Randomization (Cycle = 21 Days):

Arm I (Standard Chemotherapy)

Phase A Chemotherapy * day 1 every 21 days x 6 cycles
Placebo (for bevacizumab) ** day 1 every 21 days beginning with cycle 2 x 5 cycles

↓

Re-registration

↓

Phase B Placebo (for bevacizumab) ** day 1 every 21 days cycles 7 through 22

Arm II (Concurrent Bevacizumab)

Phase A Chemotherapy * day 1 every 21 days x 6 cycles
bevacizumab ** day 1 every 21 days beginning with cycle 2 x 5 cycles

↓

Re-registration

↓

Phase B Placebo (for bevacizumab) ** day 1 every 21 days cycles 7 through 22

Arm III (Extended Bevacizumab)

Phase A Chemotherapy * day 1 every 21 days x 6 cycles
bevacizumab ** day 1 every 21 days beginning with cycle 2 x 5 cycles

↓

Re-registration

↓

Phase B bevacizumab ** day 1 every 21 days cycles 7 through 22

*Paclitaxel 175mg/m^2 IV over 3 hours followed by Carboplatin AUC 6 IV over 30 minutes day 1 of cycles 1 through 6 only (Note: docetaxel 75mg/m^2 IV over 1 hour may be substituted for paclitaxel.)

**bevacizumab / Placebo 15mg/kg IV day 1 of each cycle beginning with cycle 2

FIG. 1

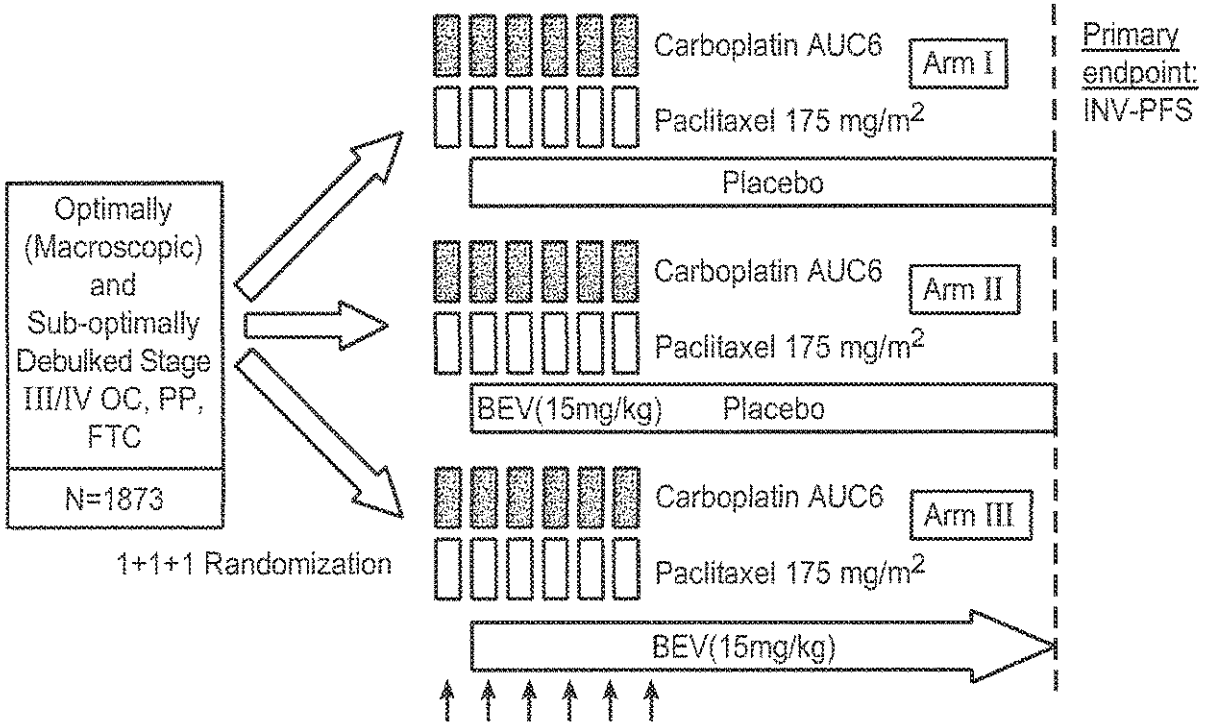


FIG. 2

Select Adverse Events

Onset Between Cycle 2 and 30 Days After Date of Last Treatment

Adverse Event (Grade When Limited), n (%)	Arm I CP (n=601)	Arm II CP + BEV (n=607)	Arm III CP + BEV → BEV (n=608)
GI events[a] (grade ≥2)	7 (1.2)	17 (2.8)	16 (2.6)
Hypertension (grade ≥3)	10 (1.7)[b]	36 (5.9)[b]	63 (10.4)[b]
Proteinuria (grade ≥3)	4 (0.7)	4 (0.7)	10 (1.6)
Pain (grade ≥3)	55 (9.2)[b]	73 (12.0)[b]	83 (13.7)[b]
Neutropenia (grade ≥4)	347 (57.7)	384 (63.3)	385 (63.3)
Febrile neutropenia	21 (3.5)	30 (4.9)	26 (4.3)
Venous thromboembolic event	35 (5.8)	32 (5.3)	41 (6.7)
Arterial thromboembolic event	5 (0.8)	4 (0.7)	4 (0.7)
CNS bleeding	0	0	2 (0.3)
Non-CNS bleeding (grade ≥3)	5 (0.8)	8 (1.3)	13 (2.1)
RPLS	0	1 (0.2)	1 (0.2)

RPLS = reversible posterior leukoencephalopathy syndrome

[a]Perforation/fistula/necrosis/leak

[b]$p<0.05$

FIG. 3

Select Adverse Events by Treatment Phase

Select Adverse Events, n (Grade When Limited)	**Arm I CP**		**Arm II CP + BEV**		**Arm III CP + BEV → BEV**	
Patients, n	**(n=601)**	**(n=483)**	**(n=607)**	**(n=457)**	**(n=608)**	**(n=464)**
Cycles, n						
Treatment Phase[a]	Cytotoxic (Cycles 2-6)	Maintenance (Cycles ≥7)	Cytotoxic (Cycles 2-6)	Maintenance (Cycles ≥7)	Cytotoxic (Cycles 2-6)	Maintenance (Cycles ≥7)
GI events[b] (grade ≥2)	6	1	16	1	15	1
Hypertension (grade ≥3)	3	7	24	12	25	38
Proteinuria (grade ≥3)	2	2	4	0	0	10
Pain (grade ≥3)	28	23	42	31	46	37
Neutropenia (grade ≥4)	345	2	382	2	385	0
Febrile neutropenia	21	0	30	0	26	0
Venous thromboembolic event	26	9	27	5	27	14
Arterial thromboembolic event	4	1	1	3	3	1
CNS bleeding	0	0	0	0	0	2
Non-CNS bleeding (grade ≥3)	3	2	8	0	10	3
RPLS	0	0	1	0	0	1

[a]Onset within 30 days of last treatment
[a]Perforation/fistula/necrosis/leak

FIG. 4

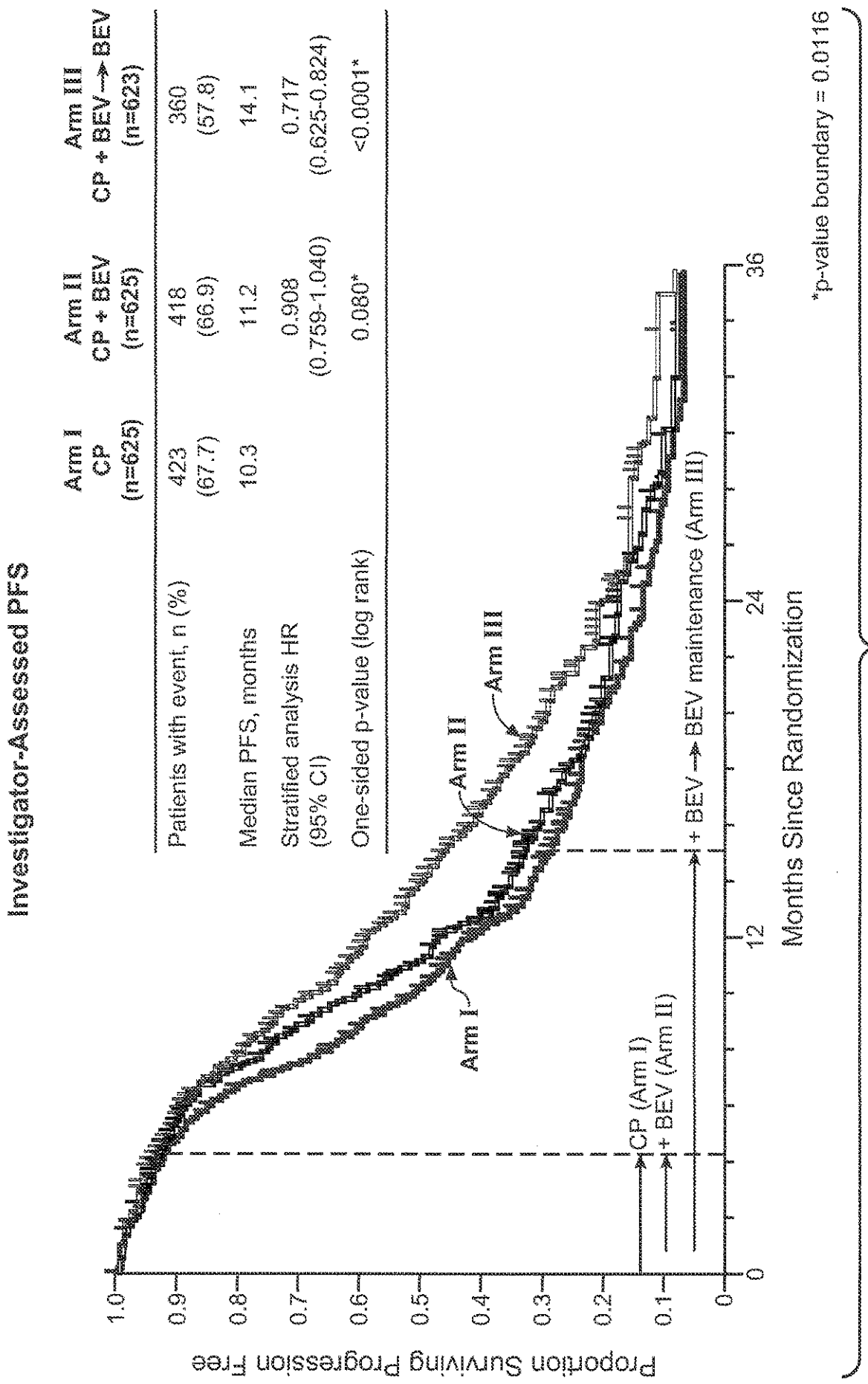

Investigator-Assessed PFS
Arm I CP (n=625)
Arm II CP + BEV (n=625)
Arm III CP + BEV → BEV (n=623)
Patients with event, n (%) 423 (67.7) 418 (66.9) 360 (57.8)
Median PFS, months 10.3 11.2 14.1
Stratified analysis HR (95% CI) 0.908 (0.759-1.040) 0.717 (0.625-0.824)
One-sided p-value (log rank) 0.080* <0.0001*
Proportion Surviving Progression Free
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Arm I
Arm II
Arm III
CP (Arm I)
+ BEV (Arm II)
+ BEV → BEV maintenance (Arm III)
0
12
24
36
Months Since Randomization
*p-value boundary = 0.0116

FIG. 5

Ramifications of Using CA-125 as Determinant of Progression

	Protocol-defined PFS Analysis	CA-125-censored PFS Analysis
Median PFS, months		
CP (Arm I)	10.3	12.0
CP + BEV → BEV (Arm III)	14.1	18.0
Absolute difference in median PFS (months)	3.8	6.0
Hazard ratio	0.717	0.645
Censored for CA-125, %		
CP (Arm I)	0	20
CP + BEV → BEV (Arm III)	0	29

FIG. 6

Subgroup Analyses

CP + BEV → BEV (Arm III) vs CP (Arm I)

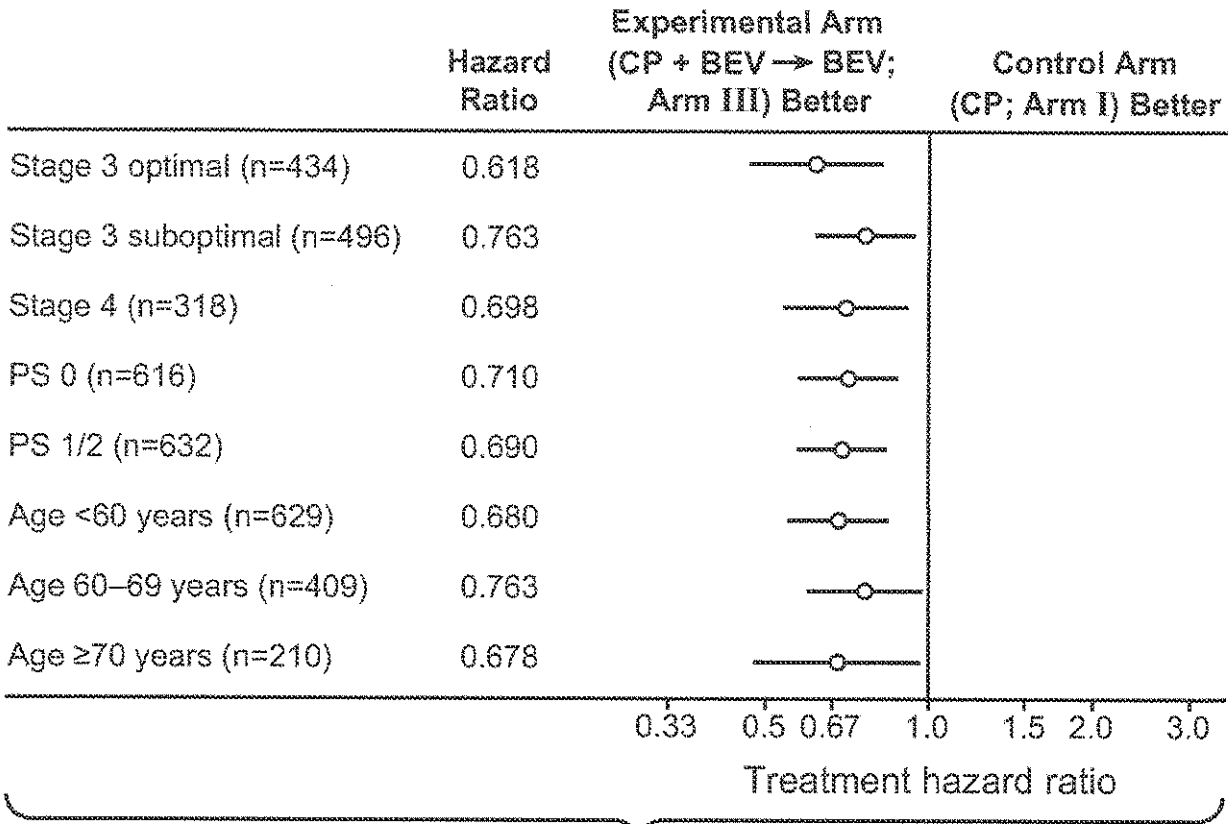
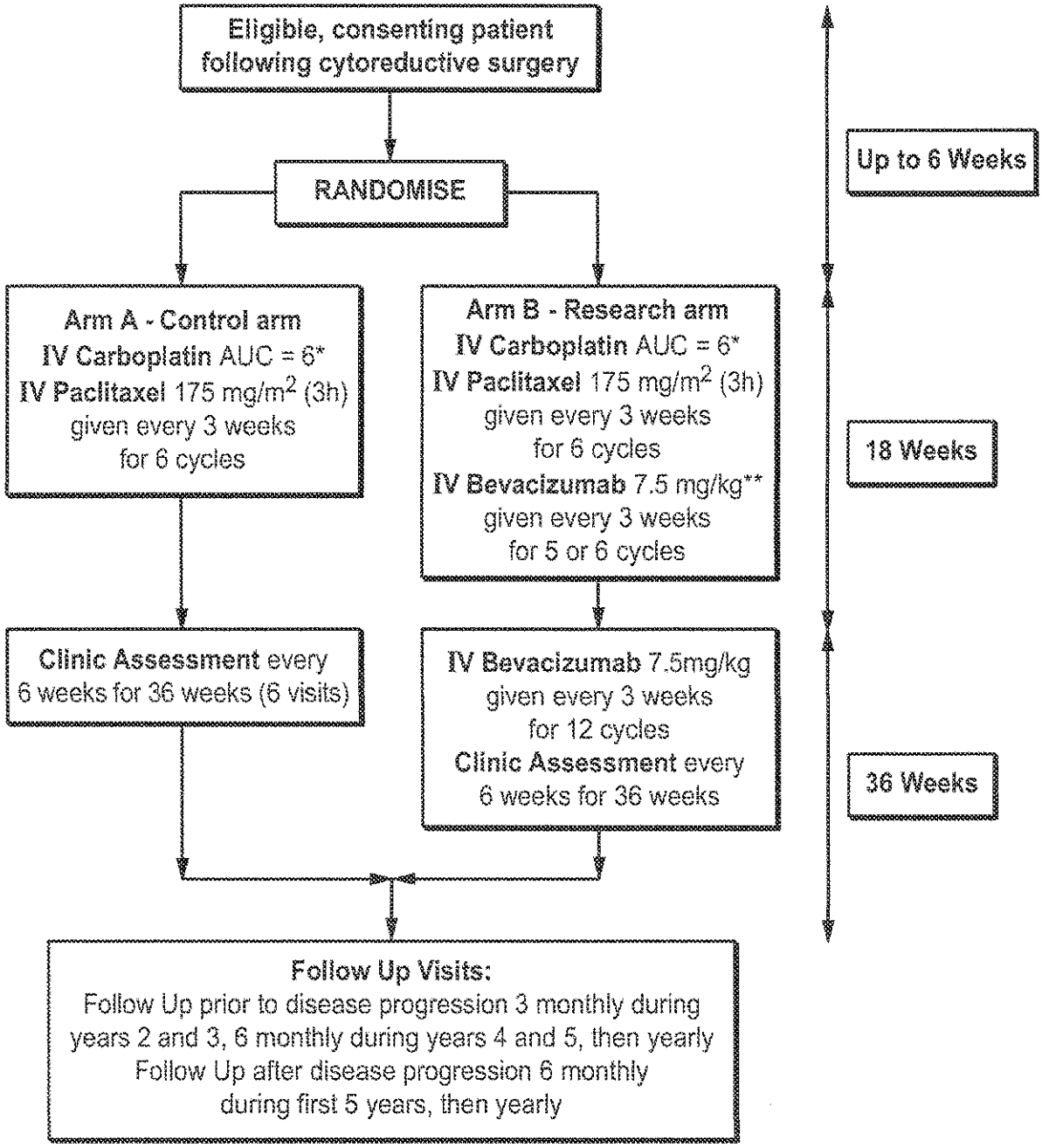


FIG. 7

1. TRIAL SCHEMA

ICON7 Trial Schema



* The carboplatin dose recommended for ICON7 is AUC6 (unless predetermined as being different by individual GCIG group,

**Bevacizumab can be omitted from the first cycle if cytotoxic chemotherapy must be started within 4 weeks of surgery.

FIG. 8

PFS Analysis for ICON7 Trial

	CP (N=764)		CPB7.5+ (N=764)
Patients with event	392 (51.3 %)		367 (48.0 %)
Patients without events	372 (48.7 %)		397 (52.0 %)
Time to event (months)			
Median#	16.0		18.3
95% CI for Median#	[14.3;17.3]		[17.8;19.1]
Range##	0.0 to 32.9		0.0 to 32.9
p-Value (Log-Rank Test)		0.0010*	
Hazard Ratio		0.79	
95% CI		[0.68;0.91]	

FIG. 9

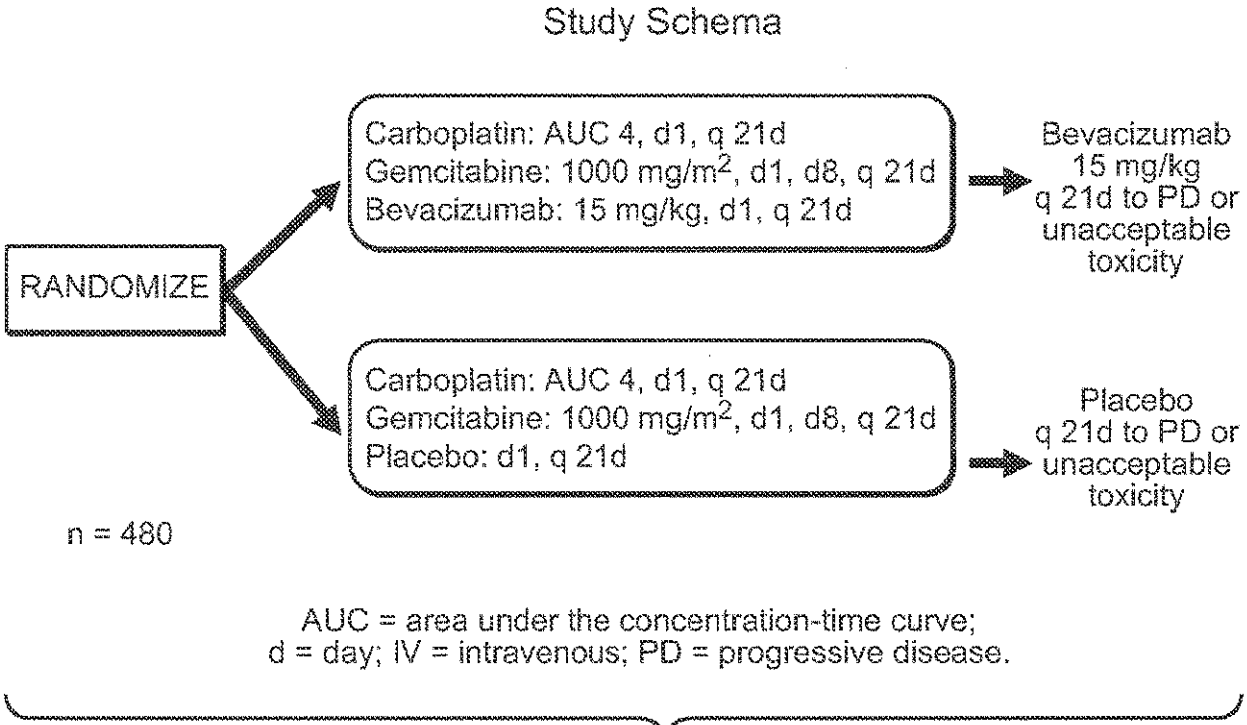


FIG. 11

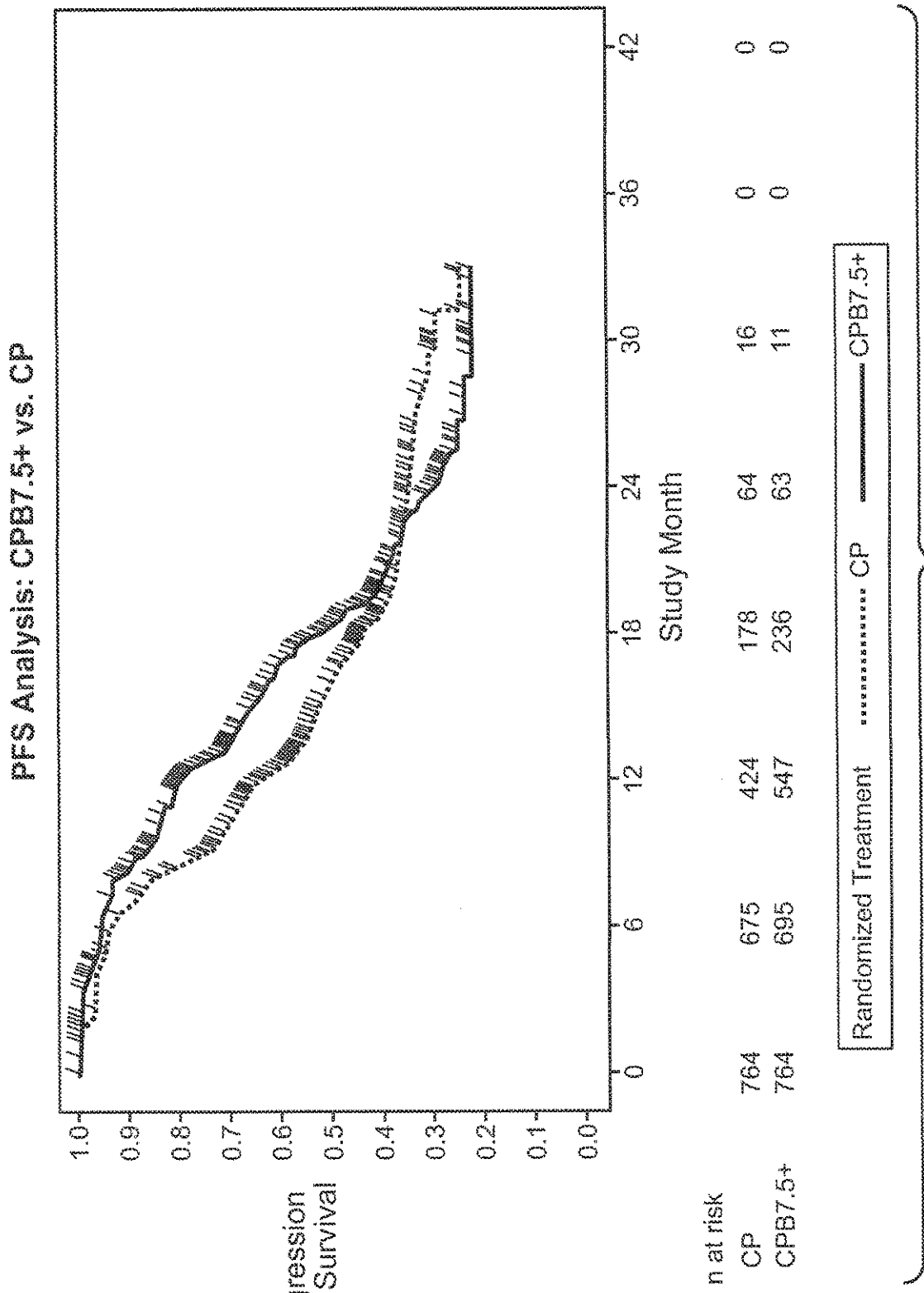

PFS Analysis: CPB7.5+ vs. CP
Progression Free Survival
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
6
12
18
24
30
36
42
Study Month
n at risk
CP 764 675 424 178 64 16 0 0
CPB7.5+ 764 695 547 236 63 11 0 0
Randomized Treatment
CP
CPB7.5+

FIG. 10