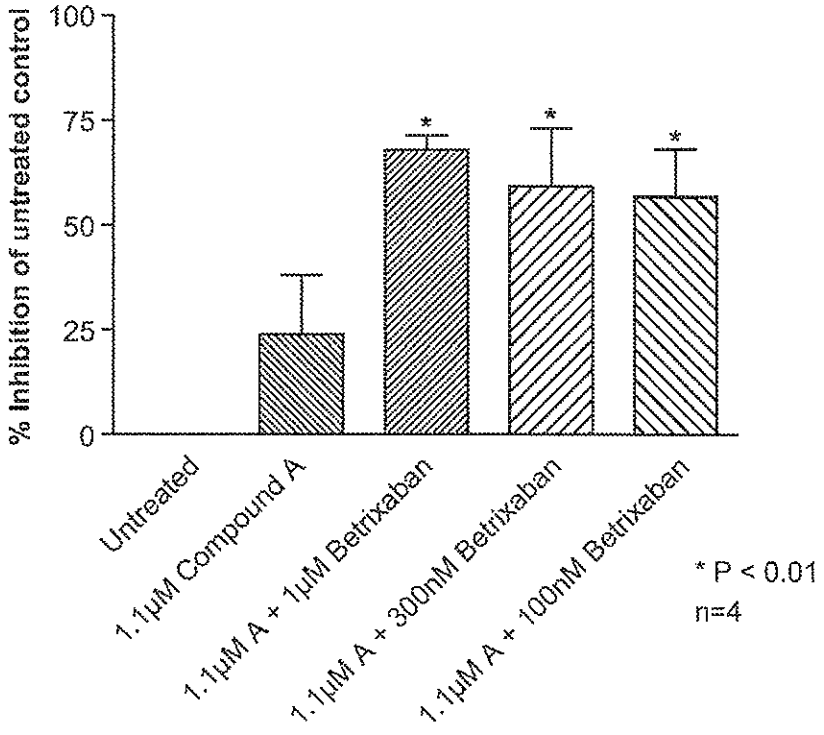

% Inhibition of untreated control
100
75
50
25
0
*
*
*
Untreated
1.1μM Compound A
1.1μM A + 1μM Betrixaban
1.1μM A + 300nM Betrixaban
1.1μM A + 100nM Betrixaban
* P < 0.01
n=4

FIG. 1

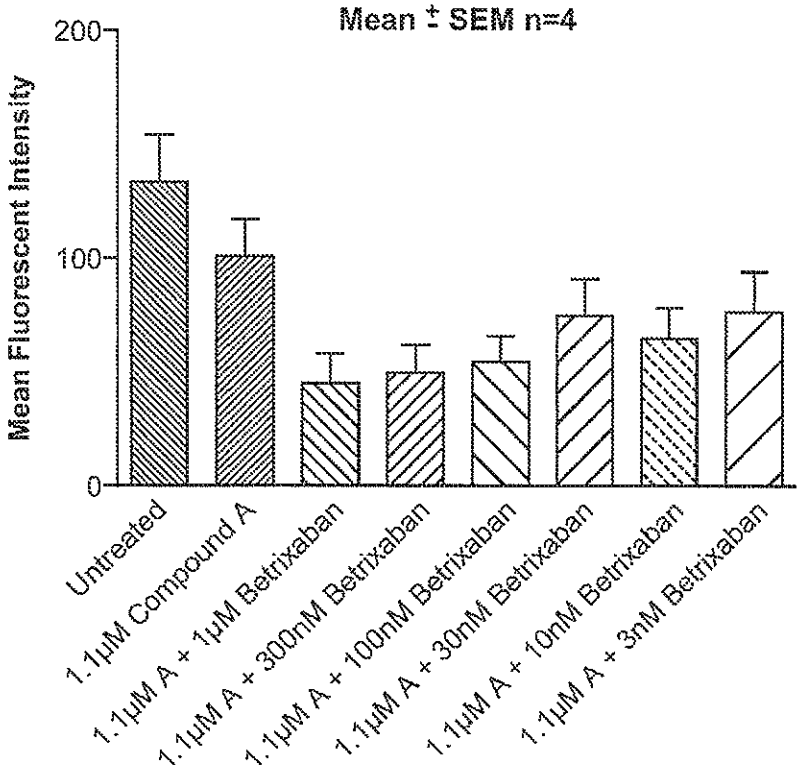

Mean ± SEM n=4
Mean Fluorescent Intensity
200
100
0
Untreated
1.1μM Compound A
1.1μM A + 1μM Betrixaban
1.1μM A + 300nM Betrixaban
1.1μM A + 100nM Betrixaban
1.1μM A + 30nM Betrixaban
1.1μM A + 10nM Betrixaban
1.1μM A + 3nM Betrixaban

FIG. 2

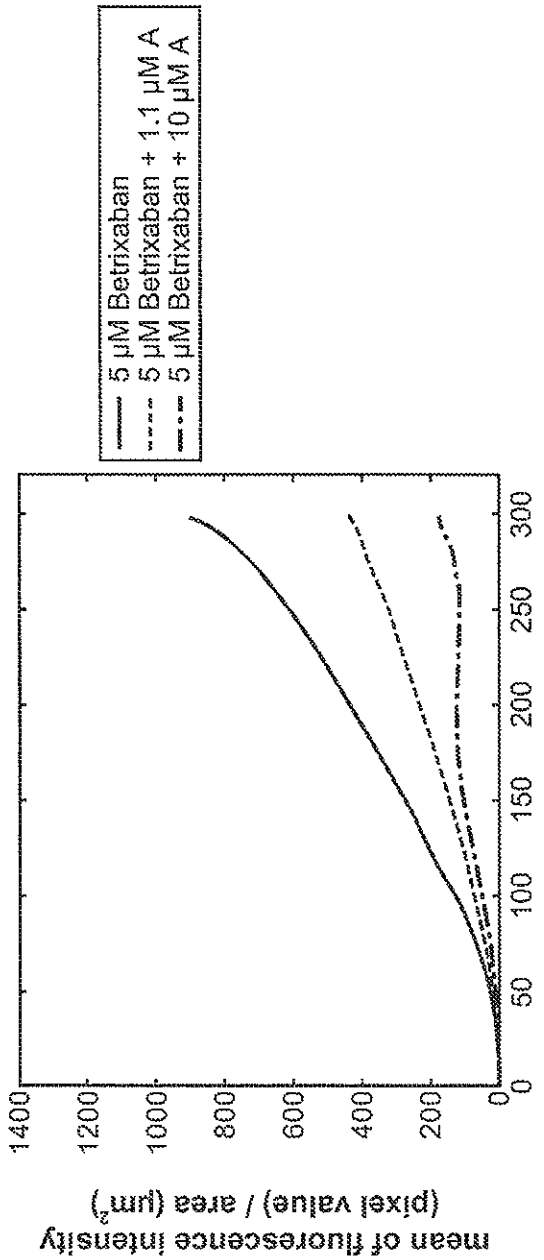

5 µM Betrixaban
5 µM Betrixaban + 1.1 µM A
5 µM Betrixaban + 10 µM A
mean of fluorescence intensity
(pixel value) / area (µm²)
0
200
400
600
800
1000
1200
1400
0
50
100
150
200
250
300

FIG. 3

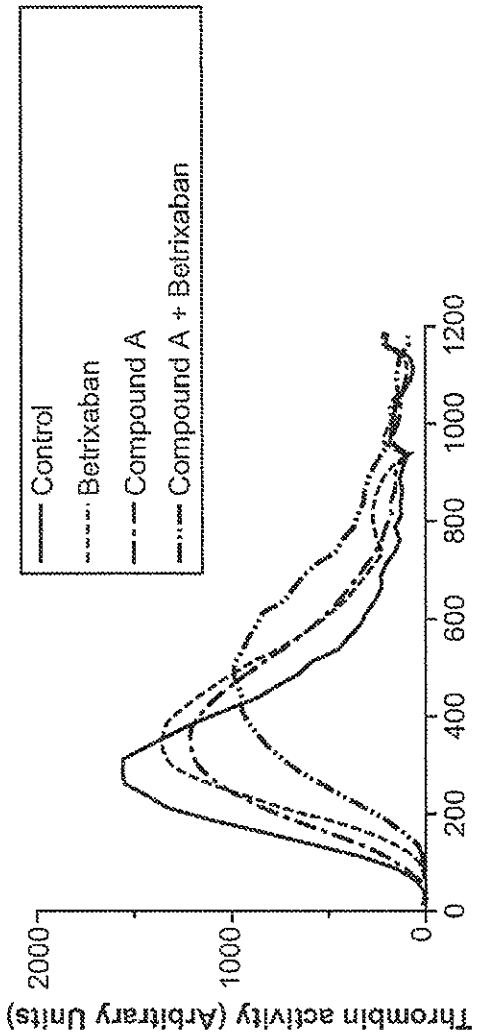

Control
Betrixaban
Compound A
Compound A + Betrixaban
Thrombin activity (Arbitrary Units)
2000
1000
0
0
200
400
600
800
1000
1200
Time (sec)

FIG. 4

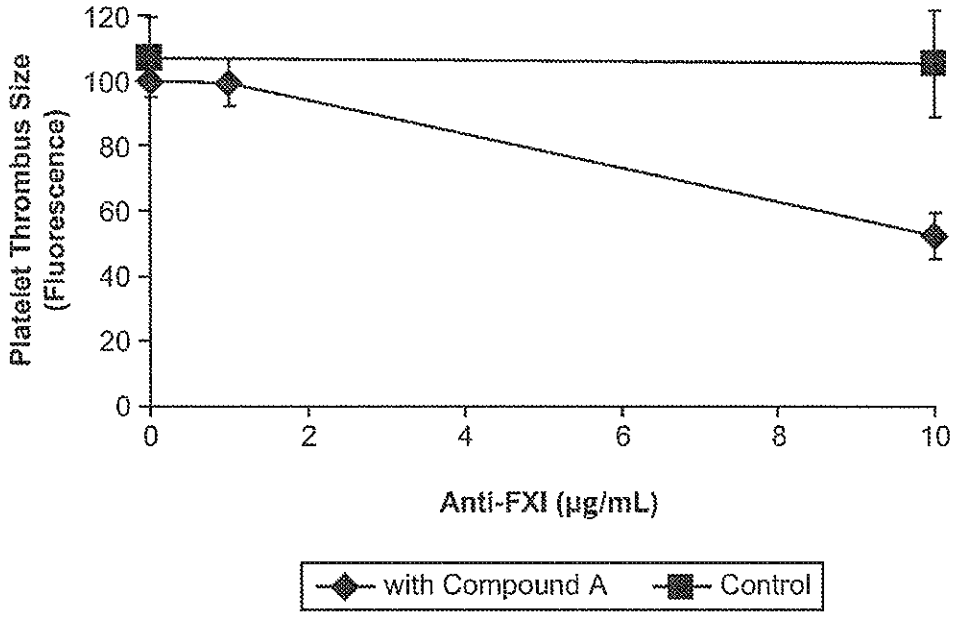

Platelet Thrombus Size (Fluorescence)
120
100
80
60
40
20
0
0
2
4
6
8
10
Anti-FXI (µg/mL)
with Compound A
Control

FIG. 5

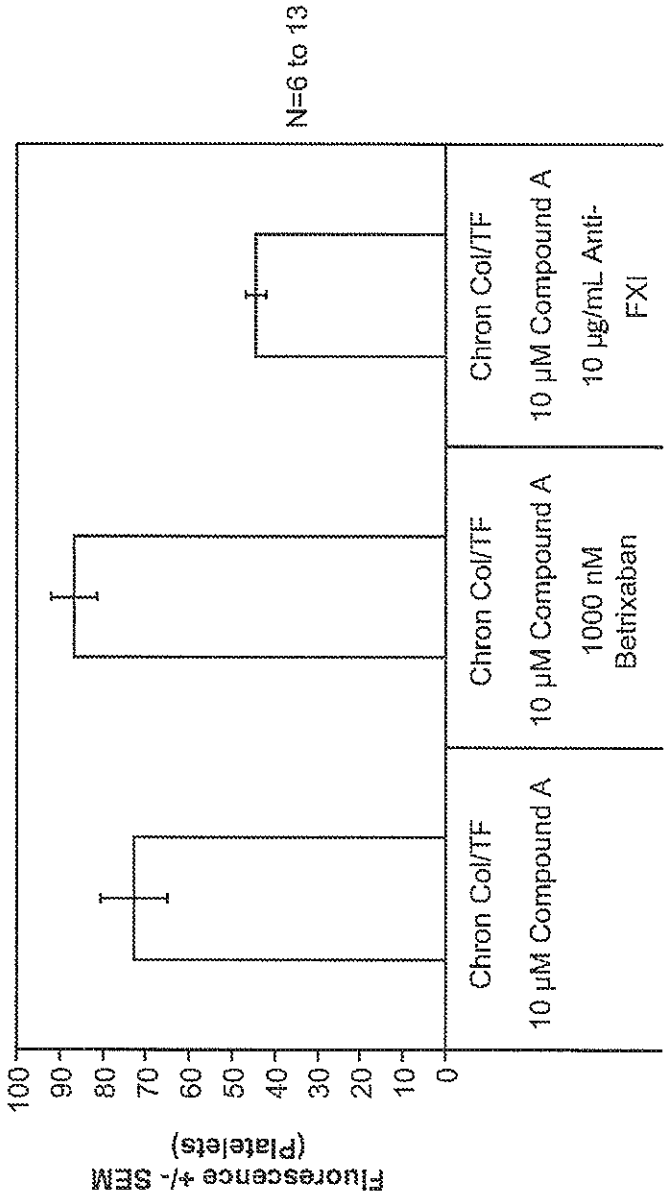

N=6 to 13
Fluorescence +/- SEM
(Platelets)
100
90
80
70
60
50
40
30
20
10
0
Chron Col/TF
10 µM Compound A
Chron Col/TF
10 µM Compound A
1000 nM
Betrixaban
Chron Col/TF
10 µM Compound A
10 µg/mL Anti-
FXI

FIG. 6

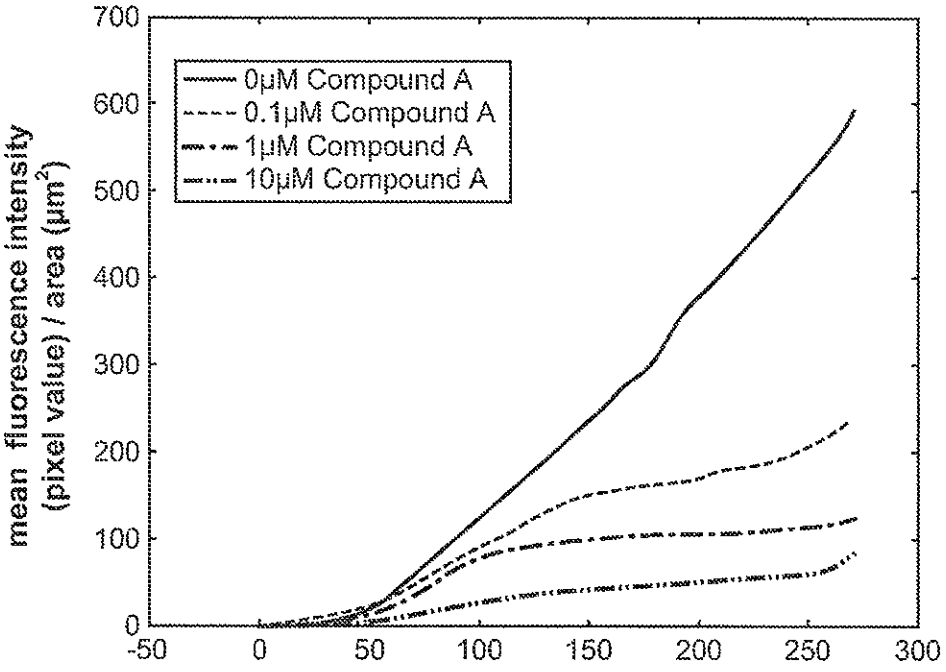

mean fluorescence intensity
(pixel value) / area (μm²)
0μM Compound A
0.1μM Compound A
1μM Compound A
10μM Compound A
700
600
500
400
300
200
100
0
-50
0
50
100
150
200
250
300

FIG. 7

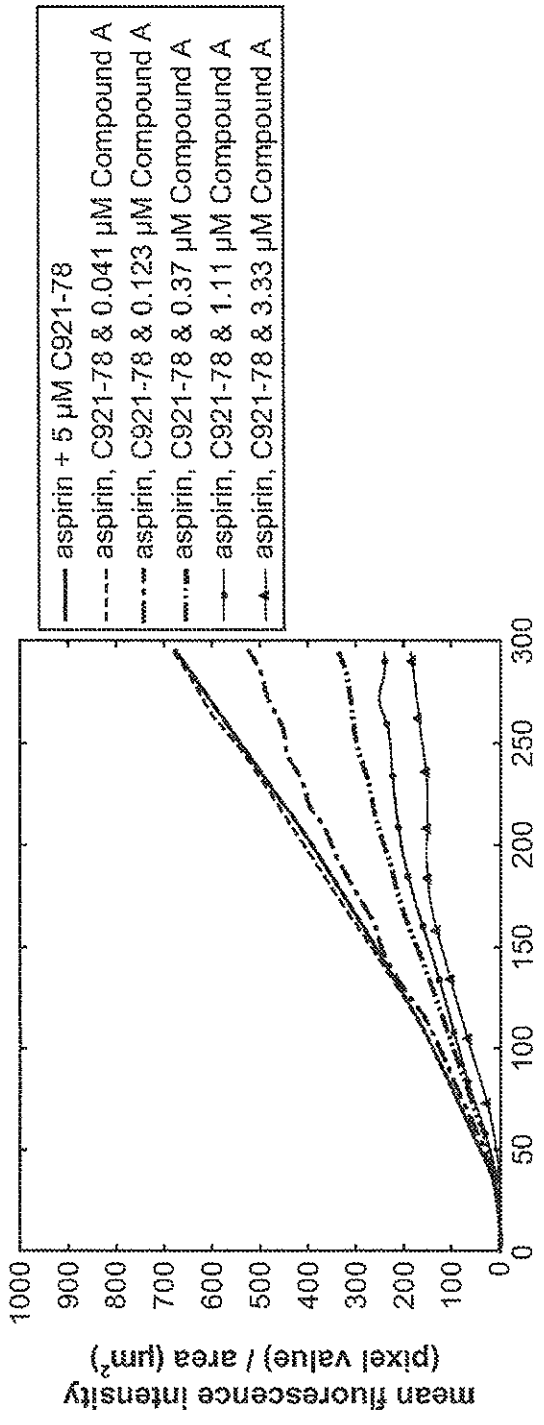

mean fluorescence intensity
(pixel value) / area (μm²)
0
100
200
300
400
500
600
700
800
900
1000
0
50
100
150
200
250
300
aspirin + 5 μM C921-78
aspirin, C921-78 & 0.041 μM Compound A
aspirin, C921-78 & 0.123 μM Compound A
aspirin, C921-78 & 0.37 μM Compound A
aspirin, C921-78 & 1.11 μM Compound A
aspirin, C921-78 & 3.33 μM Compound A

FIG. 8

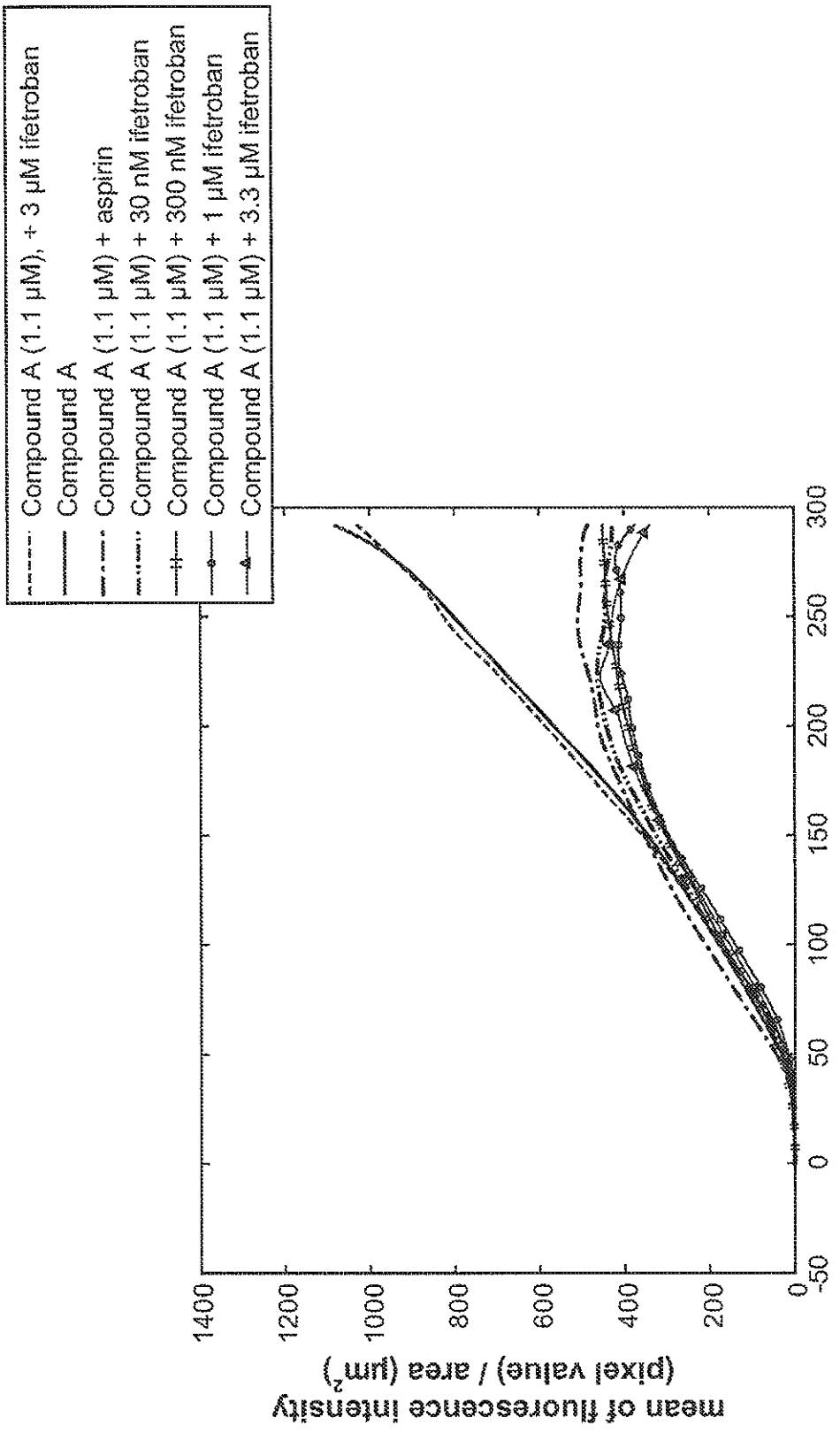

Compound A (1.1 µM), + 3 µM ifetroban
Compound A
Compound A (1.1 µM) + aspirin
Compound A (1.1 µM) + 30 nM ifetroban
Compound A (1.1 µM) + 300 nM ifetroban
Compound A (1.1 µM) + 1 µM ifetroban
Compound A (1.1 µM) + 3.3 µM ifetroban
mean of fluorescence intensity
(pixel value) / area (µm²)
1400
1200
1000
800
600
400
200
0
-50
0
50
100
150
200
250
300

FIG. 9

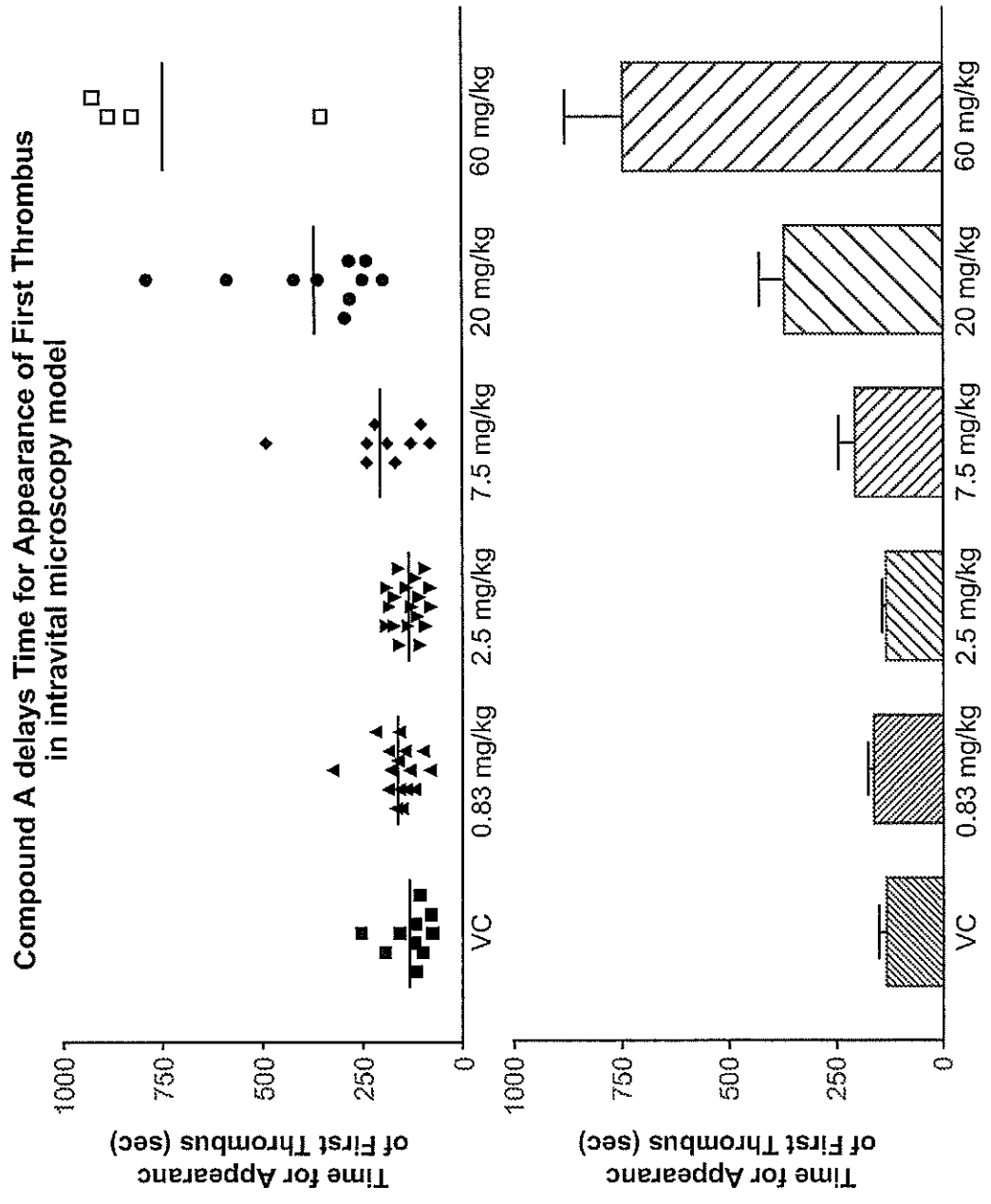

Compound A delays Time for Appearance of First Thrombus in intravital microscopy model
Time for Appearanc of First Thrombus (sec)
1000
750
500
250
0
VC
0.83 mg/kg
2.5 mg/kg
7.5 mg/kg
20 mg/kg
60 mg/kg

FIG. 10

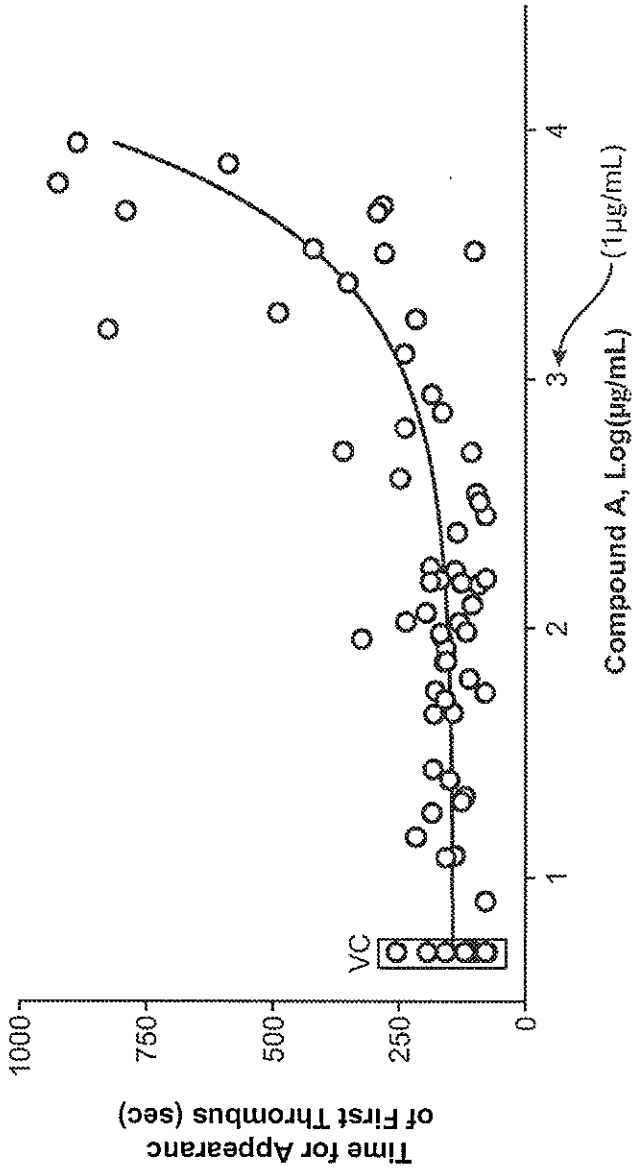

Time for Appearanc
of First Thrombus (sec)
1000
750
500
250
0
VC
1
2
3
4
Compound A, Log(µg/mL)
(1µg/mL)

FIG. 11

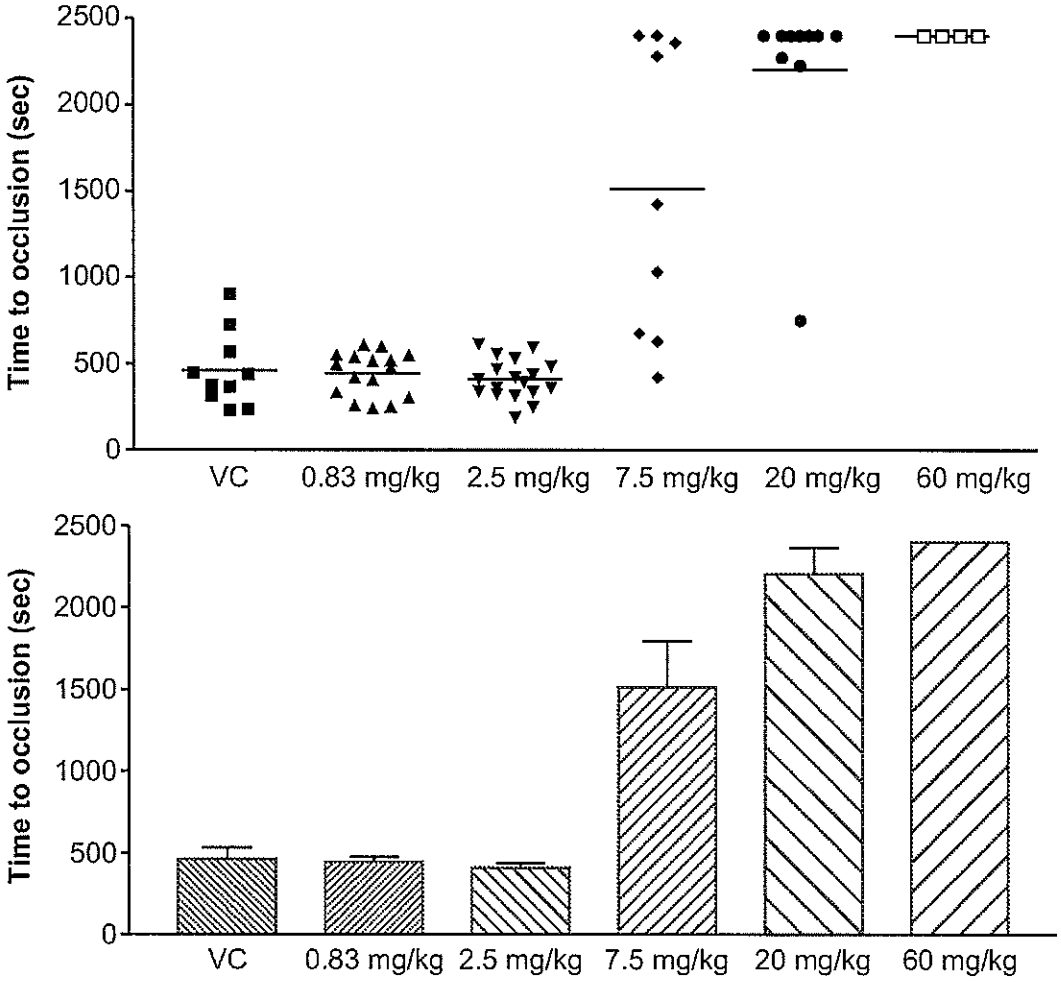

Time to occlusion (sec)
2500
2000
1500
1000
500
0
VC
0.83 mg/kg
2.5 mg/kg
7.5 mg/kg
20 mg/kg
60 mg/kg
Time to occlusion (sec)
2500
2000
1500
1000
500
0
VC
0.83 mg/kg
2.5 mg/kg
7.5 mg/kg
20 mg/kg
60 mg/kg

FIG. 12

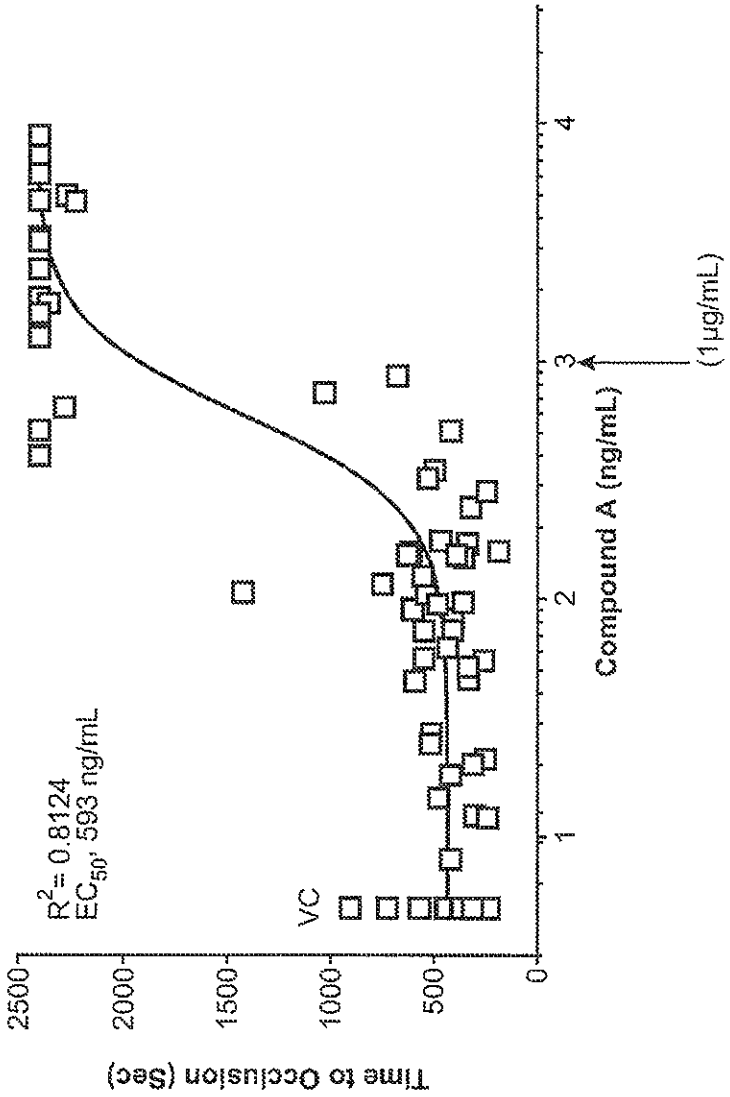

Time to Occlusion (Sec)
2500
2000
1500
1000
500
0
1
2
3
4
Compound A (ng/mL)
(1µg/mL)
VC
R2= 0.8124
EC50, 593 ng/mL

FIG. 13

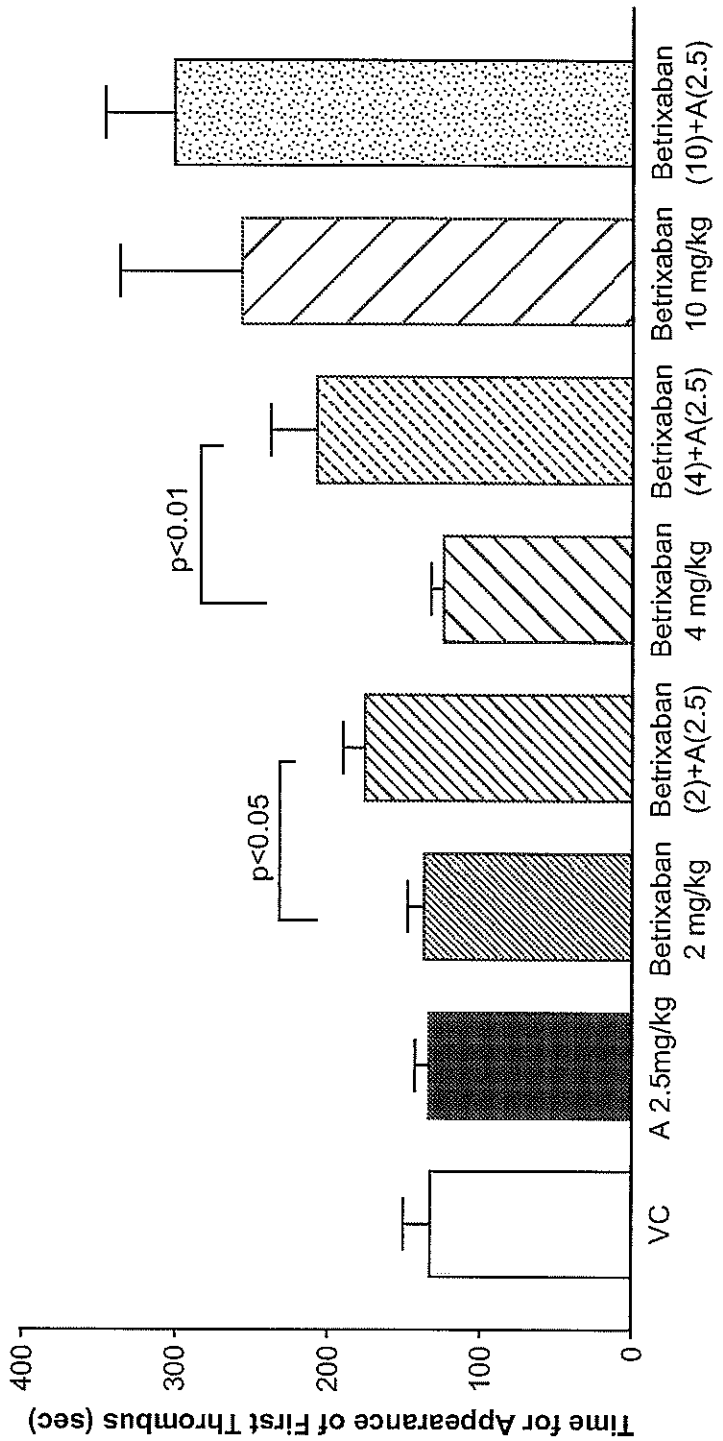

Time for Appearance of First Thrombus (sec)
400
300
200
100
0
p<0.05
p<0.01
VC
A 2.5mg/kg
Betrixaban 2 mg/kg
Betrixaban (2)+A(2.5)
Betrixaban 4 mg/kg
Betrixaban (4)+A(2.5)
Betrixaban 10 mg/kg
Betrixaban (10)+A(2.5)

FIG. 14

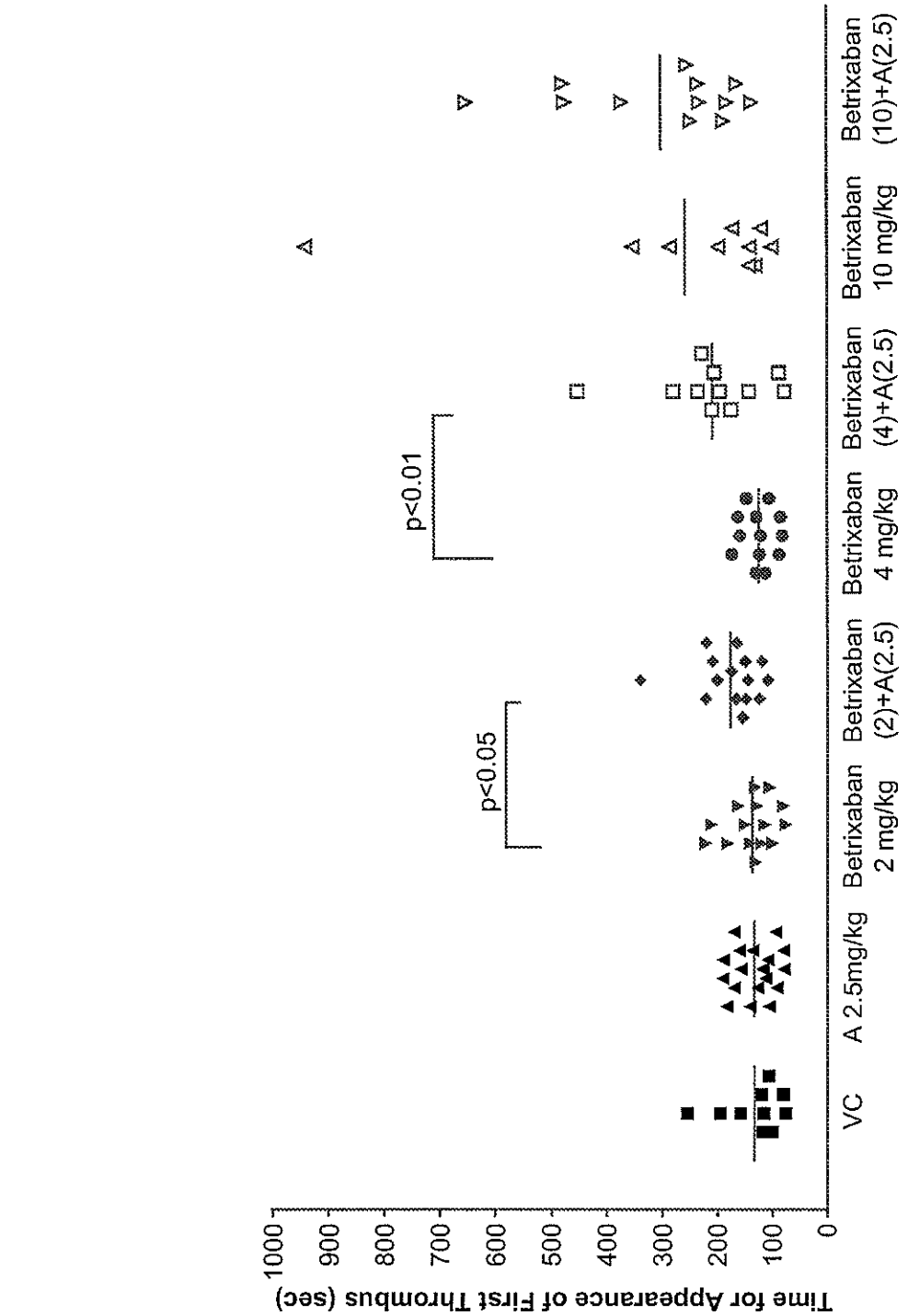

Time for Appearance of First Thrombus (sec)
1000
900
800
700
600
500
400
300
200
100
0
p<0.01
p<0.05
VC
A 2.5mg/kg
Betrixaban 2 mg/kg
Betrixaban (2)+A(2.5)
Betrixaban 4 mg/kg
Betrixaban (4)+A(2.5)
Betrixaban 10 mg/kg
Betrixaban (10)+A(2.5)

FIG. 15

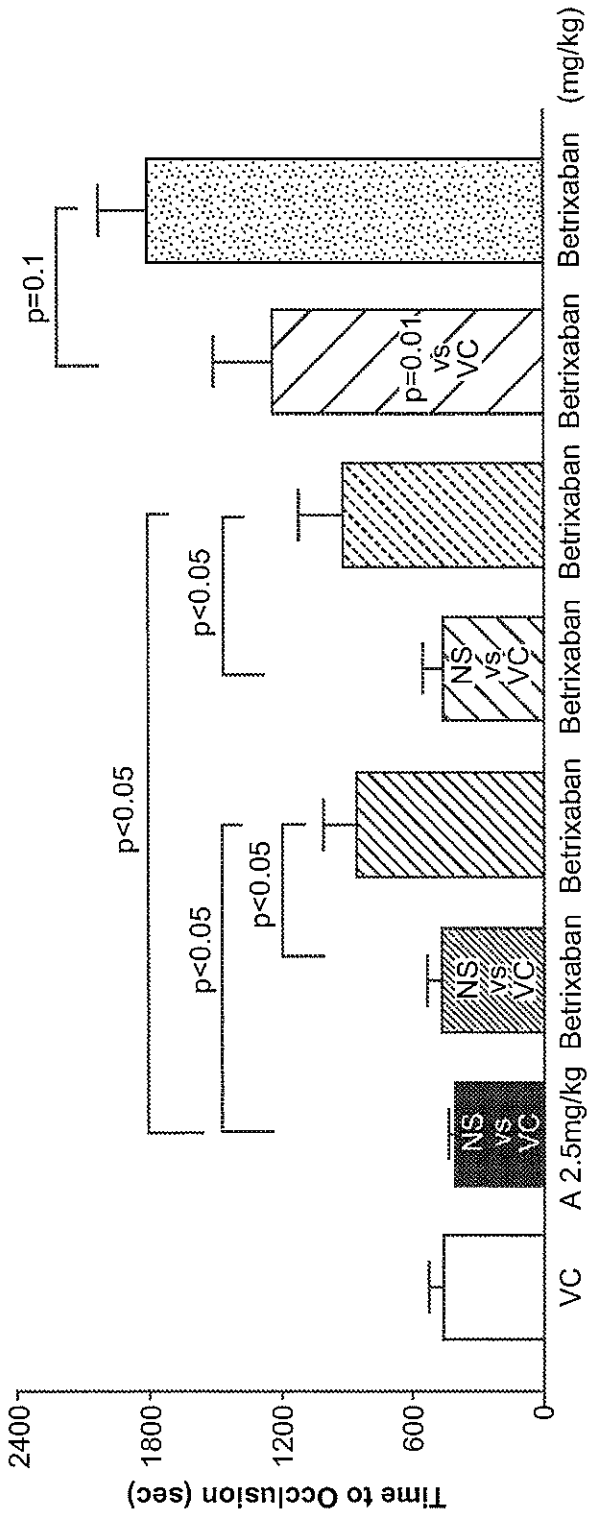

Time to Occlusion (sec)
2400
1800
1200
600
0
VC
A 2.5mg/kg
Betrixaban 2 mg/kg
Betrixaban (2)+A(2.5)
Betrixaban 4 mg/kg
Betrixaban (4)+A(2.5)
Betrixaban 10 mg/kg
Betrixaban (10)+A(2.5)
(mg/kg)
NS vs VC
p<0.05
p<0.05
p<0.05
p<0.05
NS vs VC
p=0.01 vs VC
p=0.1

FIG. 16

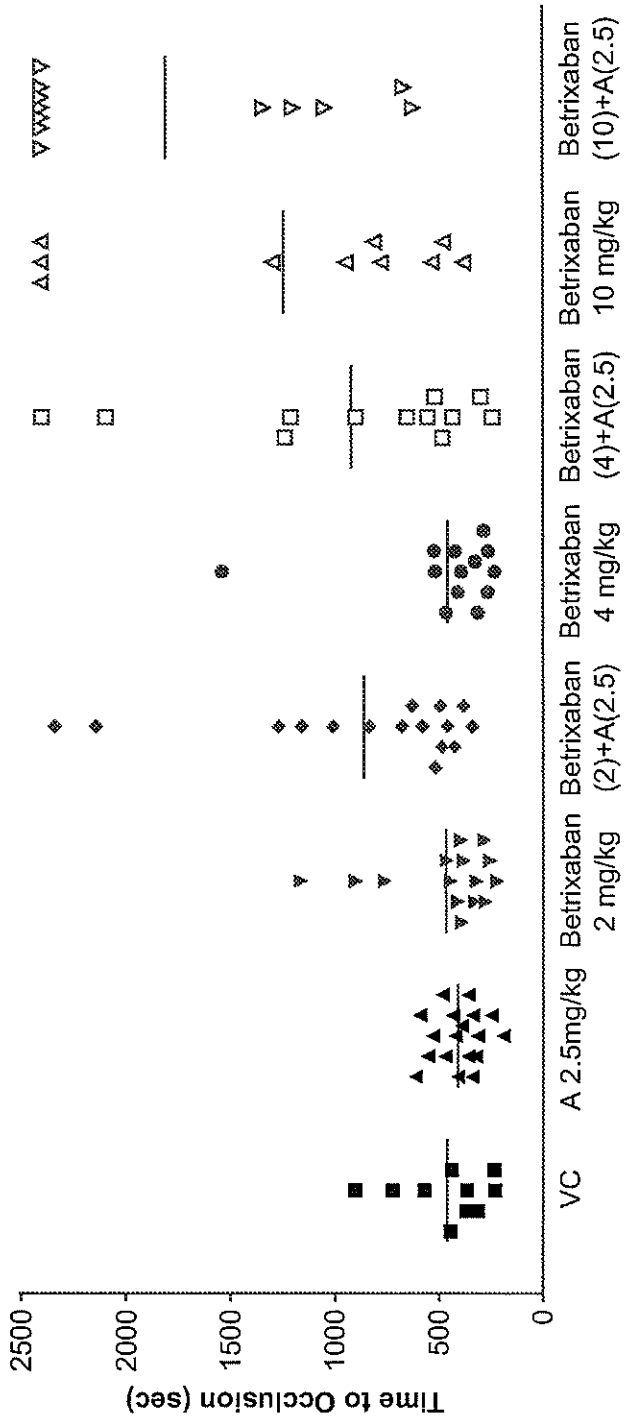

Time to Occlusion (sec)
2500
2000
1500
1000
500
0
VC
A 2.5mg/kg
Betrixaban 2 mg/kg
Betrixaban (2)+A(2.5)
Betrixaban 4 mg/kg
Betrixaban (4)+A(2.5)
Betrixaban 10 mg/kg
Betrixaban (10)+A(2.5)

FIG. 17