

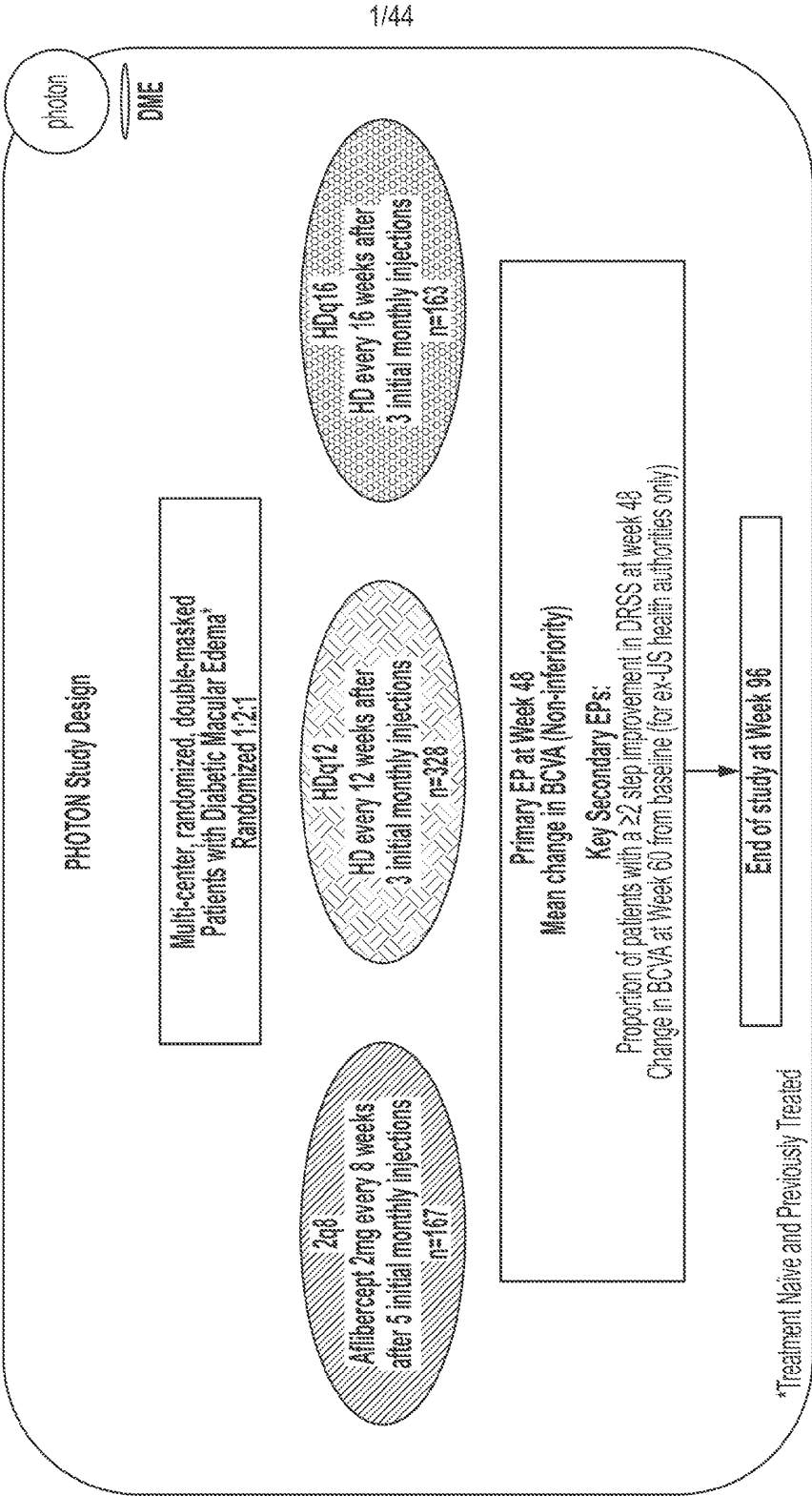


FIG. 1

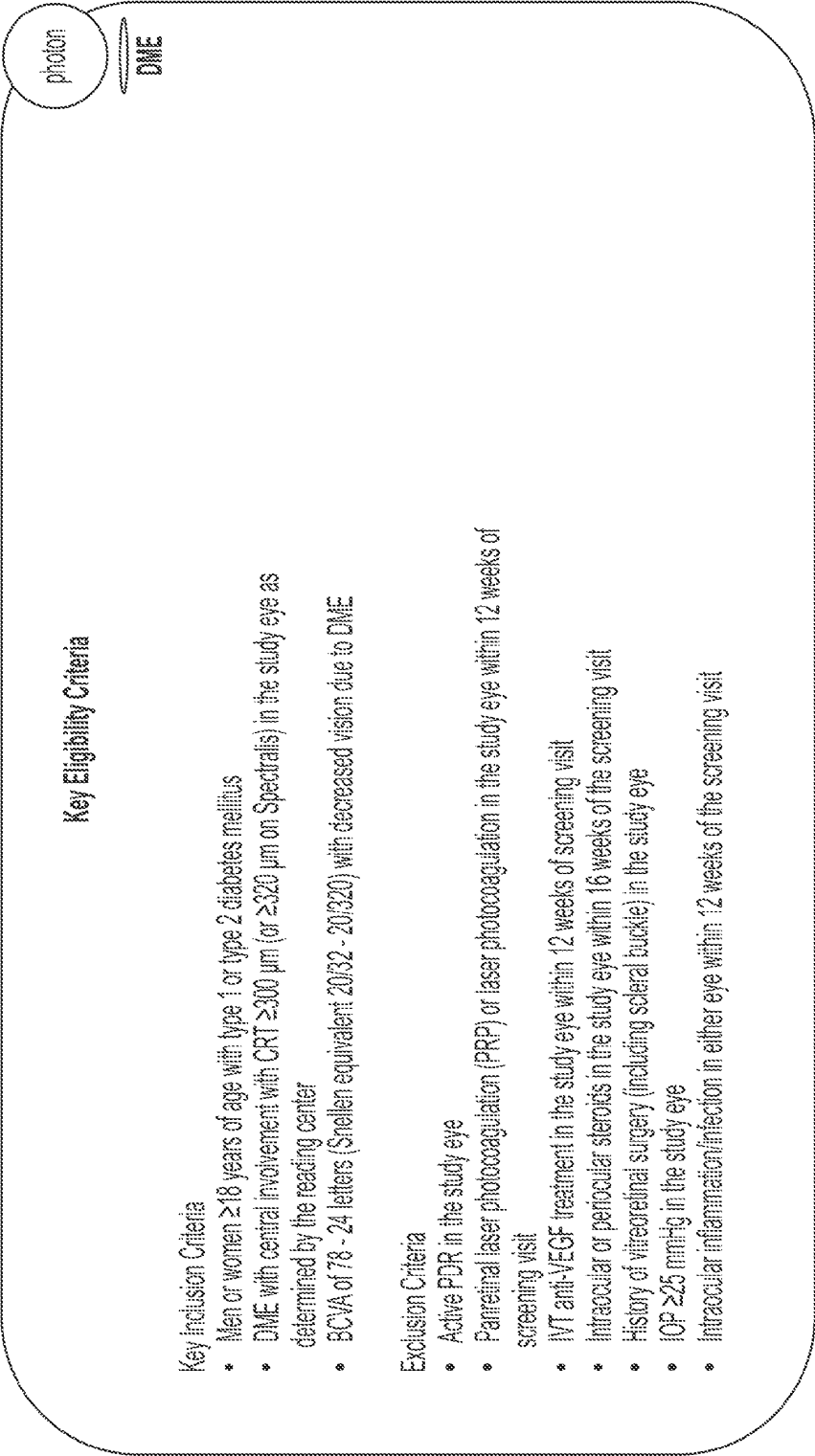
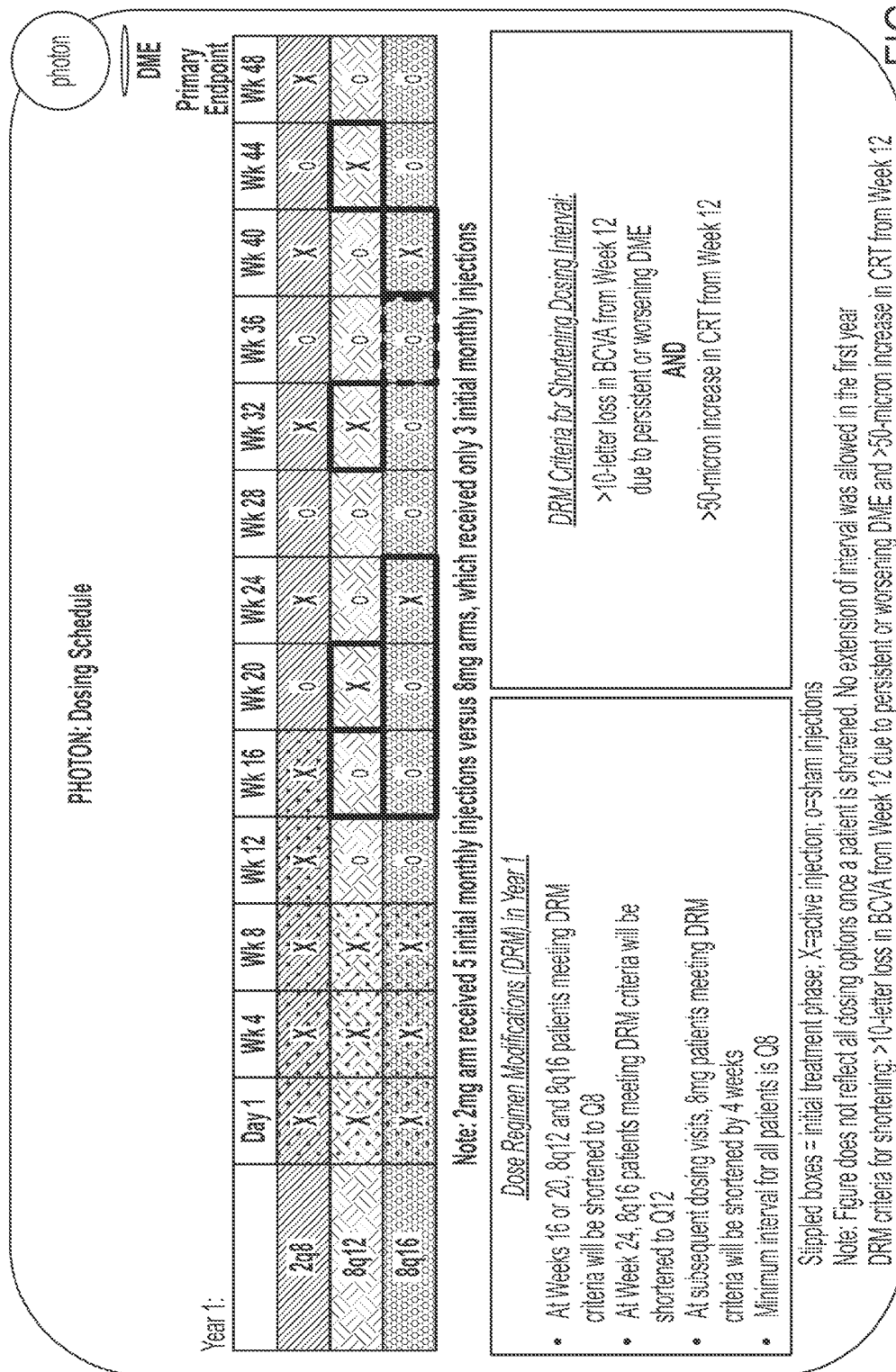


FIG. 2



3
G
L

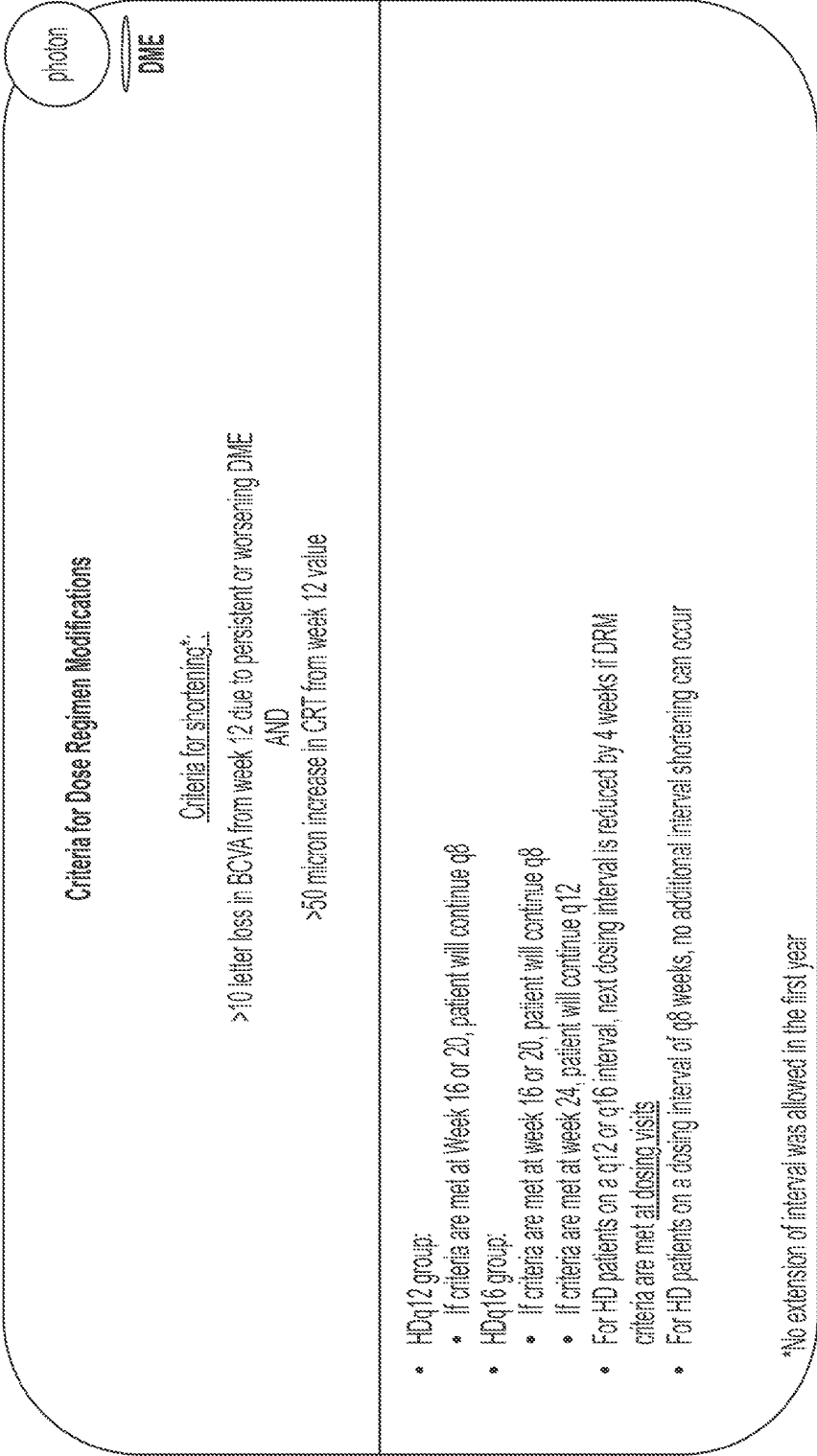


FIG. 4

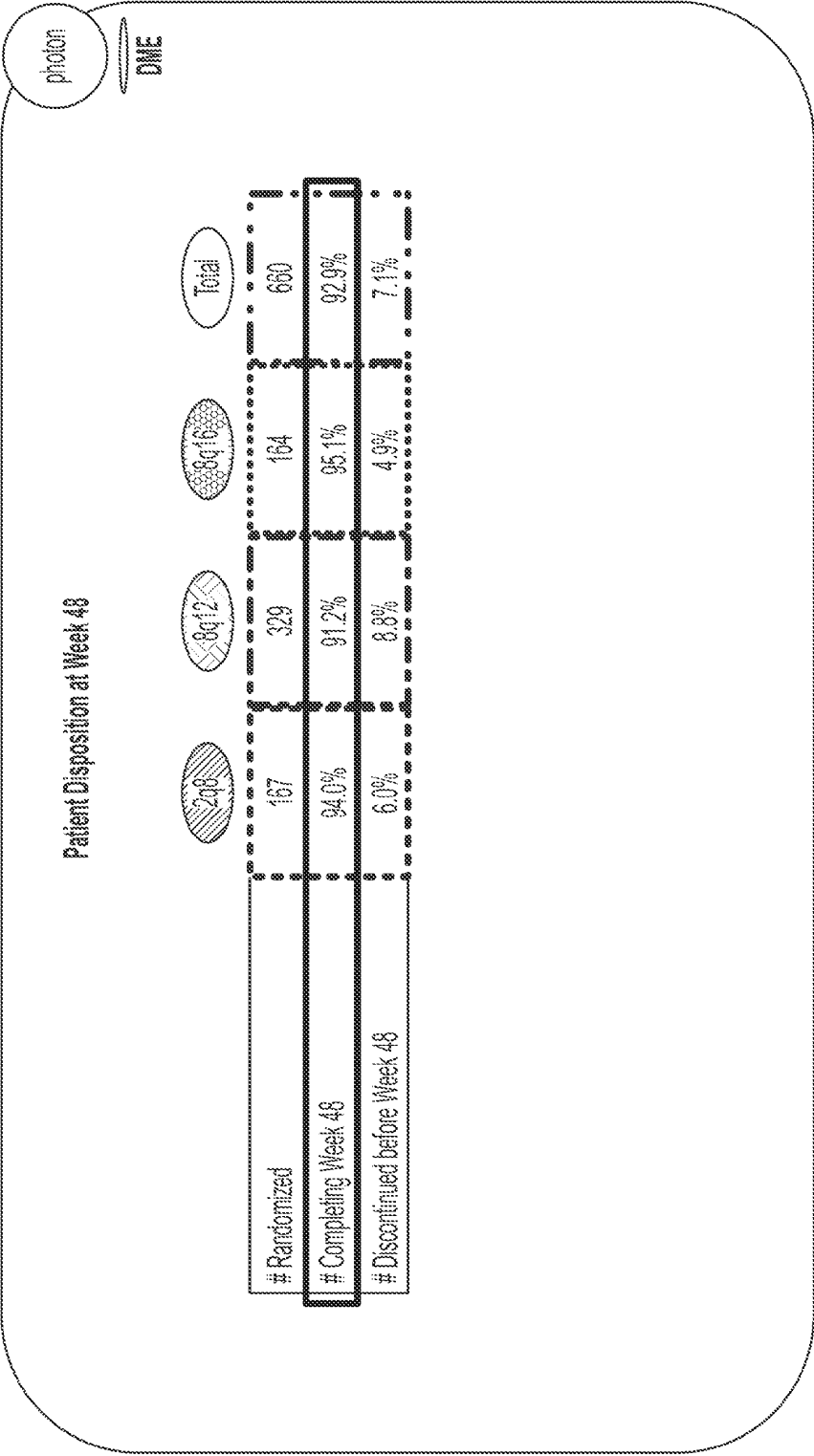


FIG. 5

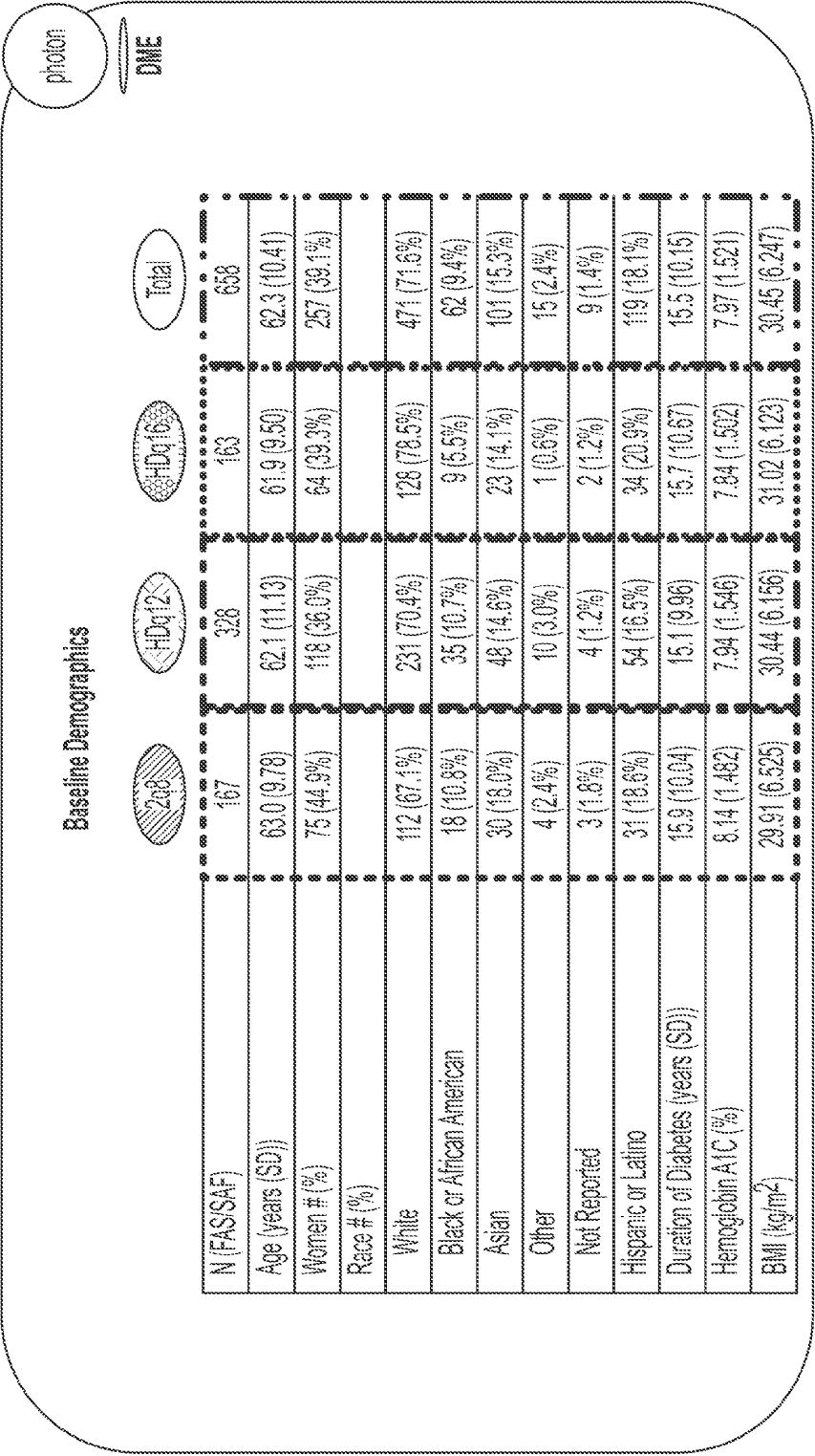


FIG. 6

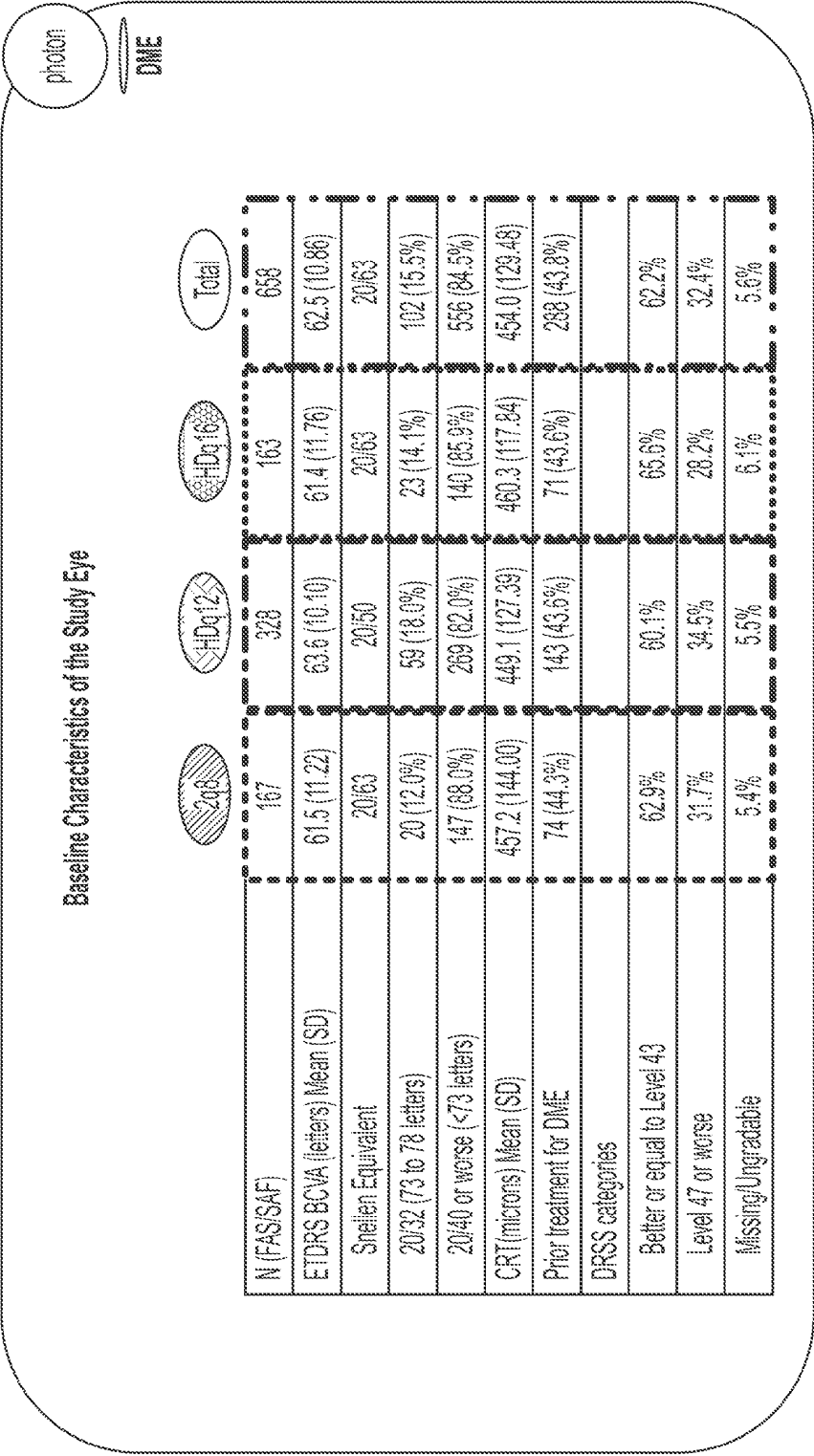


FIG. 7

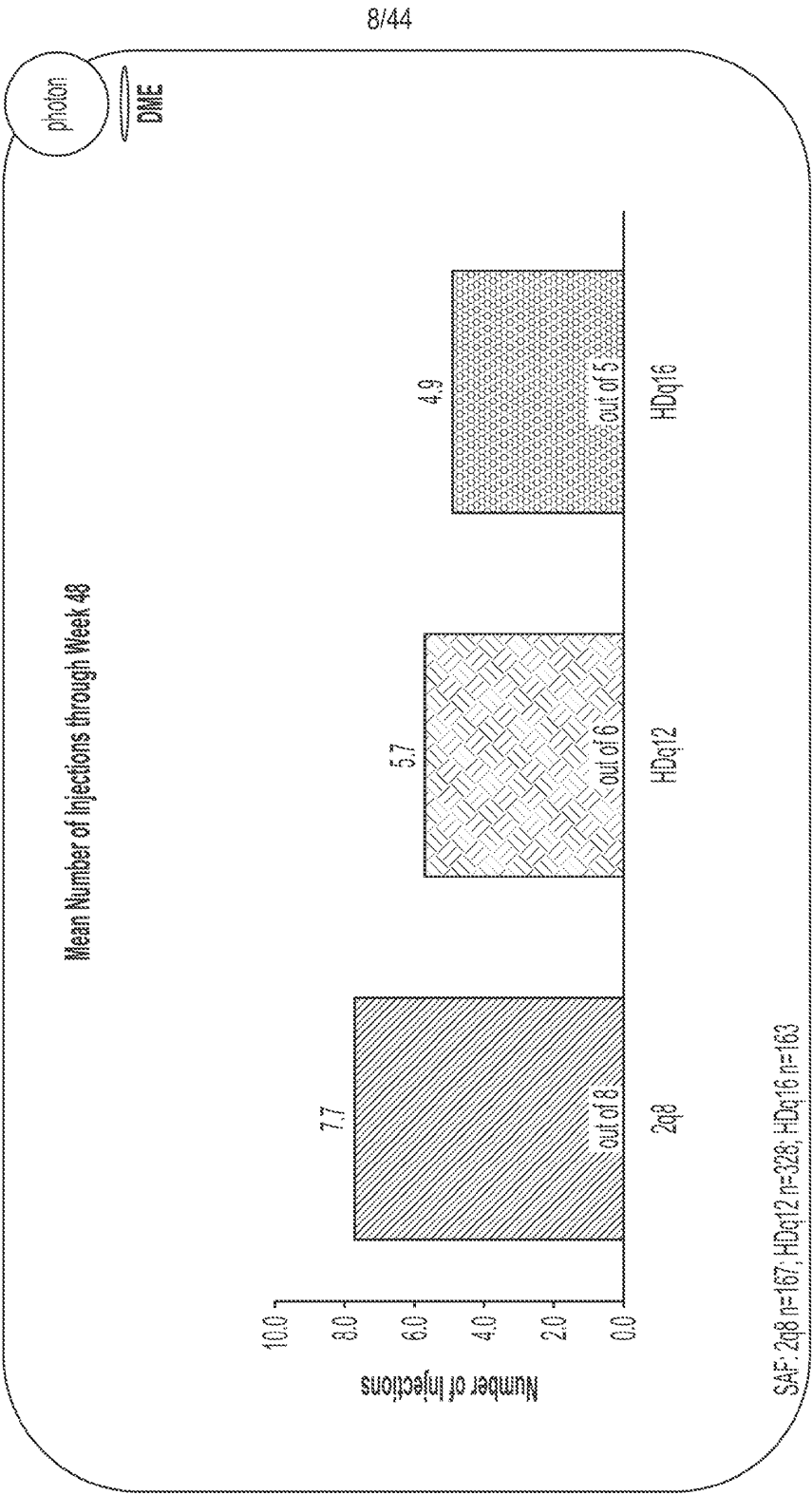


FIG. 8

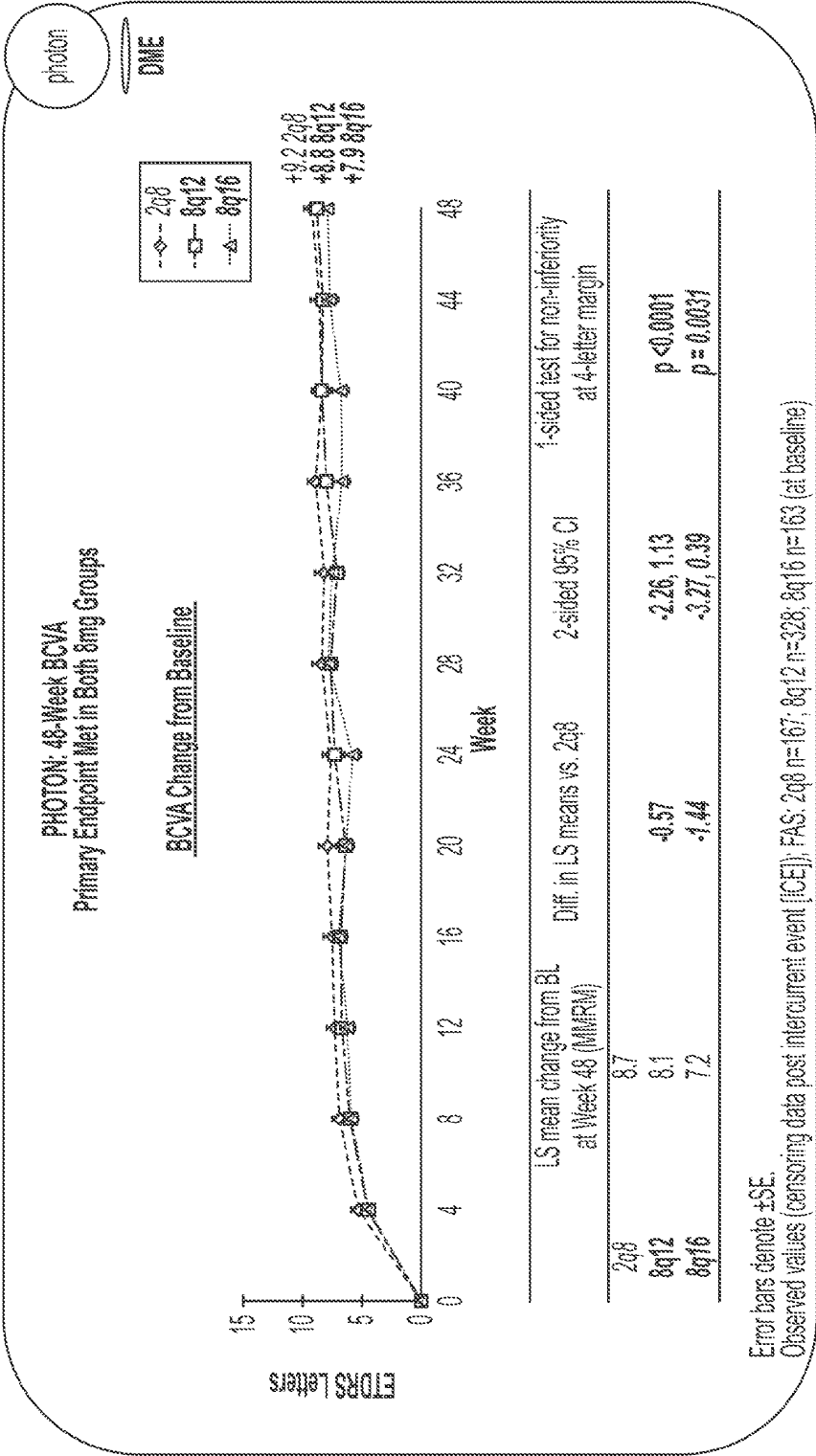


FIG. 9

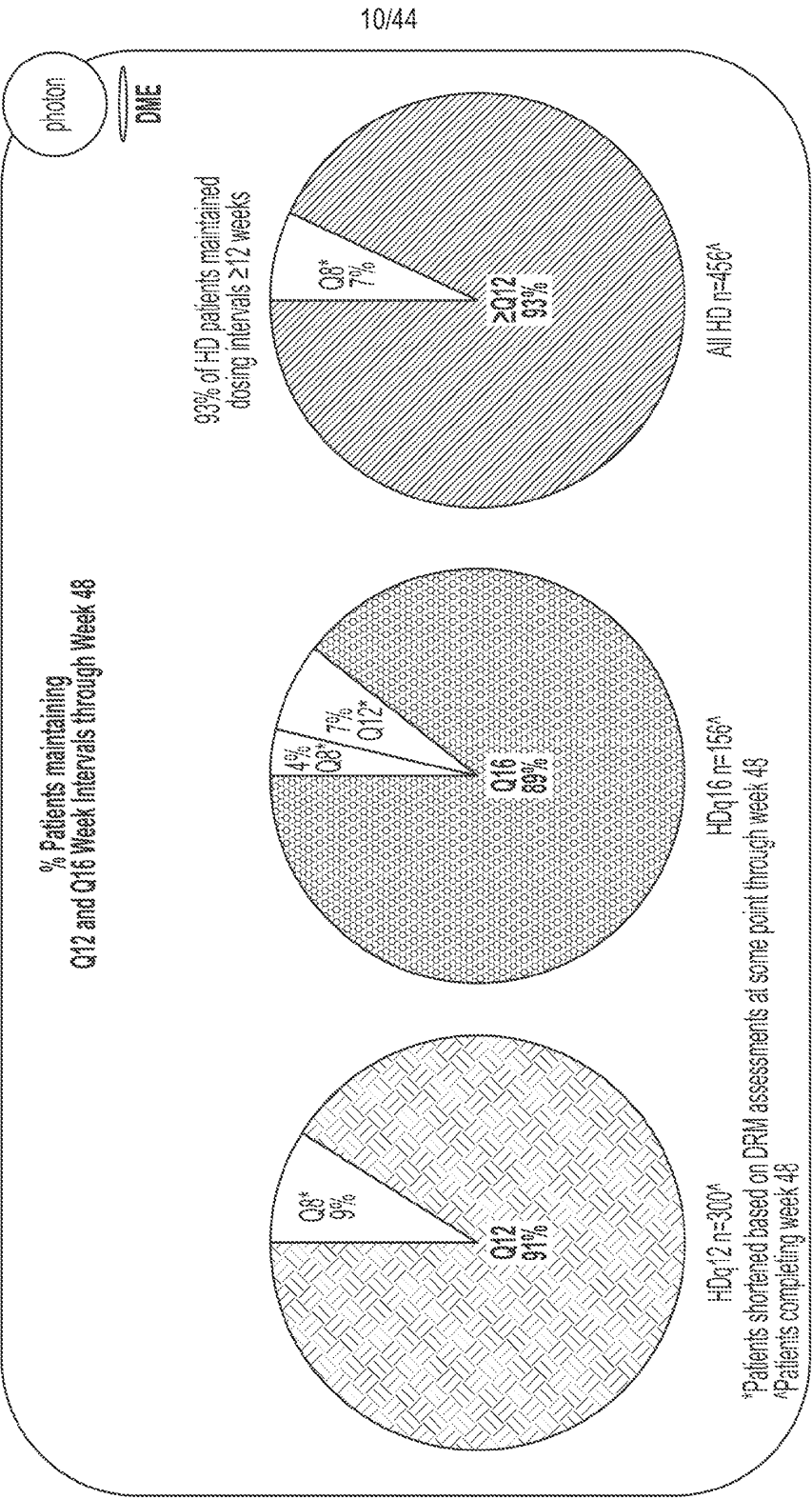


FIG. 10

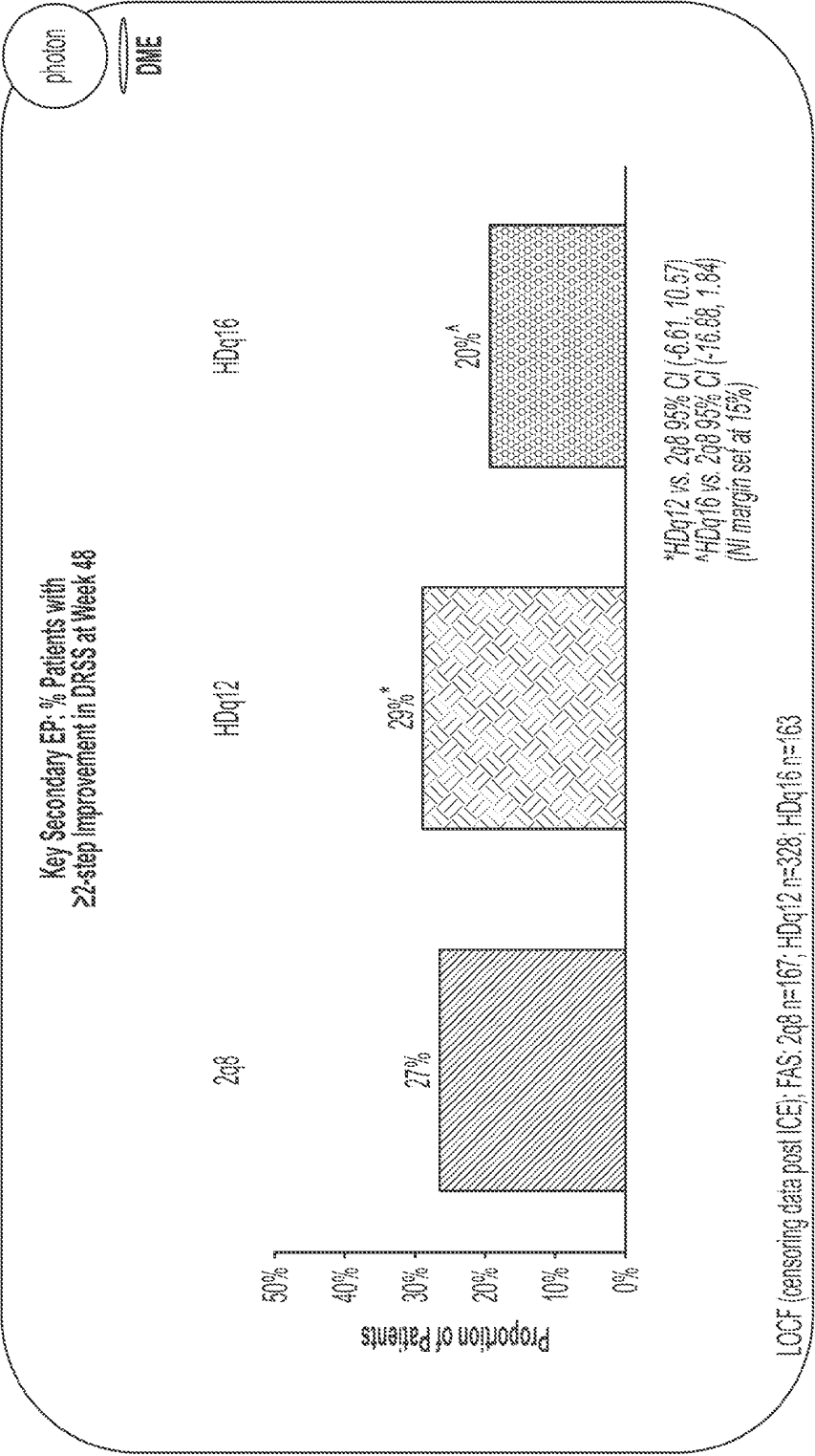


FIG. 11

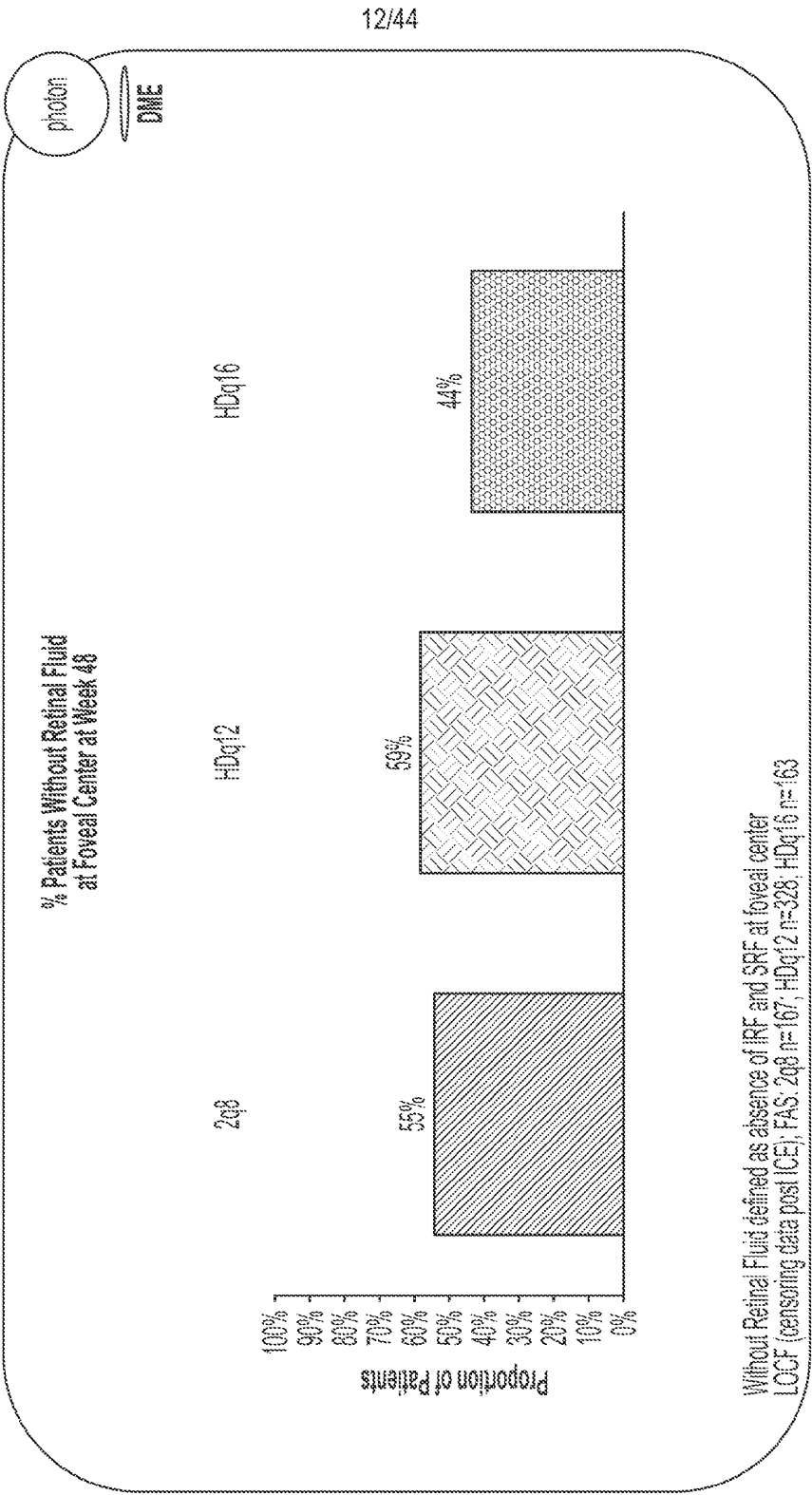


FIG. 12

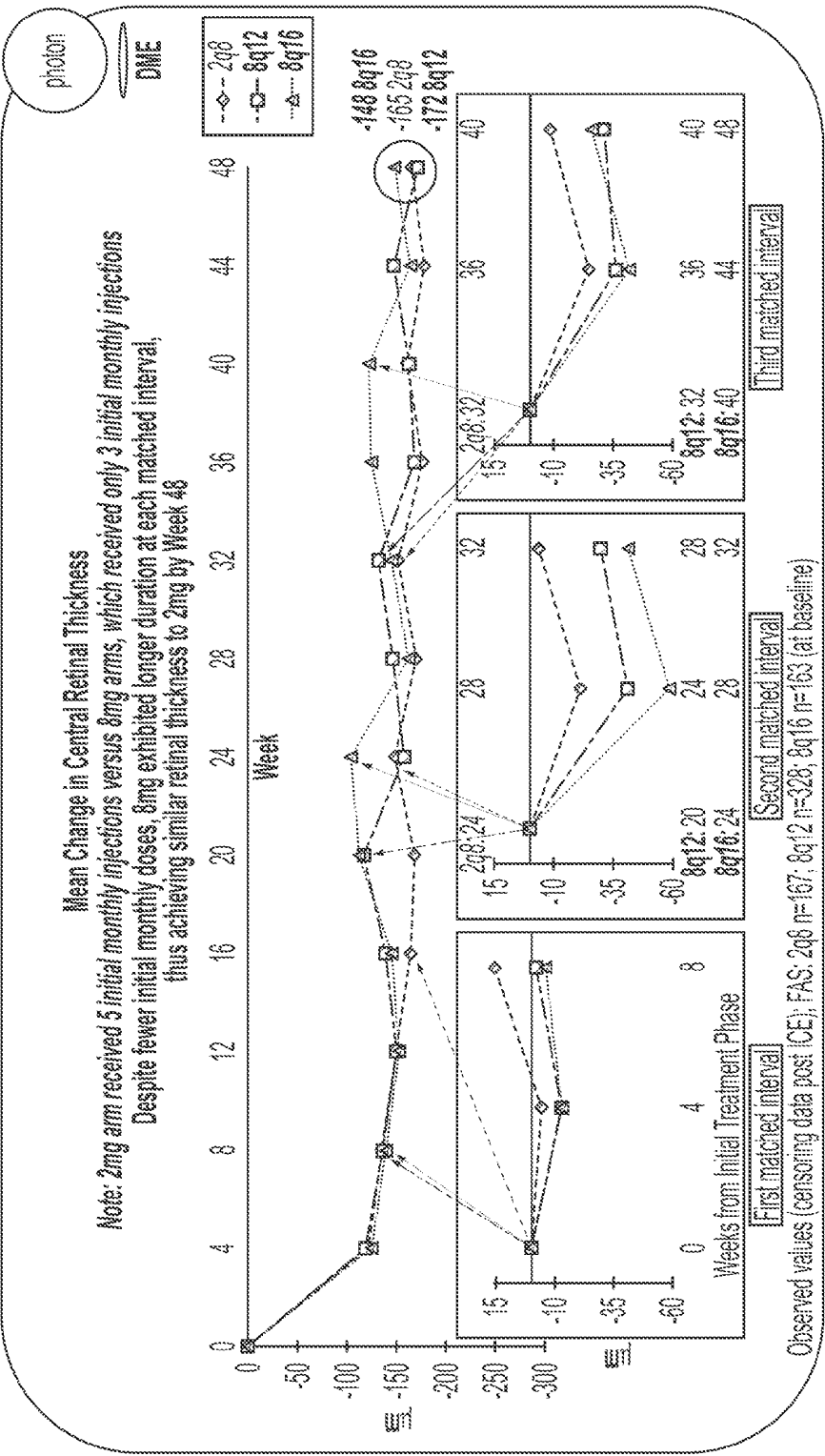
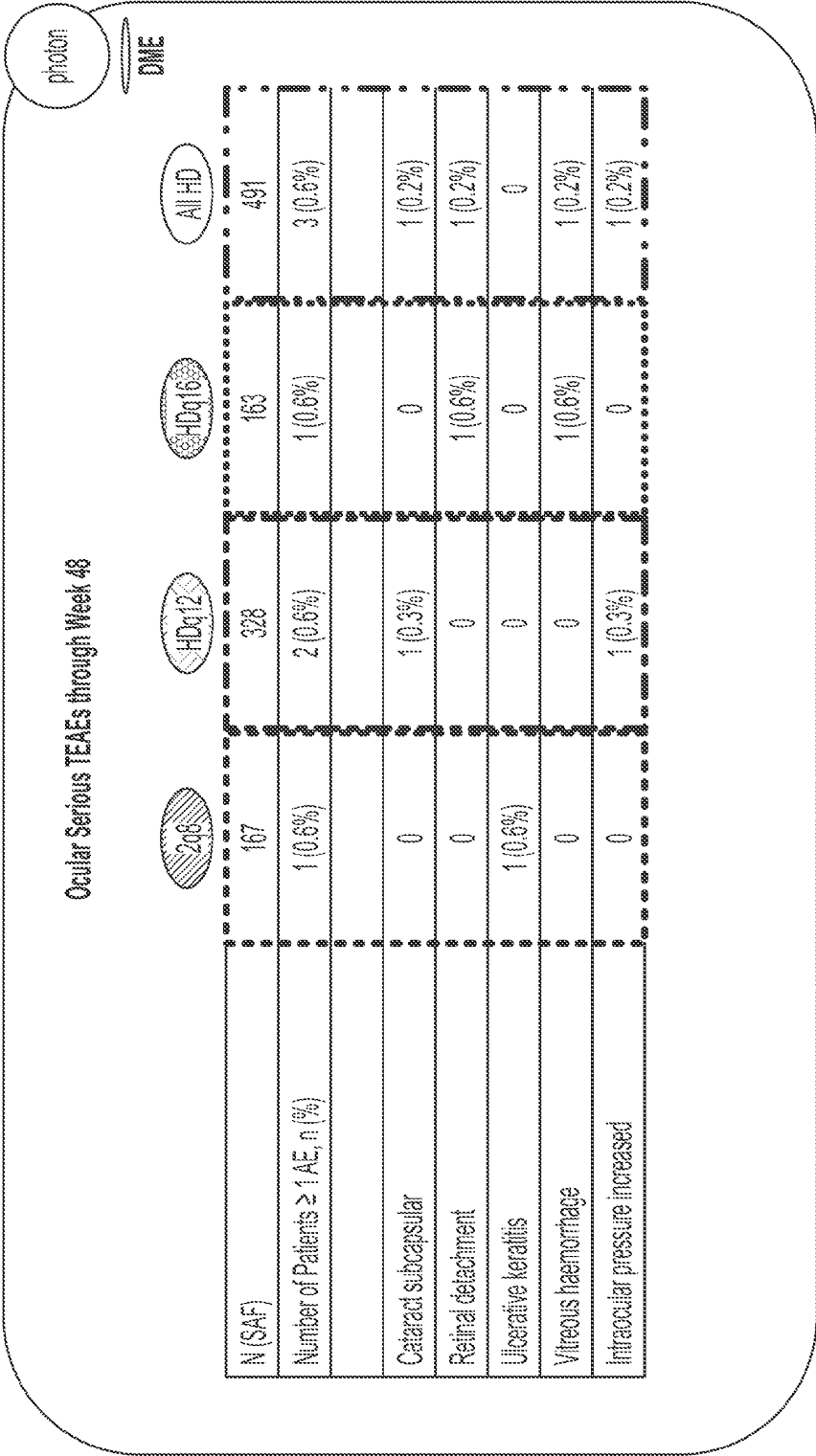


FIG. 13



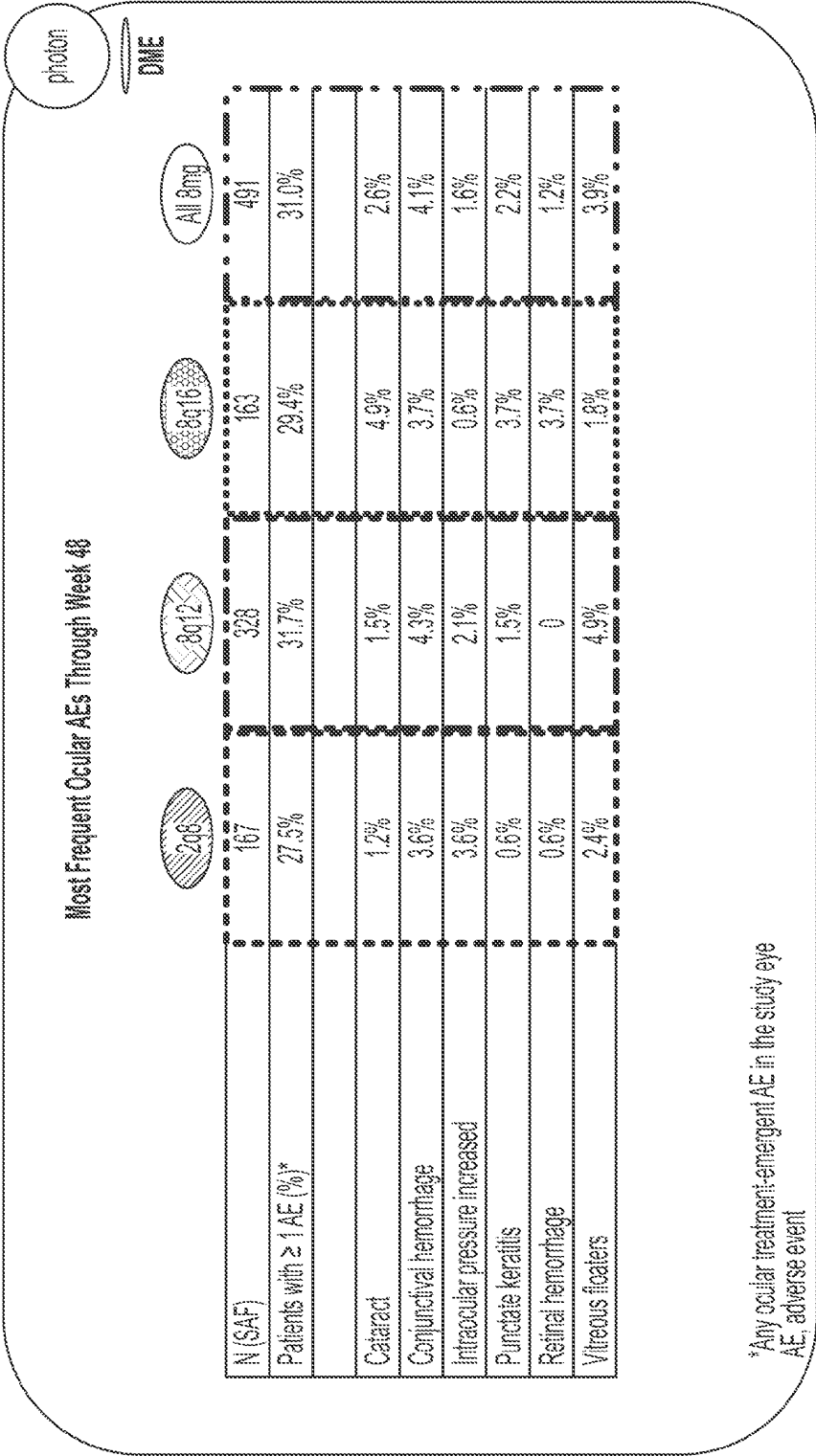


FIG. 14B

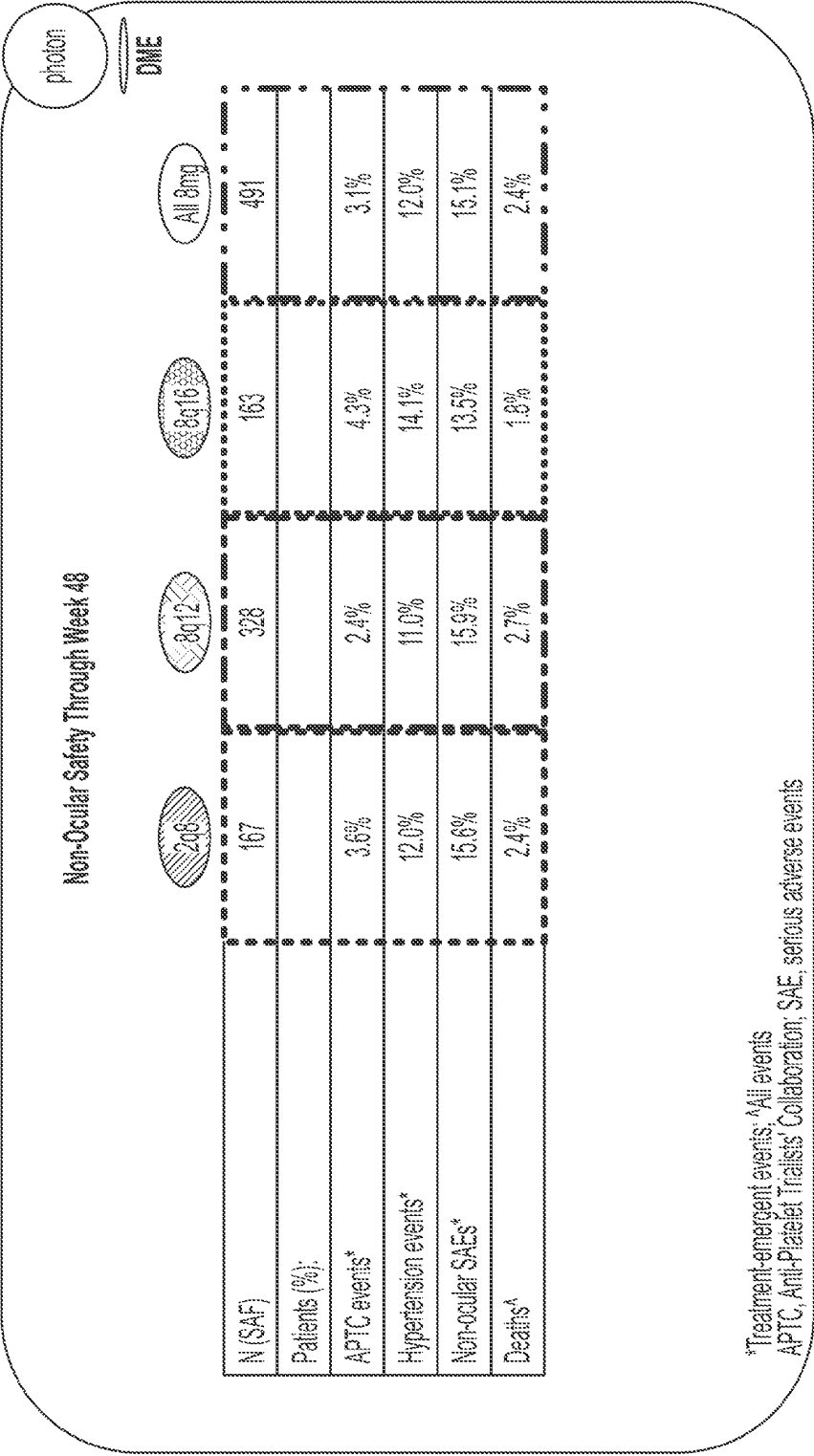


FIG. 14C

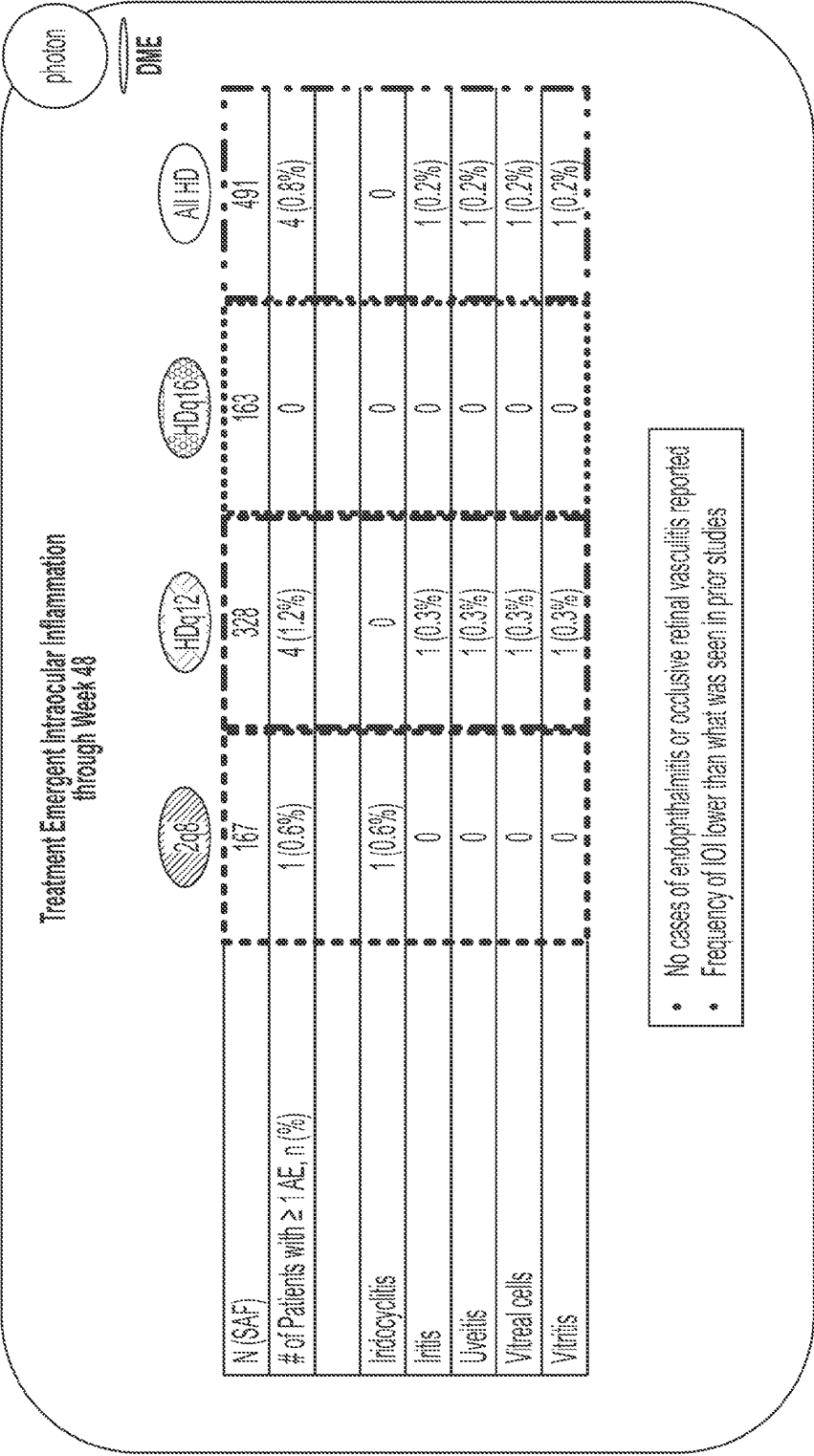


FIG. 15

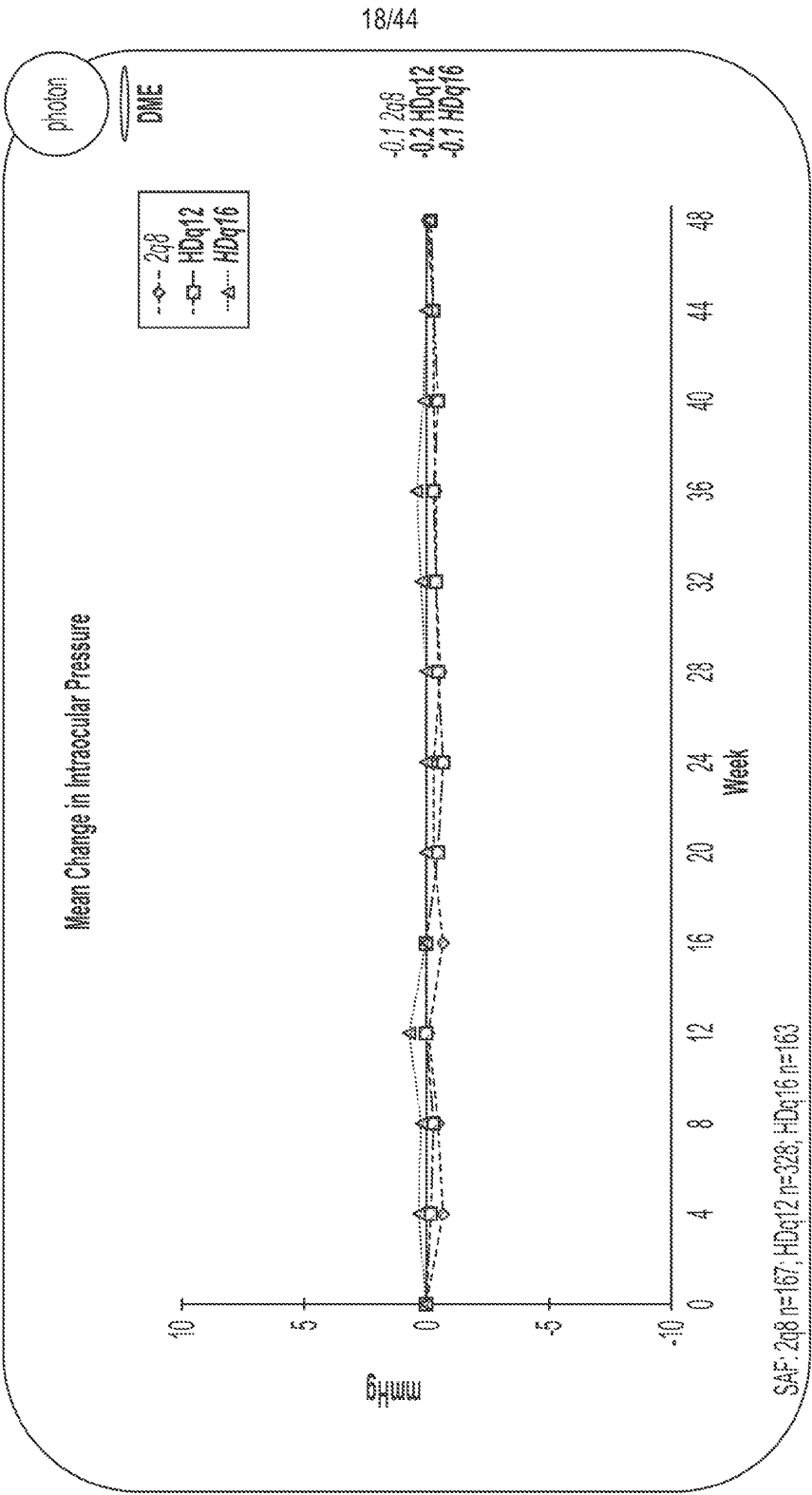
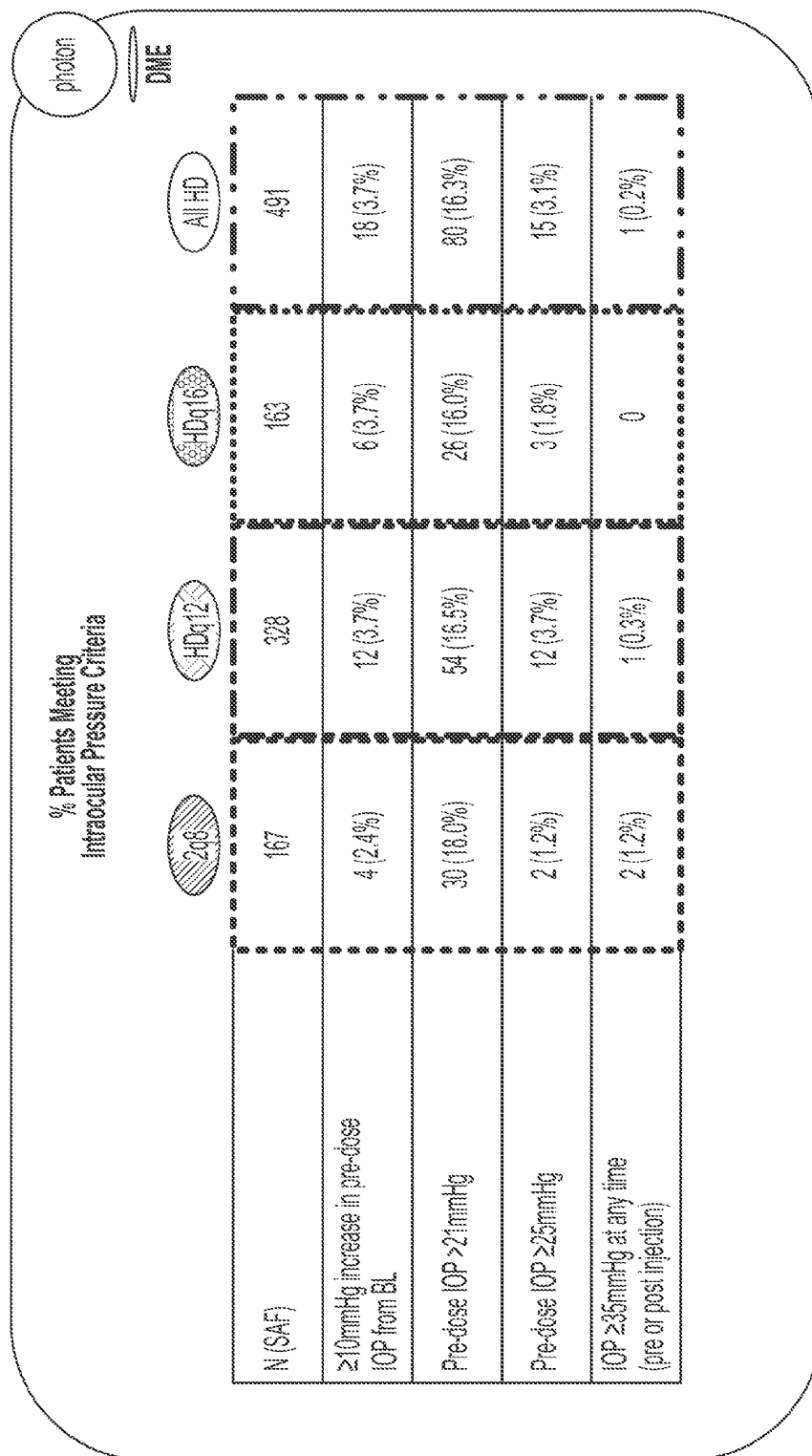


FIG. 16



photon

DME

Non-Ocular Serious TEAEs ≥1% through Week 48

	206	HDq12	HDq16	All HD
N (SAF)	167	328	163	491
Number of Patients ≥ 1 AE, n (%)	26 (15.6%)	52 (15.9%)	20 (12.3%)	72 (14.7%)
Acute left ventricular failure	3 (1.8%)	1 (0.3%)	0	1 (0.2%)
Acute myocardial infarction	2 (1.2%)	1 (0.3%)	1 (0.6%)	2 (0.4%)
Cardiac arrest	2 (1.2%)	2 (0.6%)	0	2 (0.4%)
Coronary artery disease	1 (0.6%)	1 (0.3%)	2 (1.2%)	3 (0.6%)
Myocardial infarction	2 (1.2%)	3 (0.9%)	1 (0.6%)	4 (0.8%)
COVID-19 pneumonia	2 (1.2%)	2 (0.6%)	0	2 (0.4%)
Gangrene	2 (1.2%)	0	0	0
Pneumonia	1 (0.6%)	4 (1.2%)	0	4 (0.8%)
Hyponatraemia	2 (1.2%)	0	0	0
Cerebrovascular accident	0	2 (0.6%)	3 (1.8%)	5 (1.0%)
Acute kidney injury	0	4 (1.2%)	0	4 (0.8%)
Acute respiratory failure	2 (1.2%)	1 (0.3%)	2 (1.2%)	3 (0.6%)

FIG. 18

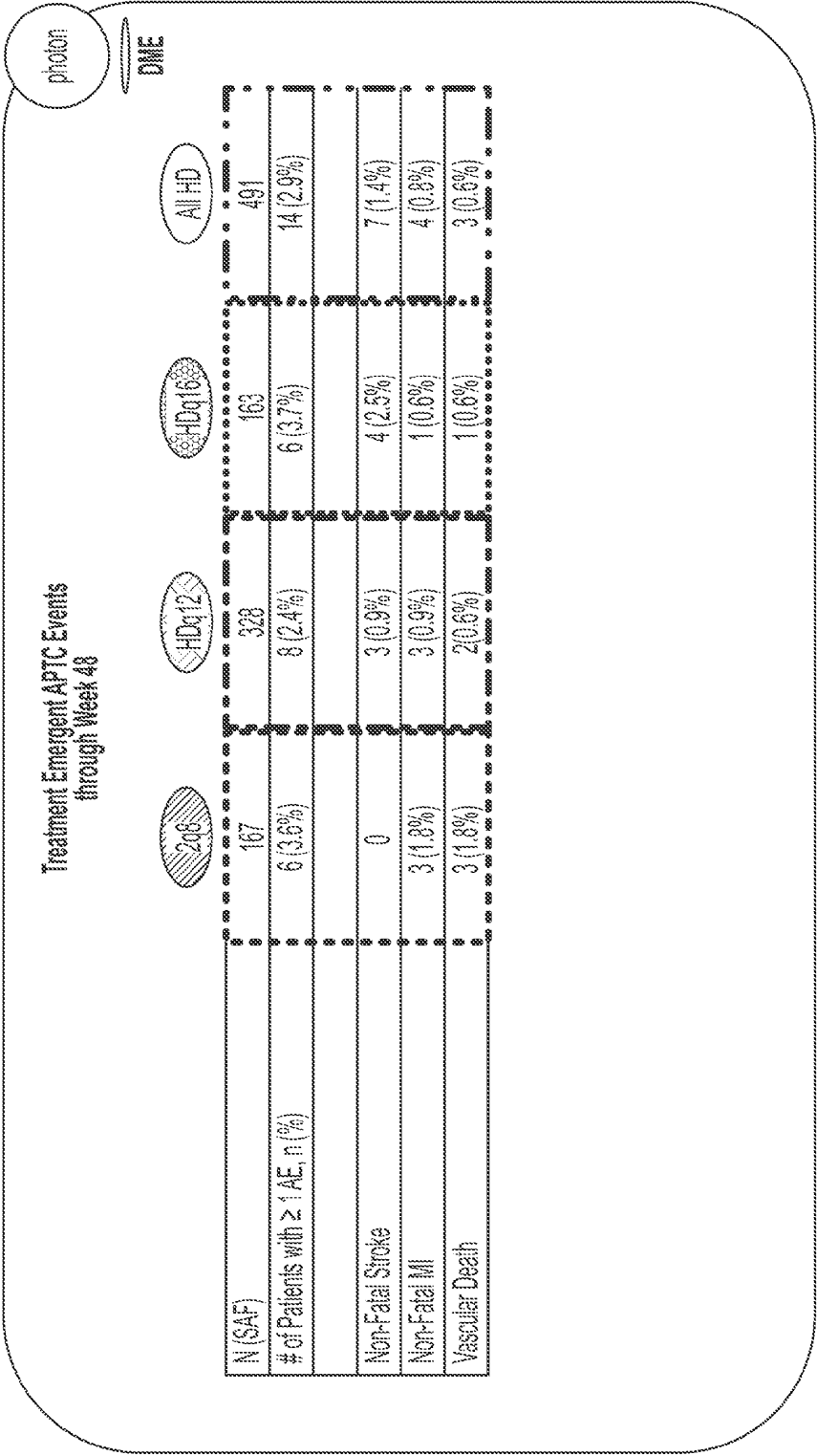


FIG. 19

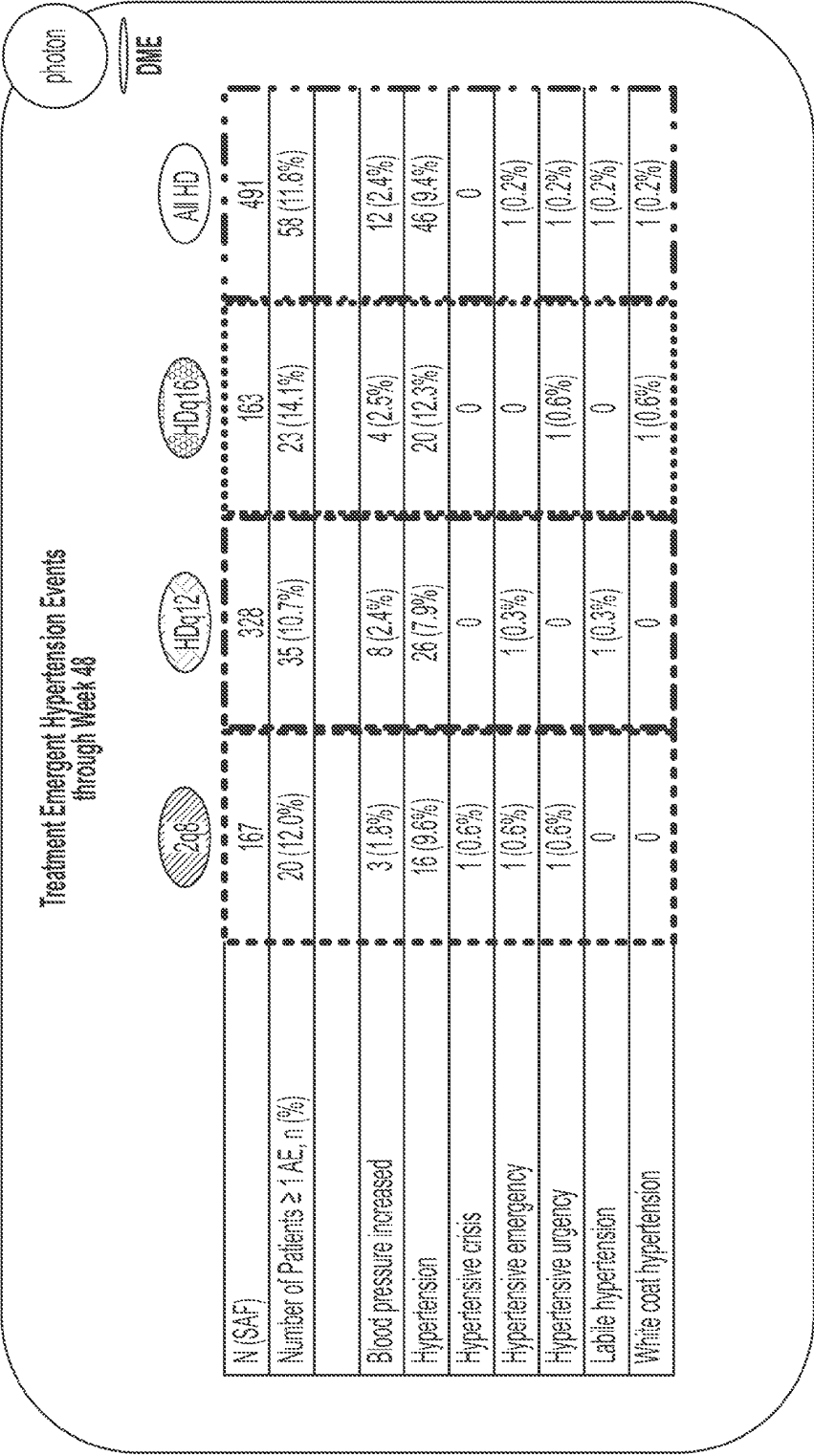


FIG. 20

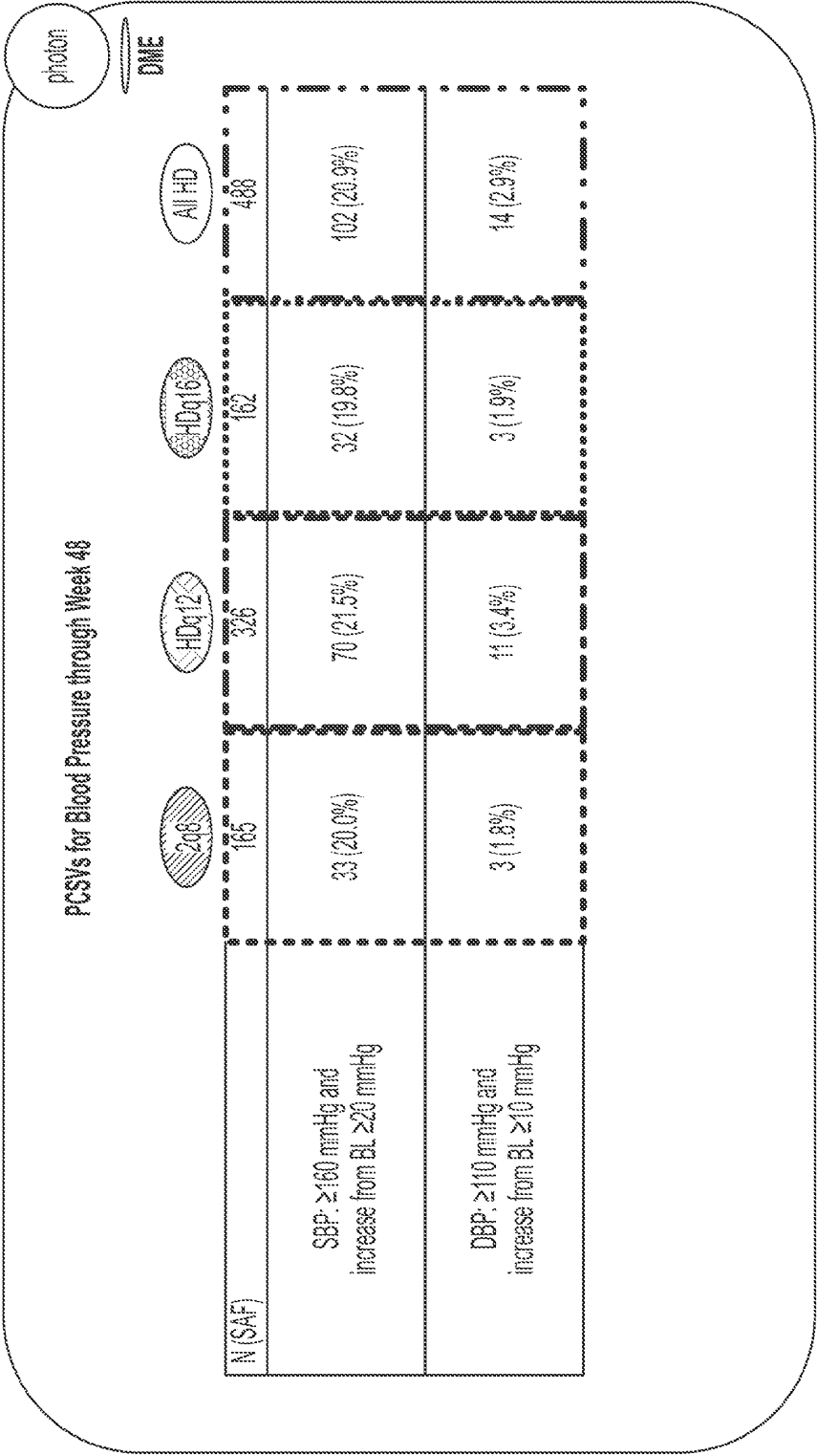


FIG. 21

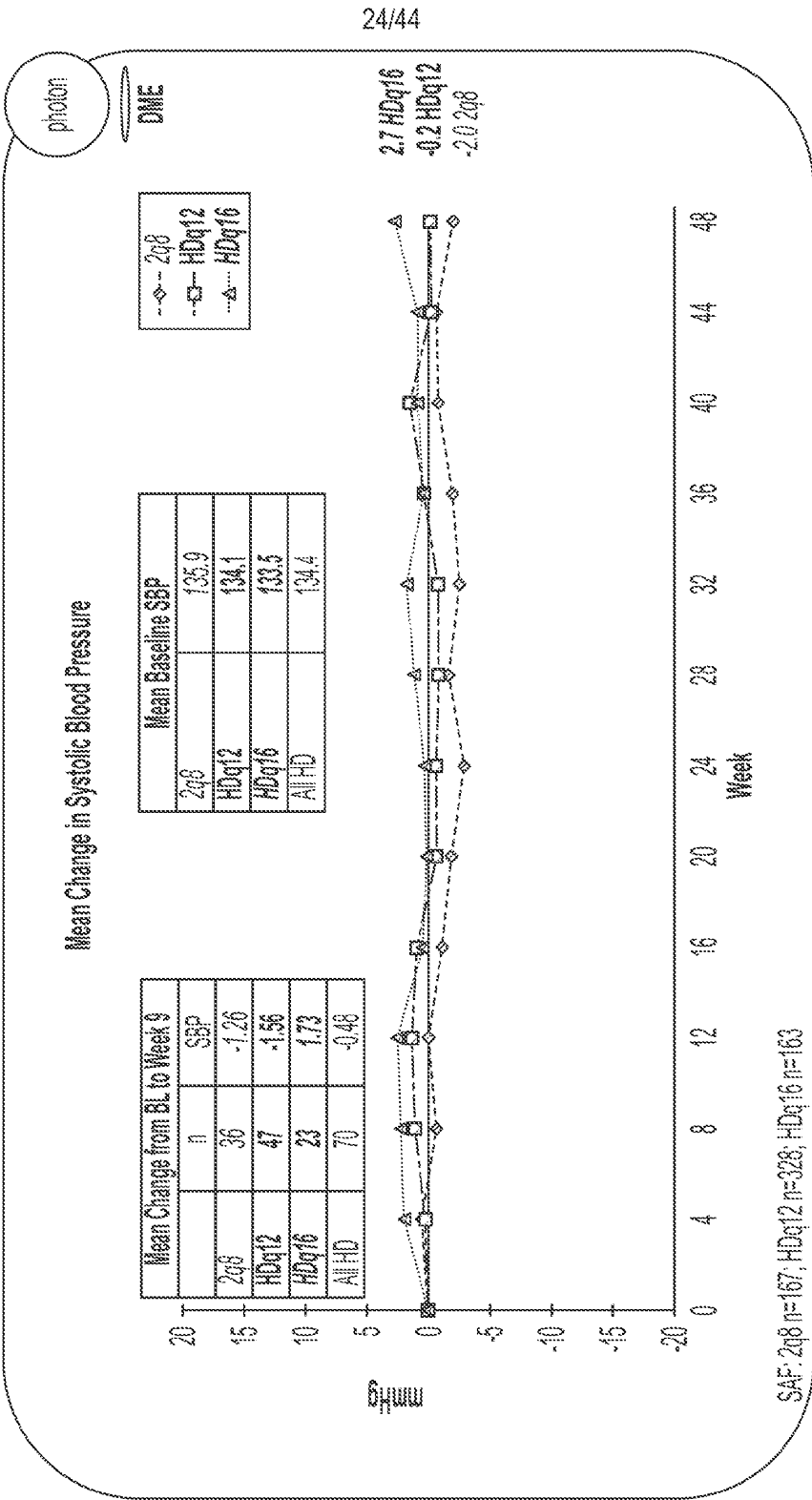


FIG. 22

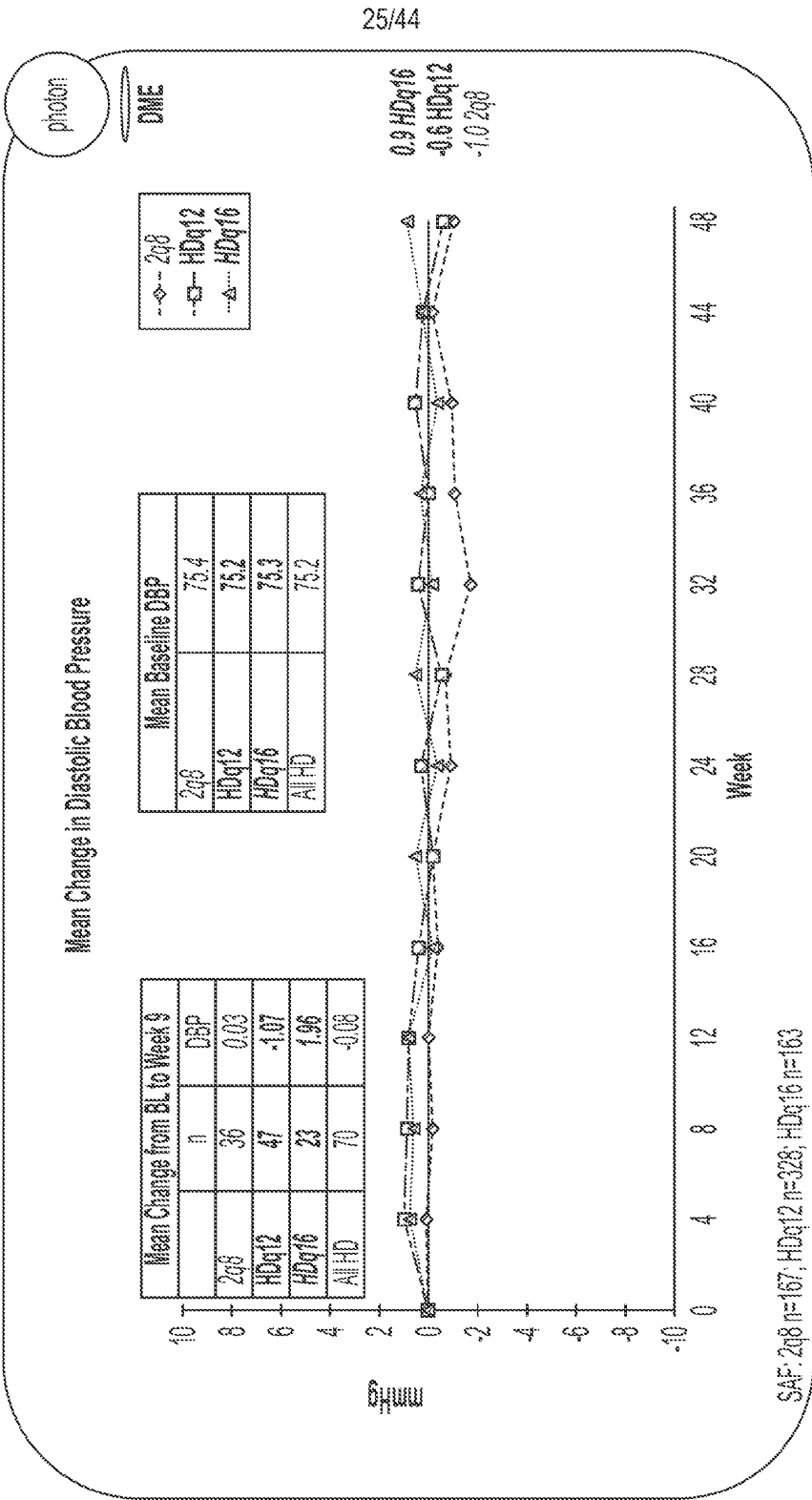


FIG. 23

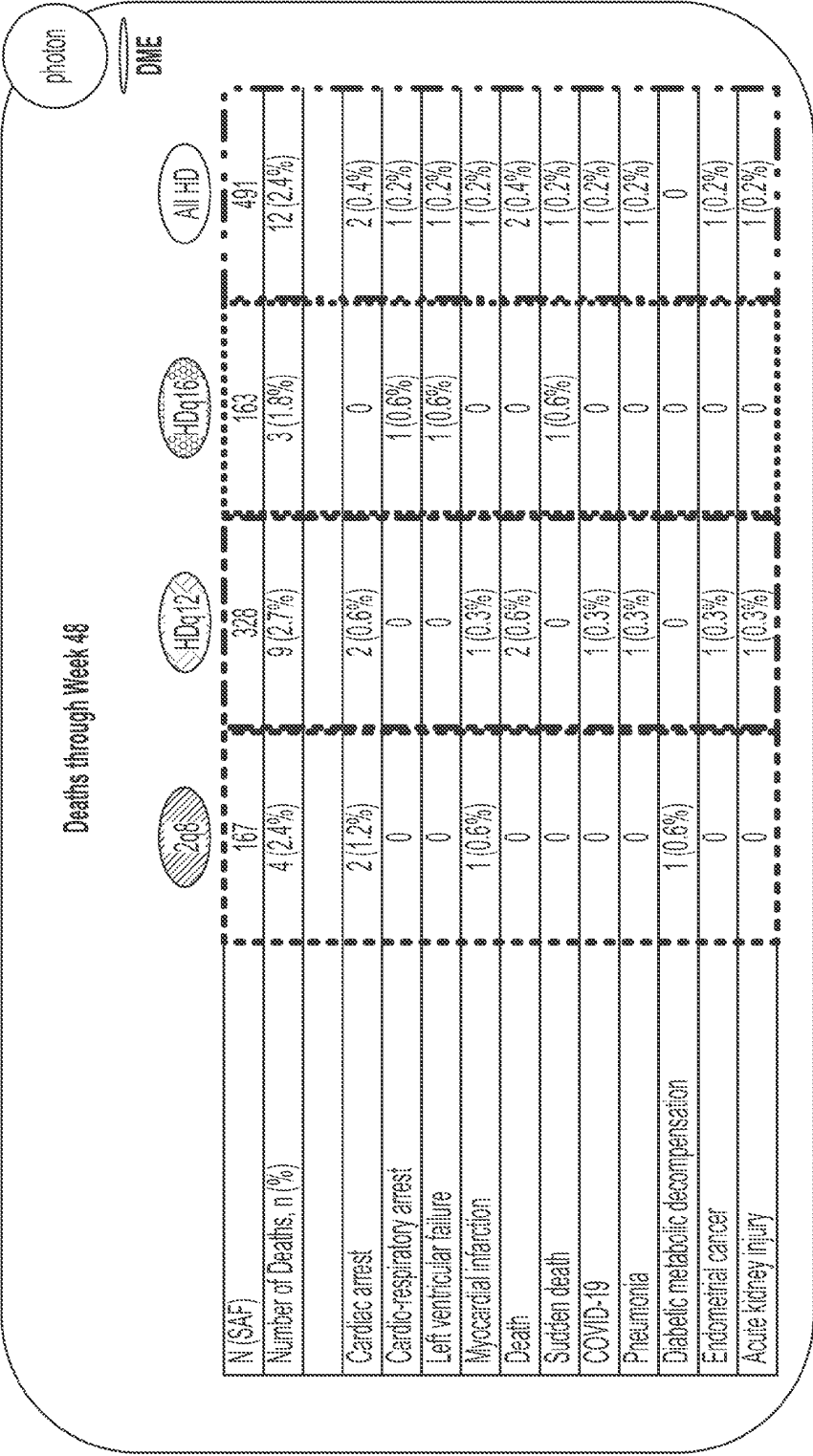
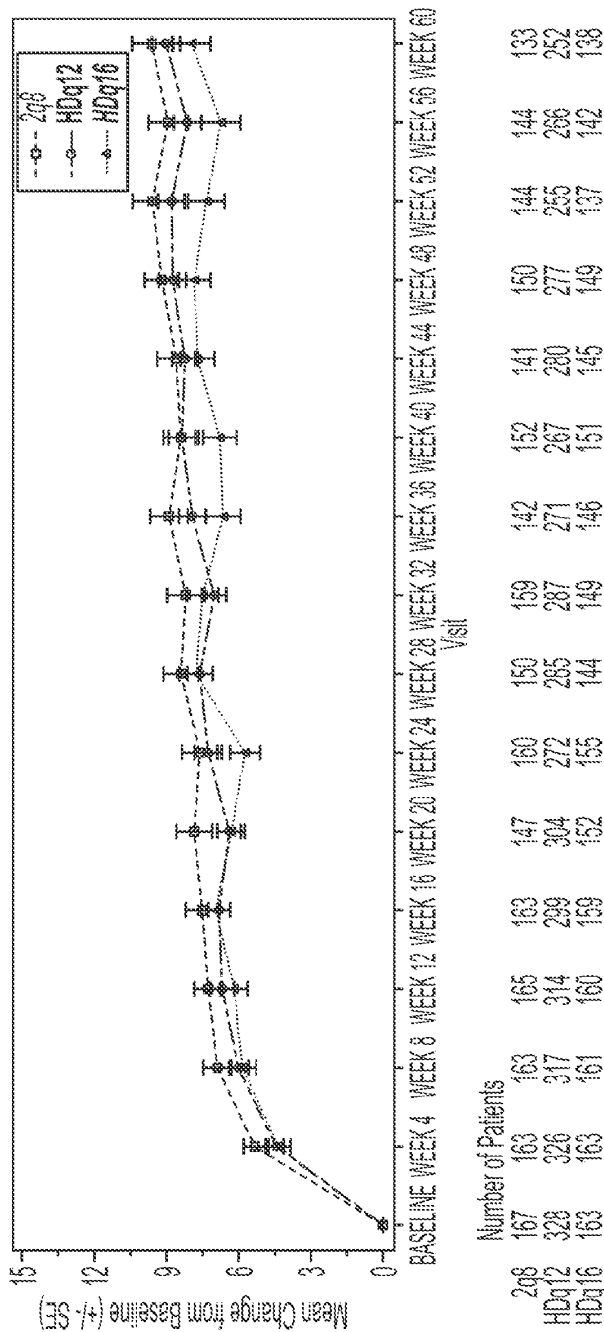


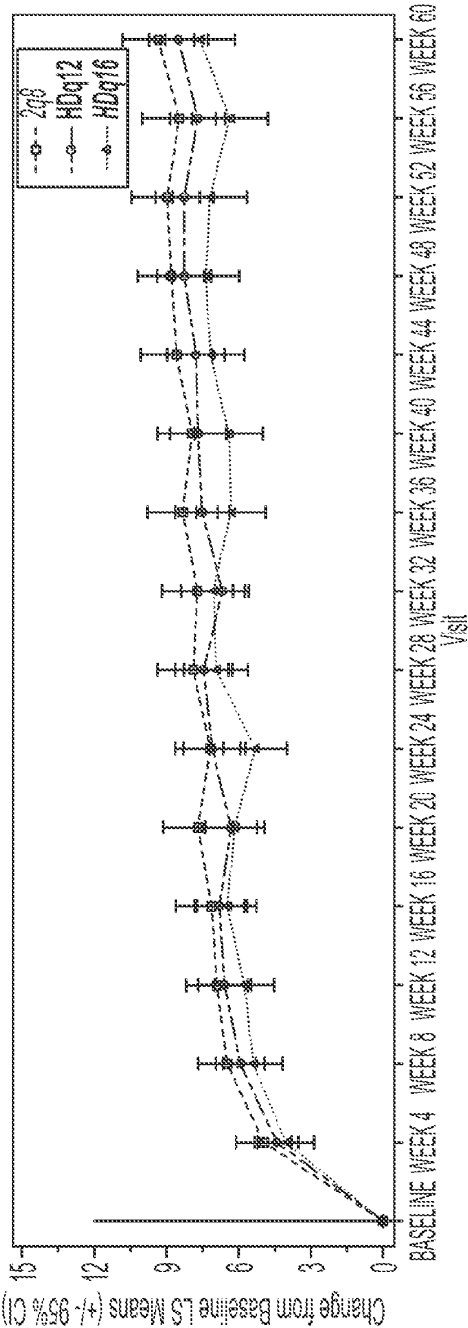
FIG. 24



BCVA=best-corrected visual activity, ETDRS=Early Treatment of Diabetic Retinopathy Study, HD=high dose;
OC=observed cases, SE=standard error.

OC: Observations after an ICE defined for the primary estimand were excluded.

FIG. 25A



Abbreviations: 2q8: Afibercept 2 mg administered every 8 weeks after 5 initial injections at 4-week intervals; HDq12: High dose aflibercept 8 mg administered every 12 weeks after 3 initial injections at 4-week intervals; HDq16: High dose aflibercept 8 mg administered every 16 weeks after 3 initial injections at 4-week intervals.

BCVA=best-corrected visual activity; ETDRS=Early Treatment of Diabetic Retinopathy Study; HD=high dose; OC=observed cases; CI=confidence interval.

Least square mean (LSM) was generated from a mixed model for repeated measurements (MMRM) with baseline BCVA measurement as a covariate, treatment group and the stratification variables (geographic region [Japan vs. Rest of World]; baseline CRT (from reading center) [$<40\mu\text{m}$ vs. $\geq 40\mu\text{m}$], prior treatment for DME (per EDC) [yes vs. no]) as fixed factors, and terms for the interaction between baseline and visit and the interaction between treatment and visit. A Kenward-Roger approximation was used for the denominator degrees of freedom. An unstructured covariance structure was used to model the within-subject error.

FIG. 25B

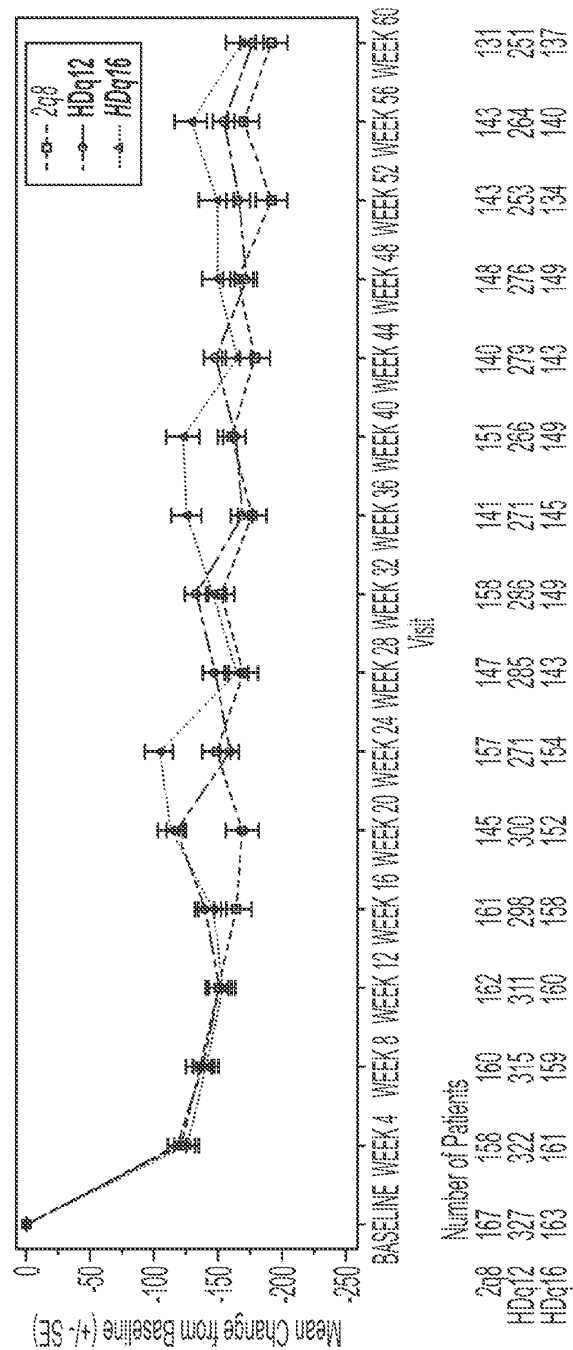
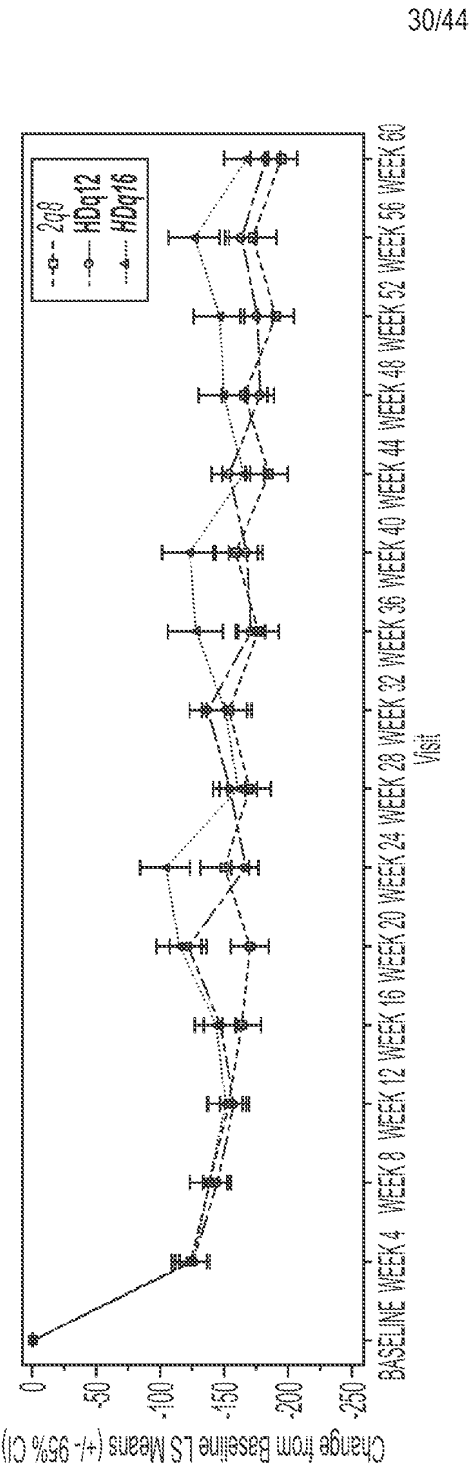


FIG. 26A



Abbreviations: 2q8: Afibercept 2 mg administered every 8 weeks after 5 initial injections at 4-week intervals; HDq12: High dose aflibercept 8 mg administered every 12 weeks after 3 initial injections at 4-week intervals; HDq16: High dose aflibercept 8 mg administered every 16 weeks after 3 initial injections at 4-week intervals.

BCVA=best-corrected visual activity; CI=confidence interval; CRT=central retinal thickness; HD=high dose; LS=least square; OC=observed cases.

Least square mean (LSM) was generated from a mixed model for repeated measurements (MMRM) with baseline CRT measurement as a covariate, treatment group and the stratification variables (geographic region [Japan vs. Rest of World], baseline CRT (from reading center) [$<40\mu\text{m}$ vs. $>=40\mu\text{m}$], prior treatment for DME (per EDC) [yes vs. no]) as fixed factors, and terms for the interaction between baseline and visit and the interaction between treatment and visit. A Kenward-Roger approximation was used for the denominator degrees of freedom. An unstructured covariance structure was used to model the within-subject error.

FIG. 26B

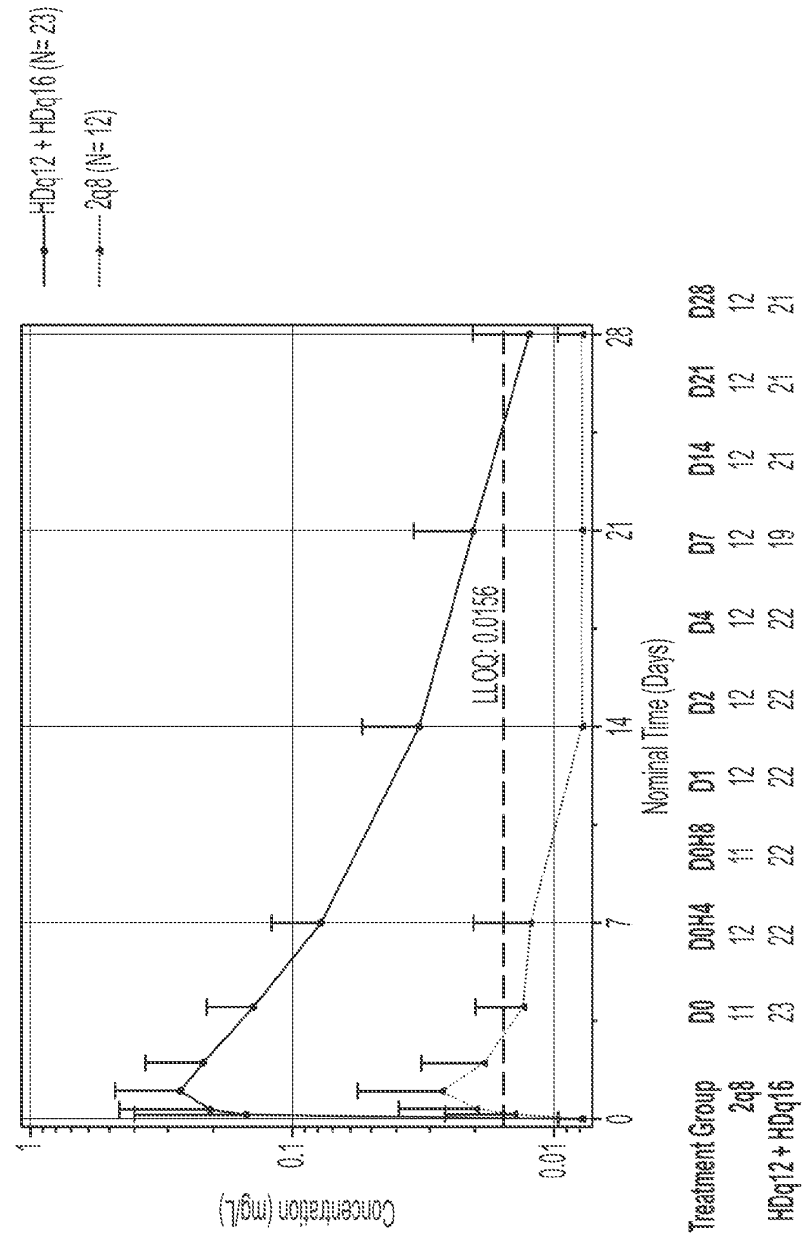


FIG. 27

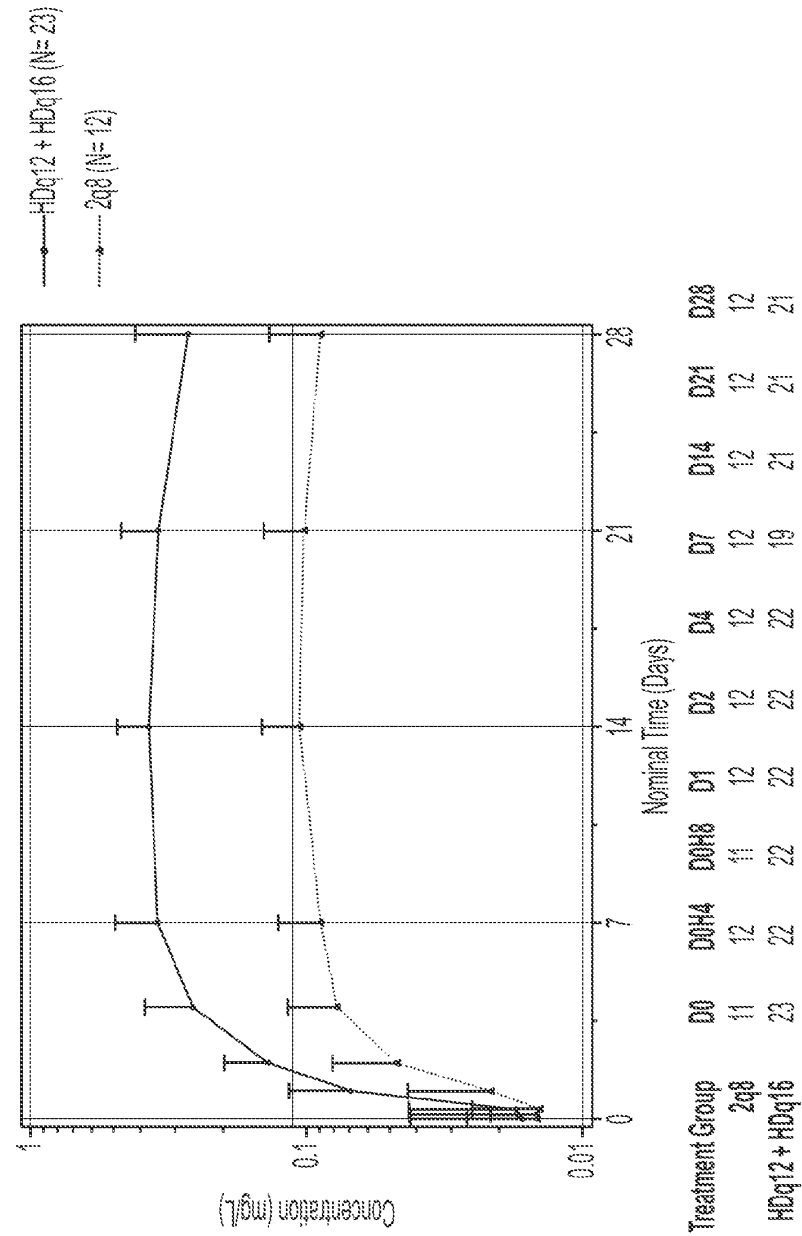


FIG. 28

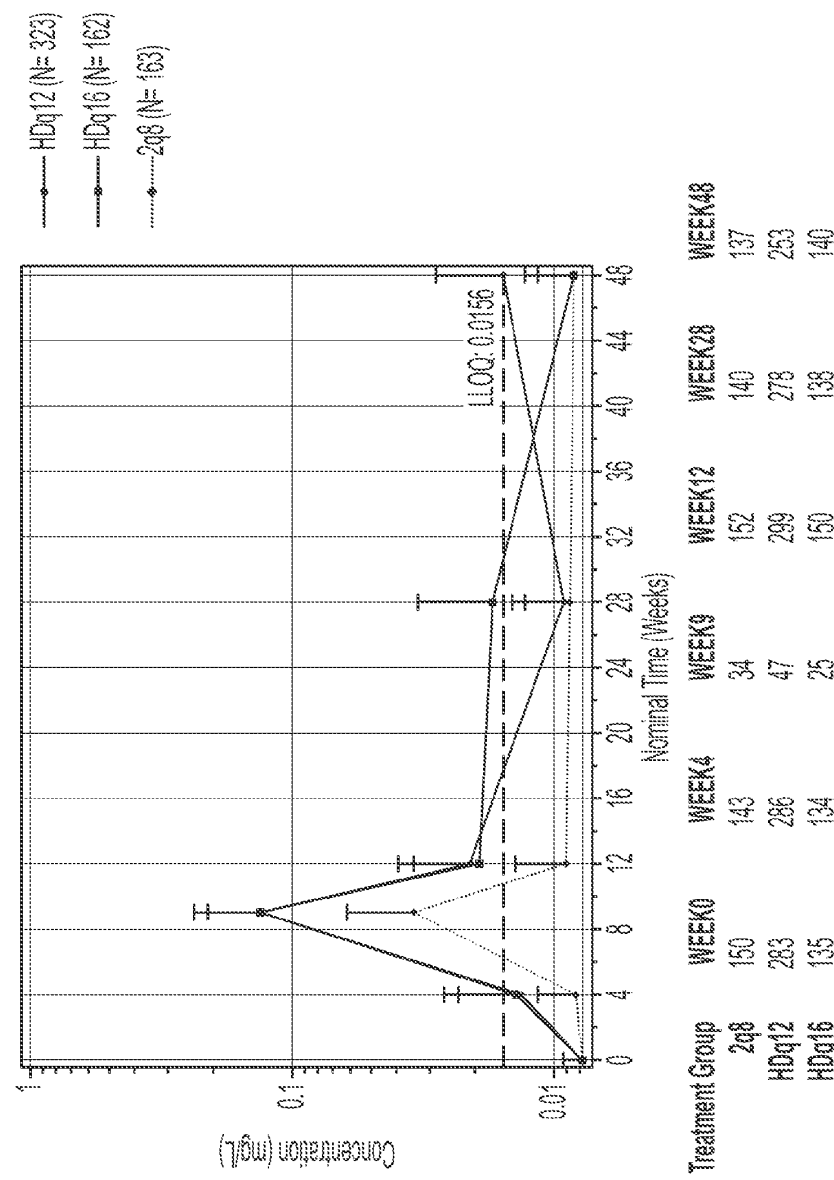


FIG. 29

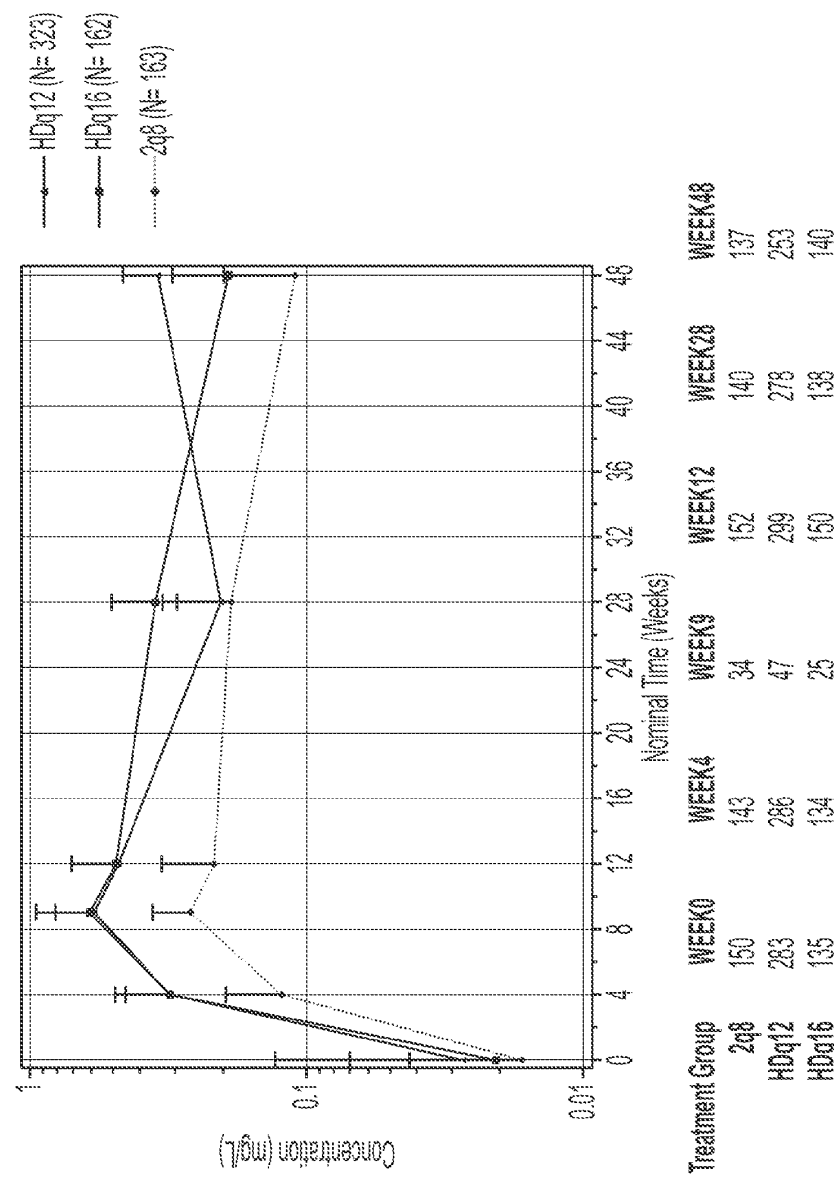


FIG. 30

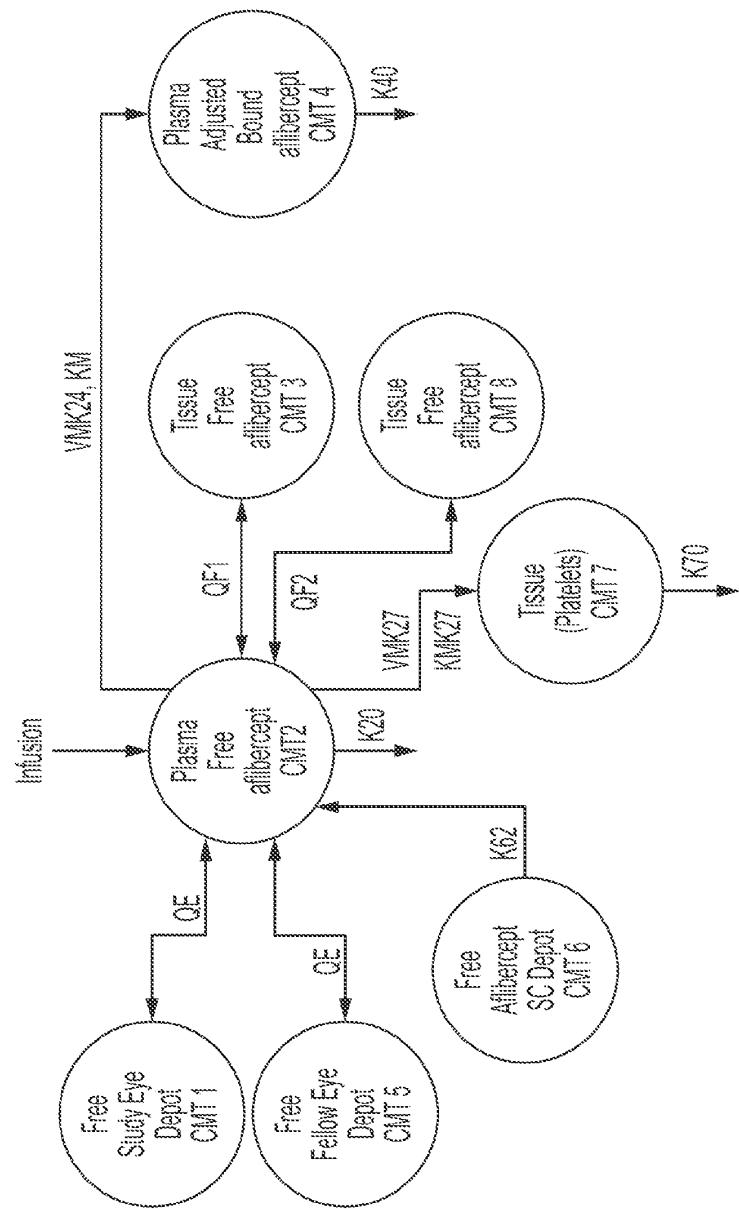


FIG. 31

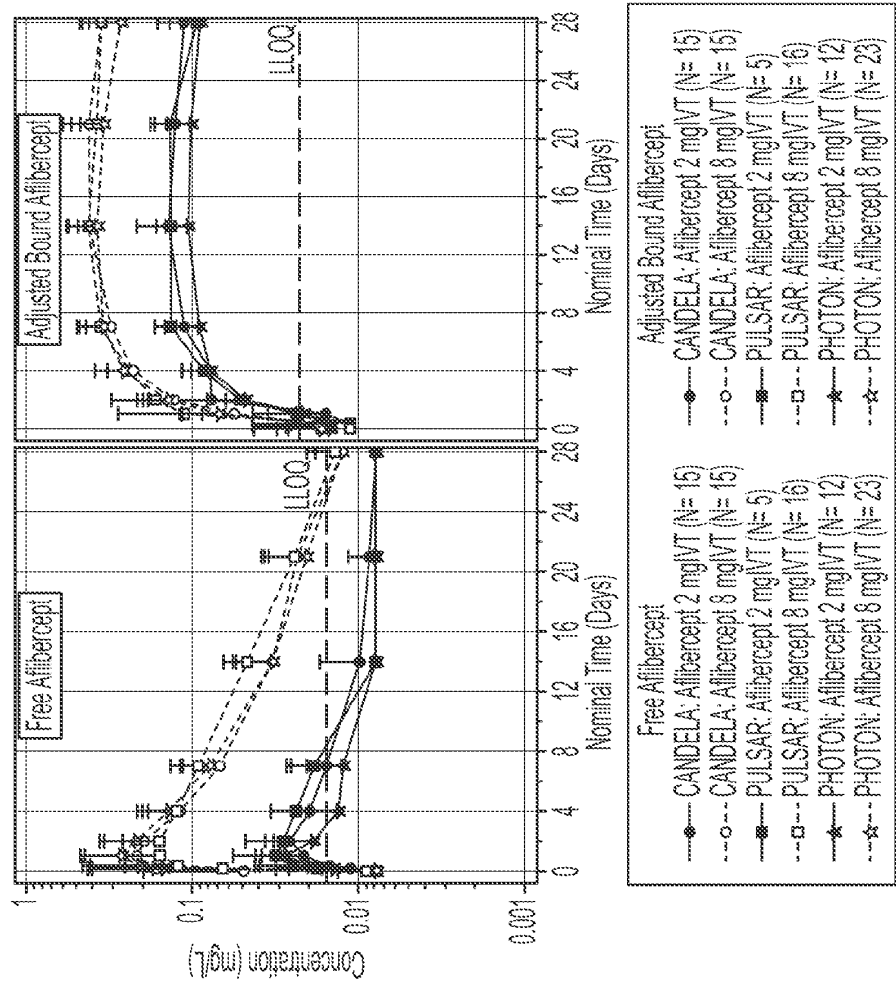


FIG. 32

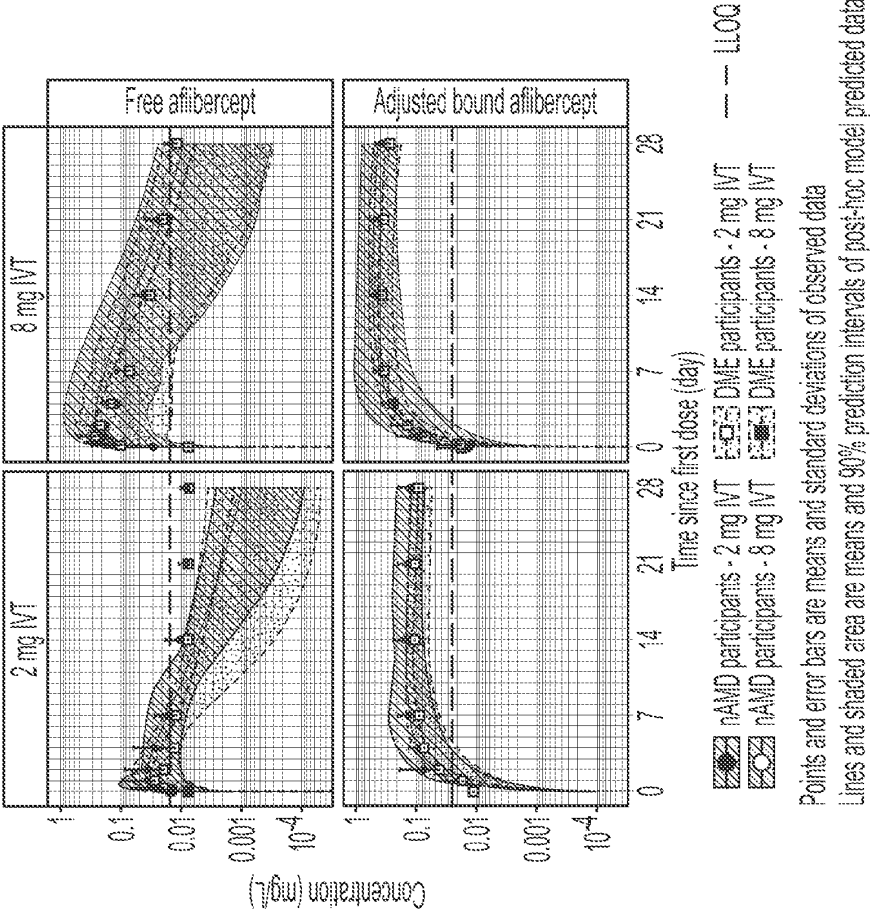


FIG. 33

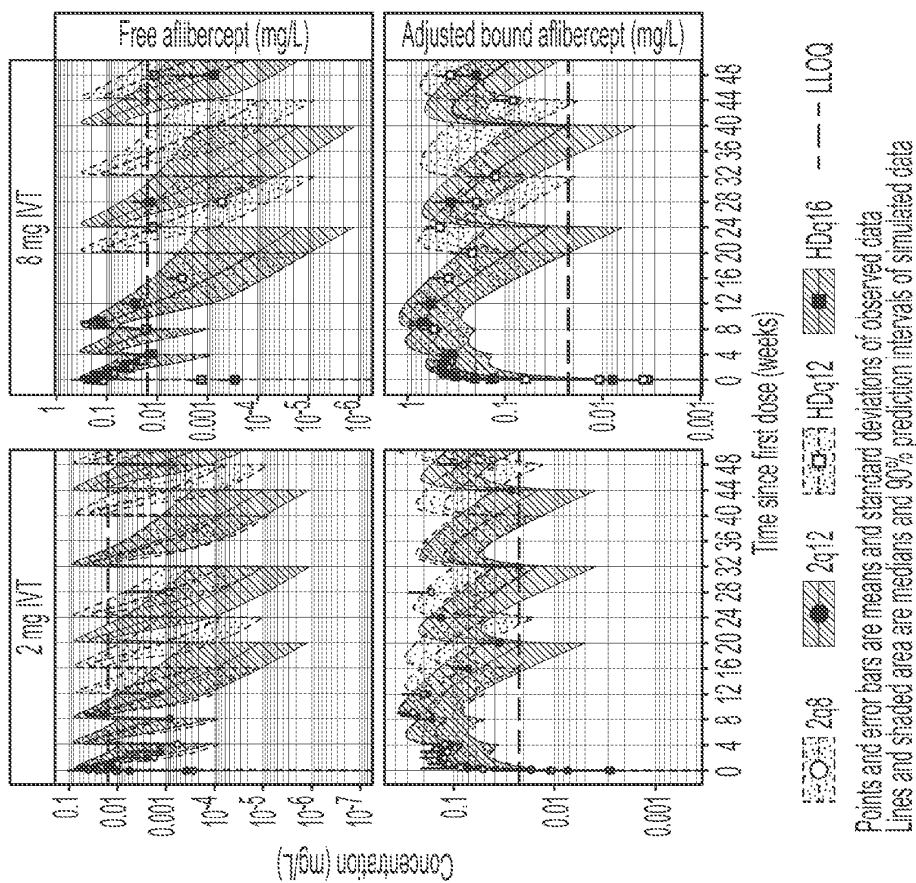


FIG. 34

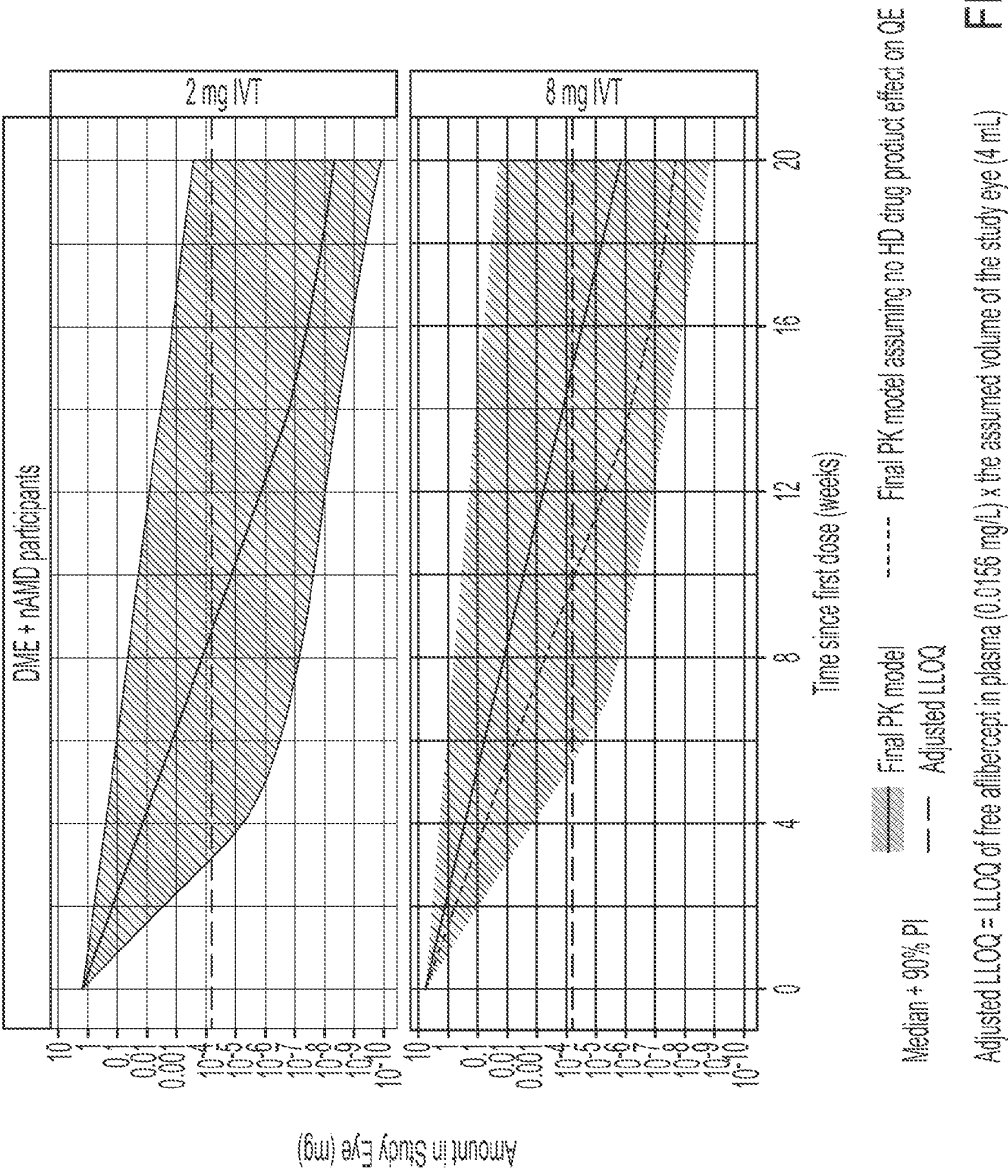


FIG. 35

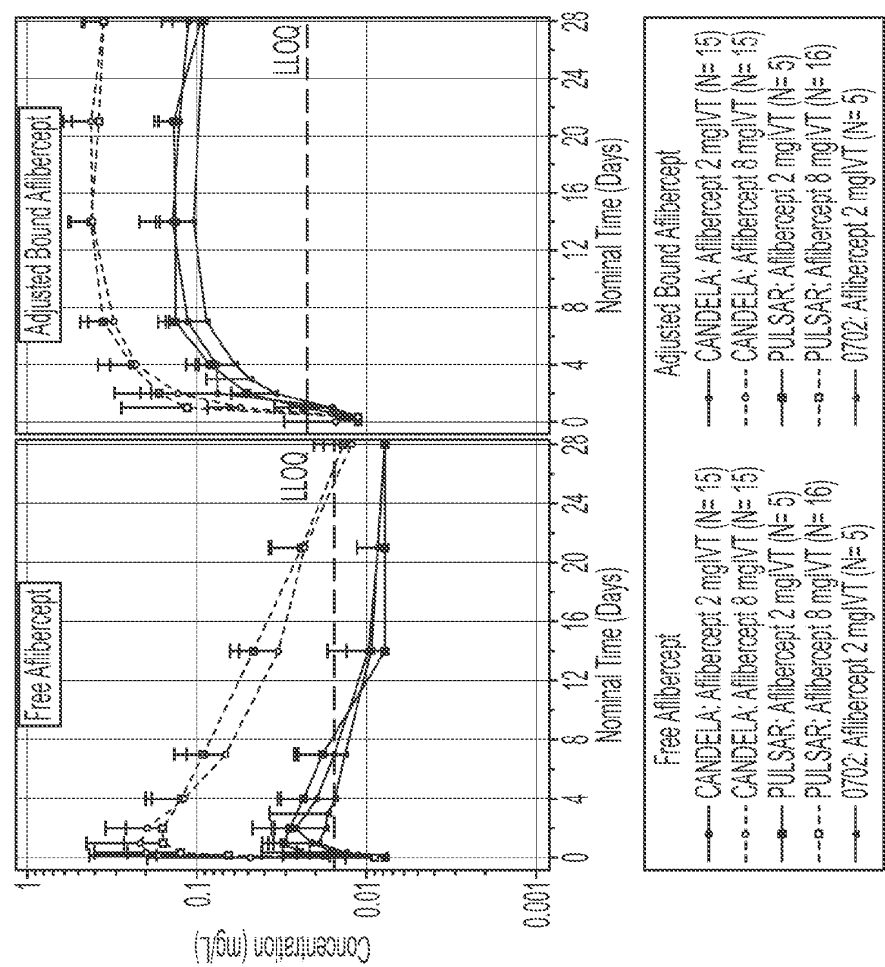


FIG. 36

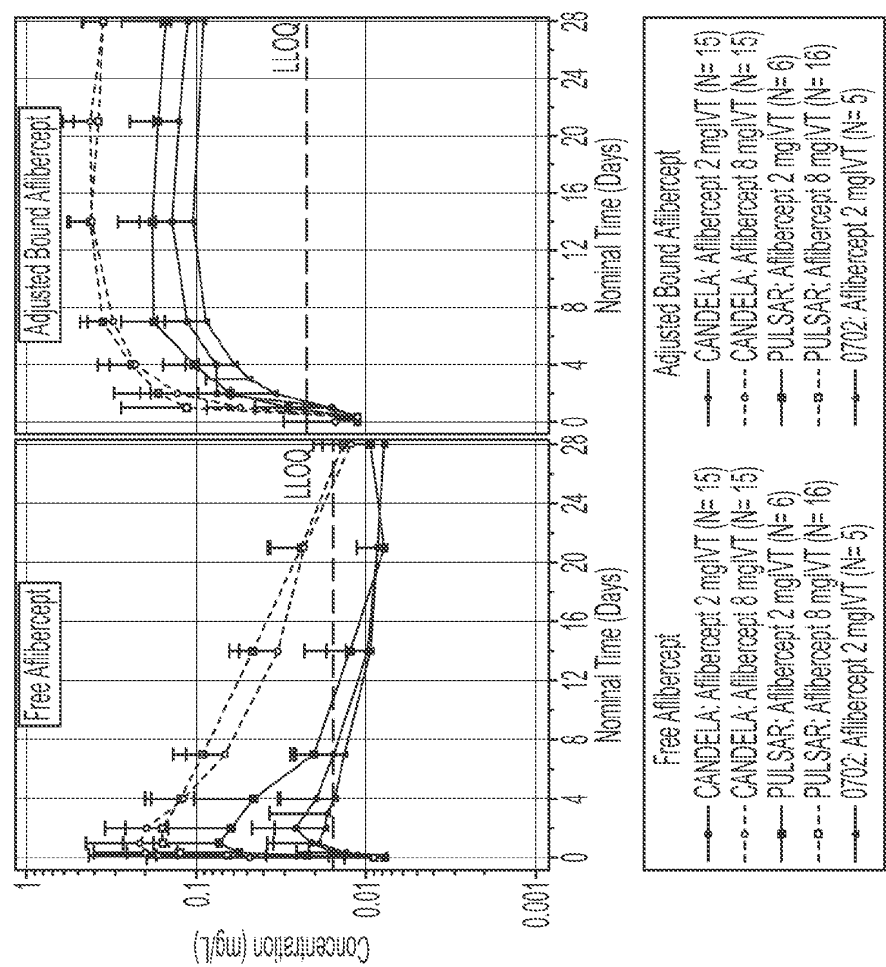


FIG. 37

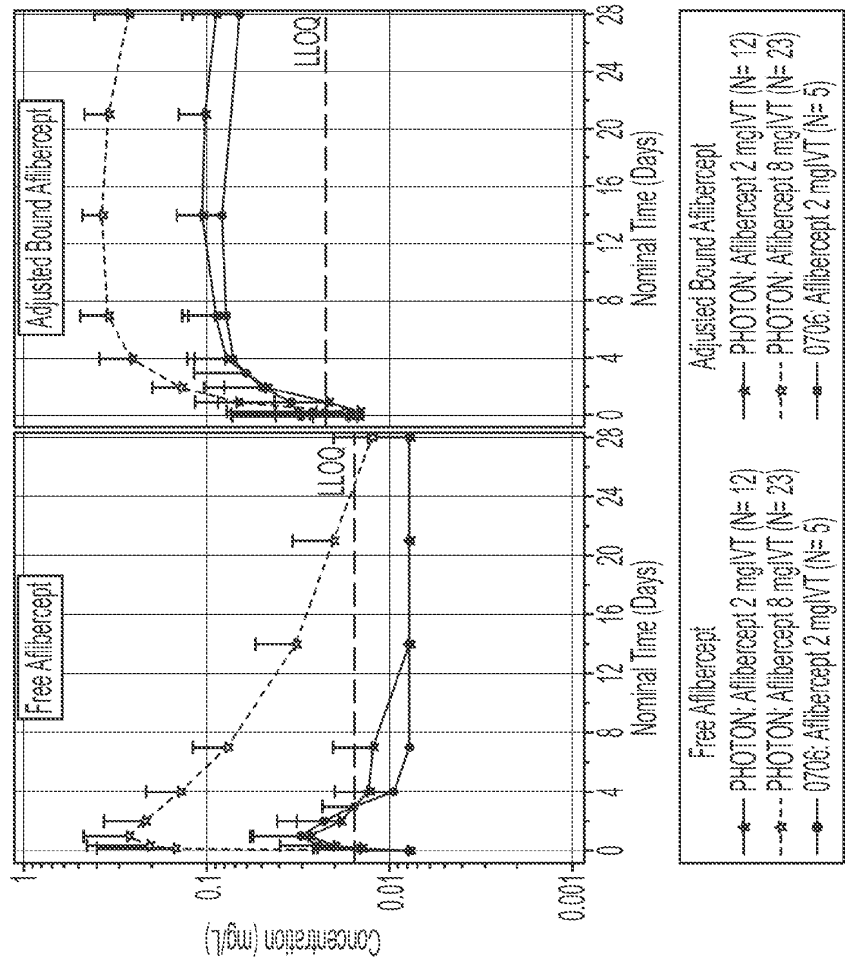


FIG. 38

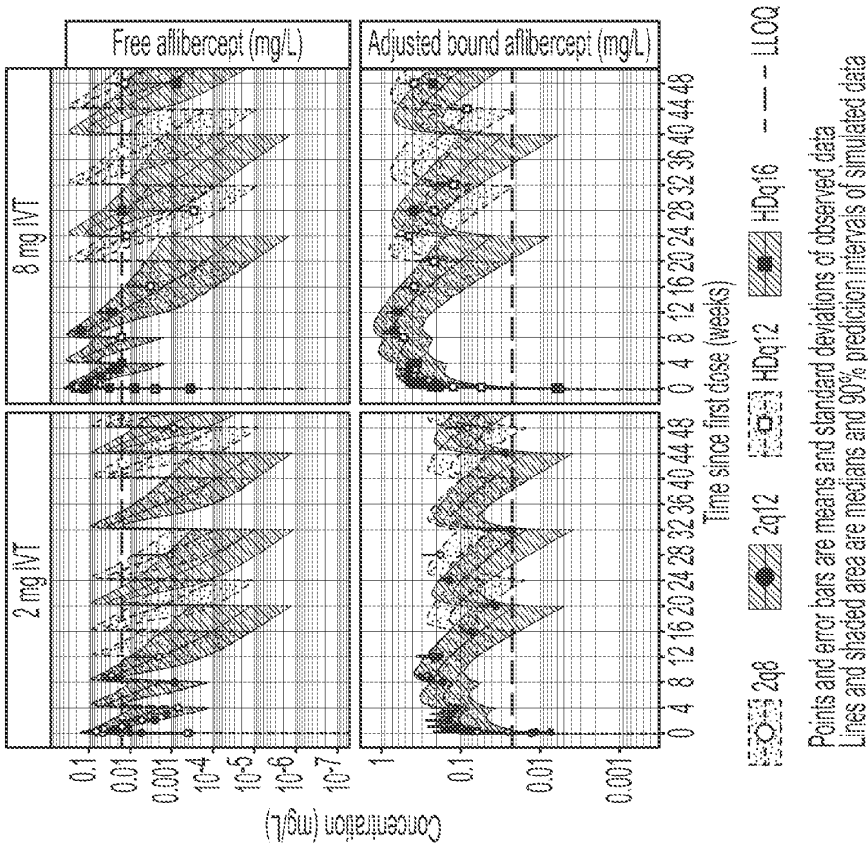


FIG. 39

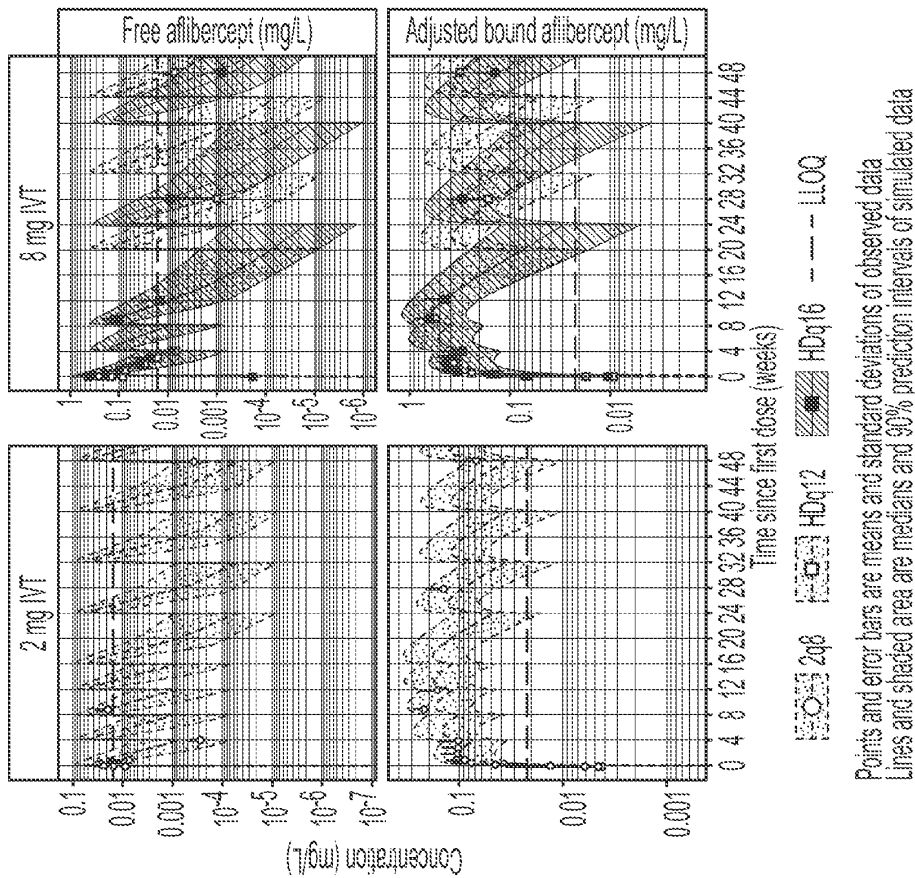


FIG. 40