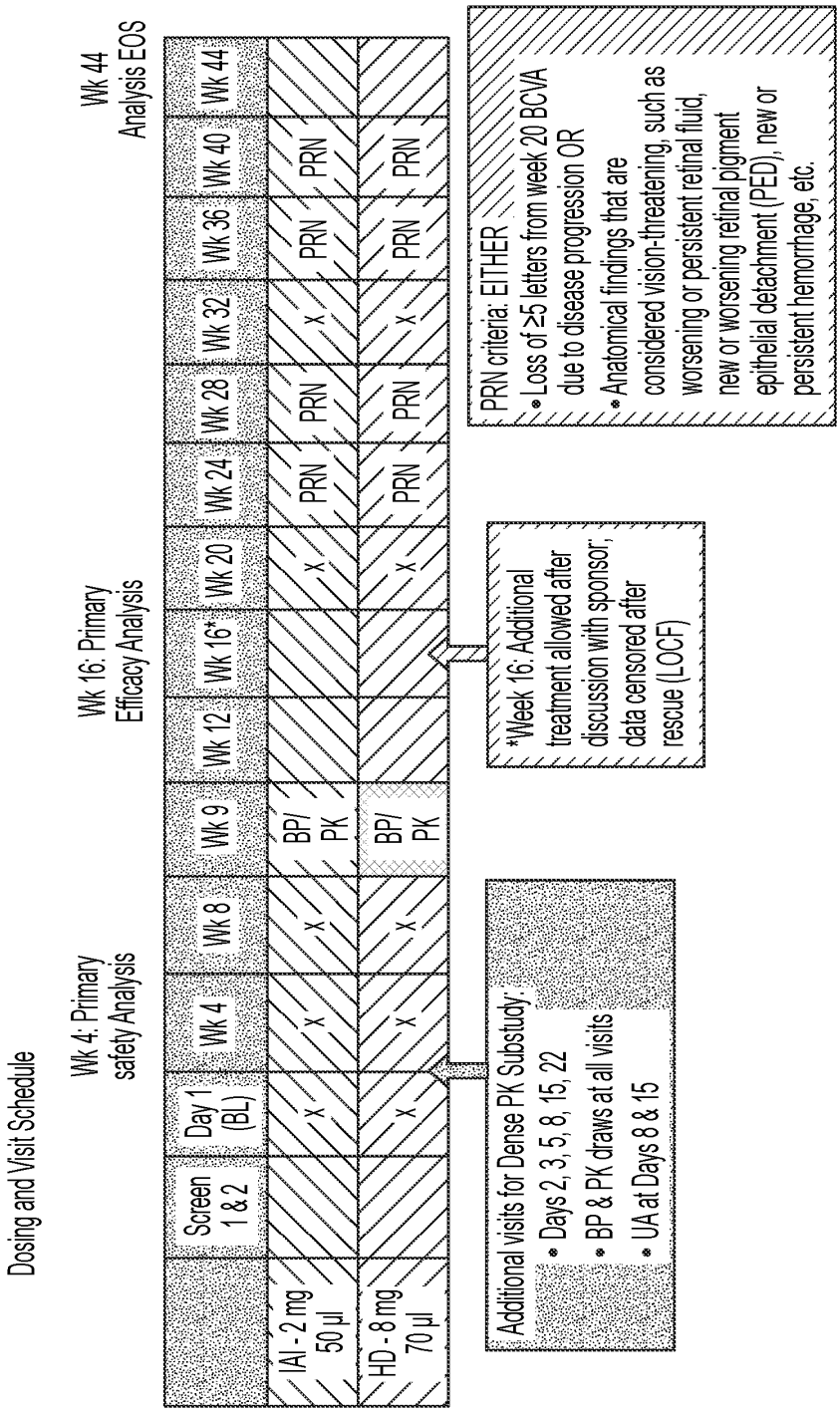

Dosing and Visit Schedule
Wk 4: Primary safety Analysis
Wk 16: Primary Efficacy Analysis
Wk 44 Analysis EOS
Screen 1 & 2
Day 1 (BL)
Wk 4
Wk 8
Wk 9
Wk 12
Wk 16*
Wk 20
Wk 24
Wk 28
Wk 32
Wk 36
Wk 40
Wk 44
IAI - 2 mg 50 µl
HD - 8 mg 70 µl
X
BP/ PK
PRN
Additional visits for Dense PK Substudy:
• Days 2, 3, 5, 8, 15, 22
• BP & PK draws at all visits
• UA at Days 8 & 15
*Week 16: Additional treatment allowed after discussion with sponsor; data censored after rescue (LOCF)
PRN criteria: EITHER
• Loss of ≥5 letters from week 20 BCVA due to disease progression OR
• Anatomical findings that are considered vision-threatening, such as worsening or persistent retinal fluid, new or worsening retinal pigment epithelial detachment (PED), new or persistent hemorrhage, etc.

FIG. 1

Baseline Demographics (All patients*)

	IAI (n=27)	HD (n=28)	ALL (n=55)
Sex			
Male	9 (33.3%)	12 (42.9%)	21 (38.2%)
Female	18 (66.7%)	16 (57.1%)	34 (61.8%)
Ethnicity			
All	27 (100%)	28 (100%)	55 (100%)
HISPANIC OR LATINO	4 (14.8%)	1 (3.6%)	5 (9.1%)
NOT HISPANIC OR LATINO	23 (85.2%)	27 (96.4%)	50 (90.9%)
Race			
All	27 (100%)	28 (100%)	55 (100%)
WHITE	27 (100%)	28 (100%)	55 (100%)
Age (years)			
Mean (SD)	76.1 (8.90)	77.7 (7.86)	76.9 (8.35)

Percentages are calculated based on N

FIG. 2

Baseline Characteristics (All patients*)

	IAI (n=27)	HD (n=28)	ALL (n=55)
Mean (SD) BL BCVA in Study Eye (ETDRS letters)	57.1 (9.24)	59.3 (13.25)	58.2 (11.41)
Mean (SD) BL CRT in Study Eye (µm)	474.0 (222.18)	497.3 (127.66)	
Mean (SD) Baseline IOP in Study Eye (mmHg)	14.5 (3.43)	14.7 (3.32)	14.6 (3.35)

FIG. 3

Baseline Blood Pressure (All patients*)

	IAI (n=27)	HD (n=28)
Systolic Pressure (Mean (SD) mmHg)	126.27 (10.1)	122.8 (11.0)
Diastolic Pressure (Mean (SD) mmHg)	71.73 (9.7)	69.89 (9.5)

FIG. 4

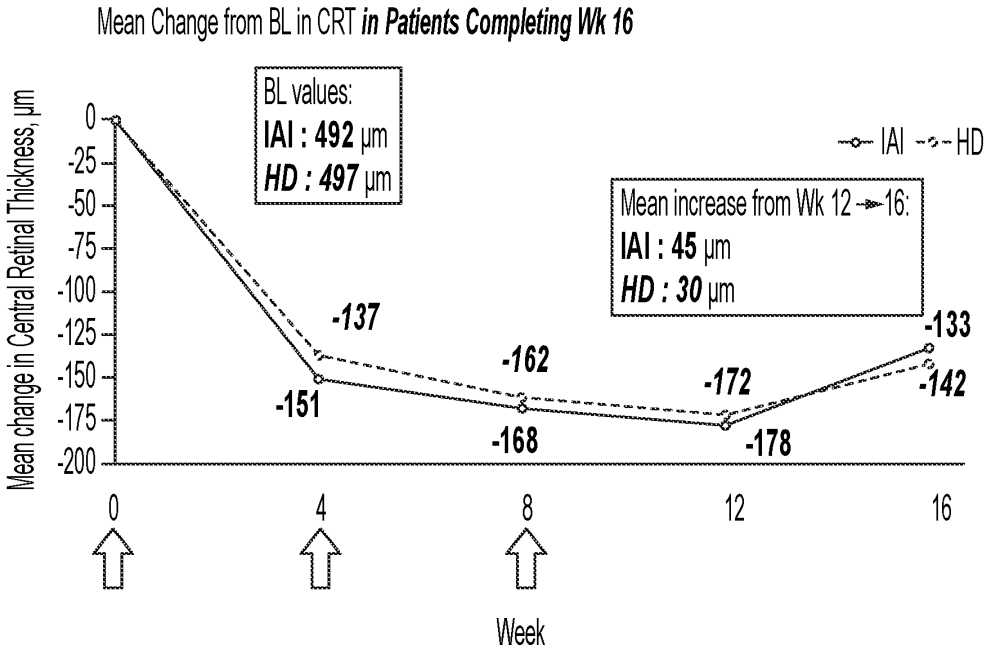
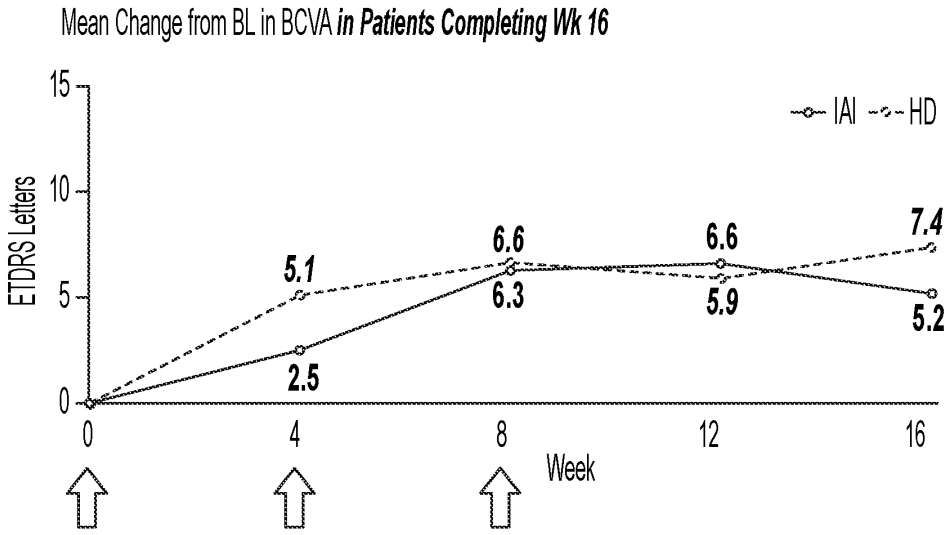

Mean Change from BL in CRT *in Patients Completing Wk 16*
BL values:
IAI : 492 µm
HD : 497 µm
IAI
HD
Mean increase from Wk 12→16:
IAI : 45 µm
HD : 30 µm
Mean change in Central Retinal Thickness, µm
0
-25
-50
-75
-100
-125
-150
-175
-200
-137
-151
-162
-168
-172
-178
-133
-142
0
4
8
12
16
Week
IAI n = 22
HD n = 27
Observed Values

FIG. 5



IAI n = 22
HD n = 27

Observed Values

FIG. 6

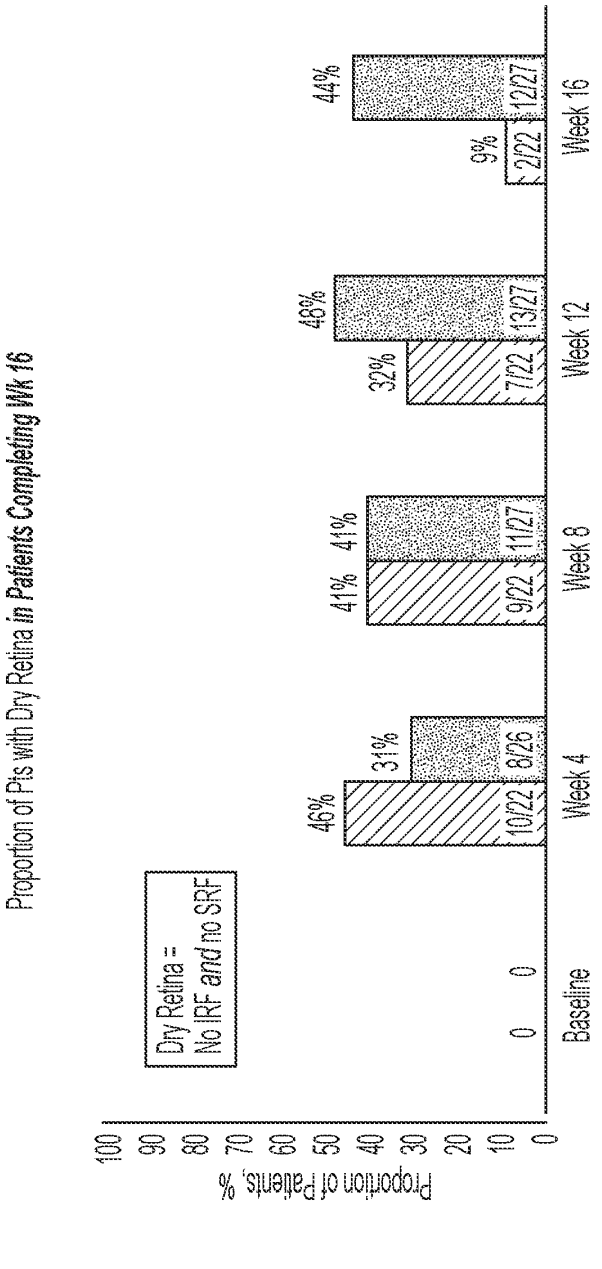

Proportion of Pts with Dry Retina in Patients Completing Wk 16
Dry Retina = No IRF and no SRF
Proportion of Patients, %
100
90
80
70
60
50
40
30
20
10
0
0 0
46% 31%
10/22 8/26
41% 41%
9/22 11/27
32% 46%
7/22 13/27
9% 44%
2/22 12/27
Baseline
Week 4
Week 8
Week 12
Week 16
IAI HD
Observed Values

FIG. 7

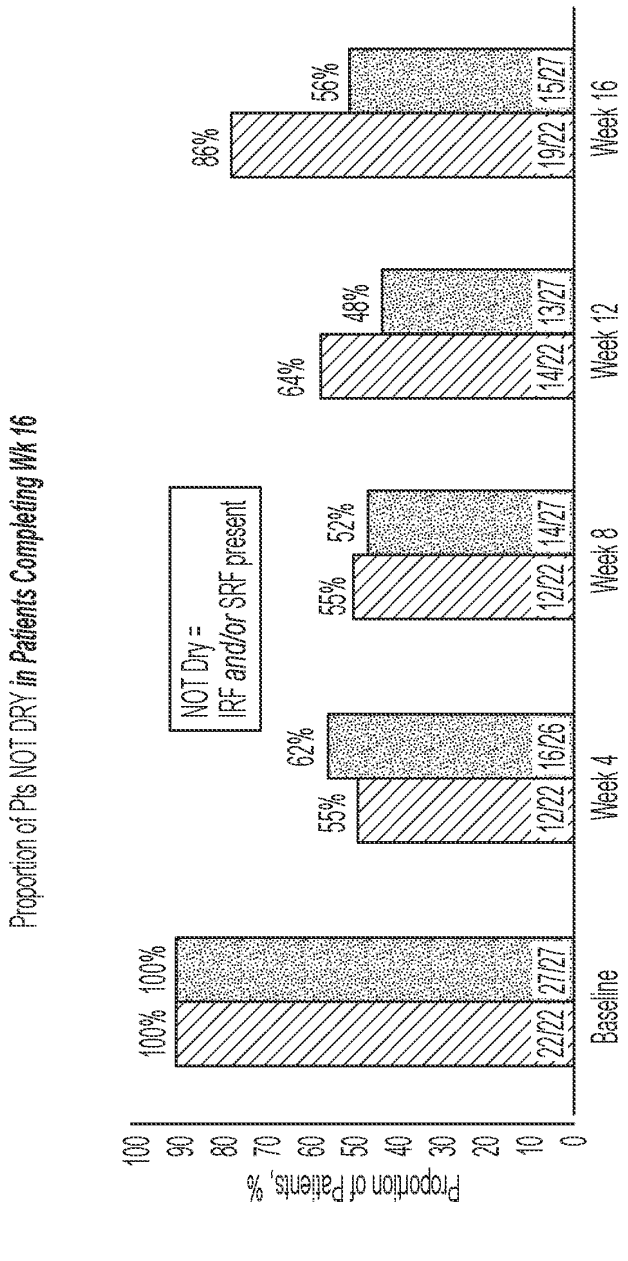

Proportion of Pts NOT DRY in Patients Completing Wk 16
NOT Dry = IRF and/or SRF present
Proportion of Patients, %
100
90
80
70
60
50
40
30
20
10
0
100%
100%
55%
62%
55%
52%
64%
48%
86%
56%
22/22
27/27
12/22
16/26
12/22
14/27
14/22
13/27
19/22
15/27
Baseline
Week 4
Week 8
Week 12
Week 16
IAI
HD
Observed Values

FIG. 8

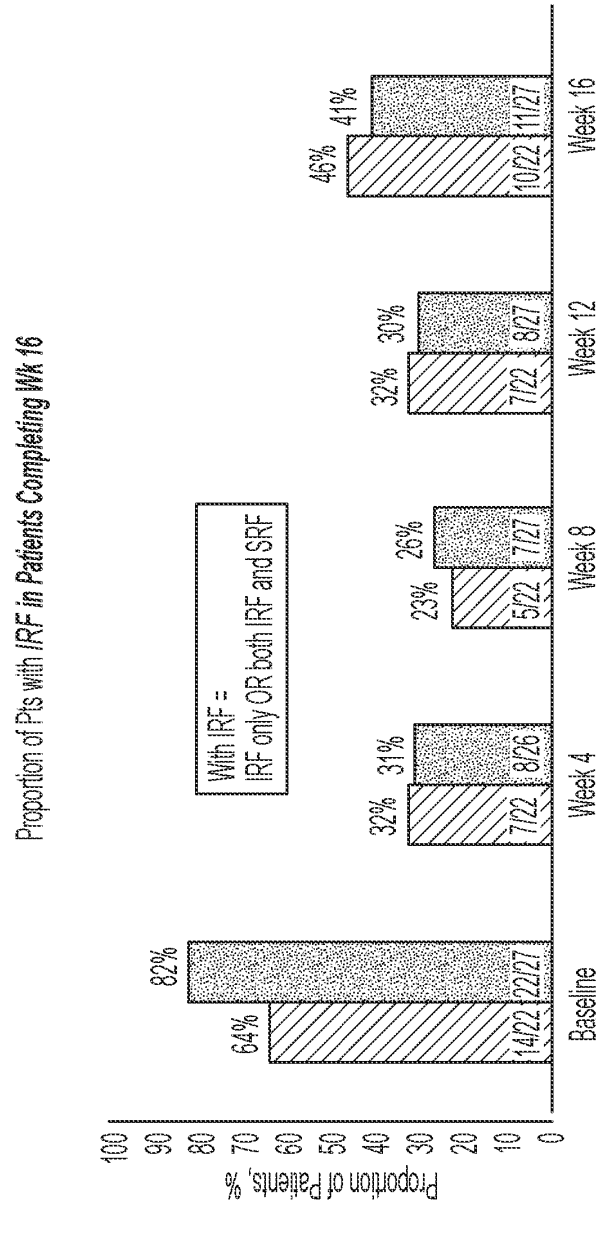

Proportion of Pts with IRF in Patients Completing Wk 16
With IRF =
IRF only OR both IRF and SRF
Proportion of Patients, %
100
90
80
70
60
50
40
30
20
10
0
82%
64%
14/22
22/27
Baseline
32%
31%
7/22
8/26
Week 4
23%
26%
5/22
7/27
Week 8
32%
30%
7/22
8/27
Week 12
46%
41%
10/22
11/27
Week 16
IAI
HD
Observed Values

FIG. 9

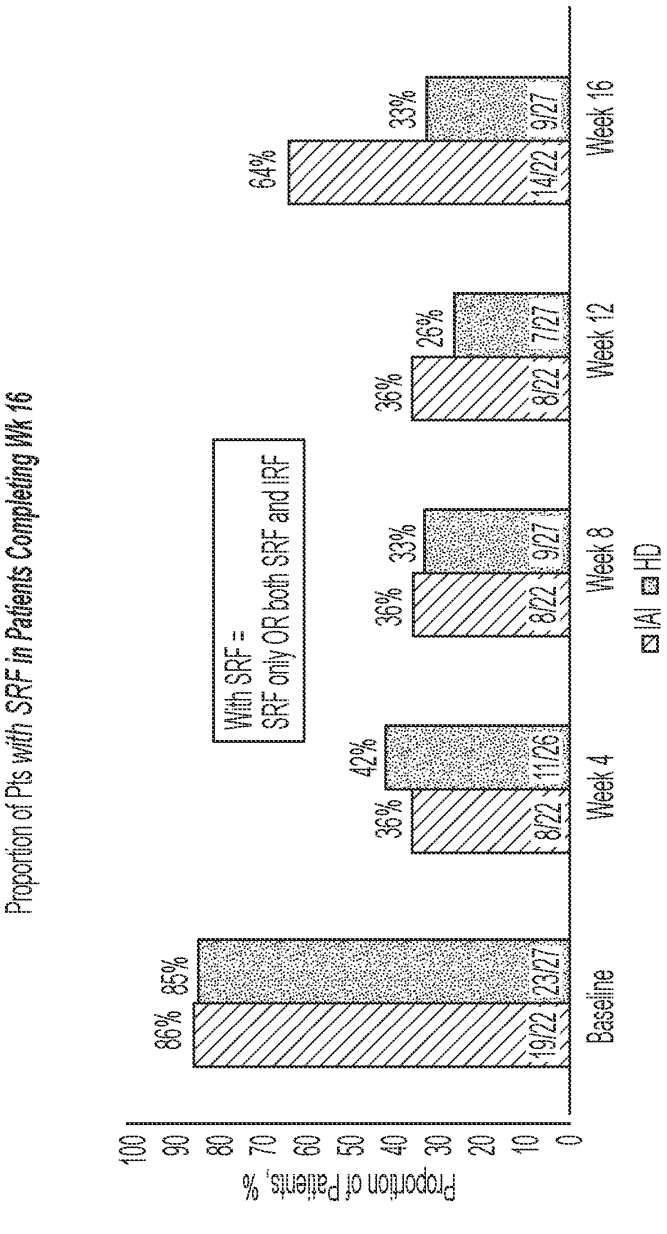

Proportion of Pts with SRF in Patients Completing Wk 16
Proportion of Patients, %
100
90
80
70
60
50
40
30
20
10
0
With SRF =
SRF only OR both SRF and IRF
86%
19/22
85%
23/27
Baseline
36%
8/22
42%
11/26
Week 4
36%
8/22
33%
9/27
Week 8
36%
8/22
26%
7/27
Week 12
64%
14/22
33%
9/27
Week 16
IAI
HD
Observed Values

FIG. 10

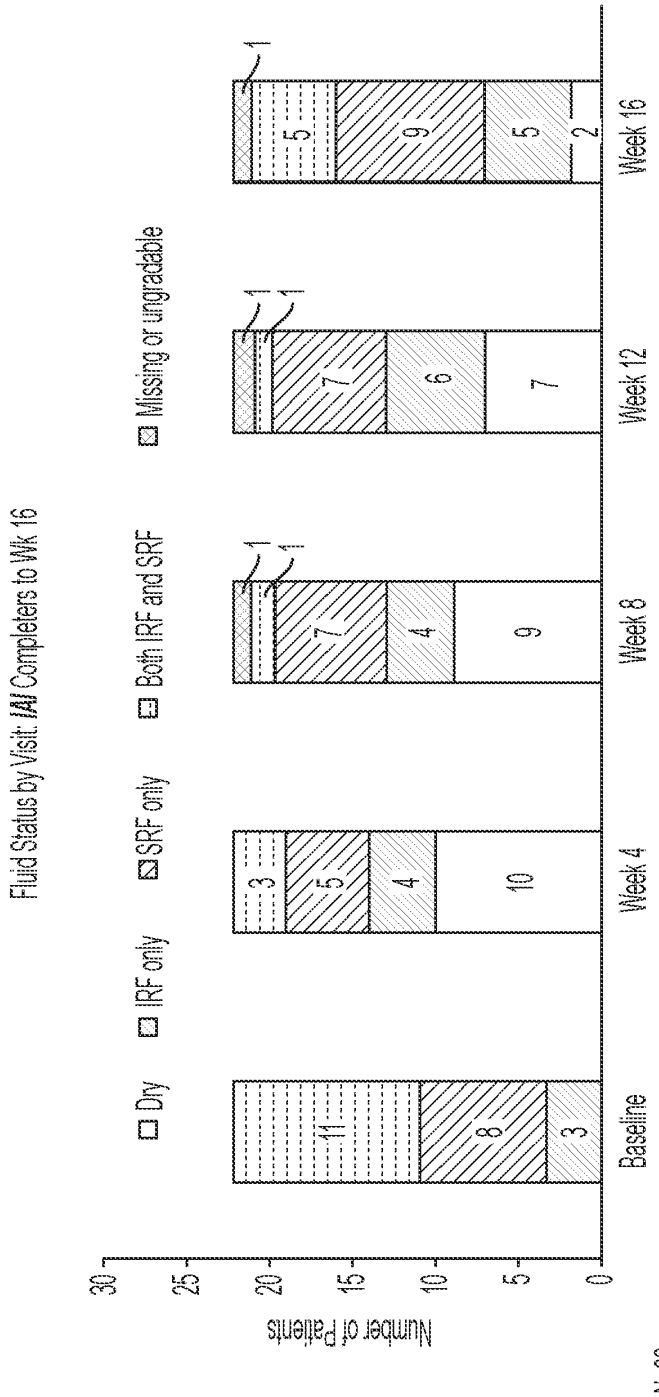

Fluid Status by Visit: IAI Completers to Wk 16
Dry
IRF only
SRF only
Both IRF and SRF
Missing or ungradable
Number of Patients
30
25
20
15
10
5
0
Baseline
Week 4
Week 8
Week 12
Week 16
11
3
8
3
10
4
5
3
9
4
7
1
1
7
6
7
1
1
5
9
5
2
1
N=22

FIG. 11

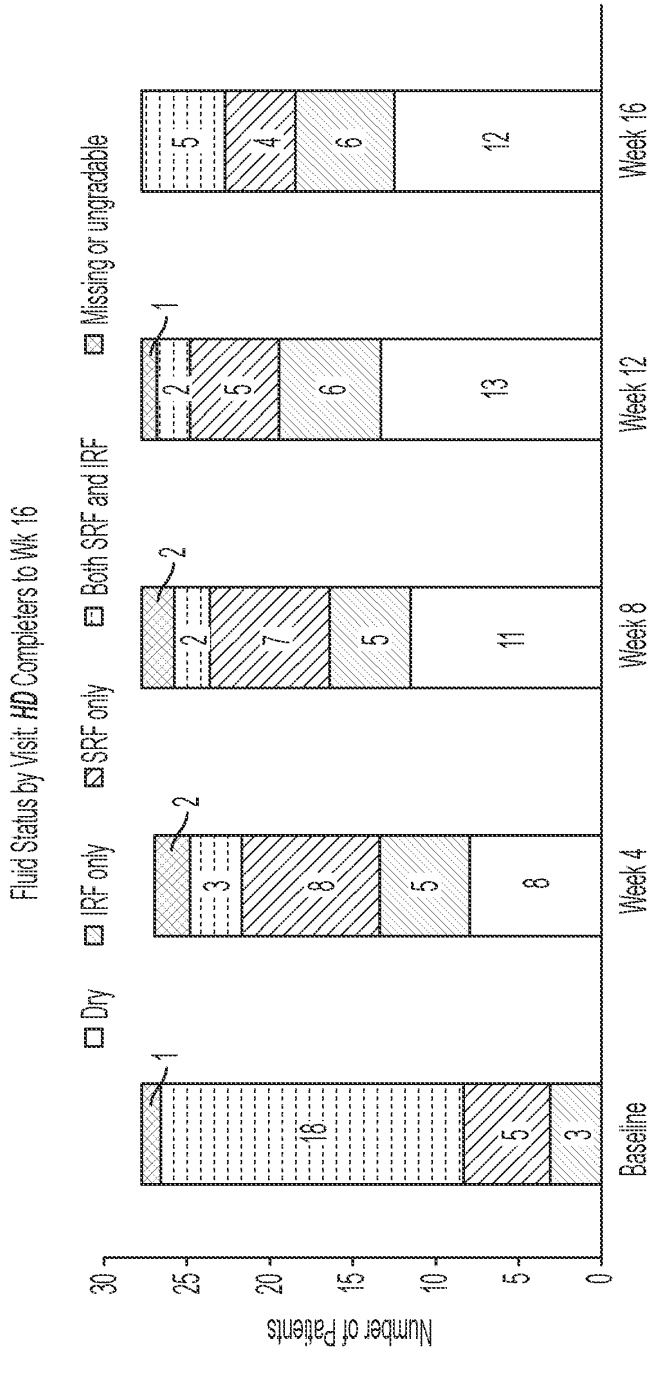

Fluid Status by Visit: HD Completers to Wk 16
Dry
IRF only
SRF only
Both SRF and IRF
Missing or ungradable
Number of Patients
30
25
20
15
10
5
0
Baseline
Week 4
Week 8
Week 12
Week 16
1
18
5
3
2
3
8
5
8
2
2
7
5
11
1
2
5
6
13
5
4
6
12
N=27 at BL, Wk8, 12, 16;
n=26 at Wk 4

FIG. 12

Treatment Exposure (All patients*)

	IAI (n=27)	HD (n=28)
Mean (SD)	4.1 (1.07)	3.9 (0.92)
Median	4.0	4.0
Q1:Q3	4.0 : 5.0	3.0 : 4.5

FIG. 13

Summary of Ocular TEAEs in Study Eye

	IAI (N=27)	HD (N=27)
Number of Patients with at Least One Such AE, n(%)	8 (29.6%)	4 (14.3%)
CHALAZION	0	1 (3.6%)
CONJUNCTIVAL DISORDER	0	1 (3.6%)
CONJUNCTIVAL HEMORRHAGE	1 (3.7%)	1 (3.6%)
CONJUNCTIVAL HYPEREMIA	0	1 (3.6%)
DRY EYE	0	1 (3.6%)
EYE PAIN	0	1 (3.6%)
MACULOPATHY	0	1 (3.6%)
NEOVASCULAR AMD	0	1 (3.6%)
PUNCTATE KERATITIS	1 (3.7%)	1 (3.6%)
RETINAL CYST	1 (3.7%)	0
RETINAL HEMORRHAGE	1 (3.7%)	0
RETINAL EDEMA	0	1 (3.6%)
SUBRETINAL FLUID	0	1 (3.6%)
TRICHIASIS	0	1 (3.6%)
VISION BLURRED	0	1 (3.6%)
VISUAL ACUITY REDUCED*	2 (7.4%)	0
VISUAL IMPAIRMENT	1 (3.7%)	0
VITREOUS DETACHMENT	2 (7.4%)	2 (7.1%)
CORNEAL ABRASION	0	1 (3.6%)

*1 of these events is an SAE

FIG. 14

Summary of TEAE IOI of Study Eye

	IAI (N=27)	HD (N=27)
Number of Patients with at Least One Such AE, n (%)	0	0

FIG. 15

Intraocular Pressure

	IAI (n=27)	HD (n=28)
# pts with ≥10 mmHg Increase in pre-injection IOP from BL	0	1 (3.6%)
# of patients with ≥10 mmHg Increase in post-injection IOP from pre-injection IOP at any visit	7 (25.9%)	4 (14.3%)
# pts with post-injection IOP > 25 mmHg at any visit	3 (11.1%)	5 (17.9%)
# pts with pre-injection IOP ≥ 25 mmHg at any visit	0	0
# pts with any visit IOP ≥ 35 mmHg at Any Time	0	0

Safety Analysis Set

Percentages are calculated based on N

FIG. 16

Summary of Non-Ocular TEAEs (1 of 2)

	IAI (N=27)	HD (N=28)
Number of Patients with at Least One Such AE, n(%)	8 (29.6%)	*10 (35.7%)*
DIARRHEA	1 (3.7%)	1 (3.6%)
GERD	1 (3.7%)	0
SMALL INTESTINAL OBSTRUCTION	1 (3.7%)	0
PERIPHERAL SWELLING	1 (3.7%)	0
EAR INFECTION FUNGAL	1 (3.7%)	0
SEASONAL ALLERGY	0	1 (3.6%)
SINUSITIS	1 (3.7%)	1 (3.6%)
BACK INJURY	0	1 (3.6%)
FALL	0	1 (3.6%)
BACTERIAL TEST POSITIVE	0	1 (3.6%)
HEPATIC ENZYME INCREASED	1 (3/7%)	0

FIG. 17

Summary of Non-Ocular TEAEs (2 of 2)

	IAI (N=27)	HD (N=28)
Number of Patients with at Least One Such AE, n(%)	*8 (29.6%)*	*10 (35.7%)*
URINE KETONE BODIES PRESENT	1 (3.7%)	0
WHITE BLOOD CELLS URINE	0	1 (3.6%)
TRANSIENT ISCHAEMIC ATTACK	0	1 (3.6%)
COUGH	0	1 (3.6%)
DERMATITIS CONTACT	0	1 (3.6%)
HYPERTENSION	1 (3.7%)	1 (3.6%)

FIG. 18

Non-Ocular Serious Adverse Events

	IAI (N=27)	HD (N=28)
Number of Patients with at Least One Non-Ocular SAE, n(%)	1 (3.7%)	1 (3.6)
Small Intestinal Obstruction	1	
TIA		1

FIG. 19

Hypertension Adverse Events

	IAI (N=27)	HD (N=28)
Number of Patients with at Least One Such AE, n(%)	1 (3.7%)	1 (3.6%)
Hypertension	1 (3.7%)	1 (3.6%)

FIG. 20

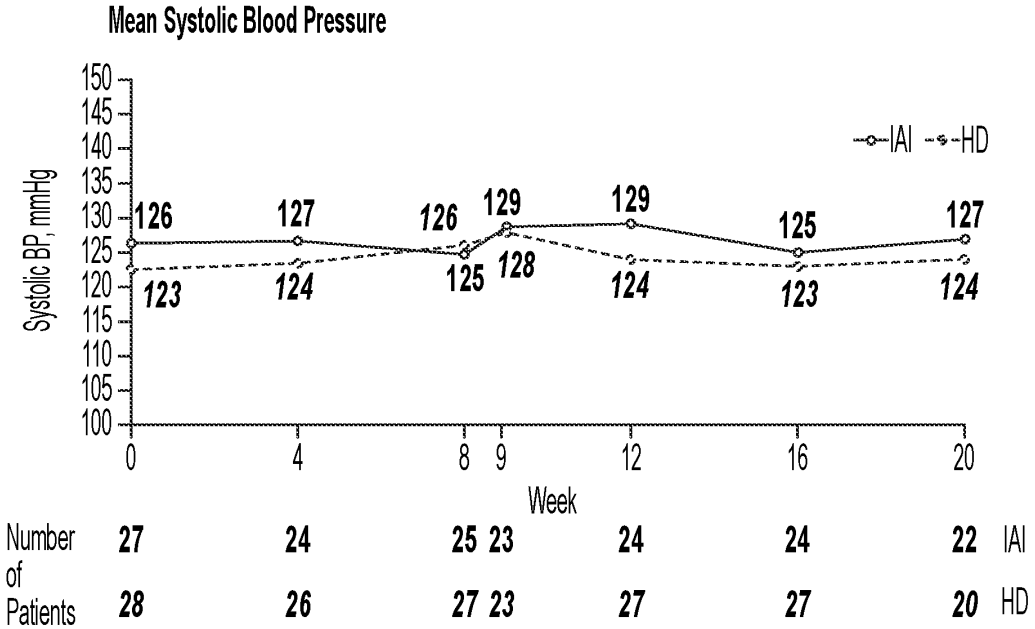

Mean Systolic Blood Pressure
Systolic BP, mmHg
150
145
140
135
130
125
120
115
110
105
100
IAI
HD
126
127
126
129
129
125
127
123
124
125
128
124
123
124
0
4
8
9
12
16
20
Week
Number of Patients
27
24
25
23
24
24
22
IAI
28
26
27
23
27
27
20
HD

FIG. 21

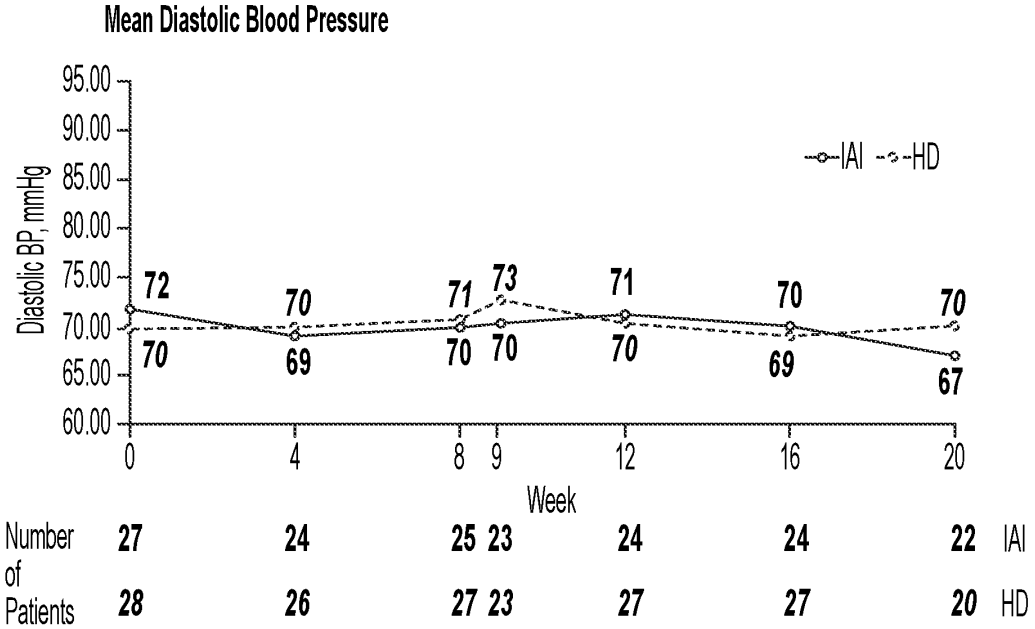

Mean Diastolic Blood Pressure
Diastolic BP, mmHg
95.00
90.00
85.00
80.00
75.00
70.00
65.00
60.00
IAI
HD
72
70
71
73
71
70
70
70
69
70
70
70
69
67
0
4
8
9
12
16
20
Week
Number of Patients
27
24
25
23
24
24
22
IAI
28
26
27
23
27
27
20
HD

FIG. 22

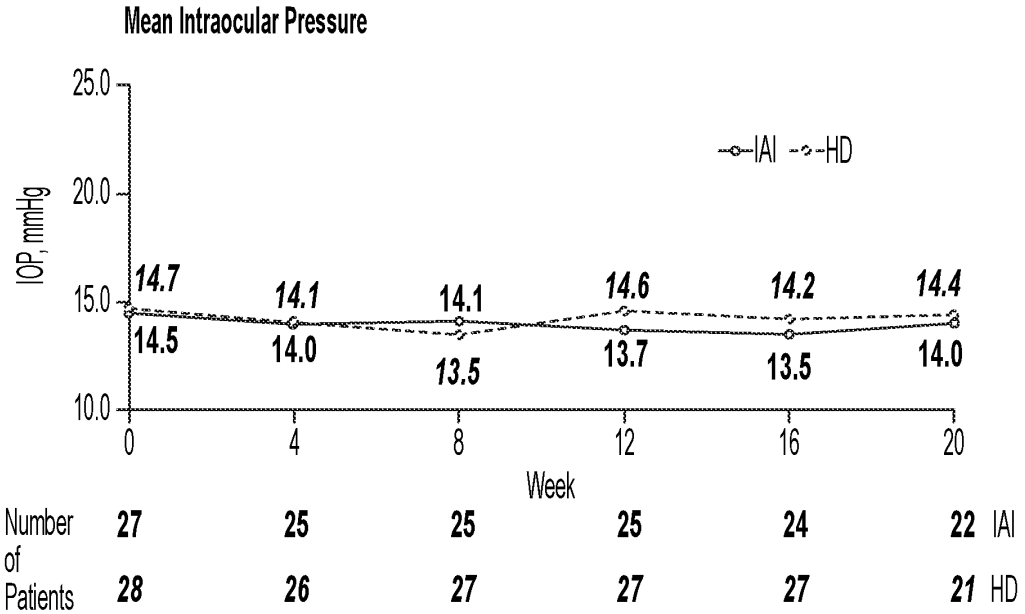

Mean Intraocular Pressure
IAI
HD
IOP, mmHg
25.0
20.0
15.0
10.0
14.7
14.1
14.1
14.6
14.2
14.4
14.5
14.0
13.5
13.7
13.5
14.0
0
4
8
12
16
20
Week
Number of Patients
27 25 25 25 24 22 IAI
28 26 27 27 27 21 HD

FIG. 23

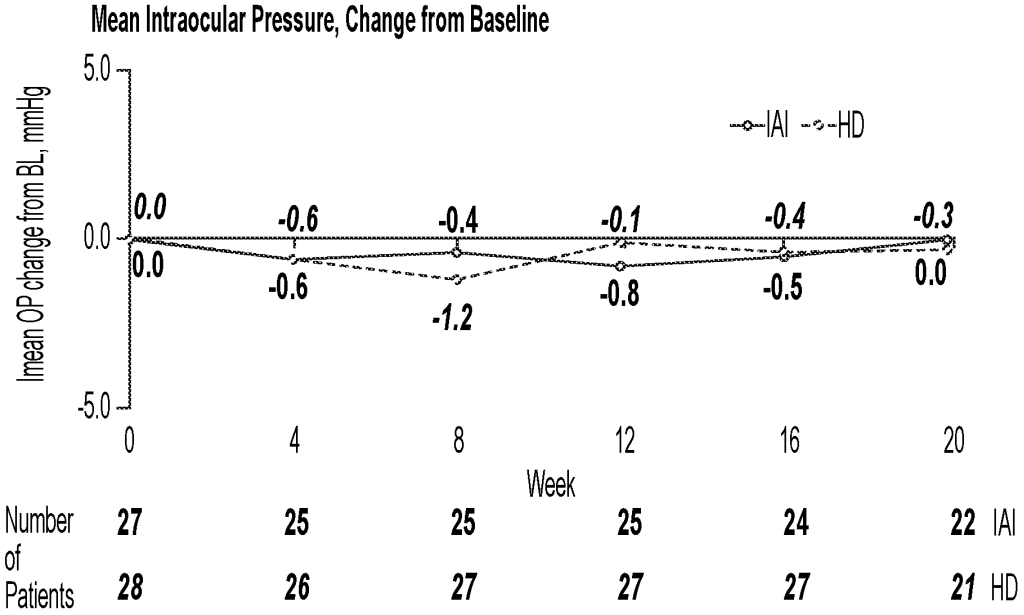

Mean Intraocular Pressure, Change from Baseline
IAI
HD
lmean OP change from BL, mmHg
5.0
0.0
-5.0
0.0
-0.6
-0.4
-0.1
-0.4
-0.3
0.0
-0.6
-1.2
-0.8
-0.5
0.0
0
4
8
12
16
20
Week
Number of Patients
27 25 25 25 24 22 IAI
28 26 27 27 27 21 HD

FIG. 24

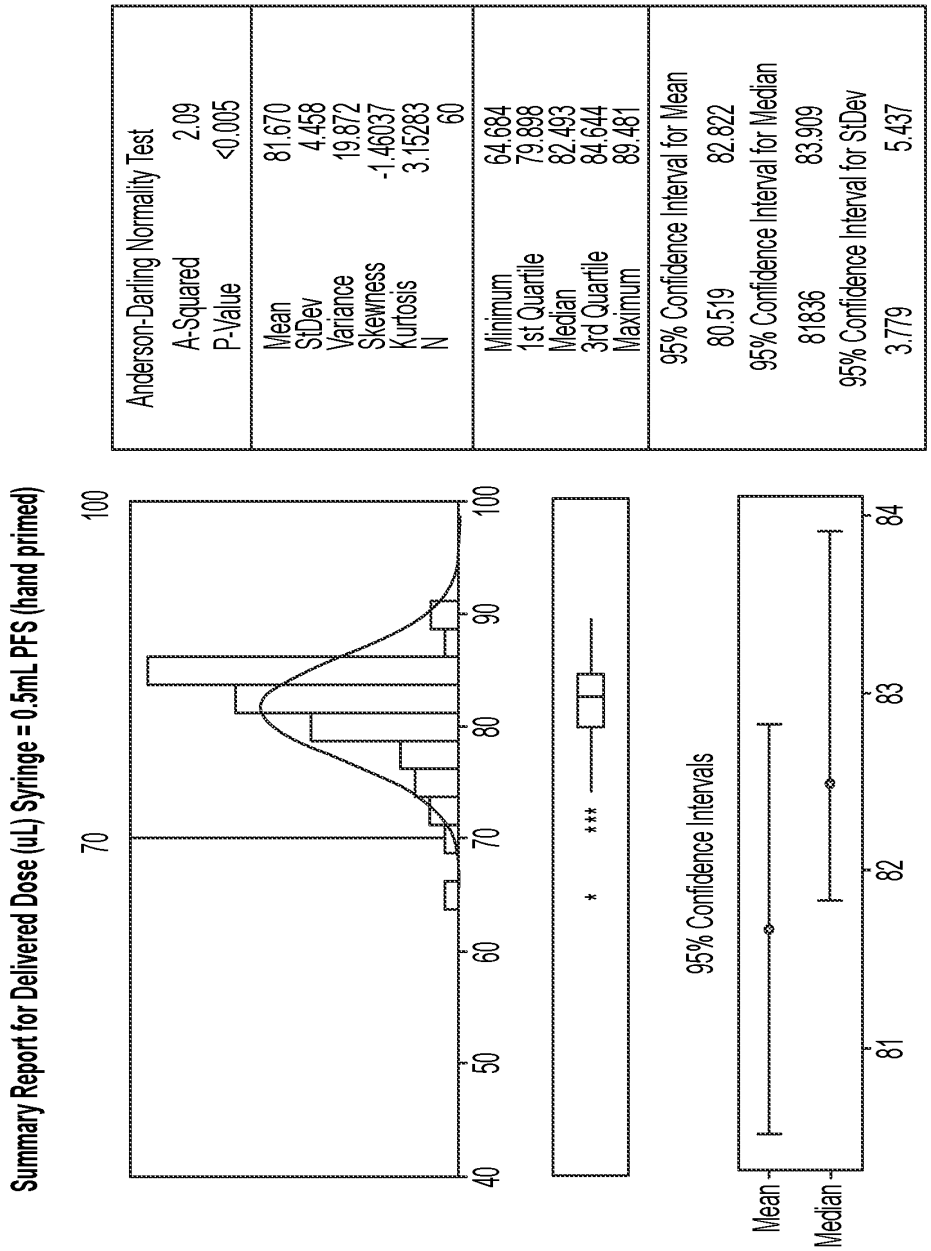

Summary Report for Delivered Dose (uL) Syringe = 0.5mL PFS (hand primed)
Anderson-Darling Normality Test
A-Squared 2.09
P-Value <0.005
Mean 81.670
StDev 4.458
Variance 19.872
Skewness -1.46037
Kurtosis 3.15283
N 60
Minimum 64.684
1st Quartile 79.898
Median 82.493
3rd Quartile 84.644
Maximum 89.481
95% Confidence Interval for Mean
80.519 82.822
95% Confidence Interval for Median
81836 83.909
95% Confidence Interval for StDev
3.779 5.437
95% Confidence Intervals
Mean
Median
40 50 60 70 80 90 100
70 100
81 82 83 84

FIG. 25A

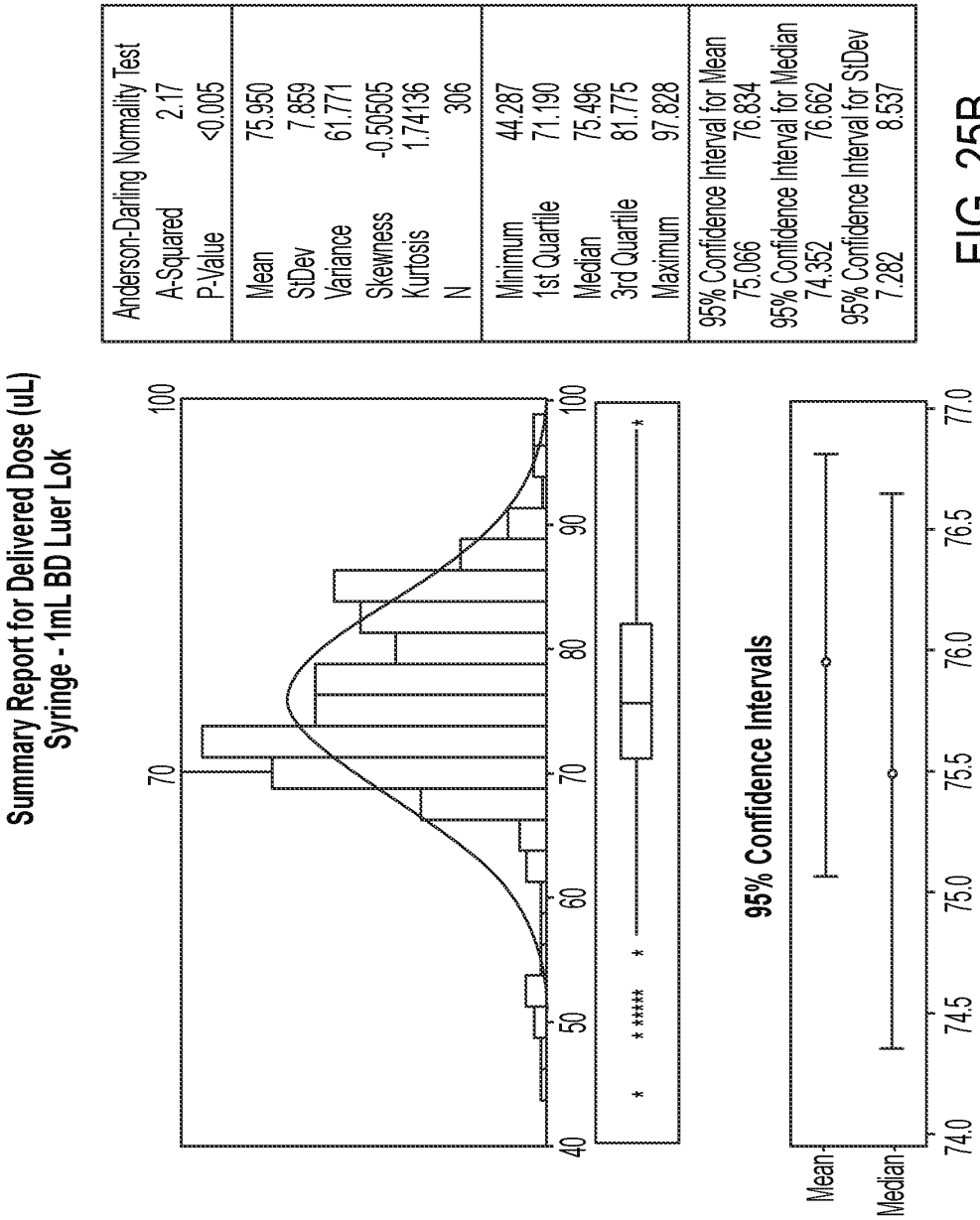

Summary Report for Delivered Dose (uL)
Syringe - 1mL BD Luer Lok
Anderson-Darling Normality Test
A-Squared 2.17
P-Value <0.005
Mean 75.950
StDev 7.859
Variance 61.771
Skewness -0.50505
Kurtosis 1.74136
N 306
Minimum 44.287
1st Quartile 71.190
Median 75.496
3rd Quartile 81.775
Maximum 97.828
95% Confidence Interval for Mean
75.066 76.834
95% Confidence Interval for Median
74.352 76.662
95% Confidence Interval for StDev
7.282 8.537
40 50 60 70 80 90 100
70 100
95% Confidence Intervals
Mean
Median
74.0 74.5 75.0 75.5 76.0 76.5 77.0

FIG. 25B

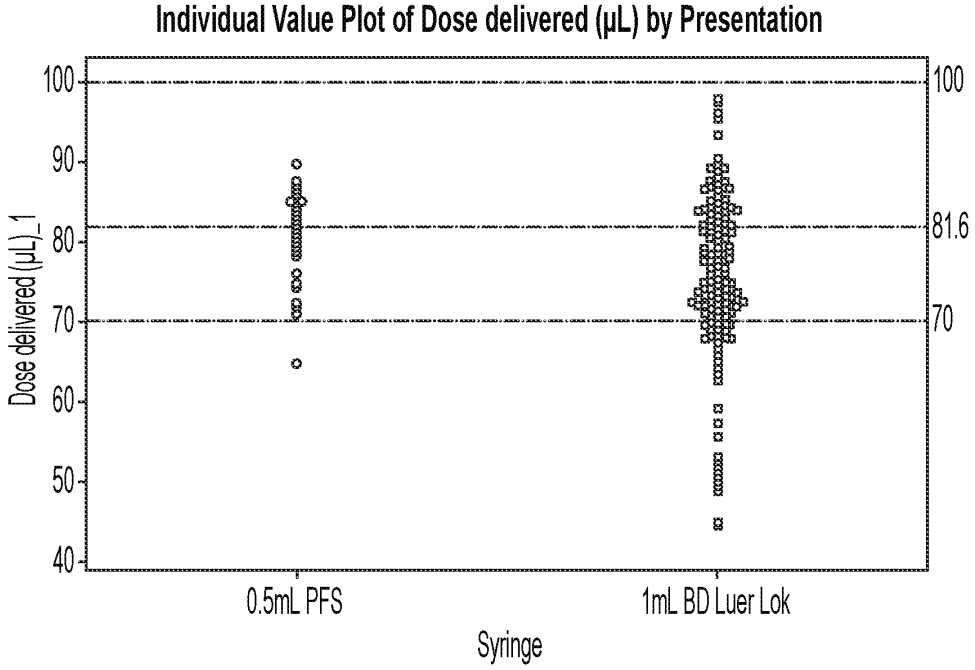

Individual Value Plot of Dose delivered (µL) by Presentation
Dose delivered (µL)_1
100
90
80
70
60
50
40
100
81.6
70
0.5mL PFS
1mL BD Luer Lok
Syringe

FIG. 25C

Disposition and Exposure Through Week 16

	IAI	HD	Total
Total Number Randomized	53	53	106
Main Study	38	38	76
Dense PK Substudy	15	15	30
Number of Patients Completing Week 16	51	53	104
Number of Patients Who Discontinued	2	0	2
Adverse Event	0	0	0
Withdrawal of consent by subject	2	0	2
Due to COVID-19	*1*	0	*1*

Exposure	IAI (n=53)	HD (n=53)
Mean (SD) number of injections (of 3 planned)	2.9 (0.47)	3.0 (0.14)

FIG. 26

Baseline Demographics

	IAI (n=53)	HD (n=53)	ALL (n=106)
Sex			
Male	17 (32.1%)	23 (43.4%)	40 (37.7%)
Female	36 (67.9%)	30 (56.6%)	66 (62.3%)
Ethnicity			
All	53 (100%)	53 (100%)	106 (100%)
Hispanic or Latino	4 (7.5%)	2 (3.8%)	6 (5.7%)
Not Hispanic or Latino	49 (92.5%)	51 (96.2%)	100 (94.3%)
Race			
White	51 (96.2%)	52 (98.1%)	103 (97.2%)
Age (years)			
Mean (SD)	77.7 (8.27)	77.0 (7.69)	77.4 (7.95)

FIG. 27

Baseline Characteristics

	IAI (n=53)	HD (n=53)	All (n=106)
Mean (SD) BL BCVA in Study Eye, ETDRS letters	58.2 (10.5)	57.9 (13.6)	58.0* (11.9)
Mean (SD) BL CRT in Study Eye, µm	488.1 (204.9)	516.2 (175.64)	502.1 (190.6)
Mean (SD) Baseline IOP in Study Eye, mmHg	14.9 (3.4)	14.8 (3.4)	14.9 (3.4)
Mean (SD) Lesion Size, mm	7.9 (6.21)	7.7 (6.84)	7.8 (6.50)
Mean (SD) CNV Size, mm	7.9 (6.20)	7.5 (6.86)	7.7 (6.51)
Baseline FA classification [%]			
Occult CNV	22 (41.5%)	26 (49.1%)	48 (45.3%)
Minimally Classic	26 (49.1%)	19 (35.8%)	45 (42.5%)
Predominantly Classic	4 (7.5%)	8 (15.1%)	12 (11.3%)
Missing	1 (1.9%)	0	1 (0.9%)

*58 ETDRS letters ≈20/60-20/70 Snellen visual acuity

FIG. 28

Baseline Blood Pressure and Medical History of Hypertension (All patients)

	IAI (n=53)	HD (n=53)
Systolic Pressure (Mean (SD) mmHg)	125.4 (10.6)	124.6 (10.6)
Diastolic Pressure (Mean (SD) mmHg)	70.7 (9.0)	71.7 (8.5)

	IAI (n=53)	HD (n=53)
Medical History of Vascular Hypertensive Disorders, n (%)	31 (58.5%)	26 (49.1%)

FIG. 29

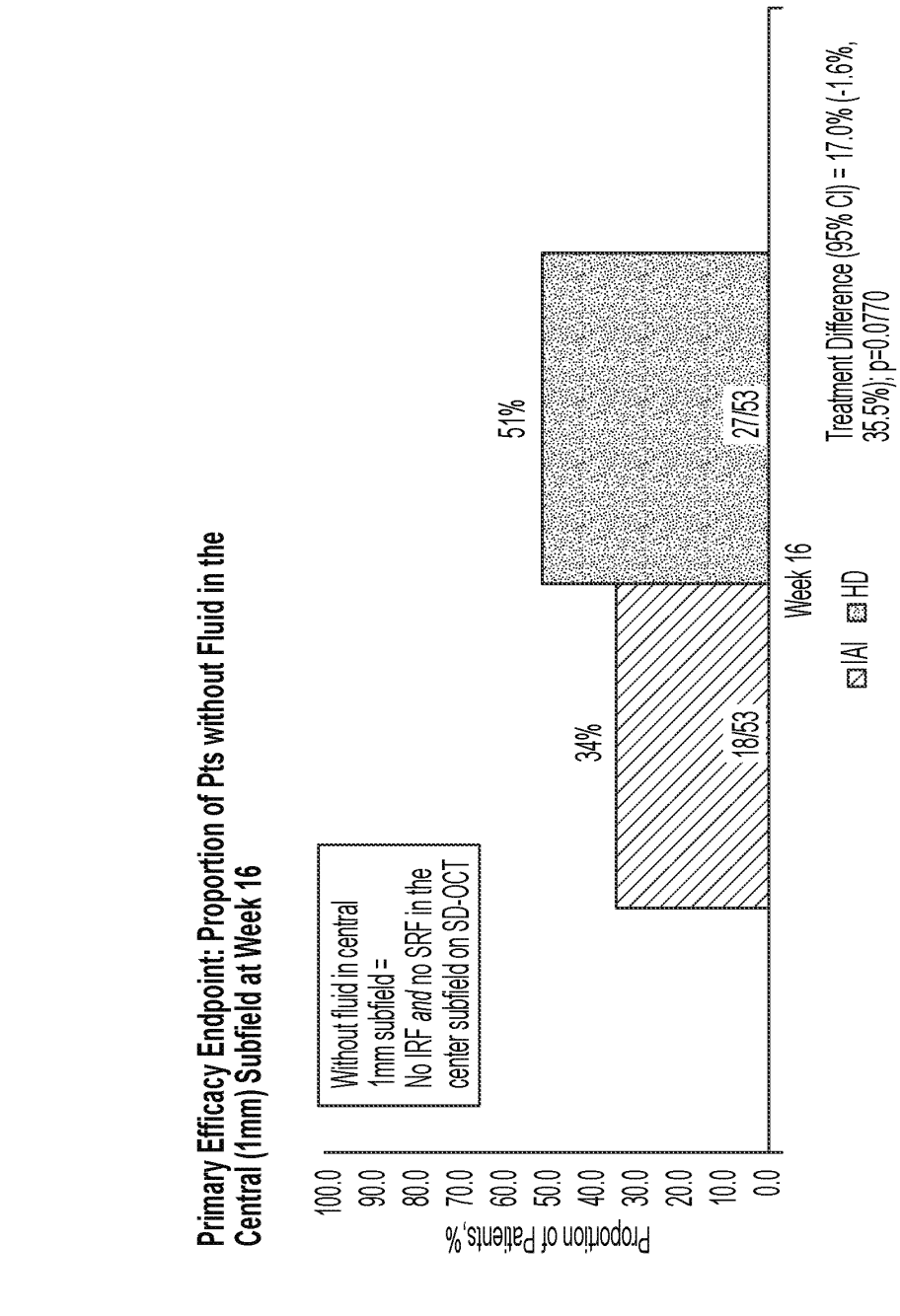

Primary Efficacy Endpoint: Proportion of Pts without Fluid in the Central (1mm) Subfield at Week 16
Without fluid in central 1mm subfield = No IRF and no SRF in the center subfield on SD-OCT
Proportion of Patients, %
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
34%
18/53
51%
27/53
Week 16
IAI
HD
Treatment Difference (95% CI) = 17.0% (-1.6%, 35.5%); p=0.0770
LOCF

FIG. 30

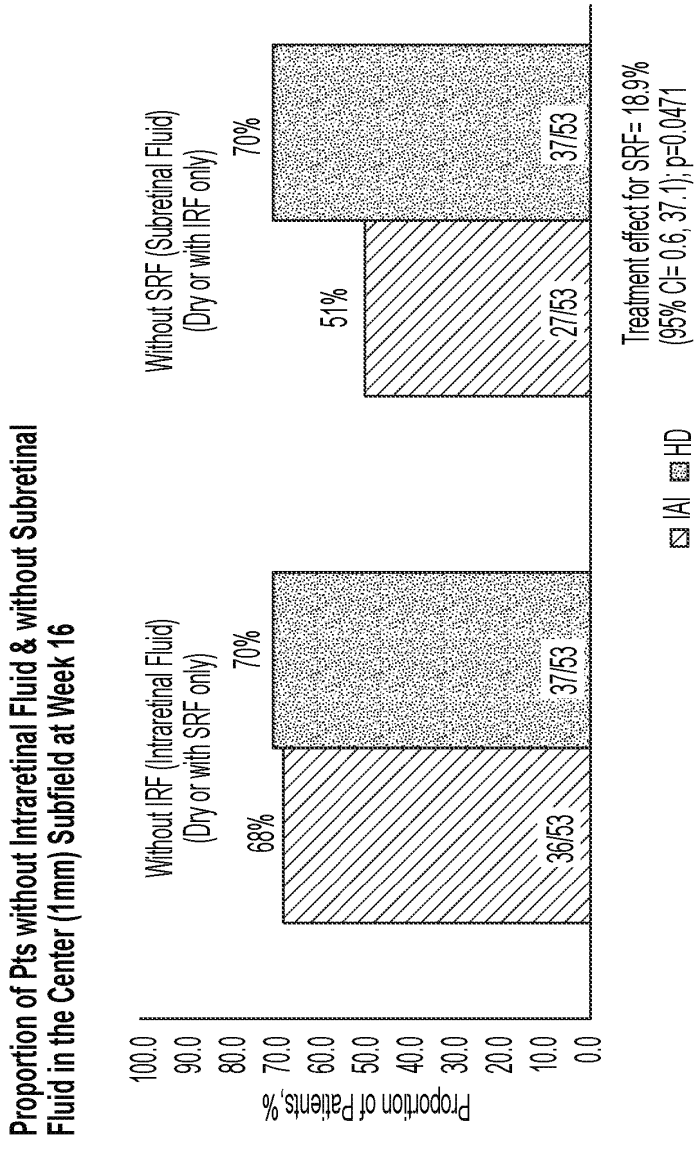

Proportion of Pts without Intraretinal Fluid & without Subretinal Fluid in the Center (1mm) Subfield at Week 16
Proportion of Patients, %
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
Without IRF (Intraretinal Fluid) (Dry or with SRF only)
68%
36/53
70%
37/53
Without SRF (Subretinal Fluid) (Dry or with IRF only)
51%
27/53
70%
37/53
IAI
HD
Treatment effect for SRF= 18.9% (95% CI= 0.6, 37.1); p=0.0471
LOCF

FIG. 31

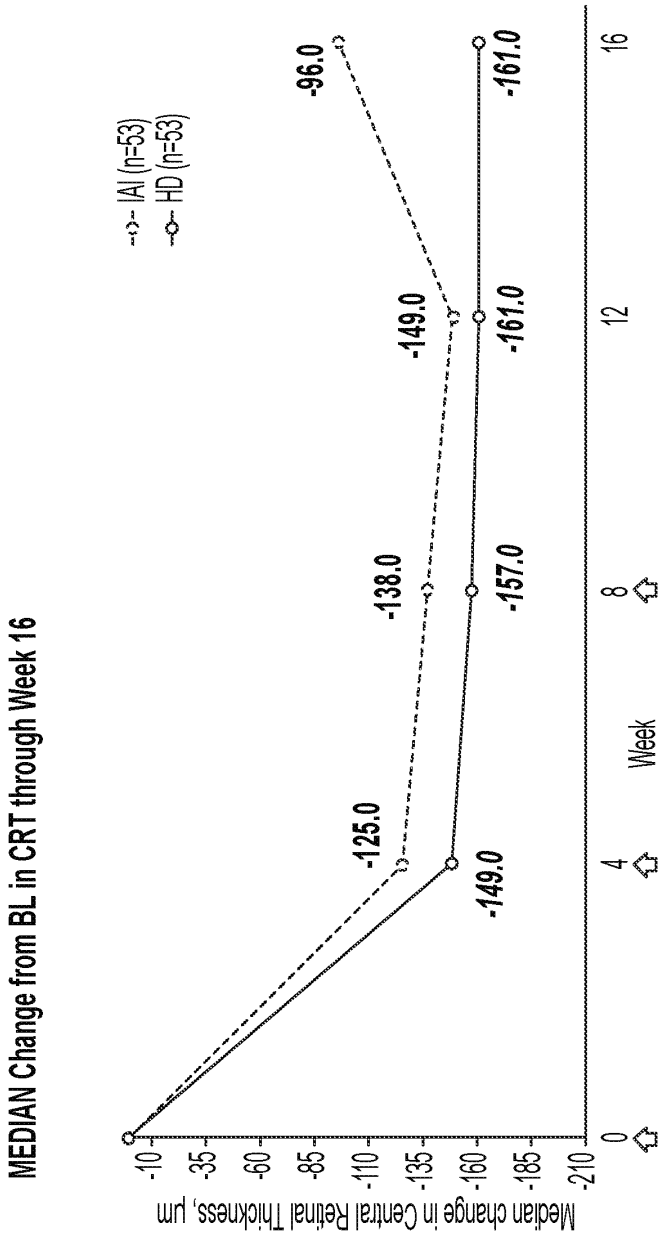


FIG. 32

FAS, LOCF

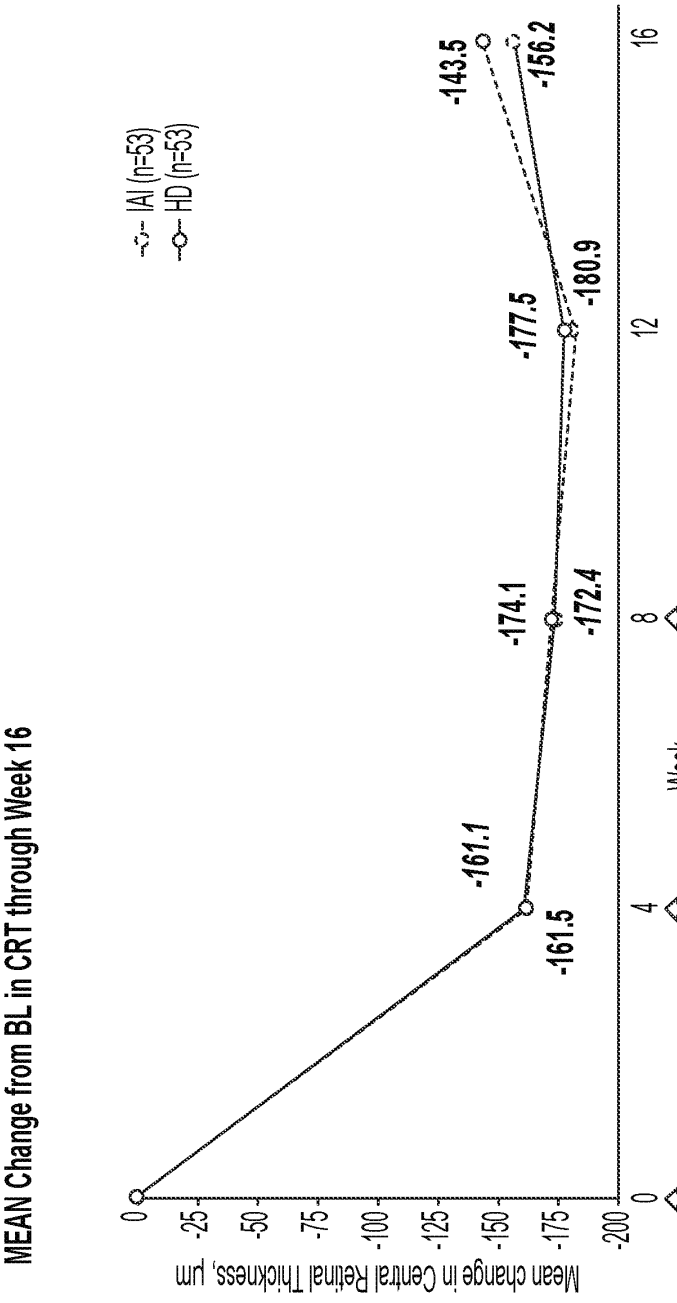


FIG. 33

FAS, LOCF

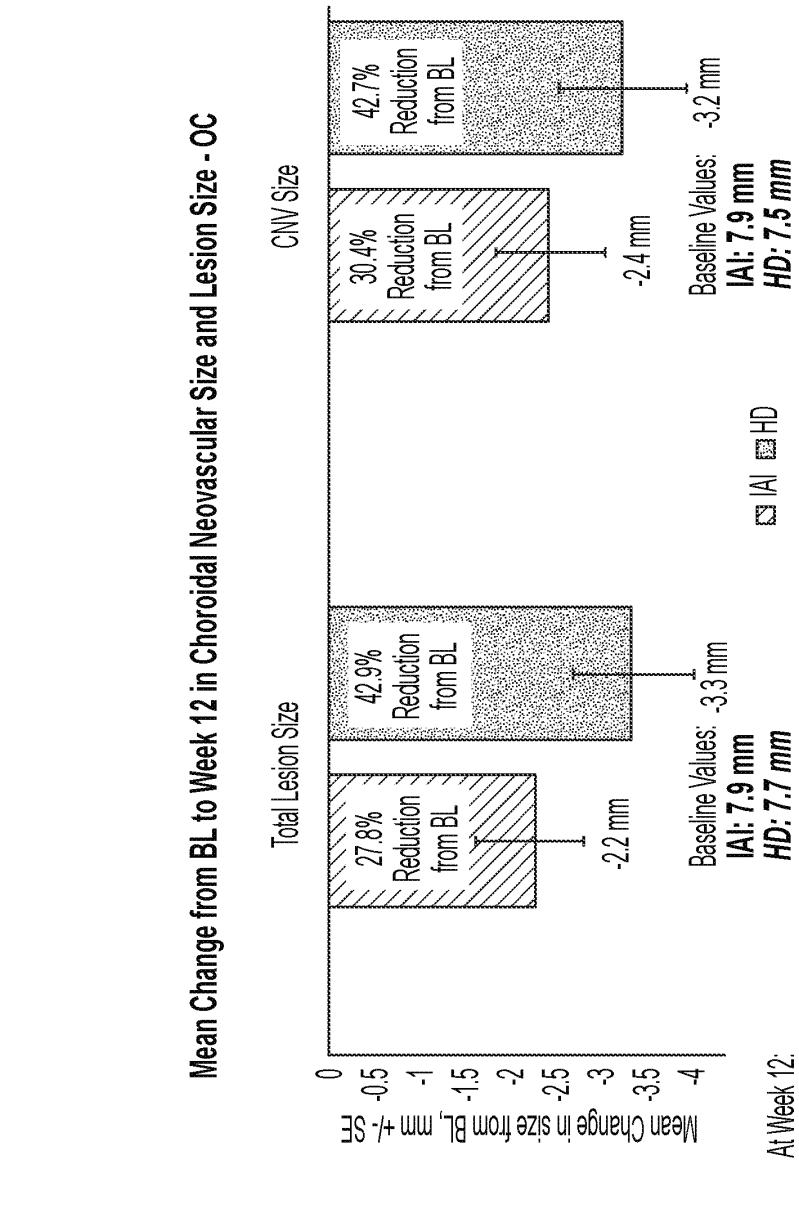

Mean Change from BL to Week 12 in Choroidal Neovascular Size and Lesion Size - OC
Total Lesion Size
CNV Size
Mean Change in size from BL, mm +/- SE
0
-0.5
-1
-1.5
-2
-2.5
-3
-3.5
-4
27.8% Reduction from BL
42.9% Reduction from BL
30.4% Reduction from BL
42.7% Reduction from BL
-2.2 mm
-3.3 mm
-2.4 mm
-3.2 mm
Baseline Values:
IAI: 7.9 mm
HD: 7.7 mm
Baseline Values:
IAI: 7.9 mm
HD: 7.5 mm
IAI
HD
At Week 12:
IAI n=44
HD n=46

FIG. 34

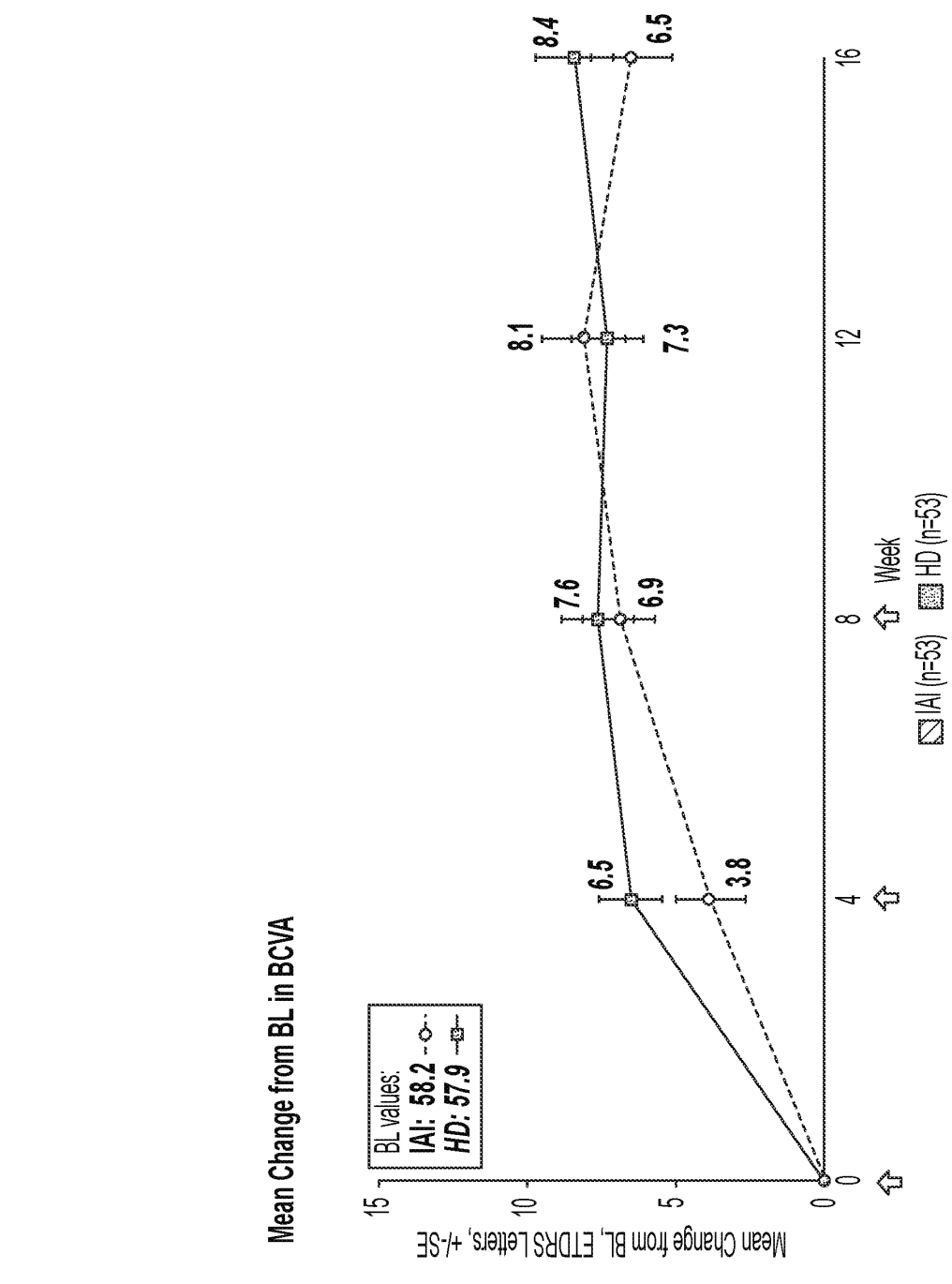

Mean Change from BL in BCVA
BL values:
IAI: 58.2
HD: 57.9
Mean Change from BL, ETDRS Letters, +/-SE
15
10
5
0
0
4
8
12
16
Week
IAI (n=53)
HD (n=53)
6.5
3.8
7.6
6.9
8.1
7.3
8.4
6.5
LOCF

FIG. 35

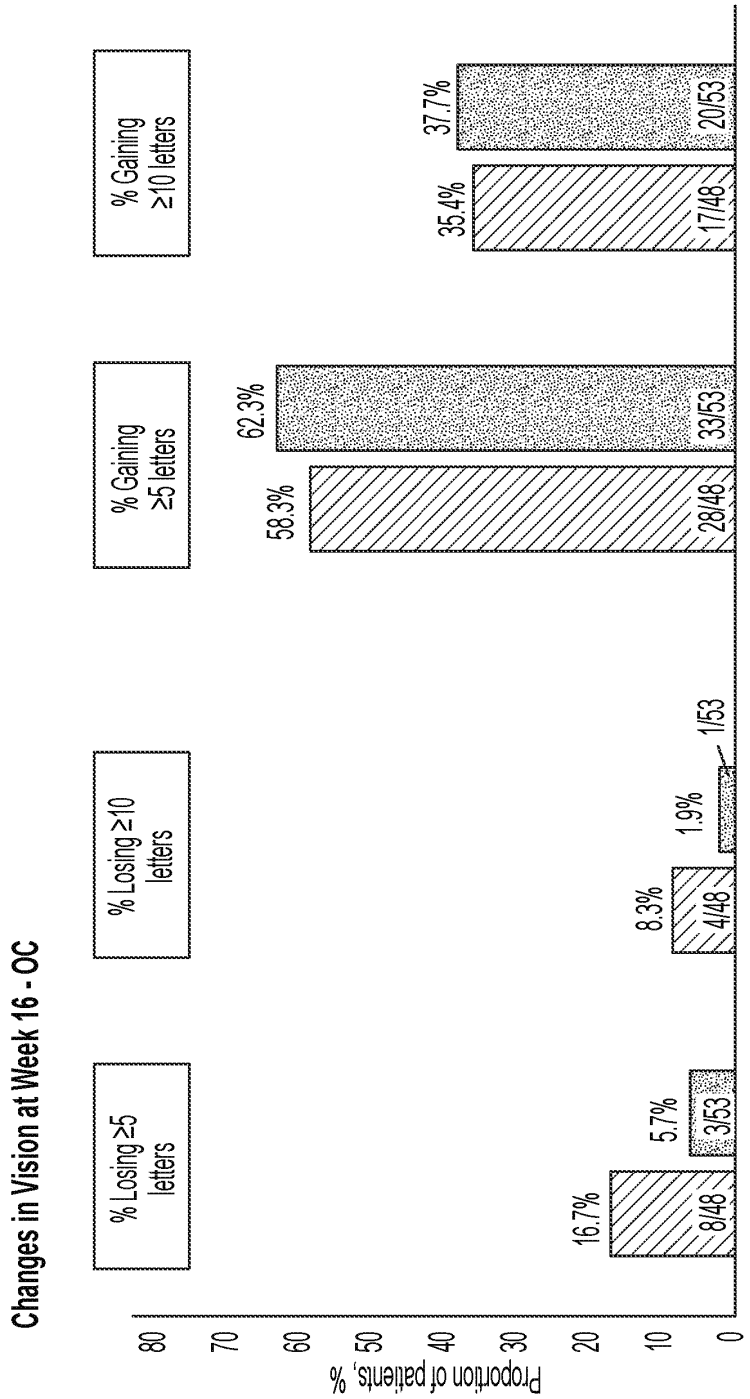

Changes in Vision at Week 16 - OC
% Losing ≥5 letters
% Losing ≥10 letters
% Gaining ≥5 letters
% Gaining ≥10 letters
Proportion of patients, %
0
10
20
30
40
50
60
70
80
16.7%
8/48
5.7%
3/53
8.3%
4/48
1.9%
1/53
58.3%
28/48
62.3%
33/53
35.4%
17/48
37.7%
20/53
IAI
HD

FIG. 36

Proportion of patients Receiving Additional Treatment at Week 16

	IAI (N=53)	HD (N=53)
Number of patients who had a Week 16 visit	48	53
Proportion of patients who had a Week 16 visit and who received Additional Treatment	27%	19%

FIG. 37

Ocular TEAEs in Study Eye Occurring in ≥2% of Patients Through Week 16

	IAI (N=53)	HD (N=53)
Number of Patients with at Least One TEAE in Study Eye, n (%)	12 (22.6%)	9 (17.0%)
CONJUNCTIVAL HAEMORRHAGE	2 (3.8%)	3 (5.7%)
NEOVASCULAR AGE-RELATED MACULAR DEGENERATION	2 (3.8%)	0
RETINAL HAEMORRHAGE	2 (3.8%)	0
VISUAL ACUITY REDUCED	2 (3.8%)	0
VISUAL IMPAIRMENT	2 (3.8%)	0
VITREOUS DETACHMENT	1 (1.9%)	2 (3.8%)

FIG. 38A

Ocular Serious Treatment Emergent Adverse Events in Study Eye Through Week 16

	IAI (N=53)	HD (N=53)
Number of Patients with at Least One Ocular SAE in the Study Eye*, n (%)	1 (1.9%)	1 (1.9%)
VISUAL ACUITY REDUCED	1 (1.9%)	0
RETINAL TEAR	0	1 (1.9%)

FIG. 38B

Intraocular Inflammation TEAEs in the Study Eye Through Week 16

	IAI (N=53)	HD (N=53)
Number of Patients with at Least One Such AE, n	0	0

FIG. 38C

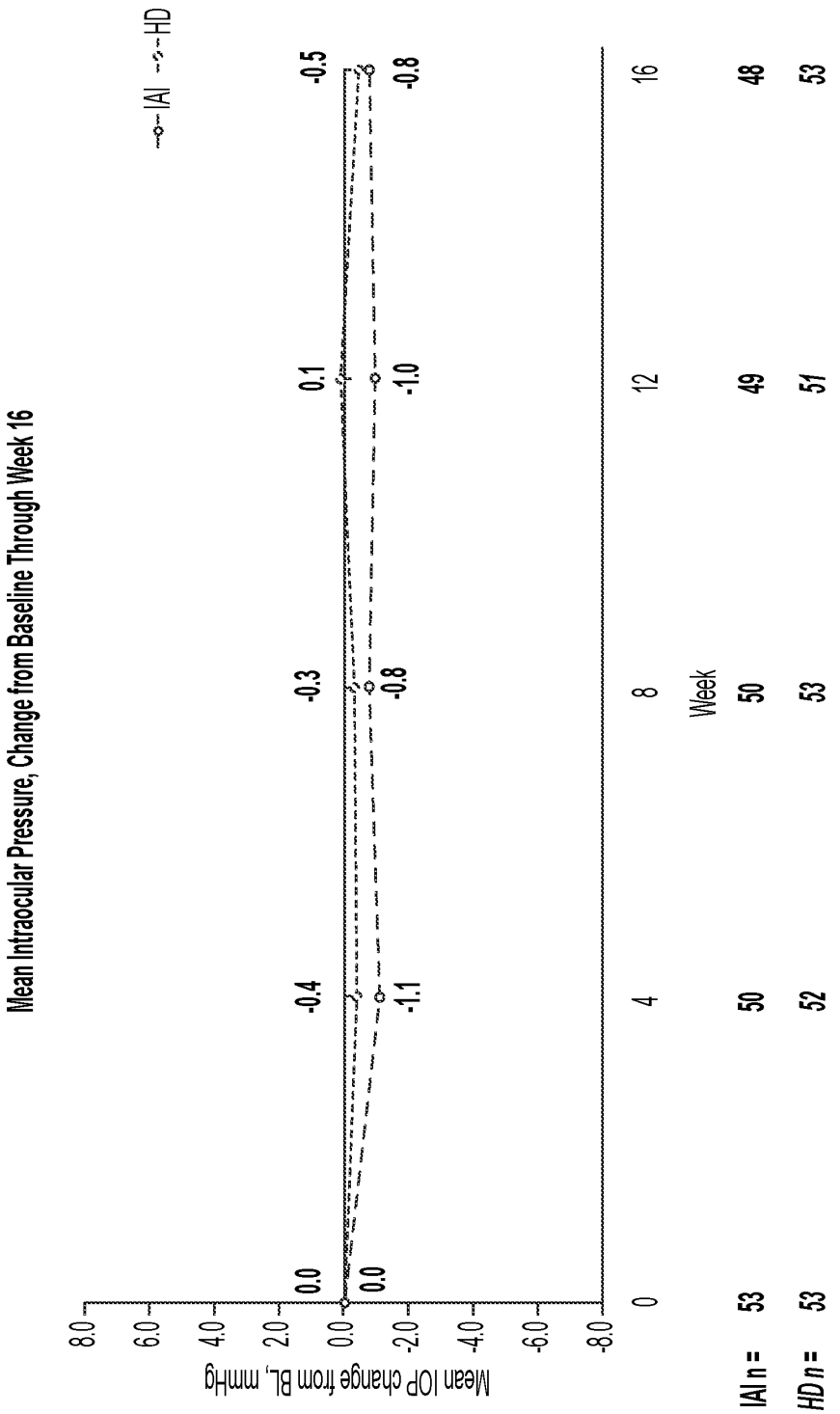

Mean Intraocular Pressure, Change from Baseline Through Week 16
IAI
HD
Mean IOP change from BL, mmHg
8.0
6.0
4.0
2.0
0.0
-2.0
-4.0
-6.0
-8.0
0.0
0.0
-0.4
-1.1
-0.3
-0.8
0.1
-1.0
-0.5
-0.8
0
4
8
12
16
Week
IAI n = 53 50 50 49 48
HD n = 53 52 53 51 53

FIG. 39

Summary of Intraocular Pressure Events Through Week 16

	IAI (N=53)	HD (N=53)
# pts with ≥10 mmHg Increase in pre-injection IOP from BL	0	0
# pts with pre-injection IOP ≥25 mmHg at any visit	0	1 (1.9%)
# pts with any visit IOP ≥35 mmHg at Any Time	0	0

Safety Analysis Set

Percentages are calculated based on N

FIG. 40

APTC Events or Deaths Through Week 16

	IAI (N=53)	HD (N=53)
Number of Patients with at Least One Such AE, n	0	0

FIG. 41

Hypertension Adverse Events Through Week 16

	IAI (N=53)	HD (N=53)
Number of Patients with at Least One Such AE, n (%)	1 (1.9%)	1 (1.9%)
Worsening Hypertension	1 (1.9%)	1 (1.9%)

FIG. 42

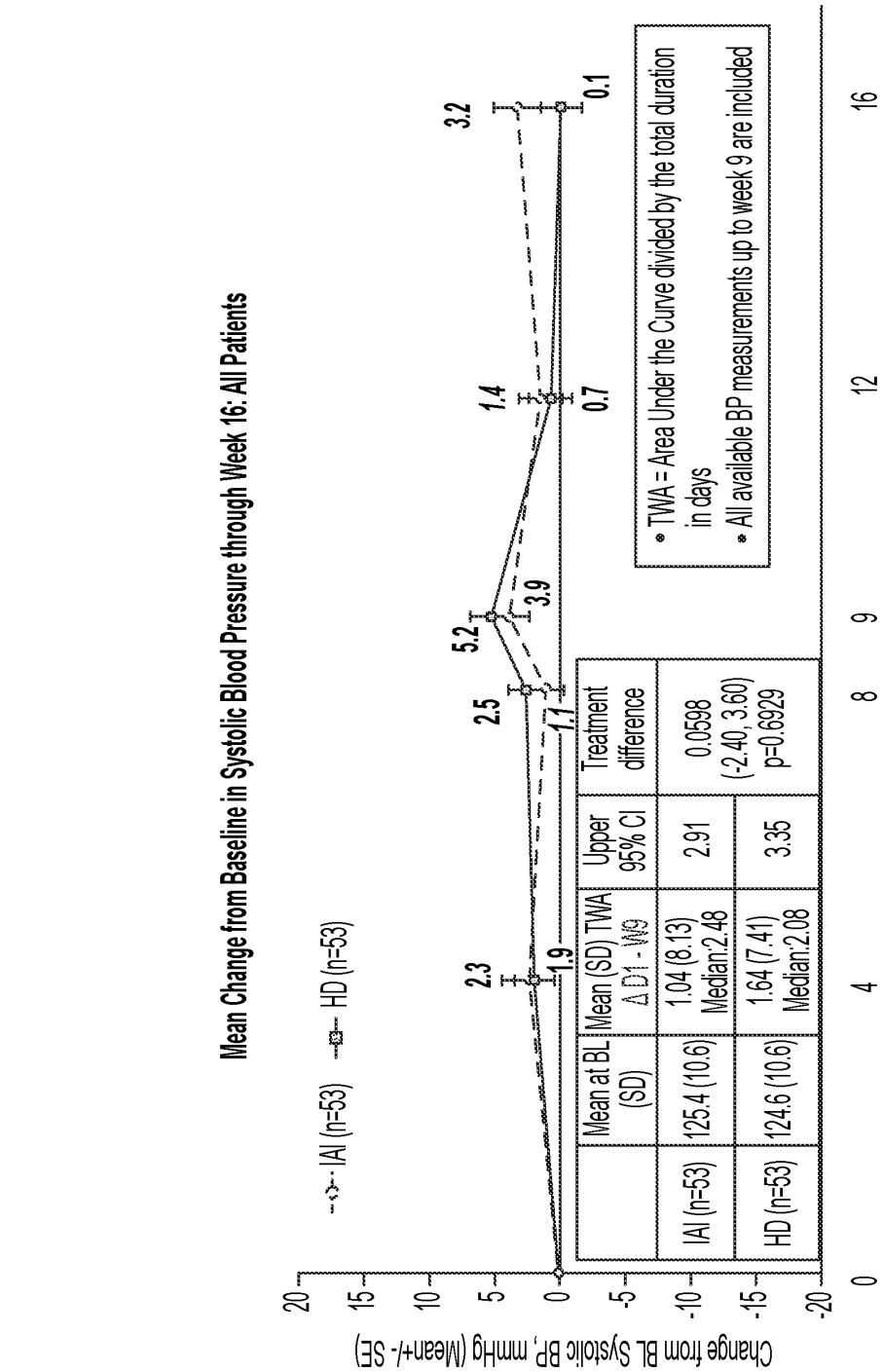

Mean Change from Baseline in Systolic Blood Pressure through Week 16: All Patients
IAI (n=53)
HD (n=53)
Change from BL Systolic BP, mmHg (Mean+/- SE)
Week
2.3
1.9
2.5
1.1
5.2
3.9
1.4
0.7
3.2
0.1
Mean at BL (SD)
Mean (SD) TWA Δ D1 - W9
Upper 95% CI
Treatment difference
IAI (n=53)
125.4 (10.6)
1.04 (8.13) Median:2.48
2.91
0.0598 (-2.40, 3.60) p=0.6929
HD (n=53)
124.6 (10.6)
1.64 (7.41) Median:2.08
3.35
* TWA = Area Under the Curve divided by the total duration in days
* All available BP measurements up to week 9 are included
Mean (SD) Baseline Values:
IAI: 125.4 (10.6)
HD: 124.6 (10.6)

FIG. 43A

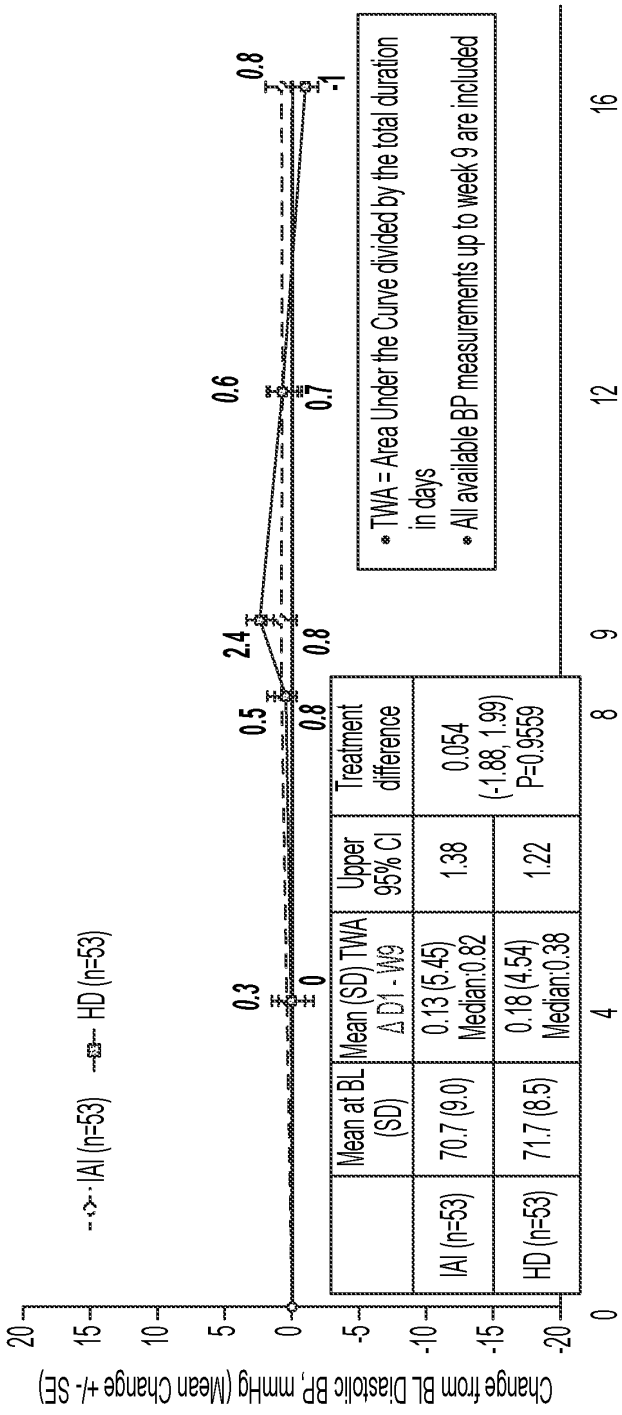

Mean Change from Baseline in Diastolic Blood Pressure through Week 16: All Patients
IAI (n=53)
HD (n=53)
Change from BL Diastolic BP, mmHg (Mean Change +/- SE)
Week
0.3
0
0.5
0.8
2.4
0.8
0.6
0.7
0.8
-1
Mean at BL (SD)
Mean (SD) TWA Δ D1 - W9
Upper 95% CI
Treatment difference
IAI (n=53)
70.7 (9.0)
0.13 (5.45) Median:0.82
1.38
0.054 (-1.88, 1.99) P=0.9559
HD (n=53)
71.7 (8.5)
0.18 (4.54) Median:0.38
1.22
* TWA = Area Under the Curve divided by the total duration in days
* All available BP measurements up to week 9 are included
Mean (SD) Baseline Values:
IAI: 70.7 (9.0)
HD: 71.7 (8.5)

FIG. 43B

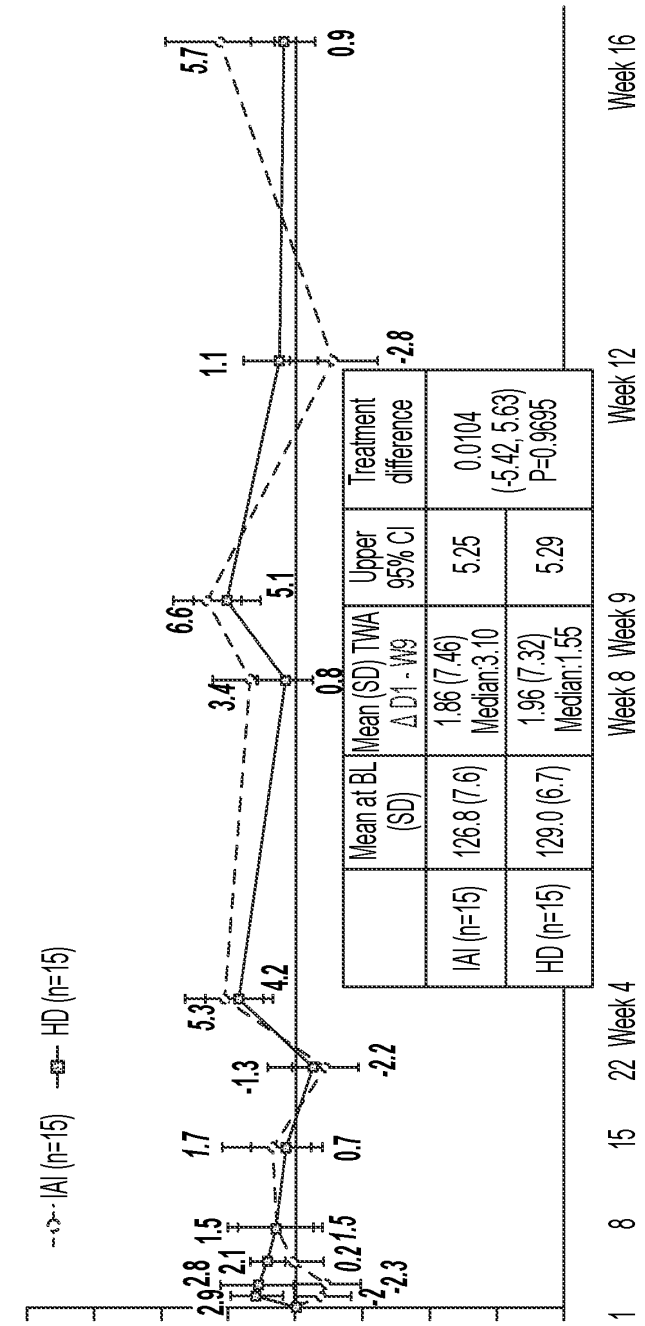

Mean Change from BL in Systolic BP through Wk 16: Dense PK Substudy Patients
IAI (n=15)
HD (n=15)
mmHg
20.0
15.0
10.0
5.0
0
-5.0
-10.0
-15.0
-20.0
1
8
15
22
Day
Week 4
Week 8
Week 9
Week 12
Week 16
2.9
2.8
2.1
1.5
0.2
1.5
-2
-2.3
1.7
0.7
-1.3
5.3
4.2
-2.2
6.6
3.4
0.8
5.1
1.1
5.7
0.9
-2.8
Mean at BL (SD)
Mean (SD) TWA Δ D1 - W9
Upper 95% CI
Treatment difference
IAI (n=15)
126.8 (7.6)
1.86 (7.46) Median:3.10
5.25
0.0104 (-5.42, 5.63) P=0.9695
HD (n=15)
129.0 (6.7)
1.96 (7.32) Median:1.55
5.29
Mean (SD) Baseline Values:
IAI: 126.8 (7.6)
HD: 129.0 (6.7)

FIG. 44A

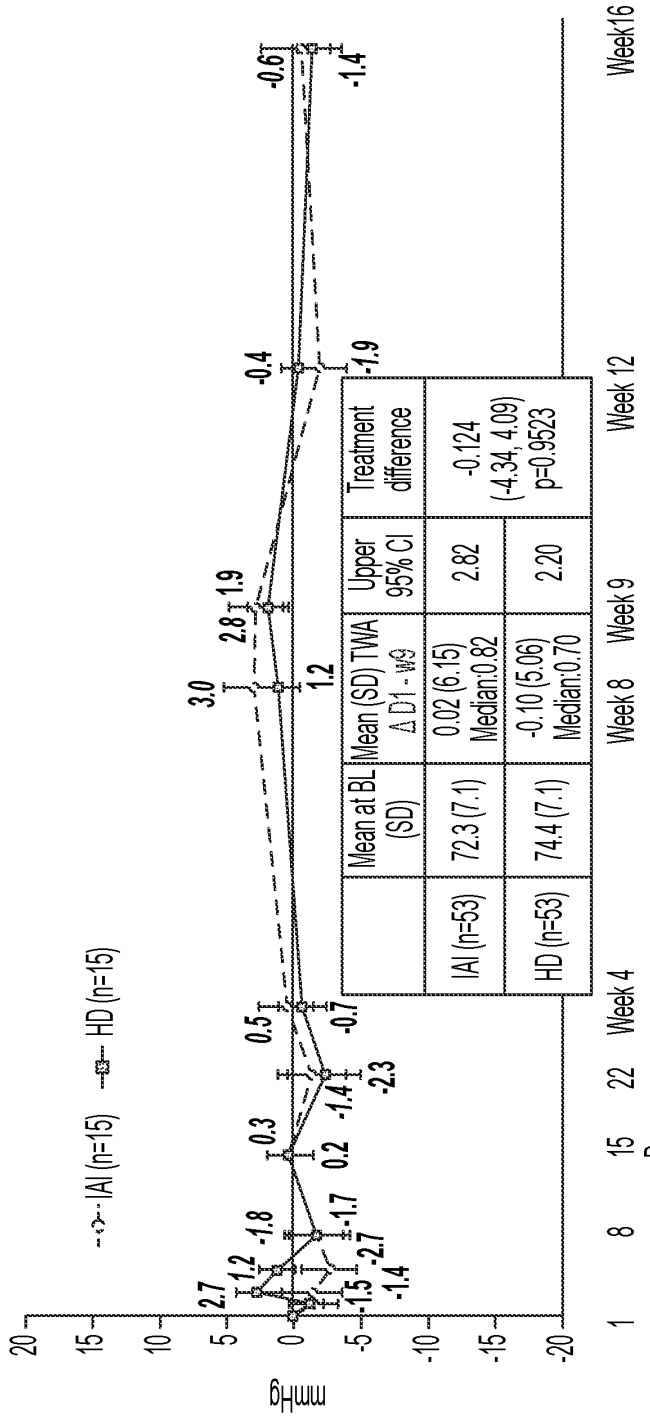

Mean Change from BL in Diastolic BP through Wk 16: Dense PK Substudy Patients
IAI (n=15)
HD (n=15)
mmHg
Day
Week 4
Week 8
Week 9
Week 12
Week16
Mean (SD) Baseline Values:
IAI: 72.3 (7.1)
HD: 74.4 (7.1)
Mean at BL (SD)
Mean (SD) TWA Δ D1 - W9
Upper 95% CI
Treatment difference
IAI (n=53) 72.3 (7.1) 0.02 (6.15) Median:0.82 2.82 -0.124 (-4.34, 4.09) p=0.9523
HD (n=53) 74.4 (7.1) -0.10 (5.06) Median:0.70 2.20

FIG. 44B

Patient Disposition

	Aflibercept 2 mg	Aflibercept 8 mg	Total
Randomized patients, n	53	53	106
Patients completing Week 16, n (%)	51 (96)	53 (100)	104 (98)
Patients completing Week 44, n (%)	49 (92)	51 (96)	100 (94)

FIG. 45

Baseline Demographics

	Aflibercept 2 mg (n=53)	Aflibercept 8 mg (n=53)	Total (N=106)
Sex, n(%)			
Male	17 (32.1)	23 (43.4)	40 (37.7)
Female	36 (67.9)	30 (56.6)	66 (62.3)
Race, n(%)			
White	51 (96.2)	52 (98.1)	103 (97.2)
Ethnicity, n (%)			
Hispanic or Latino	4 (7.5)	2 (3.8)	6 (5.7)
Not Hispanic or Latino	49 (92.5)	51 (96.2)	100 (94.3)
Age, mean (SD), years	77.7 (8.3)	77.0 (7.7)	77.4 (8.0)

SD. standard deviation.

FIG. 46

Baseline Characteristics - Study Eye

	Aflibercept 2 mg (n=53)	Aflibercept 8 mg (n=53)	Total (N=106)
BCVA, mean (SD), ETDRS letters	58.2 (10.5)	57.9 (13.6)	58.0[a] (11.9)
CRT, mean (SD), µm	488.1 (204.9)	516.2 (175.6)	502.1 (190.6)
IOP, mean (SD), mm Hg	14.9 (3.4)	14.8 (3.4)	14.9 (3.4)
Lesion size, mean (SD), mm^2	7.9 (6.2)	7.7 (6.8)	7.8 (6.5)
CNV size, mean (SD), mm^2	7.9 (6.2)	7.5 (6.9)	7.7 (6.5)
FA classification, n (%)			
Occult	22 (41.5)	26 (49.1)	48 (45.3)
Minimally classic	26 (49.1)	19 (35.8)	45 (42.5)
Predominantly classic	4 (7.5)	8 (15.1)	12 (11.3)
Missing	1 (1.9)	0	1 (0.9)

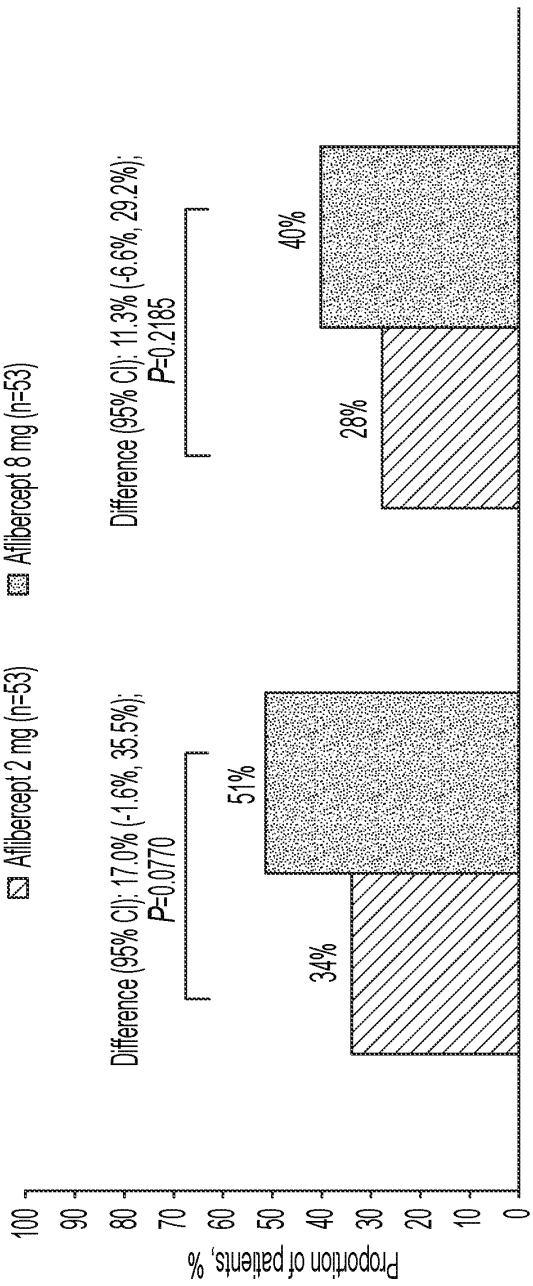
*58 ETDRS letters ≈ 20/60-20/70 Snellen visual acuity.
CRT, central retinal thickness; IOP, intraocular pressure.

FIG. 47

Treatment Exposure and PRN Treatment through Week 44

Exposure	Aflibercept 2 mg (n=53)	Aflibercept 8 mg (n=53)
Mean number of aflibercept injections through Week 44	5.8	5.8
Proportion of patients who did NOT receive additional or PRN treatment	24 (45%)	28 (53%)
Total number of PRN injections given	38	33

FIG. 48



FAS, LOCF
Without fluid in central subfield defined as no IRF and no SRF in the center subfield on SD-OCT
LOCF: Patients receiving treatment at Week 16 were considered not dry from Week 16 onward
FAS, full analysis set; IRF, intra-retinal fluid; SD-OCT, spectral domain optical coherence tomography; SRF, sub-retinal fluid

FIG. 49

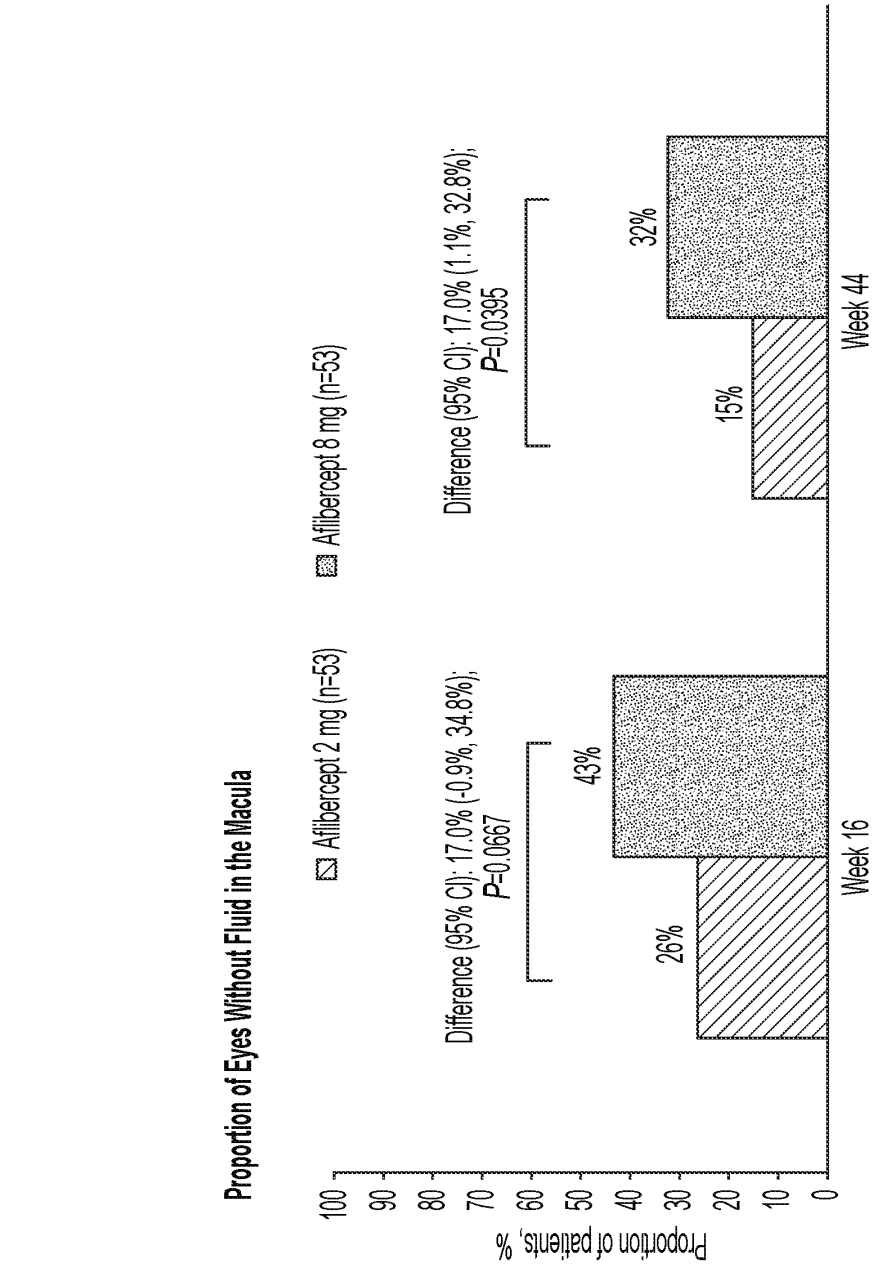

Proportion of Eyes Without Fluid in the Macula
Aflibercept 2 mg (n=53)
Aflibercept 8 mg (n=53)
Difference (95% CI): 17.0% (-0.9%, 34.8%); P=0.0667
Difference (95% CI): 17.0% (1.1%, 32.8%); P=0.0395
26%
43%
15%
32%
Week 16
Week 44
Proportion of patients, %
100
90
80
70
60
50
40
30
20
10
0
FAS. LOCF
Without fluid in macula defined as no IRF and no SRF in the macula on SD-OCT
LOCF: Patients receiving treatment at Week 16 were considered not dry from Week 16 onward

FIG. 50

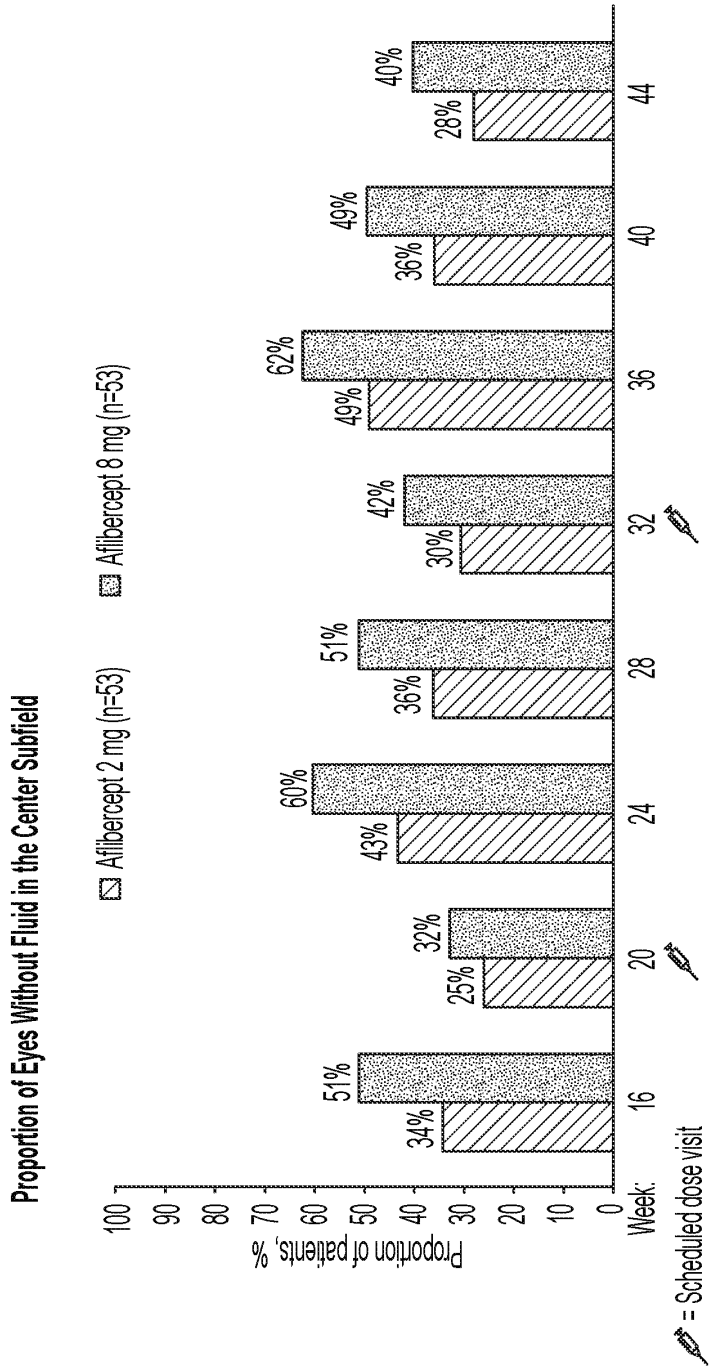

Proportion of Eyes Without Fluid in the Center Subfield
Aflibercept 2 mg (n=53)
Aflibercept 8 mg (n=53)
Proportion of patients, %
100
90
80
70
60
50
40
30
20
10
0
34%
51%
25%
32%
43%
60%
36%
51%
30%
42%
49%
62%
36%
49%
28%
40%
Week:
16
20
24
28
32
36
40
44
= Scheduled dose visit
FAS, LOCF;
Without fluid in central subfield defined as no IRF and no SRF in the center subfield on SD-OCT
LOCF: Patients receiving treatment at Week 16 were considered not dry from Week 16 onward

FIG. 51

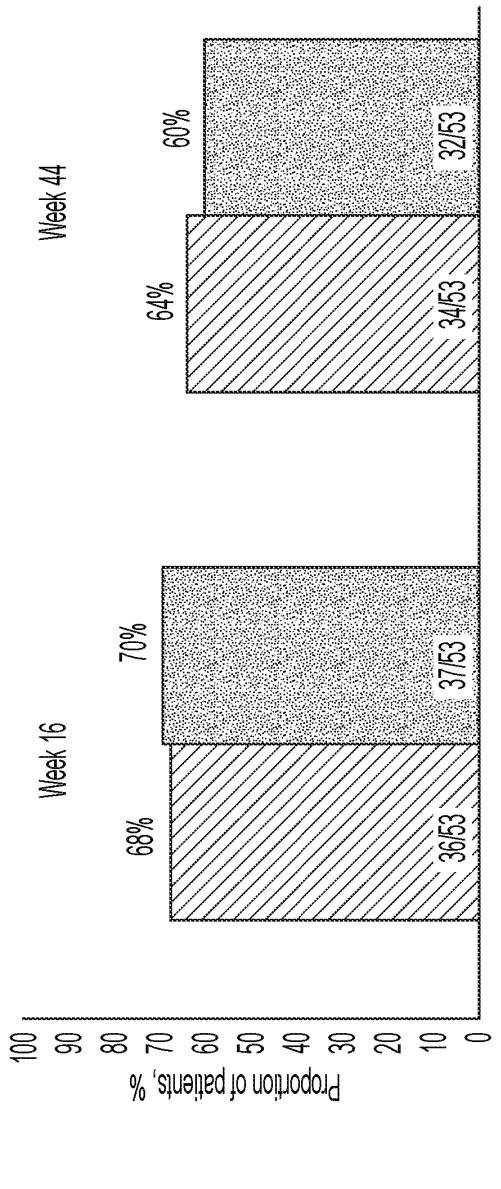

Proportion of Eyes without Intraretinal Fluid* in the Center Subfield at Weeks 16 & 44
Proportion of patients, %
100
90
80
70
60
50
40
30
20
10
0
Week 16
Week 44
68%
70%
64%
60%
36/53
37/53
34/53
32/53
IAI
HD
FAS: 2 mg N=53; 8 mg N=53; LOCF
*Without Intraretinal Fluid = Dry or with Subretinal Fluid only

FIG. 52

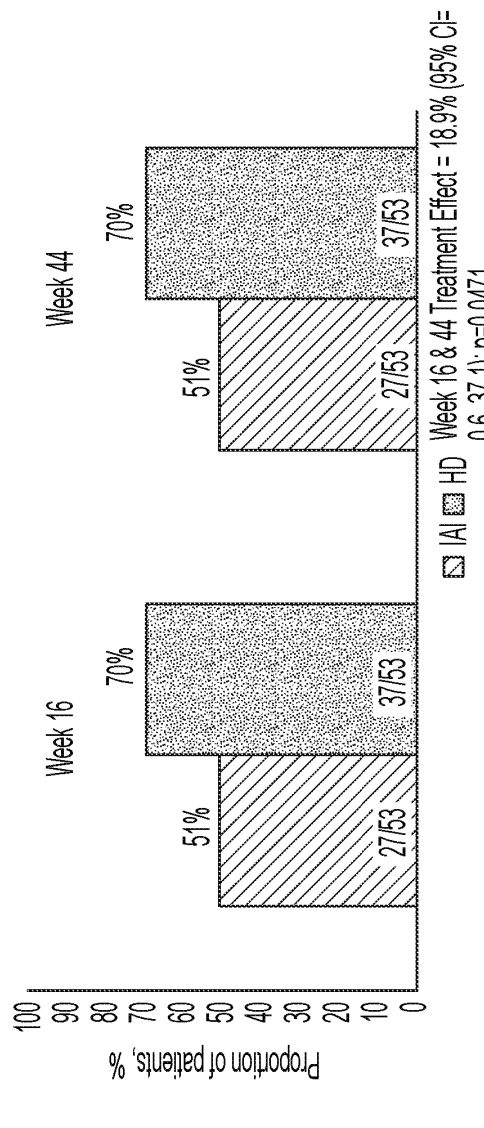

Proportion of Eyes without Subretinal Fluid* in the Center Subfield at Weeks 16 & 44
Proportion of patients, %
100
90
80
70
60
50
40
30
20
10
0
Week 16
Week 44
51%
70%
51%
70%
27/53
37/53
27/53
37/53
IAI
HD
IAI HD Week 16 & 44 Treatment Effect = 18.9% (95% CI= 0.6, 37.1); p=0.0471
FAS: 2 mg N=53; 8 mg N=53; LOCF
Week 16 & 44 Treatment Effect = 18.9% (95% CI= 0.6, 37.1); p=0.0471
*Without Subretinal Fluid = Dry or with Intraretinal Fluid only

FIG. 53

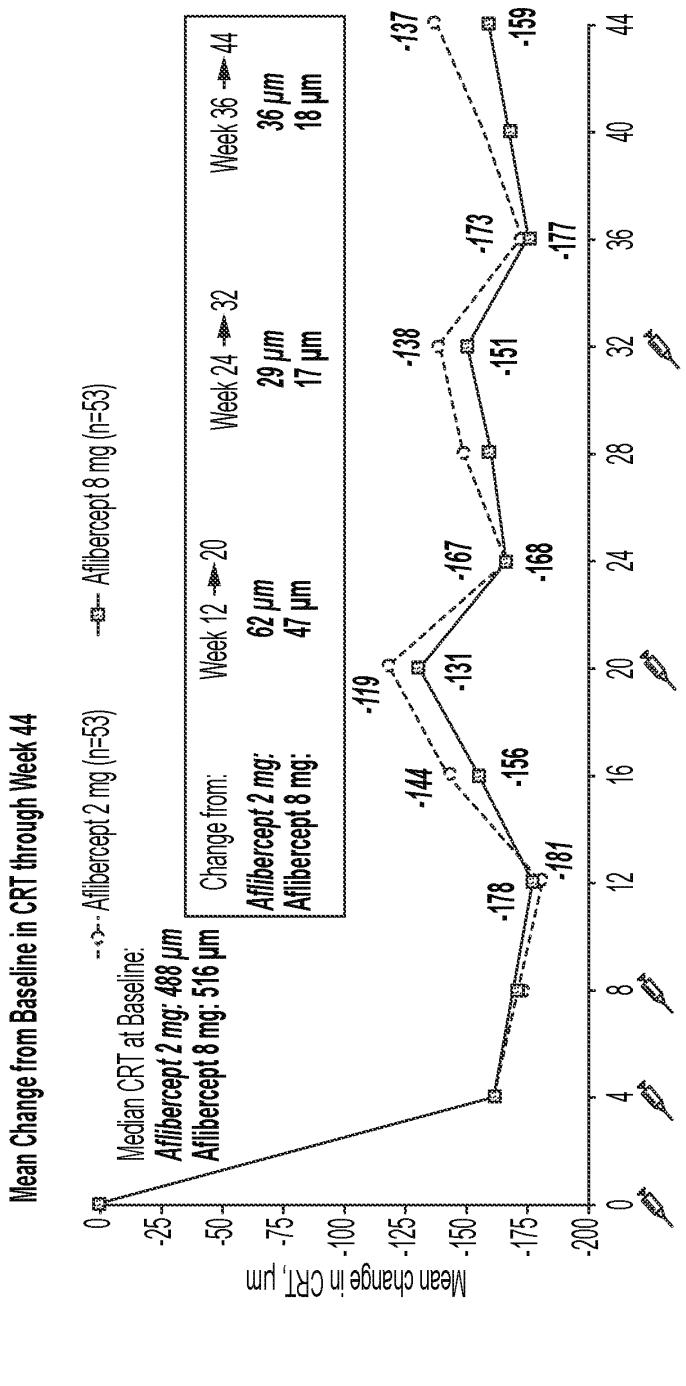

Mean Change from Baseline in CRT through Week 44
Aflibercept 2 mg (n=53)
Aflibercept 8 mg (n=53)
Median CRT at Baseline:
Aflibercept 2 mg: 488 µm
Aflibercept 8 mg: 516 µm
Change from: Week 12 Week 24 Week 36
Aflibercept 2 mg: 62 µm 29 µm 36 µm
Aflibercept 8 mg: 47 µm 17 µm 18 µm
Mean change in CRT, µm
0
-25
-50
-75
-100
-125
-150
-175
-200
-119
-144
-178
-131
-156
-181
-167
-168
-138
-151
-173
-177
-137
-159
0 4 8 12 16 20 24 28 32 36 40 44
Week
= Scheduled dose visit
FAS, LOCF
LOCF: Patients receiving treatment at Week 16 were considered not dry from Week 16 onward

FIG. 54

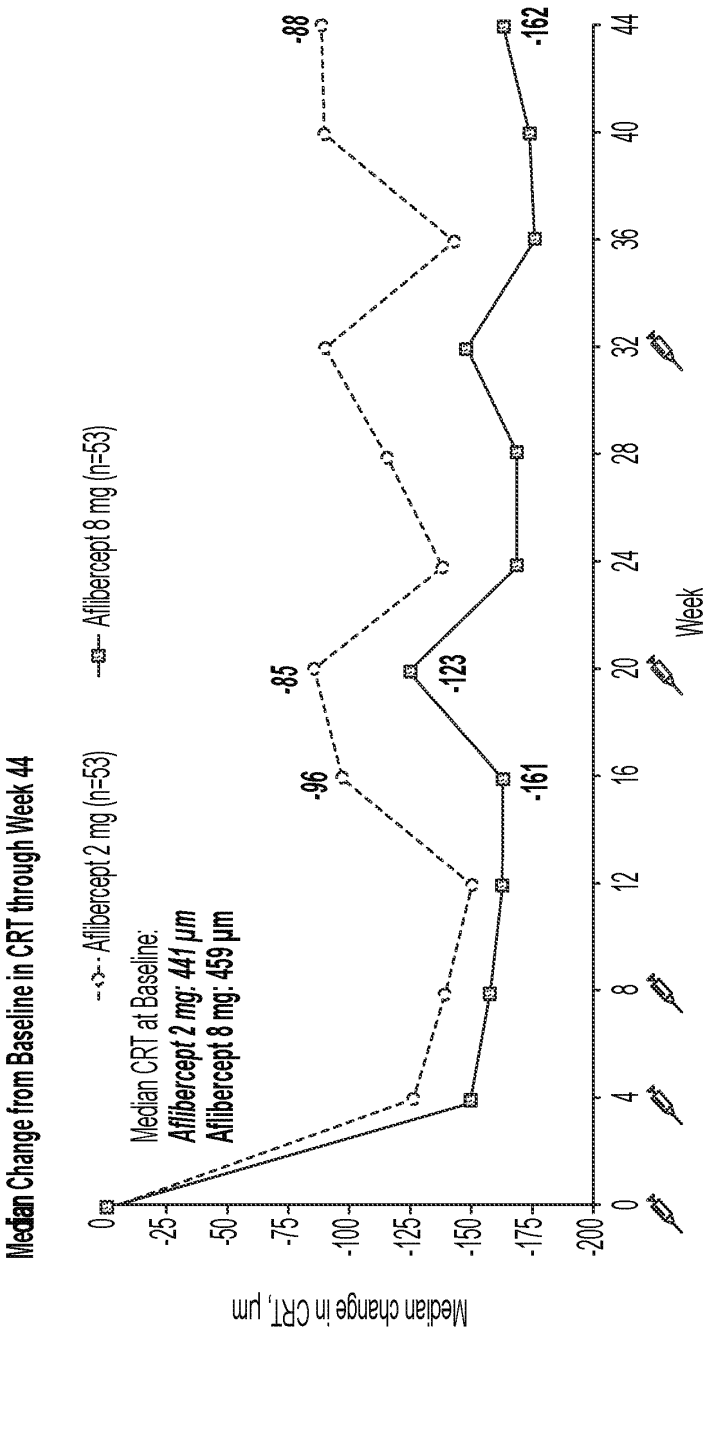

Median Change from Baseline in CRT through Week 44
Aflibercept 2 mg (n=53)
Aflibercept 8 mg (n=53)
Median CRT at Baseline:
Aflibercept 2 mg: 441 µm
Aflibercept 8 mg: 459 µm
Median change in CRT, µm
0
-25
-50
-75
-100
-125
-150
-175
-200
-96
-85
-161
-123
-88
-162
0
4
8
12
16
20
24
28
32
36
40
44
Week
= Scheduled dose visit
FAS, LOCF
LOCF: Patients receiving treatment at Week 16 were considered not dry from Week 16 onward

FIG. 55

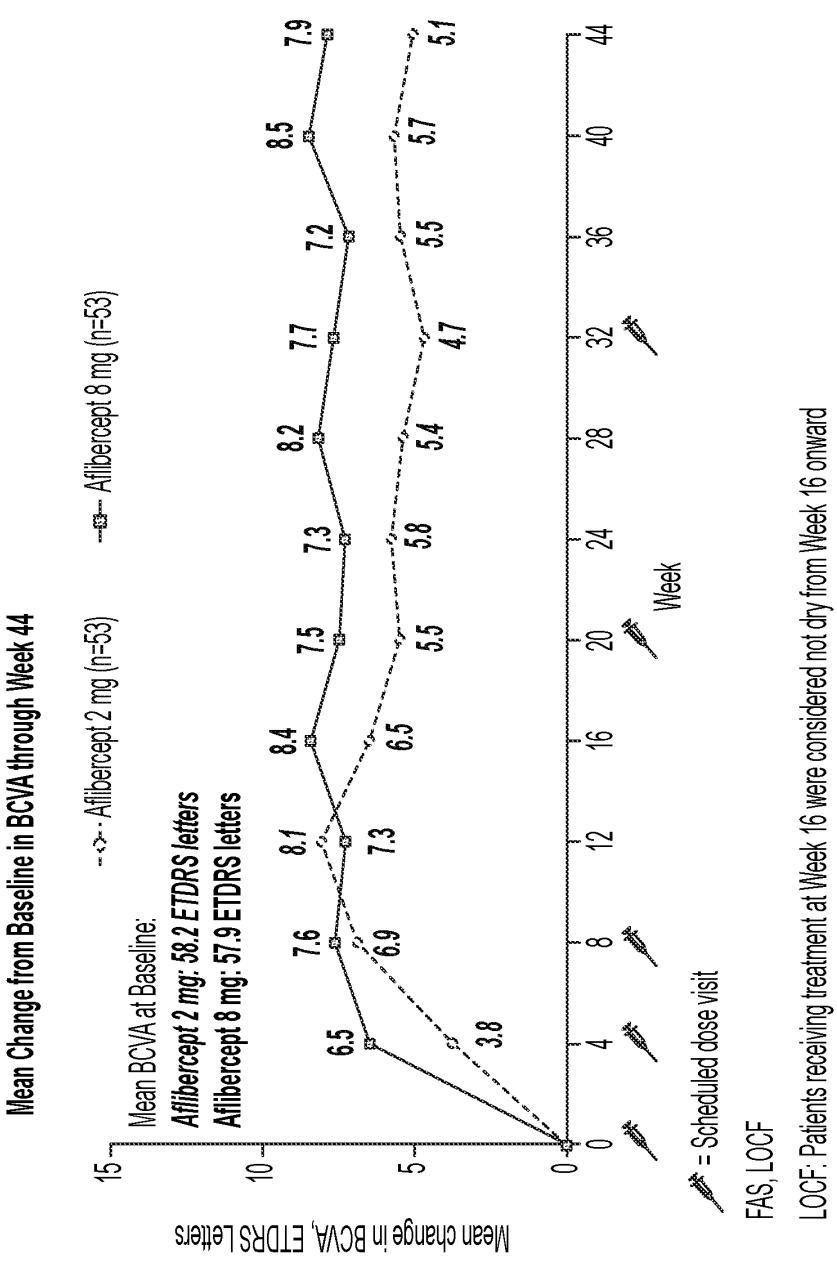

Mean Change from Baseline in BCVA through Week 44
Aflibercept 2 mg (n=53)
Aflibercept 8 mg (n=53)
Mean BCVA at Baseline:
Aflibercept 2 mg: 58.2 ETDRS letters
Aflibercept 8 mg: 57.9 ETDRS letters
Mean change in BCVA, ETDRS Letters
15
10
5
0
6.5
7.6
8.1
8.4
7.5
7.3
8.2
7.7
7.2
8.5
7.9
3.8
6.9
7.3
6.5
5.5
5.8
5.4
4.7
5.5
5.7
5.1
0
4
8
12
16
20
24
28
32
36
40
44
Week
= Scheduled dose visit
FAS, LOCF
LOCF: Patients receiving treatment at Week 16 were considered not dry from Week 16 onward

FIG. 56

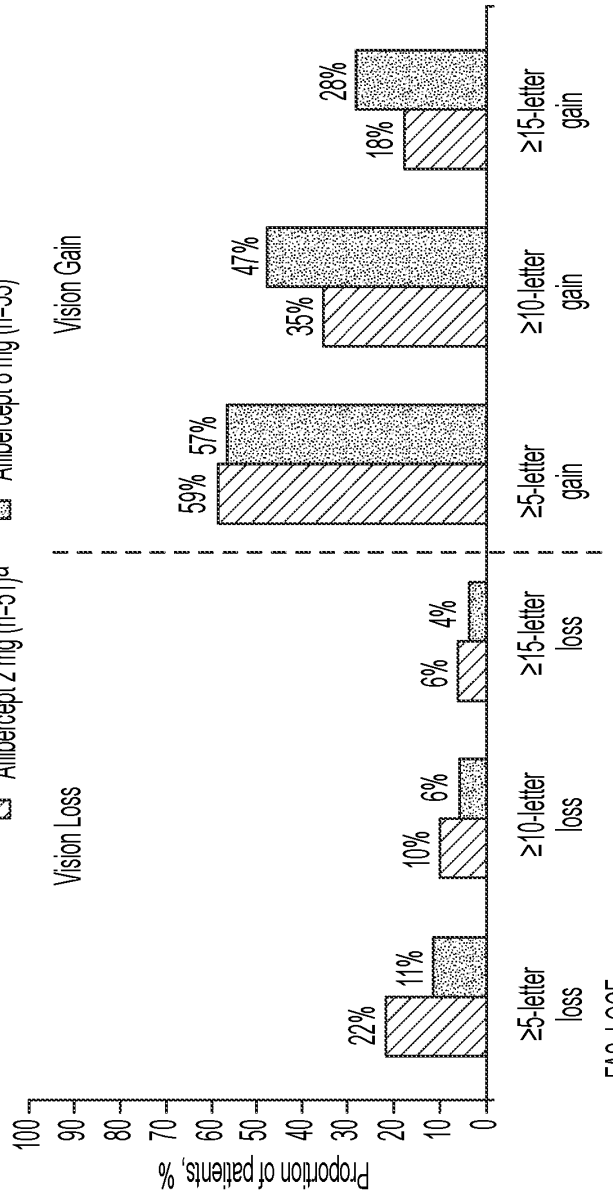

Proportion of Patients with Vision Loss or Gain at Week 44
Aflibercept 2 mg (n=51)a
Aflibercept 8 mg (n=53)
Vision Loss
Vision Gain
Proportion of patients, %
100
90
80
70
60
50
40
30
20
10
0
22%
11%
10%
6%
6%
4%
59%
57%
35%
47%
18%
28%
≥5-letter loss
≥10-letter loss
≥15-letter loss
≥5-letter gain
≥10-letter gain
≥15-letter gain
FAS, LOCF
aTwo patients in the aflibercept 2 mg group did not have post-baseline values

FIG. 57

Ocular TEAEs in Study Eye Occurring in ≥2% of Pts

	IAI (N=53)	HD (N=53)
Number of Patients with at Least One Ocular TEAE in Study Eye, n(%)	20 (37.7%)	20 (37.7%)
CONJUNCTIVAL HAEMORRHAGE	2 (3.8%)	3 (5.7%)
DRY EYE	2 (3.8%)	2 (3.8%)
MACULAR DEGENERATION	1 (1.9%)	1 (1.9%)
NEOVASCULAR AGE-RELATED MACULAR DEGENERATION	4 (7.5%)	2 (3.8%)
PUNCTATE KERATITIS	2 (3.8%)	1 (1.9%)
RETINAL HAEMORRHAGE	2 (3.8%)	1 (1.9%)
RETINAL TEAR	0	2 (3.8%)
SUBRETINAL FLUID	1 (1.9%)	1 (1.9%)
VISUAL ACUITY REDUCED	2 (3.8%)	1 (1.9%)
VISUAL IMPAIRMENT	2 (3.8%)	1 (1.9%)
VITREOUS DETACHMENT	2 (3.8%)	4 (7.5%)

FIG. 58

Ocular Serious TEAEs in Study Eye

	IAI (N=53)	HD (N=53)
Number of Patients with at Least One Ocular SAE in the Study Eye*, n (%)	1 (1.9%)	2 (3.8)
VISUAL ACUITY REDUCED	1 (1.9%)	0
RETINAL TEAR	0	1 (1.9%)
VISUAL IMPAIRMENT	0	1 (1.9%)

**No Ocular SAEs occurred in the Fellow Eye*

FIG. 59

Intraocular Inflammation TEAEs in Study Eye

	IAI (N=53)	HD (N=53)
Number of Patients with at Least One Such AE, n (%)	0	1 (1.9%)
IRITIS	0	1 (1.9%)

Iritis was characterized as mild cells in the anterior chamber which resolved within 1 month with topical therapy

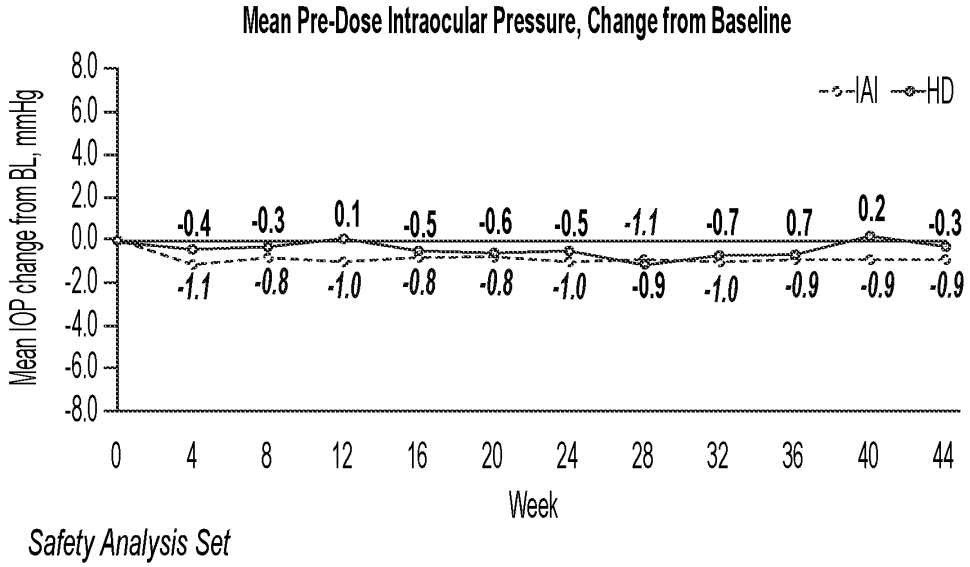
FIG. 60

Summary of Intraocular Pressure Events

	IAI (n=53)	HD (n=53)
# pts with ≥10 mmHg Increase in pre-injection IOP from BL	0/51	2/53 (3.8%)
# pts with pre-injection IOP ≥25 mmHg at any visit	0/53	2/53 (3.8%)
# pts with any visit IOP ≥35 mmHg at Any Time	0/53	0/53

Safety Analysis Set
Percentages are calculated based on N

FIG. 61



Safety Analysis Set

FIG. 62

Non-Ocular TEAEs Occurring in ≥2% of Patients

	IAI (N=53)	HD (N=53)
Number of Patients with at Least One Non-Ocular TEAE, n(%)	24 (45.3%)	28 (52.8%)
DIARRHEA	1 (1.9%)	2 (3.8%)
GASTRITIS	1 (1.9%)	1 (1.9%)
GASTROOESOPHAGEAL REFLUX DISEASE	2 (3.8%)	0
NAUSEA	0	2 (3.8%)
CHEST PAIN	0	2 (3.8%)
COVID-19	2 (3.8%)	2 (3.8%)
SINUSITIS	2 (3.8%)	1 (1.9%)
URINARY TRACT INFECTION	1 (1.9%)	2 (3.8%)
FALL	2 (3.8%)	3 (5.7%)
ARTHRALGIA	2 (3.8%)	0
CARPAL TUNNEL SYNDROME	1 (1.9%)	1 (1.9%)
DIZZINESS	0	3 (5.7%)
HYPERTENSION	1 (1.9%)	1 (1.9%)

FIG. 63

Non-Ocular Serious TEAEs

	IAI (N=53)	HD (N=53)
Number of Patients with at Least One Non-Ocular SAE, n(%)	4 (7.5%)	5 (9.4%)
ACUTE LEFT VENTRICULAR FAILURE	0	1 (1.9%)
COLITIS	1 (1.9%)	0
SMALL INTESTINAL OBSTRUCTION	1 (1.9%)	0
CHEST PAIN	0	1 (1.9%)
NON-CARDIAC CHEST PAIN	0	1 (1.9%)
COVID-19	1 (1.9%)	0
FEMUR FRACTURE	1 (1.9%)	0
LUMBAR SPINAL STENOSIS	0	1 (1.9%)
HEPATIC ENCEPHALOPATHY	0	1 (1.9%)
TRANSIENT ISCHEMIC ATTACK	0	1 (1.9%)
ACUTE RESPIRATORY FAILURE	0	1 (1.9%)

FIG. 64

Hypertension TEAEs

	IAI (N=53)	HD (N=53)
Number of Patients with at Least One Such AE, n (%)	1 (1.9%)	1 (1.9%)
Worsening Hypertension	1 (1.9%)	1 (1.9%)

FIG. 65

Adjudicated APTC Events and Deaths

	IAI (N=53)	HD (N=53)
Adjudicated APTC Events, n	0	0
Deaths, n	0	1*

*Death due to glioblastoma

FIG. 66