Citrulline by 6-Month Mortality
p(Group)= 0.3134 , p(Days)=<0.0001 , p(Group*Days)= 0.4260

Legend: ● Survivor, ○ Non-Survivor

Y-axis: (Citrulline μM)

Day :	0	3	7	14	21	28
(#Survivor)	(102)	(100)	(93)	(72)	(50)	(53)
(#Non-Survivor)	(44)	(39)	(38)	(29)	(19)	(15)

Days on Study
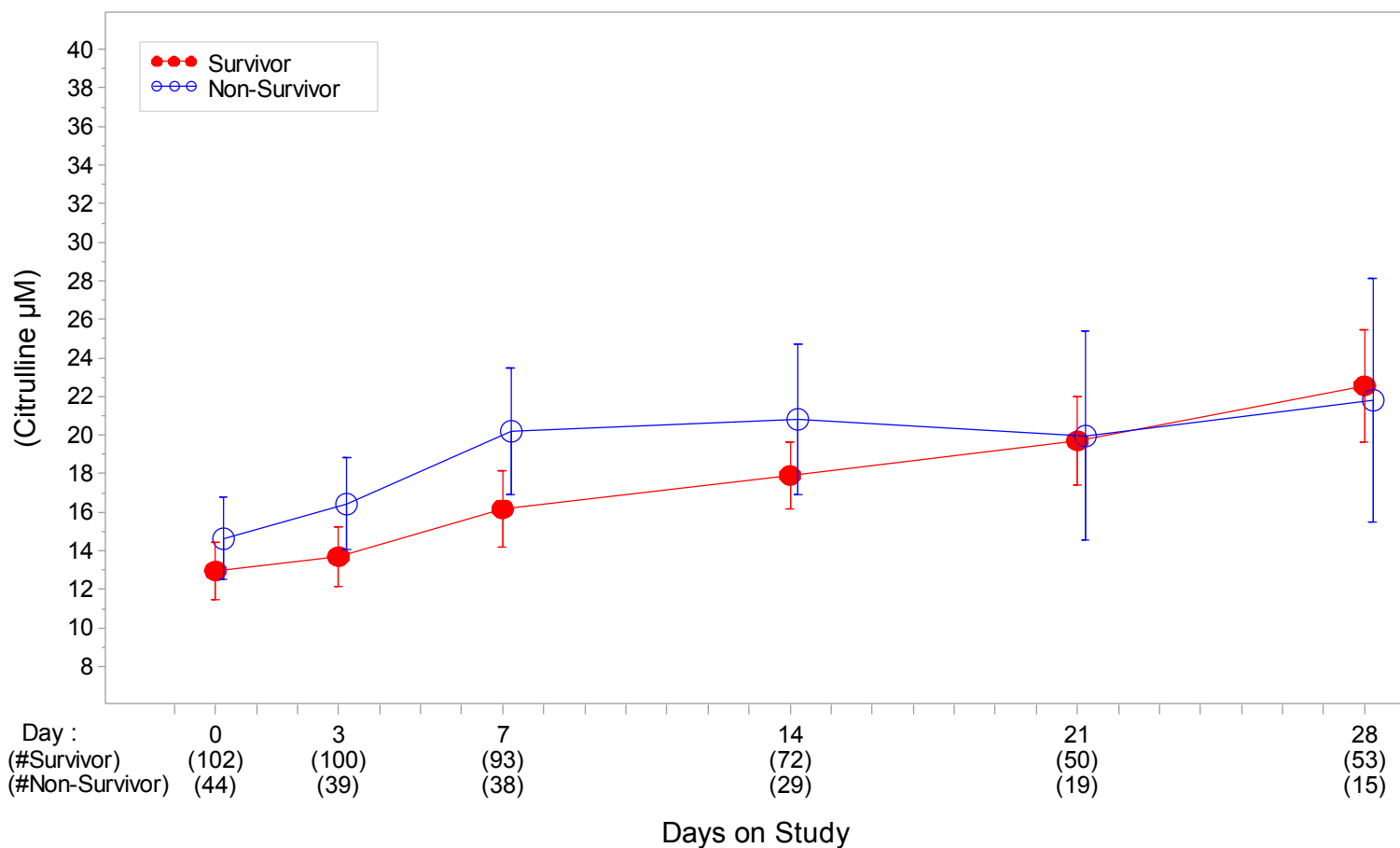
Citrulline by In-Hospital Mortality
p(Group)= 0.4512 , p(Days)=<0.0001 , p(Group*Days)= 0.2473

Legend: ● Survivor, ○ Non-Survivor

Y-axis: (Citrulline μM)

Day :	0	3	7	14	21	28
(#Survivor)	(123)	(119)	(114)	(87)	(60)	(64)
(#Non-Survivor)	(23)	(20)	(17)	(14)	(9)	(4)

Days on Study

13
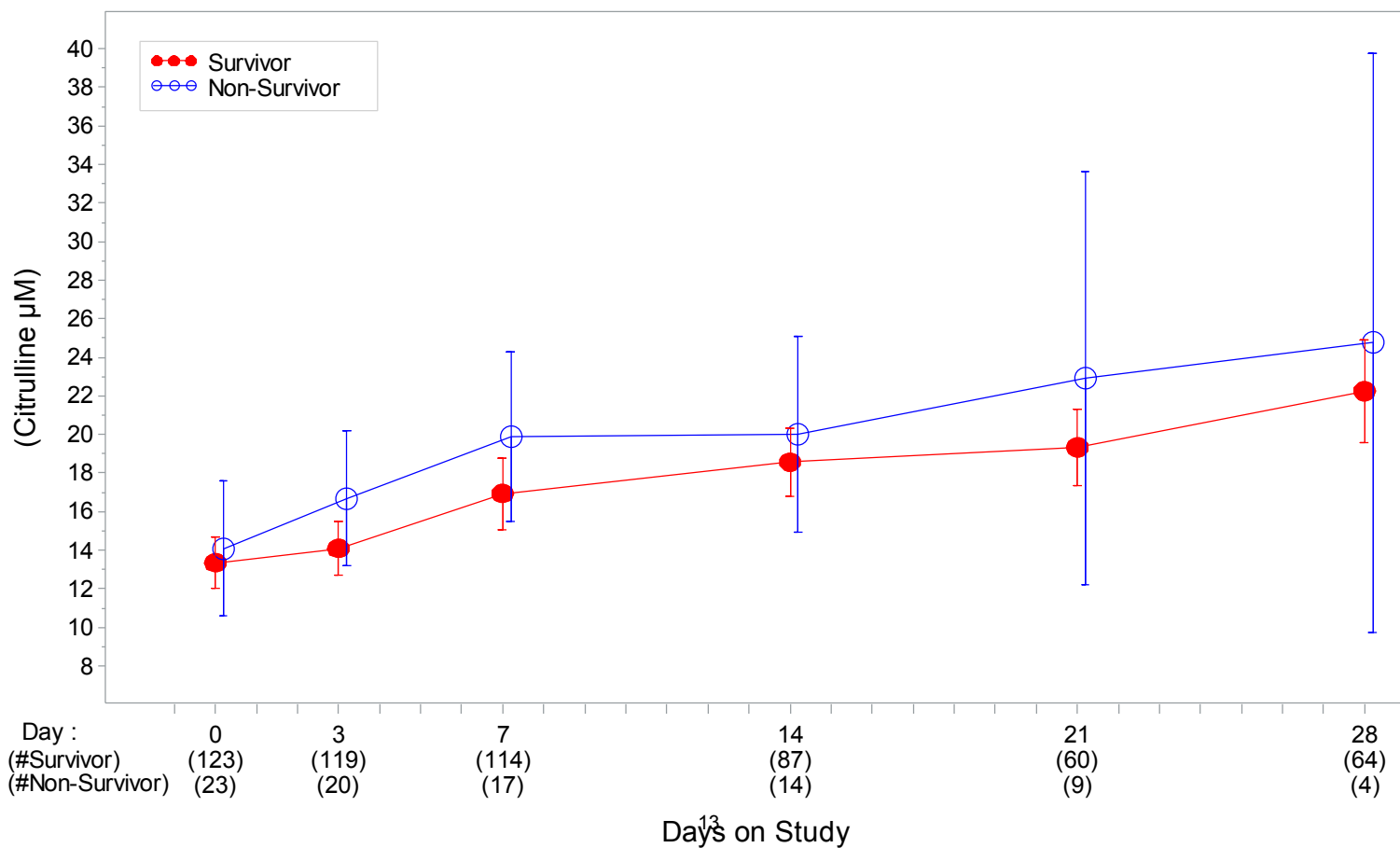
Citrulline by Treatment
p(Group)= 0.6980 , p(Days)=<0.0001 , p(Group*Days)= 0.3067

Day :	0	3	7	14	21	28
(#AG-PN)	(74)	(72)	(67)	(56)	(37)	(35)
(#STD-PN)	(72)	(67)	(64)	(45)	(32)	(33)

Days on Study
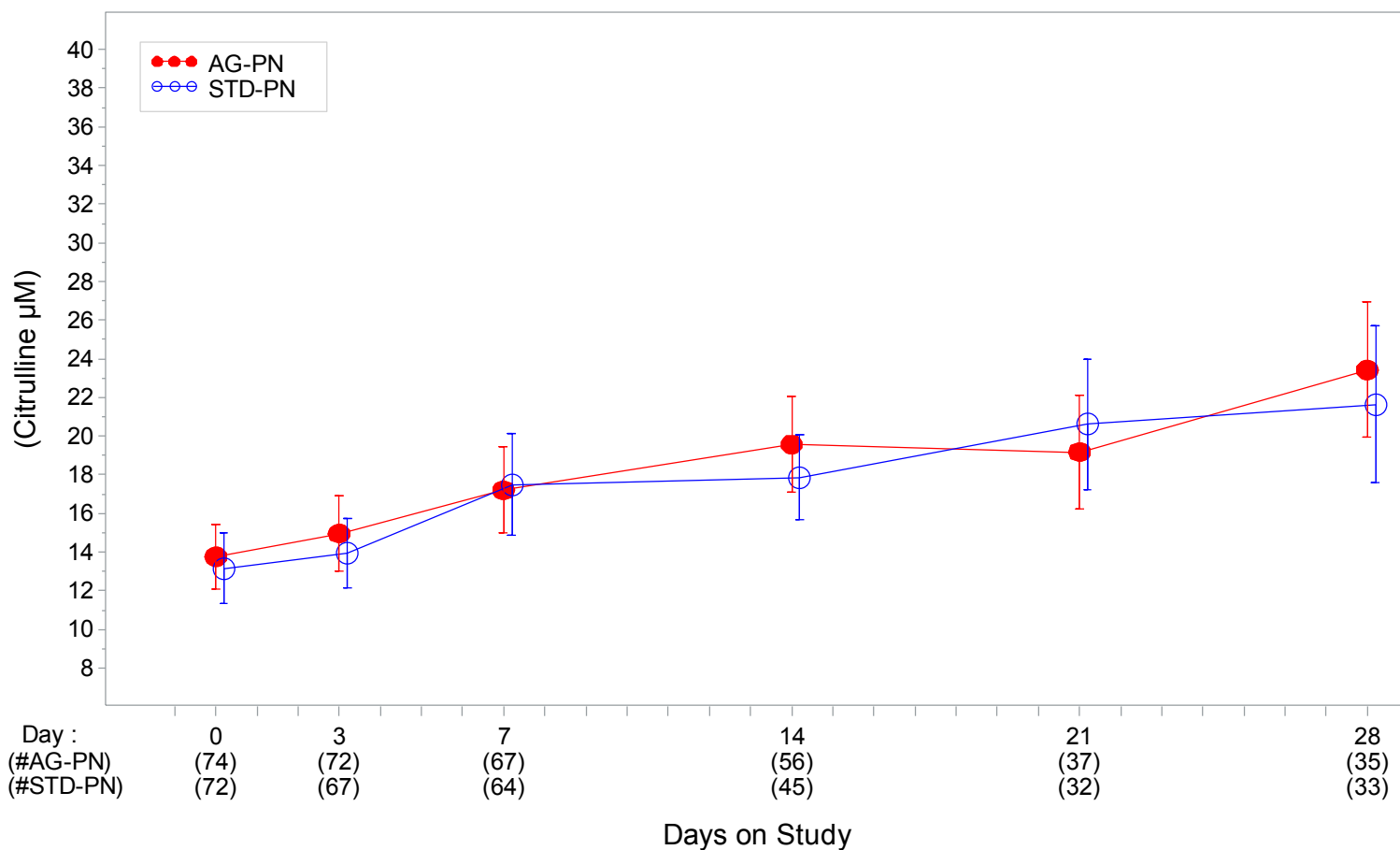
Citrulline by Apache II Score at Randomization
p(Group)= 0.0017 , p(Days)=<0.0001 , p(Group*Days)= 0.0707

Day :	0	3	7	14	21	28
(#ApacheII <=15)	(70)	(65)	(60)	(45)	(33)	(36)
(#ApacheII >15)	(76)	(74)	(71)	(56)	(36)	(32)
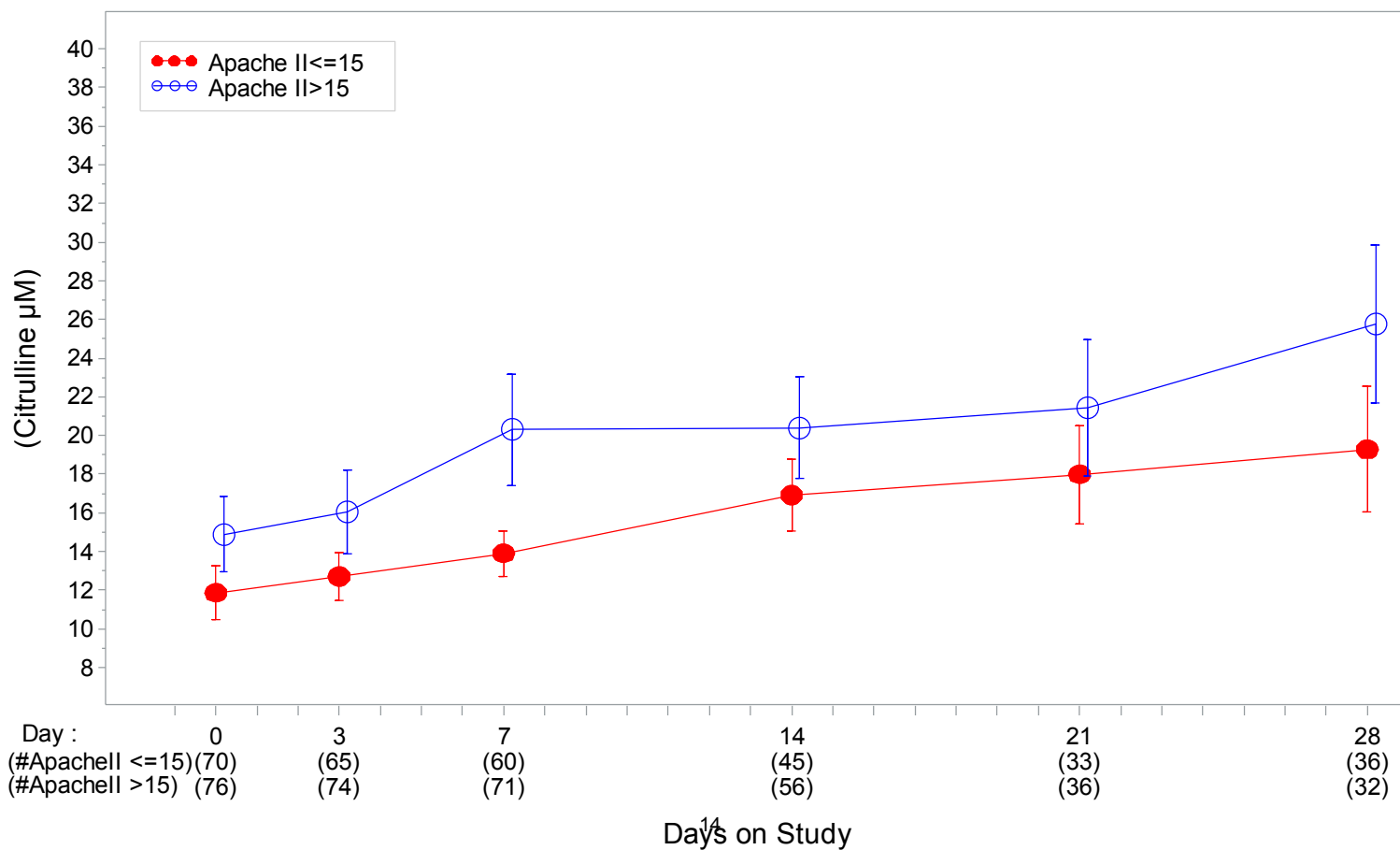
Days on Study

Citrulline by SOFA Score at Randomization
p(Group)= 0.0758 , p(Days)=<0.0001 , p(Group*Days)= 0.2423

Legend:
- ● ● ● SOFA<=6
- ○ ○ ○ SOFA>6

Y-axis: (Citrulline µM)

Day :	0	3	7	14	21	28
(#SOFA <=6)	(76)	(72)	(67)	(51)	(32)	(41)
(#SOFA >6)	(70)	(67)	(64)	(50)	(37)	(27)

Days on Study

15
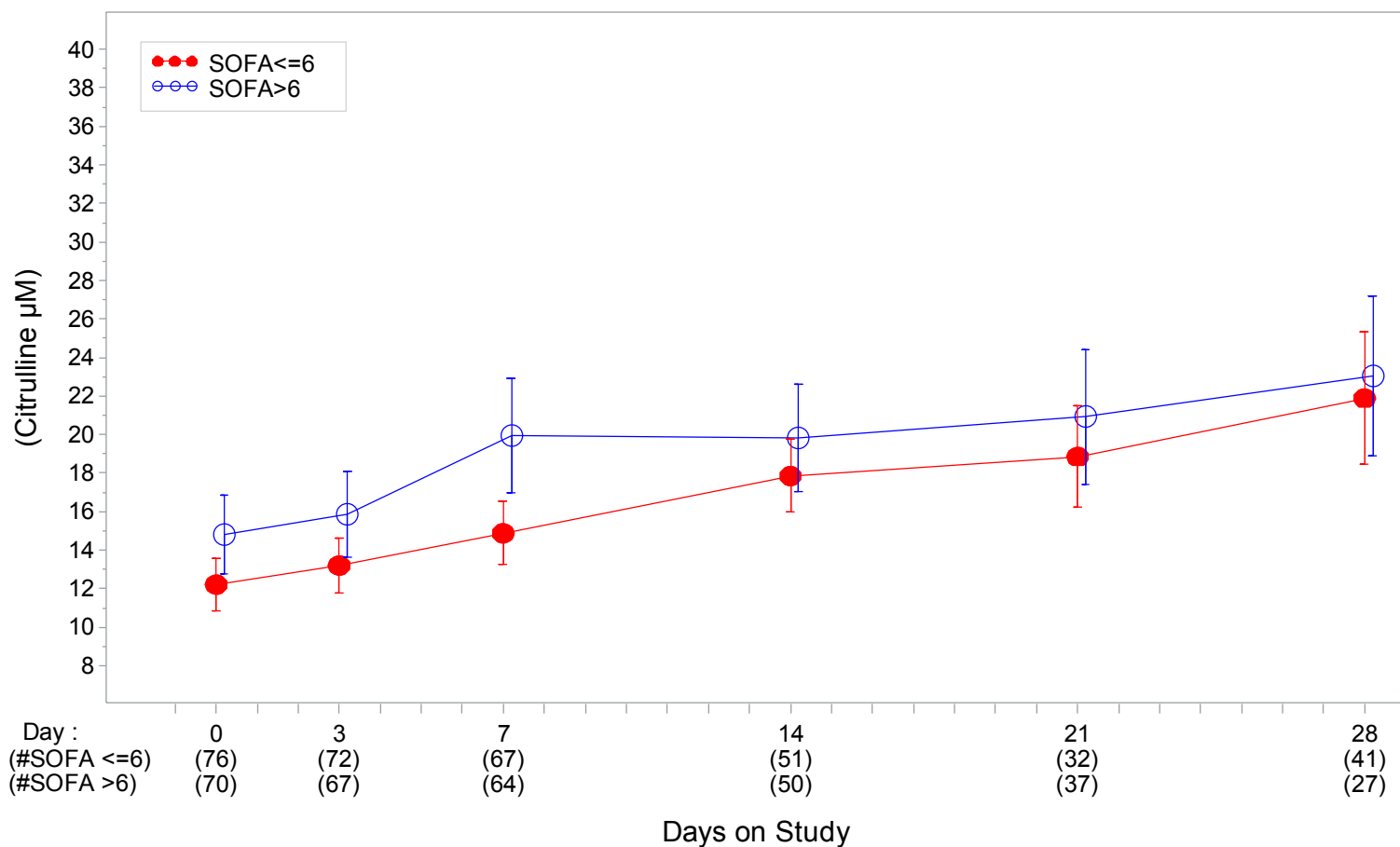
Model Based Estimate of Citrulline by 6-Month Mortality and Days on Study

Day	Survivor Mean[95%CI], N	Non-Survivor Mean[95%CI], N
0	13.0(11.5, 14.5), 102	14.6(12.5, 16.8), 44
3	13.7(12.1, 15.2), 100	16.4(14.0, 18.8), 39
7	16.2(14.2, 18.1), 93	20.2(16.9, 23.5), 38
14	17.9(16.2, 19.6), 72	20.8(16.9, 24.7), 29
21	19.7(17.4, 22.0), 50	20.0(14.5, 25.4), 19
28	22.6(19.7, 25.4), 53	21.8(15.5, 28.1), 15

Model Based Estimate of Citrulline by In-Hospital Mortality and Days on Study

Day	Survivor Mean[95%CI], N	Non-Survivor Mean[95%CI], N
0	13.3(12.0, 14.7), 123	14.1(10.6, 17.6), 23
3	14.1(12.7, 15.5), 119	16.7(13.2, 20.2), 20
7	16.9(15.1, 18.8), 114	19.9(15.5, 24.3), 17
14	18.6(16.8, 20.3), 87	20.0(14.9, 25.1), 14
21	19.3(17.3, 21.3), 60	22.9(12.2, 33.6), 9
28	22.3(19.6, 24.9), 64	24.8(9.8, 39.8), 4

Model Based Estimate of Citrulline by Treatment and Days on Study

Day	AG-PN Mean[95%CI], N	STD-PN Mean[95%CI], N
0	13.8(12.1, 15.4), 74	13.1(11.3, 15.0), 72
3	15.0(13.0, 16.9), 72	14.0(12.2, 15.8), 67
7	17.2(15.0, 19.4), 67	17.5(14.9, 20.1), 64
14	19.6(17.1, 22.0), 56	17.9(15.7, 20.0), 45
21	19.2(16.3, 22.1), 37	20.6(17.2, 24.0), 32
28	23.4(19.9, 26.9), 35	21.6(17.6, 25.7), 33

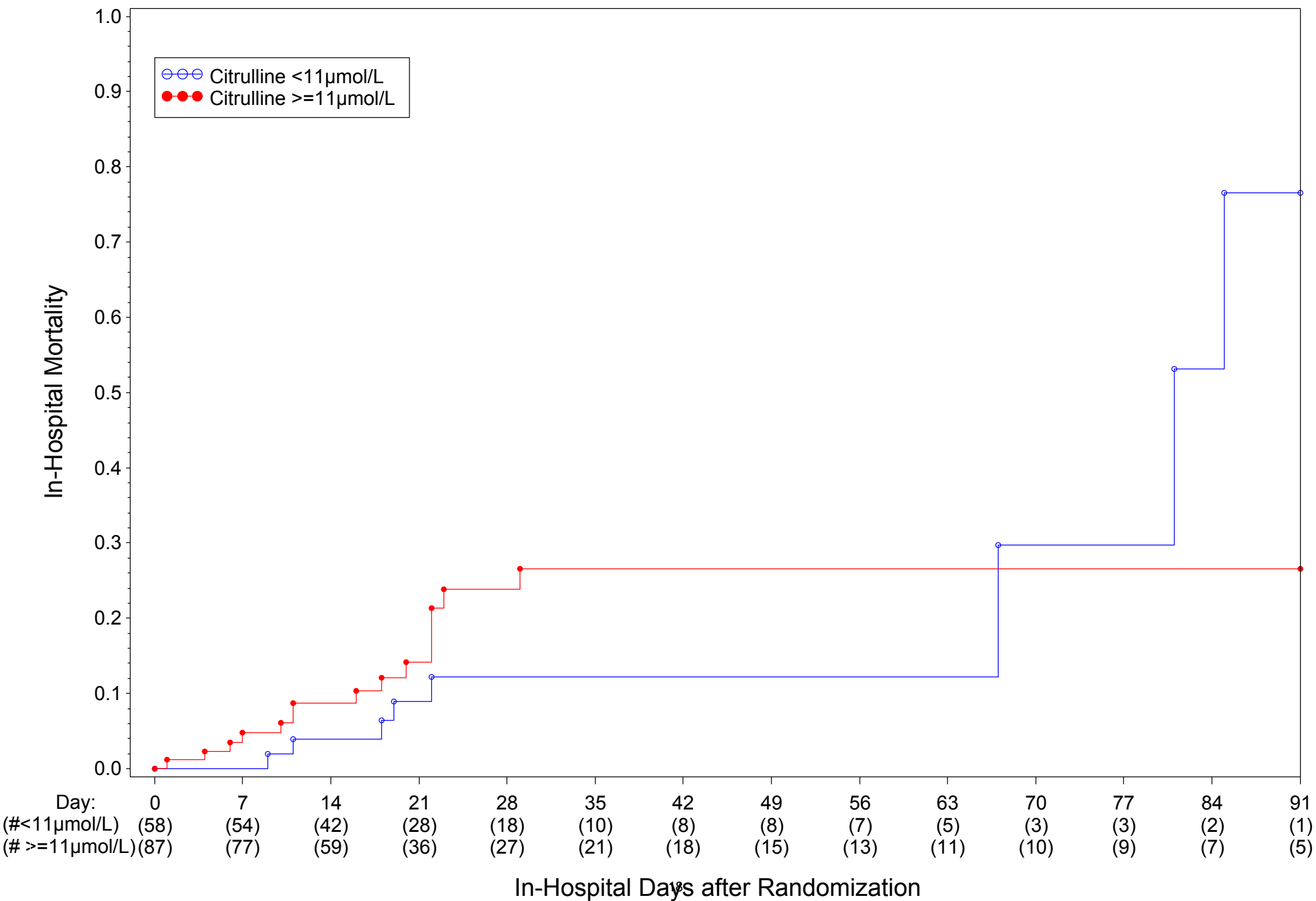**Model Based Estimate of Citrulline by Apache>15 and Days on Study**

Day	Apache<=15 Mean[95%CI], N	Apache>15 Mean[95%CI], N
0	11.9(10.5, 13.2), 70	14.9(13.0, 16.8), 76
3	12.7(11.4, 14.0), 65	16.1(13.9, 18.2), 74
7	13.9(12.7, 15.1), 60	20.3(17.4, 23.2), 71
14	16.9(15.1, 18.8), 45	20.4(17.8, 23.0), 56
21	18.0(15.4, 20.5), 33	21.4(17.9, 24.9), 36
28	19.3(16.0, 22.5), 36	25.8(21.7, 29.8), 32

Model Based Estimate of Citrulline by SOFA>6(Median) and Days on Study

Day	SOFA<=6 Mean[95%CI], N	SOFA>6 Mean[95%CI], N
0	12.2(10.8, 13.6), 76	14.8(12.7, 16.9), 70
3	13.2(11.8, 14.7), 72	15.9(13.6, 18.1), 67
7	14.9(13.2, 16.5), 67	20.0(17.0, 22.9), 64
14	17.9(16.0, 19.8), 51	19.8(17.0, 22.6), 50
21	18.9(16.2, 21.5), 32	20.9(17.4, 24.4), 37
28	21.9(18.4, 25.3), 41	23.1(18.9, 27.2), 27

In-Hospital Mortality by Baseline Plasma Citrulline Levels (Number of Death=23)
Log-Rank Test: p=0.59

Legend:
- Citrulline <11µmol/L
- Citrulline >=11µmol/L

Y-axis: In-Hospital Mortality

X-axis: In-Hospital Days after Randomization

Day:	0	7	14	21	28	35	42	49	56	63	70	77	84	91
(#<11µmol/L)	(58)	(54)	(42)	(28)	(18)	(10)	(8)	(8)	(7)	(5)	(3)	(3)	(2)	(1)
(# >=11µmol/L)	(87)	(77)	(59)	(36)	(27)	(21)	(18)	(15)	(13)	(11)	(10)	(9)	(7)	(5)

Citrulline	Days on Study	Motality(%)	Survival Standard Error	Number Left
<11 µmol/L	30	0.1220	0.0524	16
>=11 µmol/L	30	0.2662	0.0633	25

6-Month Mortality by Baseline Plasma Citrulline Levels (Number of Death=44)
Log-Rank Test: p=0.68
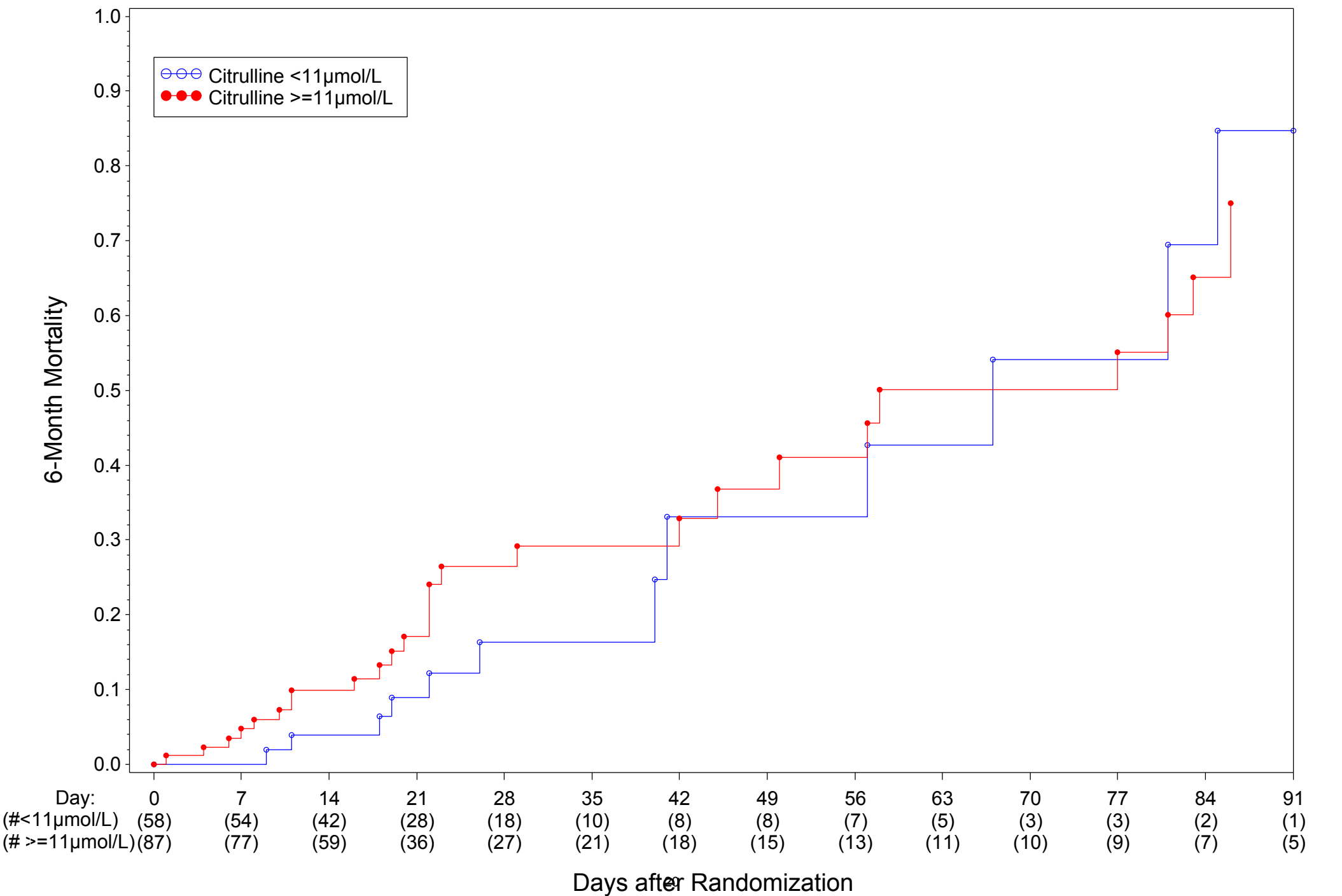
Legend:
- Citrulline <11μmol/L
- Citrulline >=11μmol/L

Y-axis: 6-Month Mortality (0.0 to 1.0)
X-axis: Days after Randomization

Day:	0	7	14	21	28	35	42	49	56	63	70	77	84	91
(#<11μmol/L)	(58)	(54)	(42)	(28)	(18)	(10)	(8)	(8)	(7)	(5)	(3)	(3)	(2)	(1)
(# >=11μmol/L)	(87)	(77)	(59)	(36)	(27)	(21)	(18)	(15)	(13)	(11)	(10)	(9)	(7)	(5)

Citrulline	Days on Study	Motality(%)	Survival Standard Error	Number Left
<11 µmol/L	30	0.1639	0.0645	16
>=11 µmol/L	30	0.2915	0.0638	25