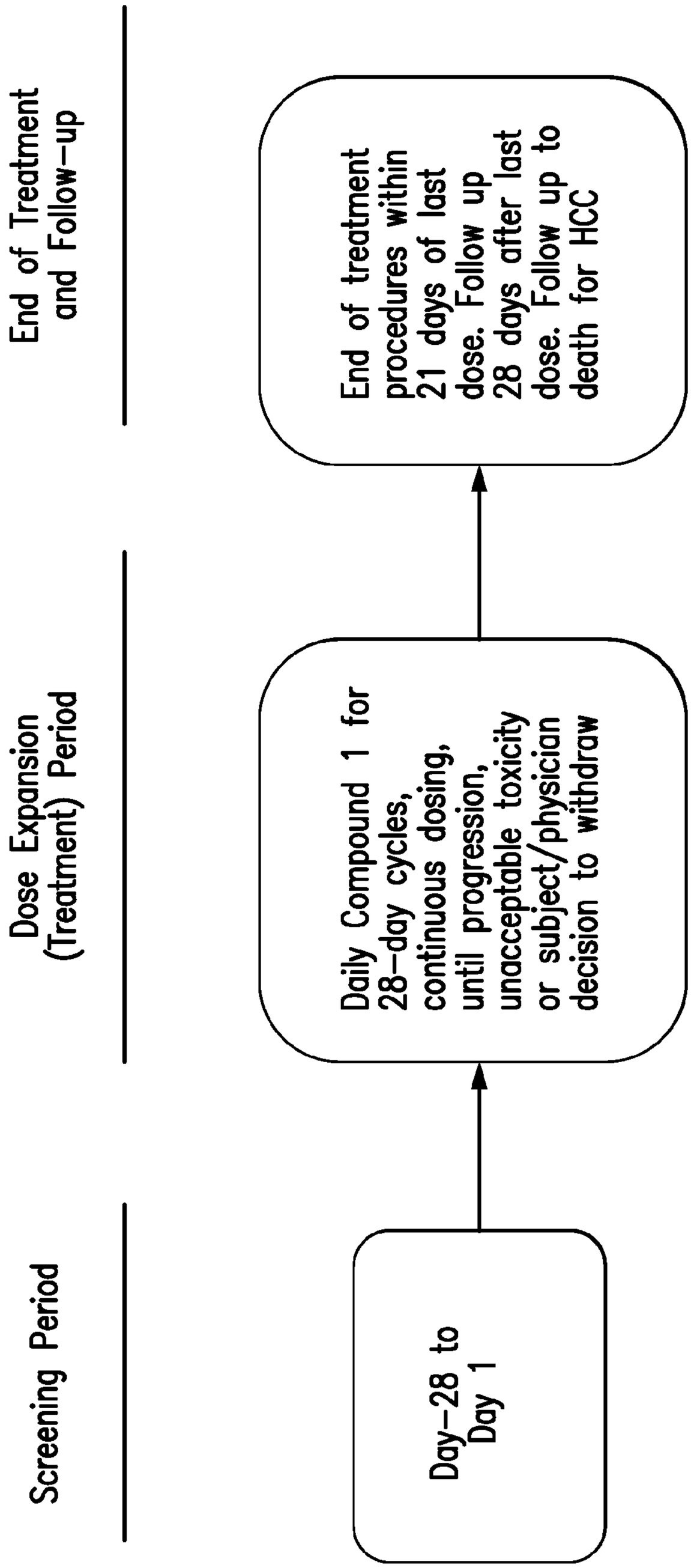

End of Treatment and Follow–up
Dose Expansion (Treatment) Period
Screening Period
End of treatment procedures within 21 days of last dose. Follow up 28 days after last dose. Follow up to death for HCC
Daily Compound 1 for 28–day cycles, continuous dosing, until progression, unacceptable toxicity or subject/physician decision to withdraw
Day –28 to Day 1

FIG. 1

SUBSTITUTE SHEET (RULE 26)

	Subject Characteristics by HBV Status (ITT)			Subject Characteristics by HBV Status (EE)		
	HBV+ (n=12)	Non HBV (n=41)	Overall (n=53)	HBV+ (n=11)	Non HBV (n=30)	Overall (n=41)
Age, mean (range) years	57.5 (42 – 77)	60.8 (25 – 84)	60.0 (25 – 84)	55.7 (42 – 67)	59.1.8 (25 – 77)	58.2 (25 – 77)
Sex, Male (%) : Female (%)	12 (100%) : 0 (%)	31 (76%) : 10 (24%)	43 (81%) : 10 (19%)	11 (100%) : 0 (0%)	24 (80%) : 6 (20%)	35 (85.4%) : 6 (14.6%)
Race:						
Asian	8 (66.7%)	2 (4.9%)	10 (18.9%)	7 (63.6%)	1 (3.3%)	8 (19.5%)
Black	1 (8.3%)	4 (9.8%)	5 (9.4%)	1 (9.1%)	1 (3.3%)	2 (4.9%)
White	1 (8.3%)	30 (73.2%)	31 (58.5%)	1 (9.1%)	23 (76.7%)	24 (58.5%)
Other/Unknown	2 (16.7%)	5 (12.2%)	7 (13.2%)	2 (18.2%)	5 (16.7%)	7 (17.2%)
ECOG PS:						
0	4 (33.3%)	15 (36.6%)	19 (35.6%)	4 (36.4%)	12 (40%)	16 (39%)
1	8 (66.7%)	24 (58.5%)	32 (60.4%)	7 (63.6%)	16 (53.3%)	23 (56.1%)
2	0 (0%)	2 (4.9%)	2 (3.8%)	0 (0%)	2 (6.7%)	2 (4.9%)
Childs–Pugh Score:						
A (5–6)	10 (83.3%)	33 (80.5%)	43 (81.1%)	9 (81.8%)	25 (83.3%)	34 (82.9%)
B ((7–9)	1 (8.3%)	3 (7.3%)	4 (7.5%)	1 (9.1%)	2 (6.7%)	3 (7.3%)
Unknown	1 (8.3%)	4 (9.8%)	5 (9.4%)	1 (9.1%)	3 (10%)	3 (7.3%)
Cirrhosis, Yes (%) : No (%)	8 (66.7%) : 4 (33.3%)	26 (63.4%) : 15 (36.6%)	34 (64.2%) : 19 (35.8%)	7 (63.6%) : 4 (36.4%)	20 (66.7%) : 10 (33.3%)	27 (65.9%) : 14 (34.1%)

FIG. 2

	Subject Characteristics by HBV Status (ITT)			Subject Characteristics by HBV Status (EE)		
	HBV+ (n=12)	Non HBV (n=41)	Overall (n=53)	HBV+ (n=11)	Non HBV (n=30)	Overall (n=41)
HCC Risk Factor:						
HBV	12 (100%)	0 (0%)	12 (22.6%)	11 (100%)	0 (0%)	11 (26.8%)
HCV	0 (0%)	15 (36.6%)	15 (28.3%)	0 (0%)	10 (33.6%)	10 (24.4%)
Alcohol	0 (0%)	3 (7.3%)	3 (5.7%)	0 (0%)	3 (10%)	3 (7.3%)
Other/Unknown	6 (50%)	23 (56.1%)	29 (54.7%)	2 (18.2%)	17 (56.7%)	19 (46.3%)
APF≥15 ng/mL at baseline, Yes (%) : No (%)	9 (75%) : 3 (25%)	27 (65.9%) : 14 (34.1%)	36 (67.9%) : 17 (32.1%)	8 (72.7%) : 3 (27.3%)	21 (70%) : 9 (30%)	29 (70.7%) : 12 (29.3%)
Median CC223 dose (mg/day) (range)	30.0 (22.8 – 45.0)	30.0 (19.1 – 45.0)	30.0 (19.1 – 45.0)	30.0 (228– 42.5)	30.0 (19.1 – 45.0)	30.0 (19.1 – 45.0)
Median treatment duration (days) (range)	112.5 (19.0 – 419.0)	56.0 (1.0 – 393.0)	64.0 (1.0 – 419.0)	113 (48.0 – 419.0)	70.0 (23.0 – 393.0)	105.0 (23.0 – 419.0)
Median number of cycles (range)	4 (1 – 15)	2 (1 – 14)	3 (1 – 15)	4 (4 – 15)	2 (1 – 14)	3 (1 – 15)

FIG. 2 continued

SUBSTITUTE SHEET (RULE 26)

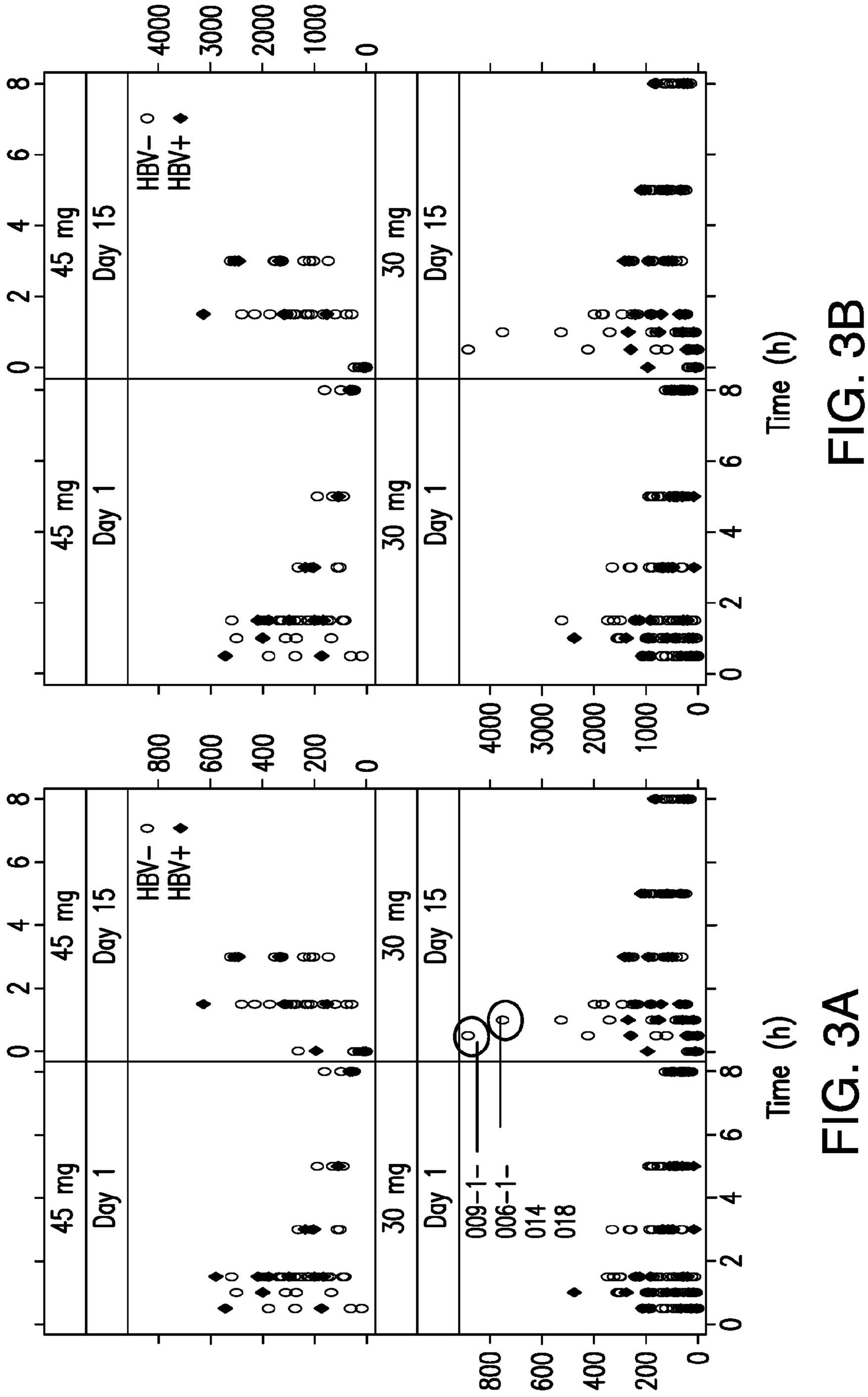

45 mg
Day 1
Day 15
30 mg
HBV− ○
HBV+ ◆
009−1−
006−1−
014
018
Plasma Concentration (ng/mL)
Time (h)

FIG. 3A

FIG. 3B

Subject Disposition by HBV Status – Part B HCC Cohort
Enrolled Population

	HBV+ (N=12) n (%)	HBV– (N=41) n (%)	Overall (N=53) n (%)
Subject Disposition			
Ongoing	2 (16.7)	5 (12.2)	7 (13.2)
Discontinued	10 (83.3)	36 (87.8)	46 (86.8)
Reason for Discontinuation			
Adverse event	3 (25.0)	11 (26.8)	14 (26.4)
Disease progression	7 (58.3)	11 (26.8)	18 (34.0)
Withdrew consent	0	4 (9.8)	4 (7.5)
Death	0	5 (12.2)	5 (9.4)
Lost to follow up	0	2 (4.9)	2 (3.8)
Other	0	3 (7.3)	3 (5.7)

FIG. 4

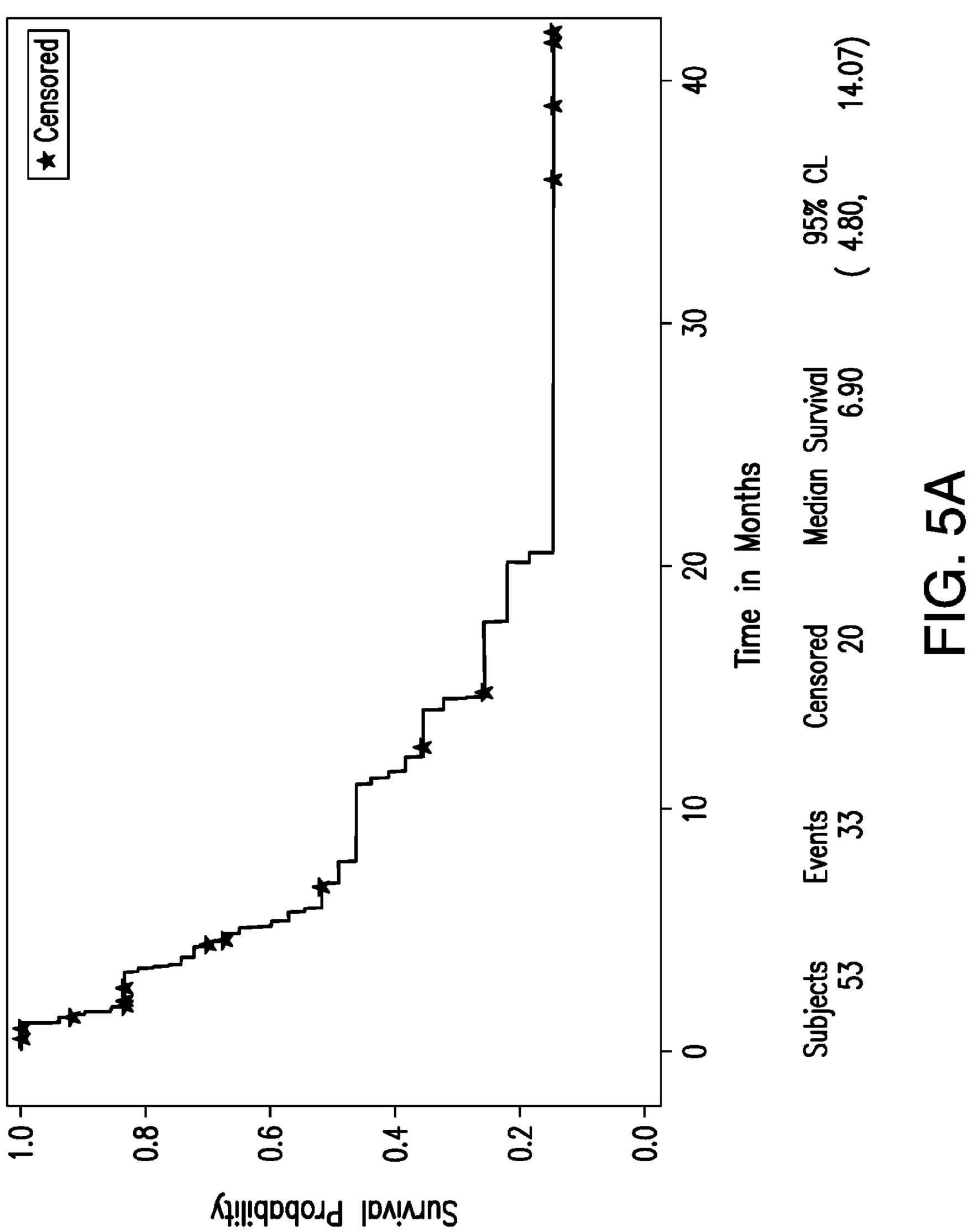

★ Censored
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
0
10
20
30
40
Time in Months
Subjects 53
Events 33
Censored 20
Median Survival 6.90
95% CL (4.80, 14.07)

FIG. 5A

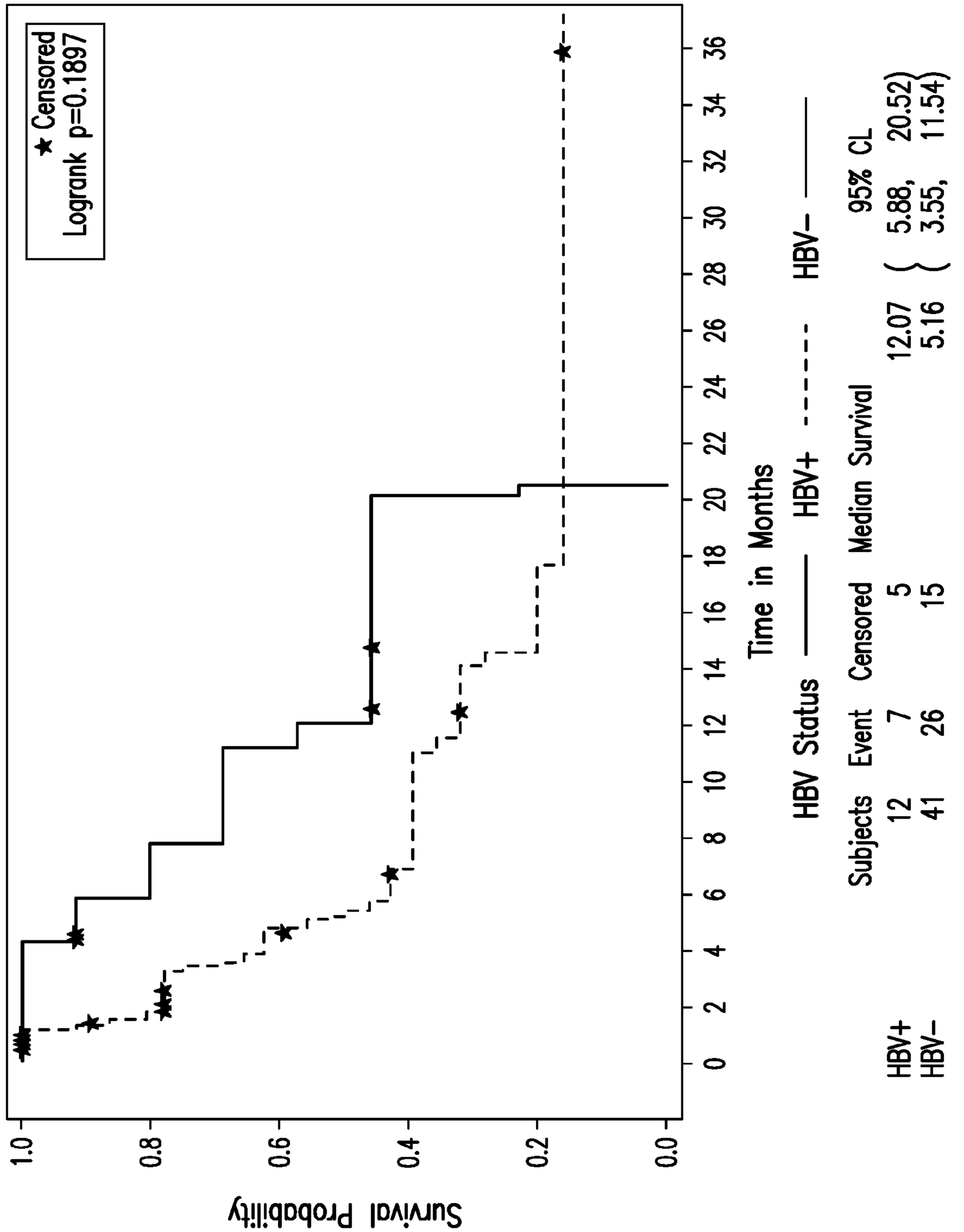

★ Censored
Logrank p=0.1897
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
Time in Months
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
HBV Status —— HBV+ - - - - HBV– ——
Subjects Event Censored Median Survival 95% CL
12 7 5 12.07 (5.88, 20.52)
41 26 15 5.16 (3.55, 11.54)
HBV+
HBV–

FIG. 5B

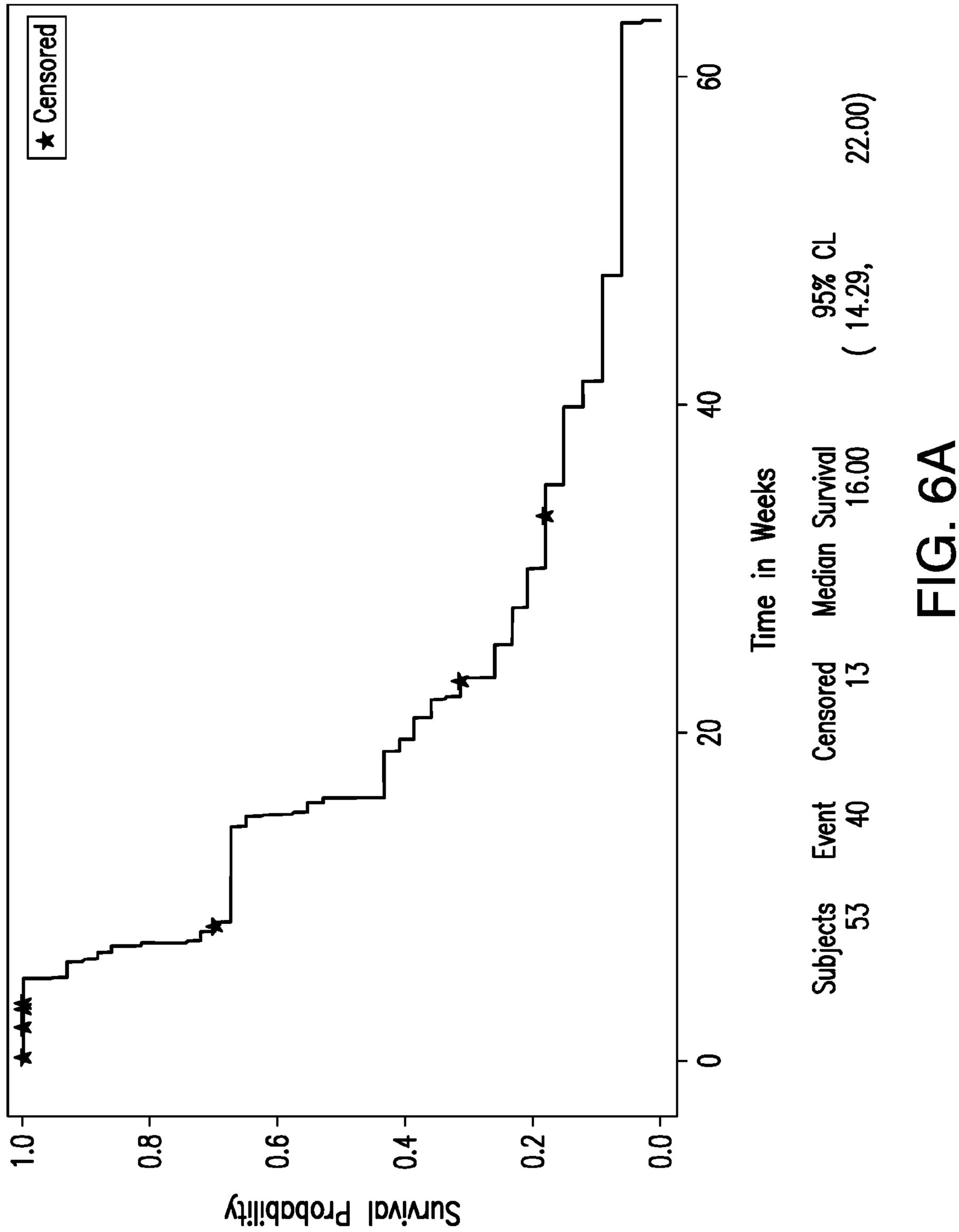

★ Censored
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
0
20
40
60
Time in Weeks
Subjects 53
Event 40
Censored 13
Median Survival 16.00
95% CL (14.29, 22.00)

FIG. 6A

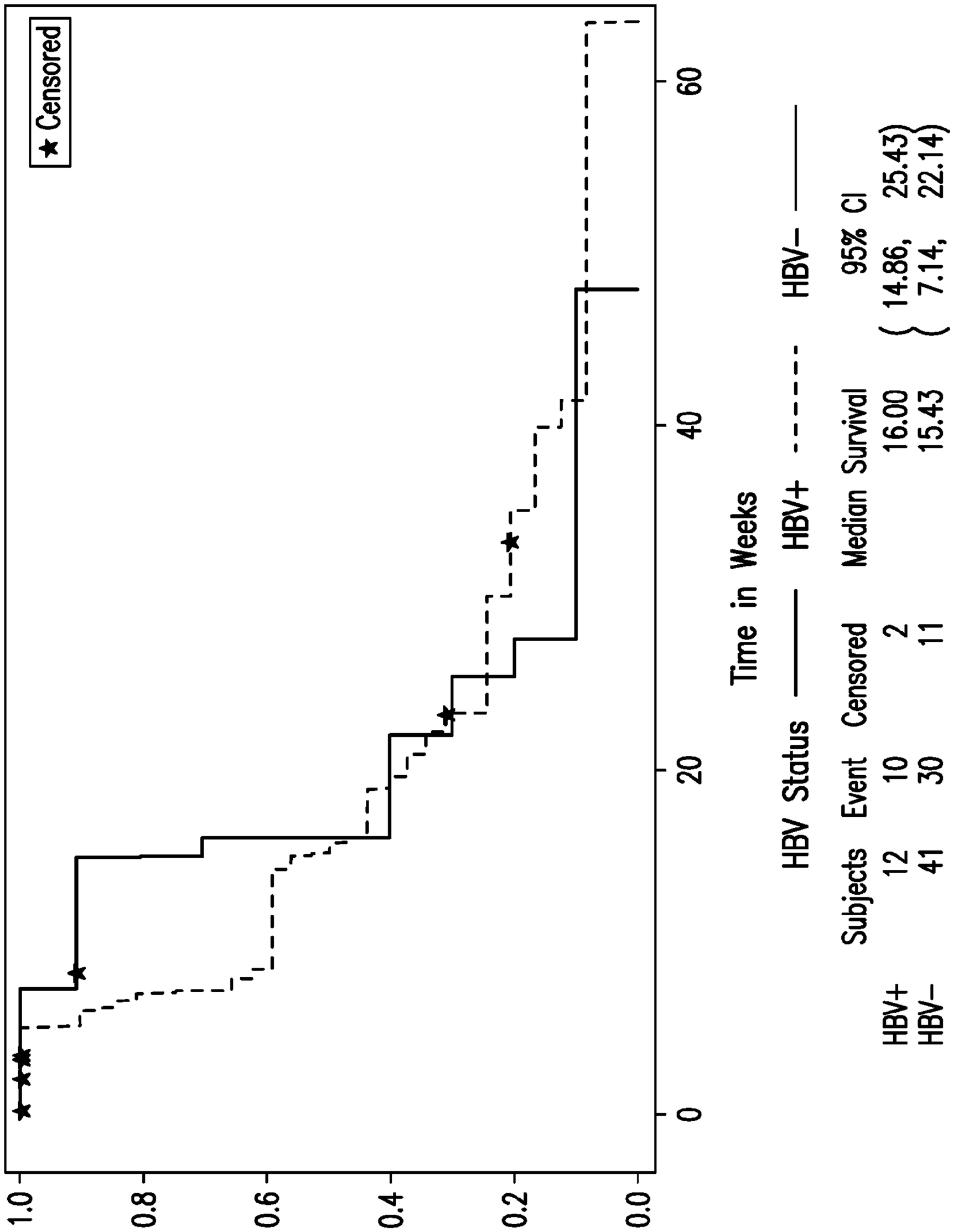

★ Censored
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
0
20
40
60
Time in Weeks
HBV Status —— HBV+ ----- HBV– ——
Subjects Event Censored Median Survival 95% CI
HBV+ 12 10 2 16.00 (14.86, 25.43)
HBV– 41 30 11 15.43 (7.14, 22.14)

FIG. 6B

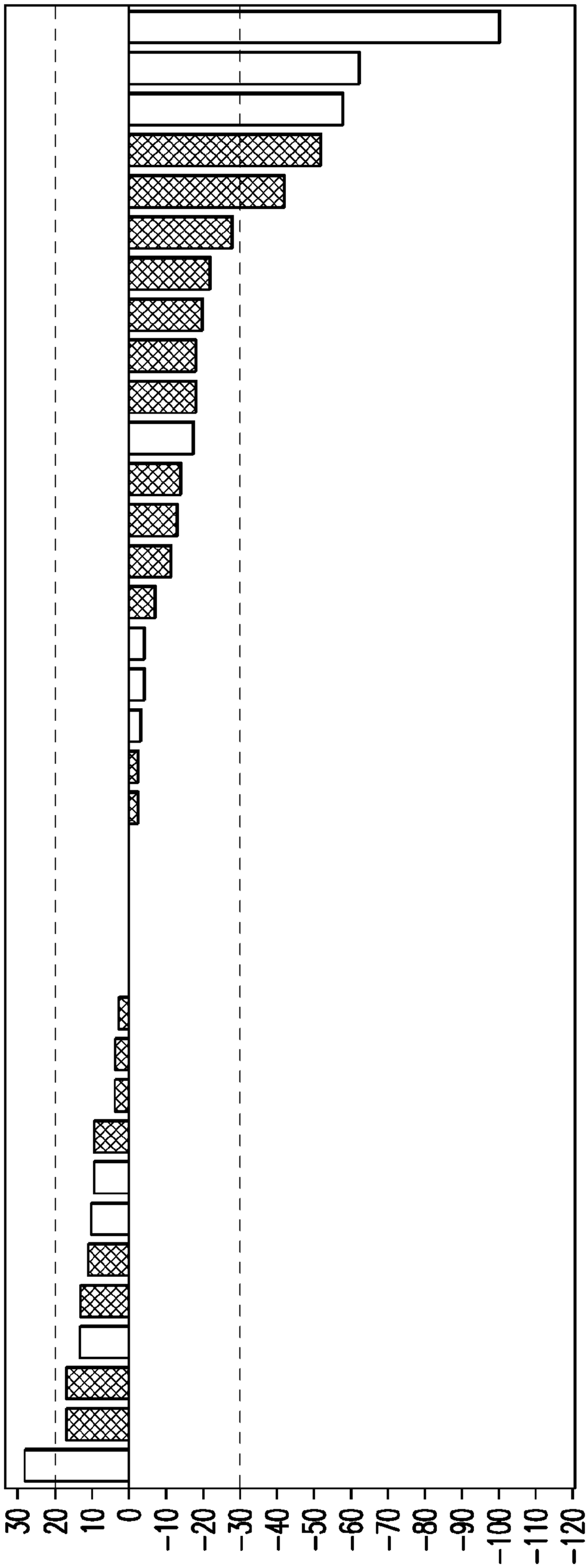

HBV Status
HBV+ (N=12)
HBV− (N=41)
30
20
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
Best Change from Baseline (%)

FIG. 7

Efficacy Results	HBV+	HBV–
Median overall survival (months)	12.07	5.16
Median overall progression free survival (weeks)	16	15.43
Objective Response Rate	25%	0%
Disease Control Rate	91.7%	43.9%
Complete Response	0	0
Partial Response	3	0
Stable disease	8	18
Progressive disease	1	5

FIG. 8

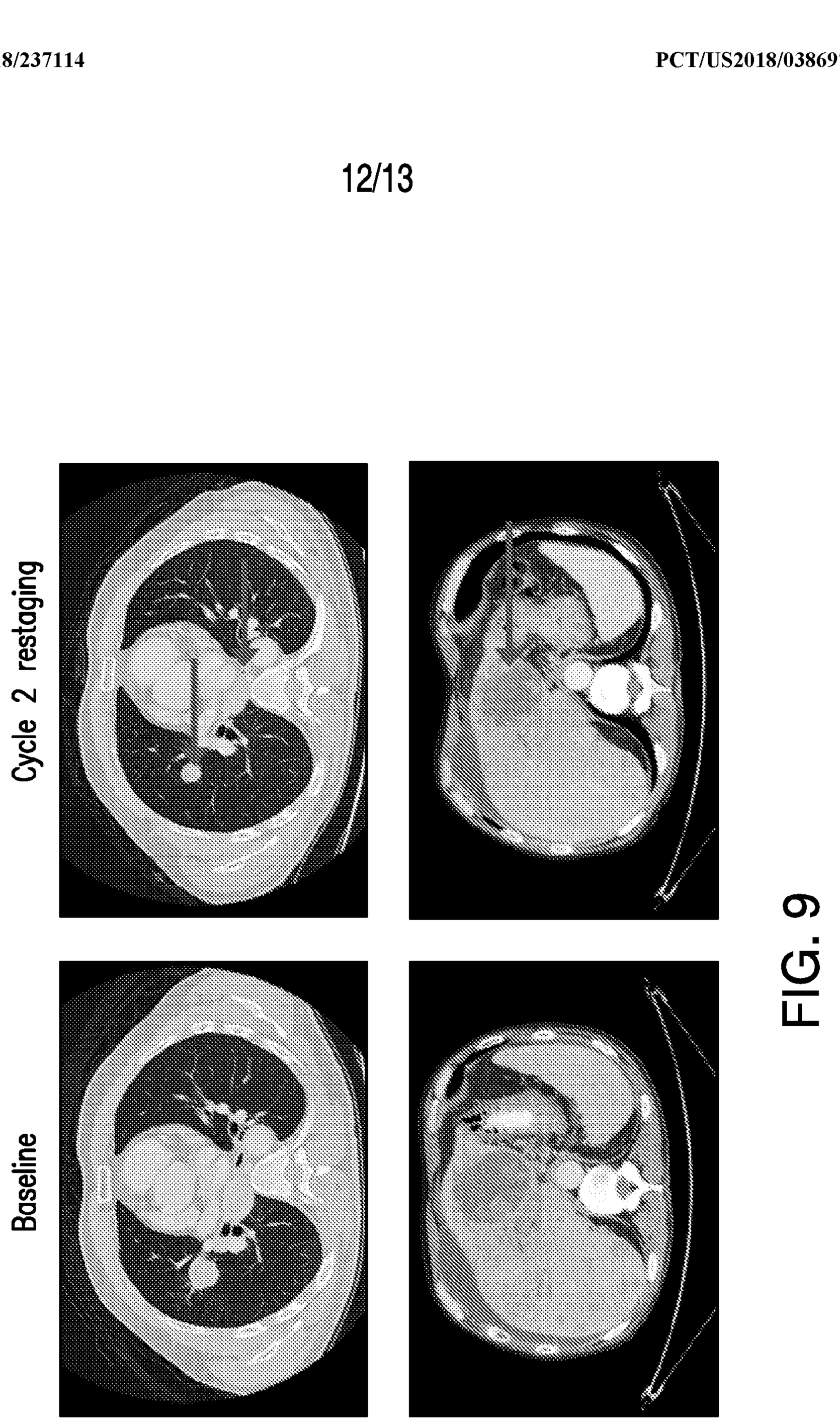


FIG. 9

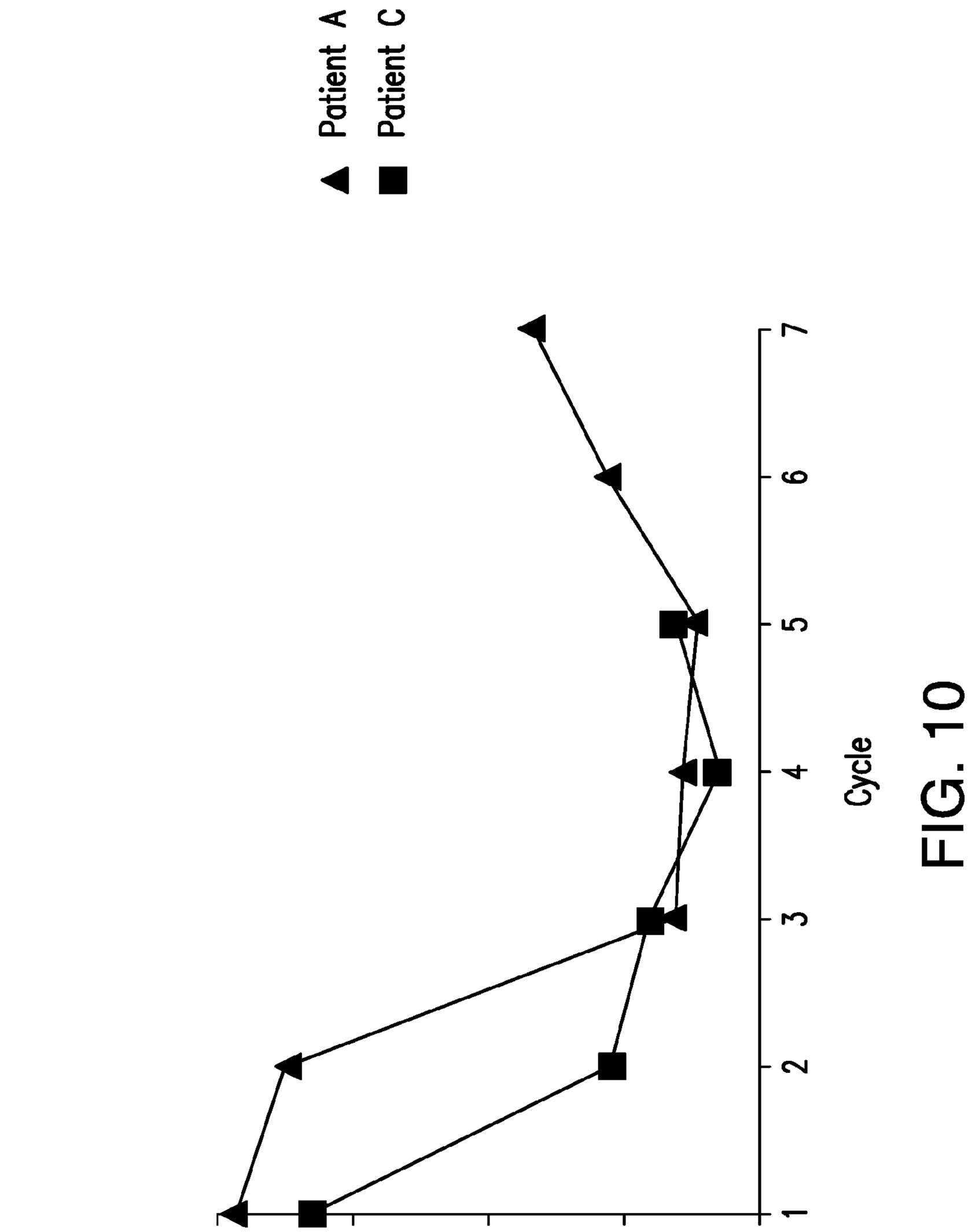

Patient A
Patient C
AFP (ng/mL)
20000
15000
10000
5000
0
1
2
3
4
5
6
7
Cycle

FIG. 10