

Figure 1

Inclusion Criteria

- 50 years of age or older
- Treatment naïve (except for laser treatment outside the subfoveal area) for choroidal neovascularization (CNV) due to AMD in the study eye
- Subfoveal CNV due to AMD
- CNV must be $\geq 50\%$ of the entire lesion
- All lesion composition types with a lesion greatest linear dimension (GLD) ≤ 5400 microns (approx ≤ 9 disc areas [DA])
- Best-corrected Early Treatment Diabetic Retinopathy Study (ETDRS) VA score of 25 - 73 letters (approximate Snellen equivalent of 20/40 - 20/320)

Figure 2

Exclusion Criteria

- Subfoveal geographic atrophy or subfoveal fibrosis in the study eye
- Intraocular surgery within 3 months of enrollment
- Uncontrolled glaucoma (i.e., subject is on >1 glaucoma medication or has glaucoma that could lead to progressive visual field deterioration
- Recent (<1 year) history of stroke
- Inability to attend the protocol-required visits
- Known allergies or hypersensitivity to any of the study treatments

Figure 3

Study Design

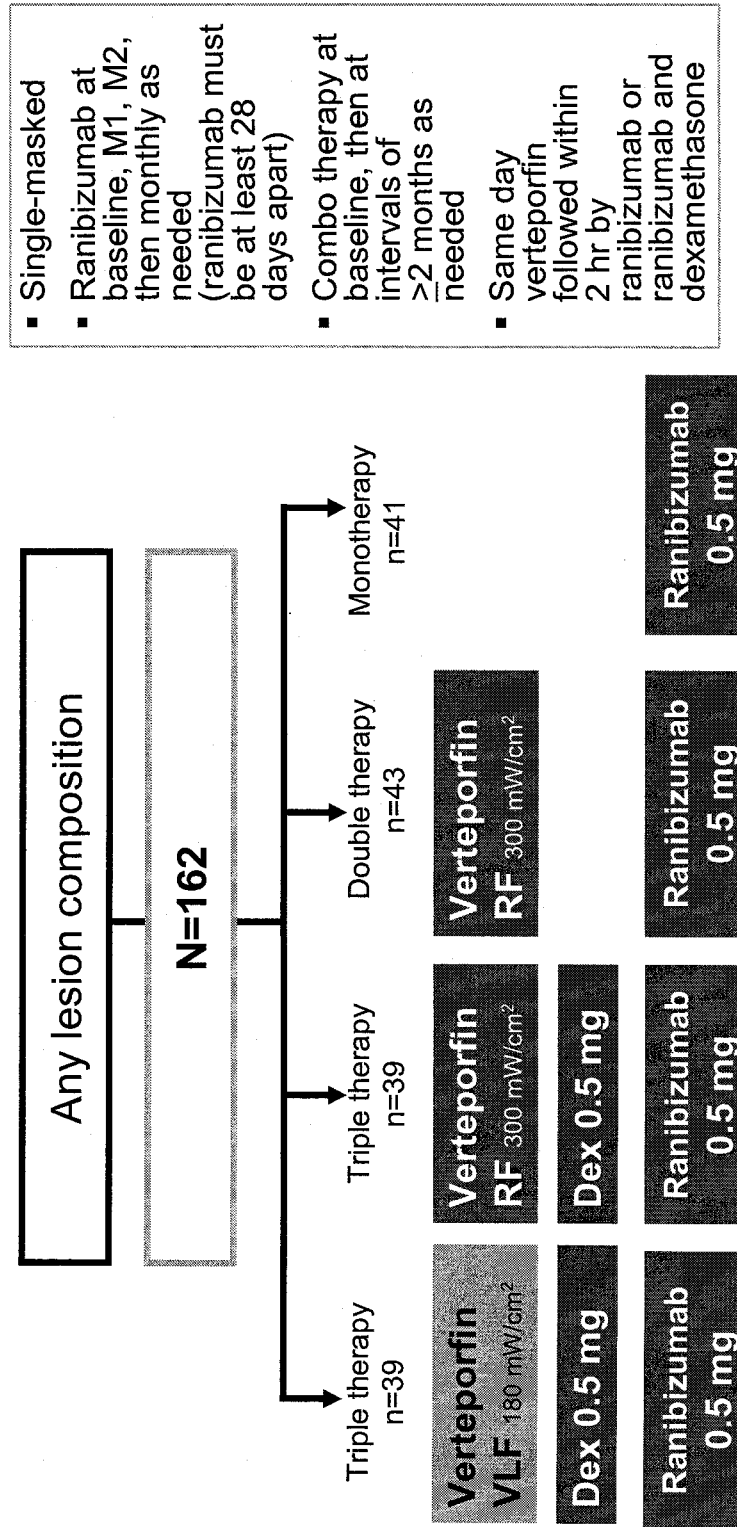


Figure 4

Treatment Schedule

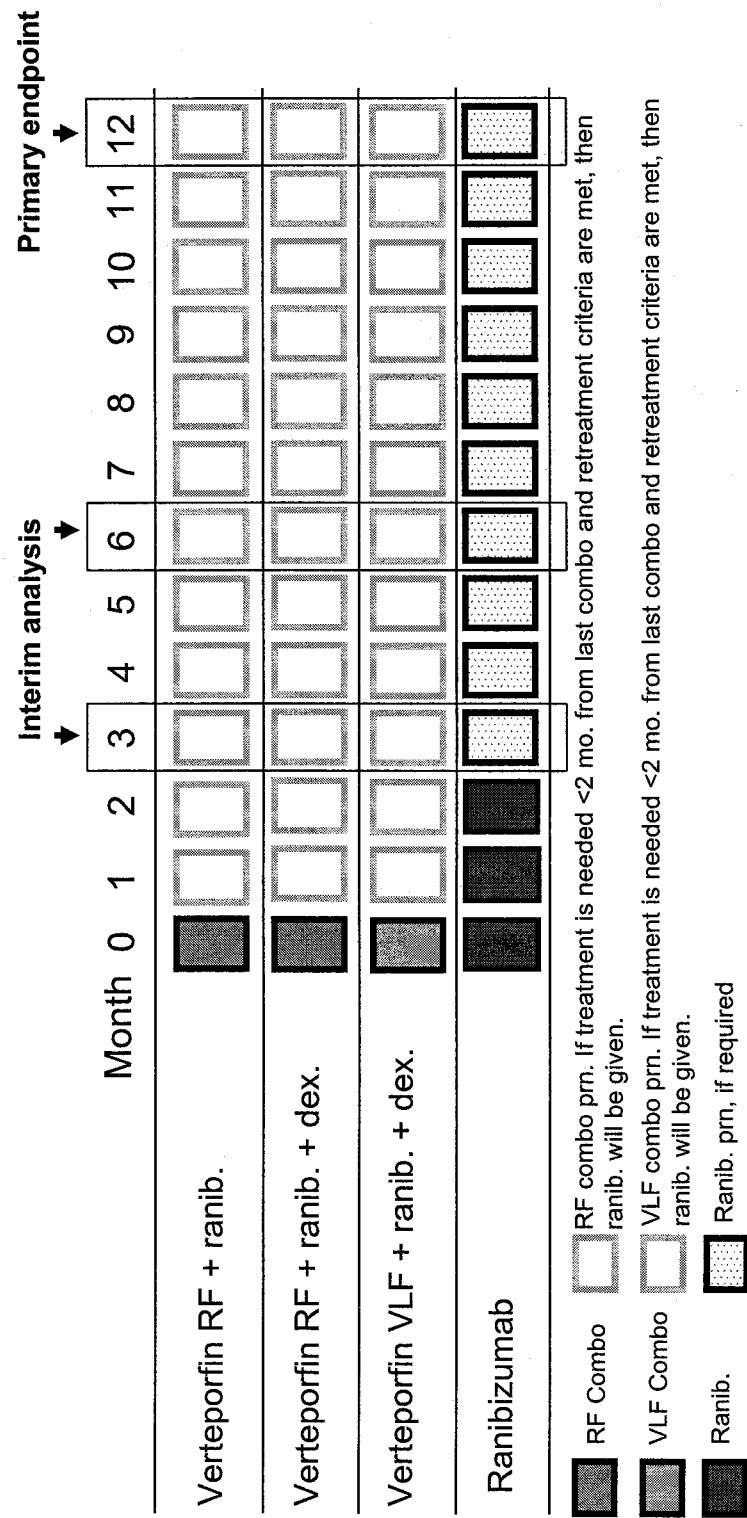


Figure 5

Retreatment Criteria

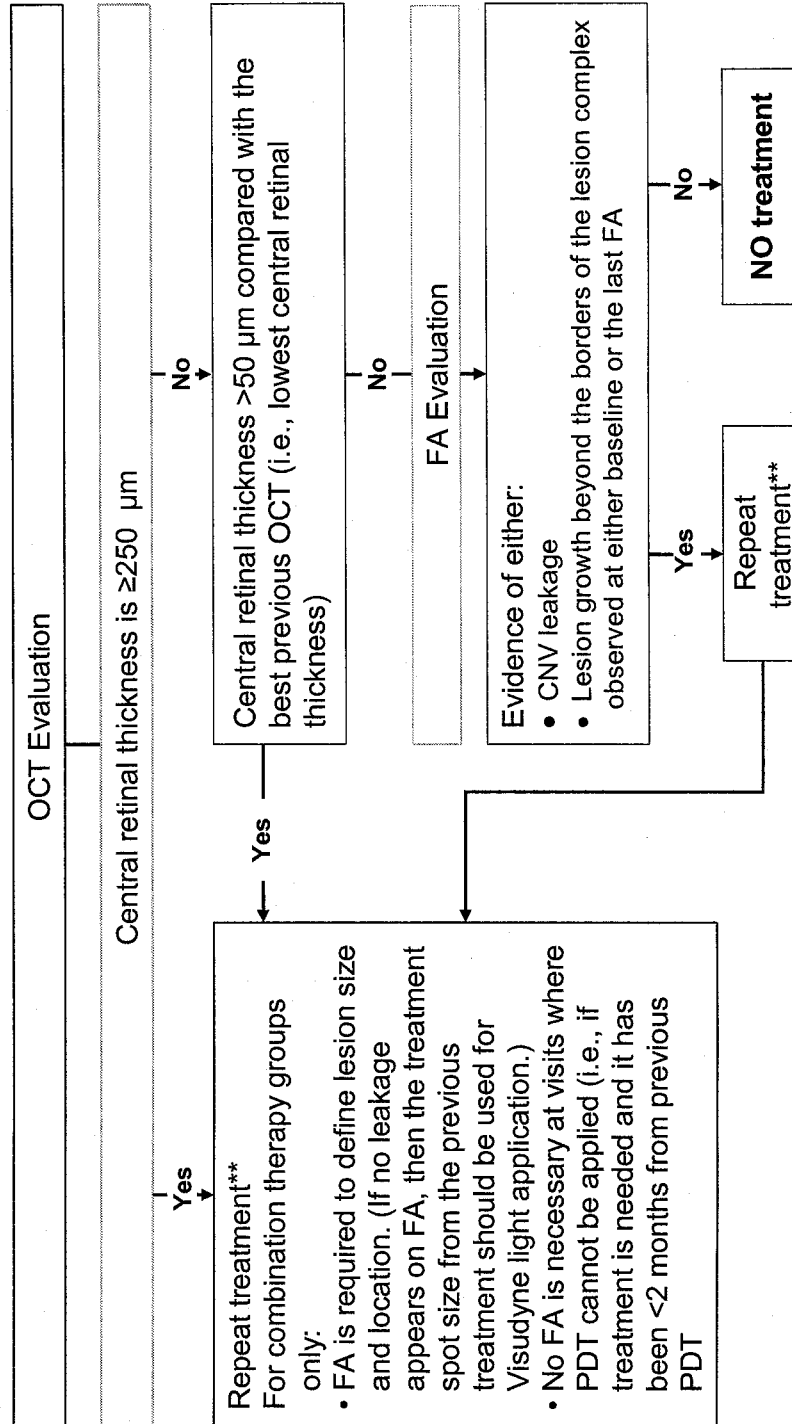


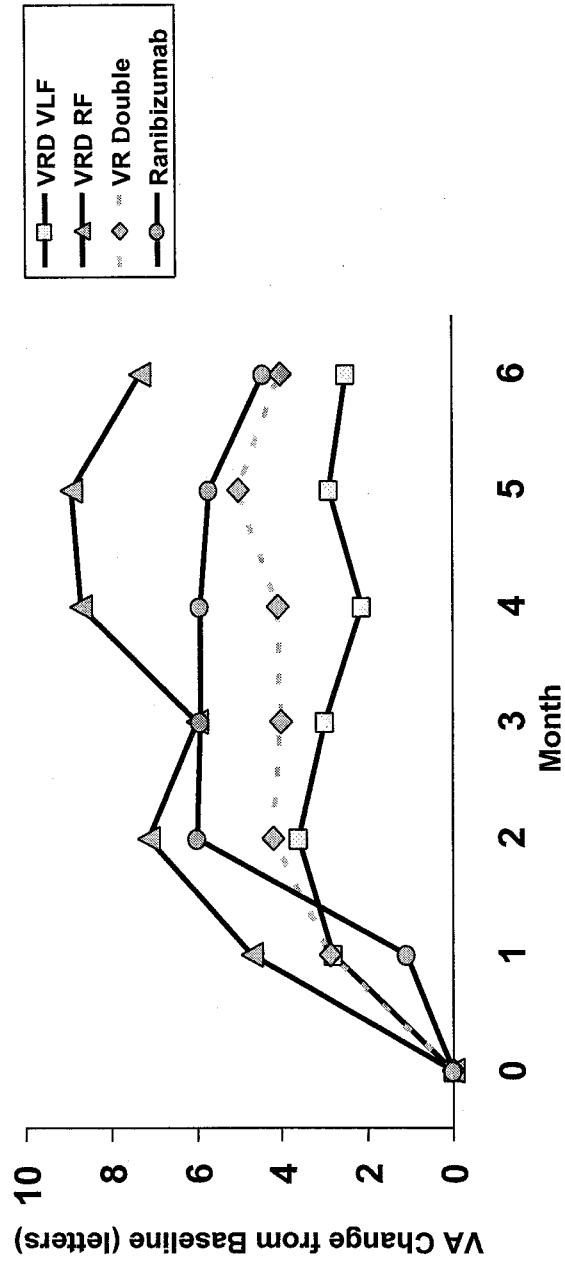
Figure 6

Patient Baseline Characteristics

Characteristic	VRD VLF N=39	VRD RF N=39	VR Double N=43	Ranibizumab N=41
Visual Acuity, letters				
Mean	58.1	55.6	53.3	56.0
Median	61.0	58.0	56.0	60.0
Central retinal thickness (μm), mean	318.3	337.3	337.3	311.9
GLD (μm), mean	2778.8	2740.1	2796.1	3118.4

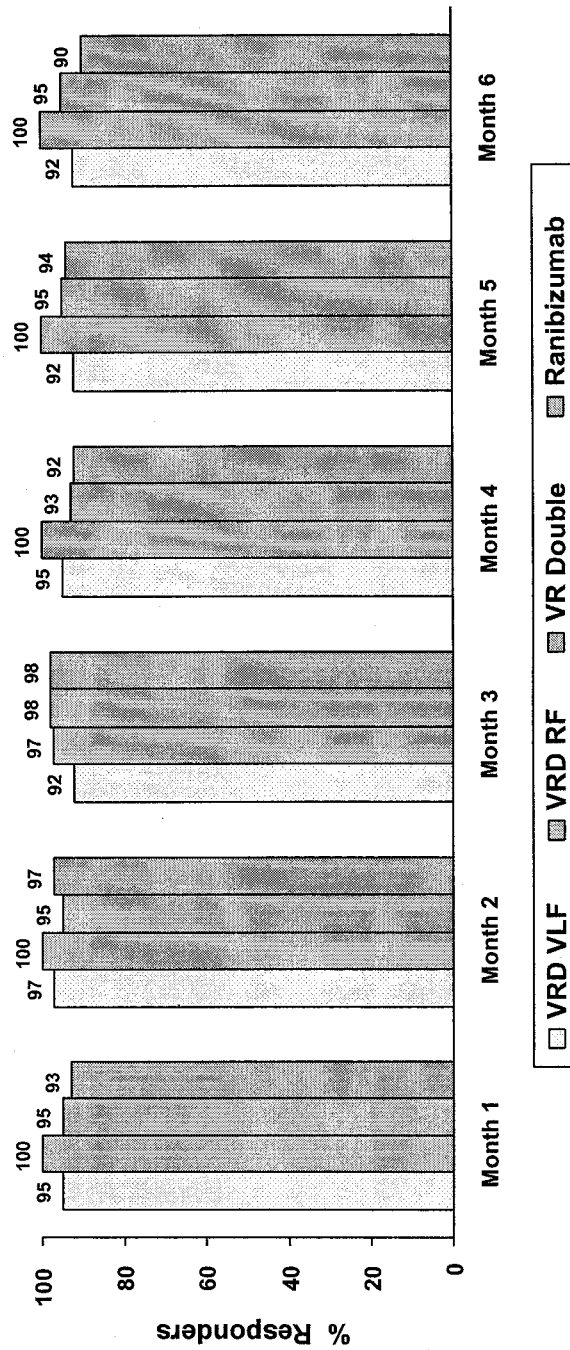
Figure 7

Mean VA Change From Baseline



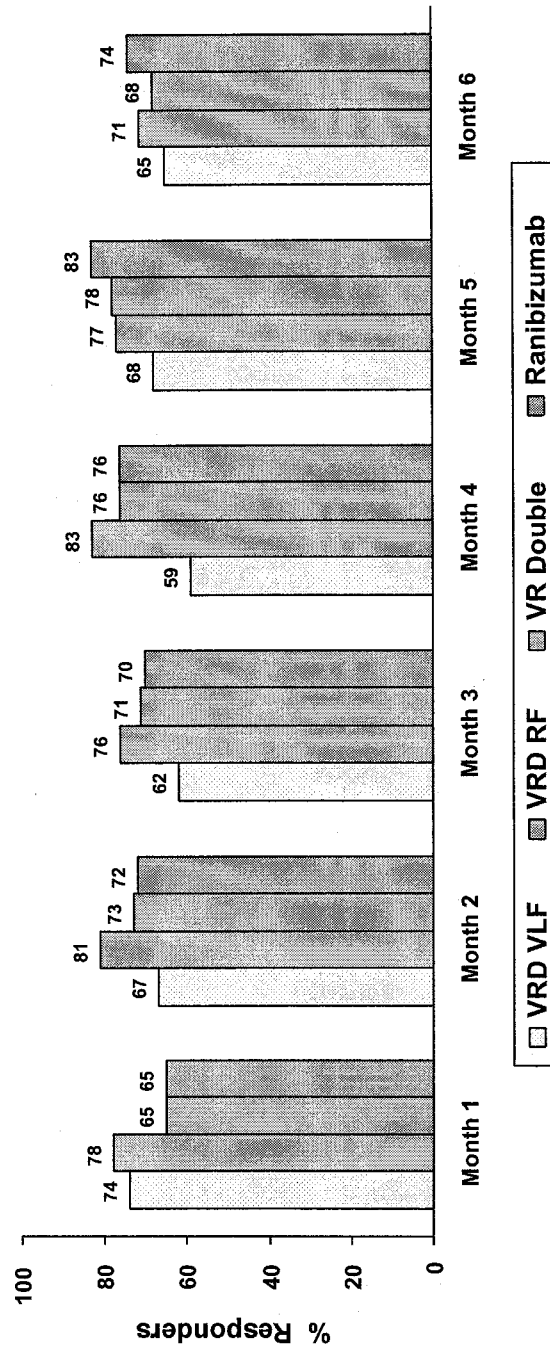
VRD VLF	N=39	39	39	39	39	37	37
VRD RF	N=39	37	36	37	35	35	35
VR Double	N=43	43	41	41	42	40	41
Ranibizumab	N=41	40	39	40	37	36	39

Figure 8
VA Change From Baseline:
% Subjects Who Lost <15 letters VA



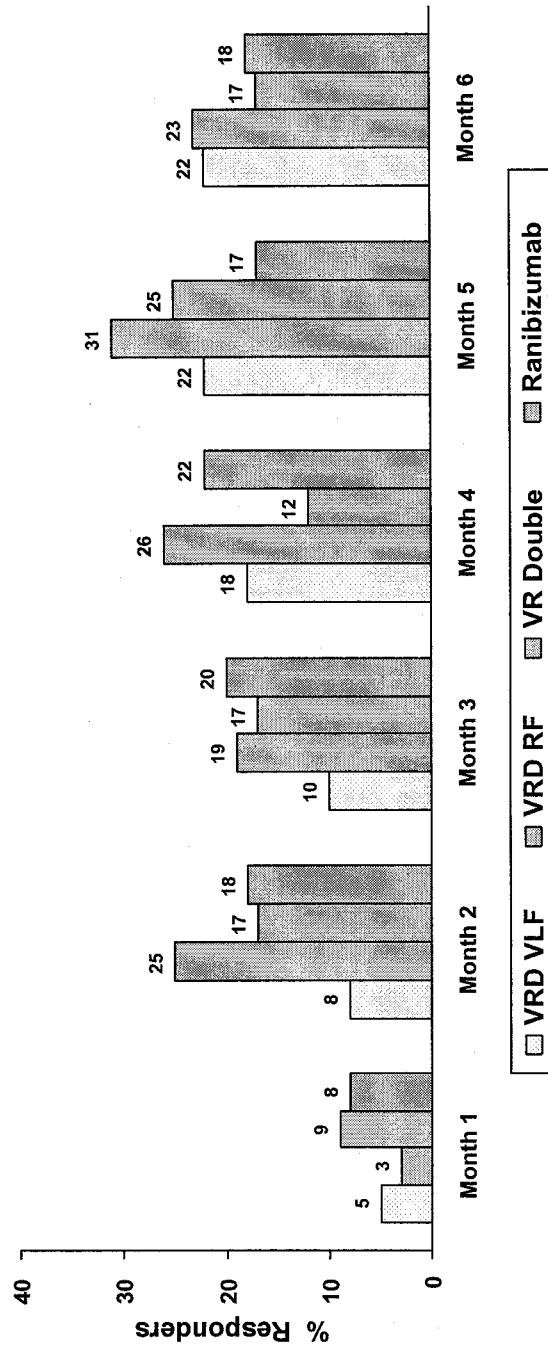
VRD VLF	N=39	39	39	39	37	37
VRD RF	N=37	36	37	35	35	35
VR Double	N=43	41	41	42	40	41
Ranibizumab	N=40	39	40	37	36	39

Figure 9
VA Change From Baseline:
% Subjects Who Gained ≥ 0 letters VA



VRD VLF	N=39	39	39	39	37	37
VRD RF	N=37	36	37	35	35	35
VR Double	N=43	41	41	42	40	41
Ranibizumab	N=40	39	40	37	36	39

Figure 10
VA Change From Baseline:
% Subjects Who Gained ≥ 15 letters VA



VRD VLF	N=39	39	39	39	37	37
VRD RF	N=37	36	37	35	35	35
VR Double	N=43	41	41	42	40	41
Ranibizumab	N=40	39	40	37	36	39

Figure 11
Central Retinal Thickness (CRT):
Mean Change from Baseline

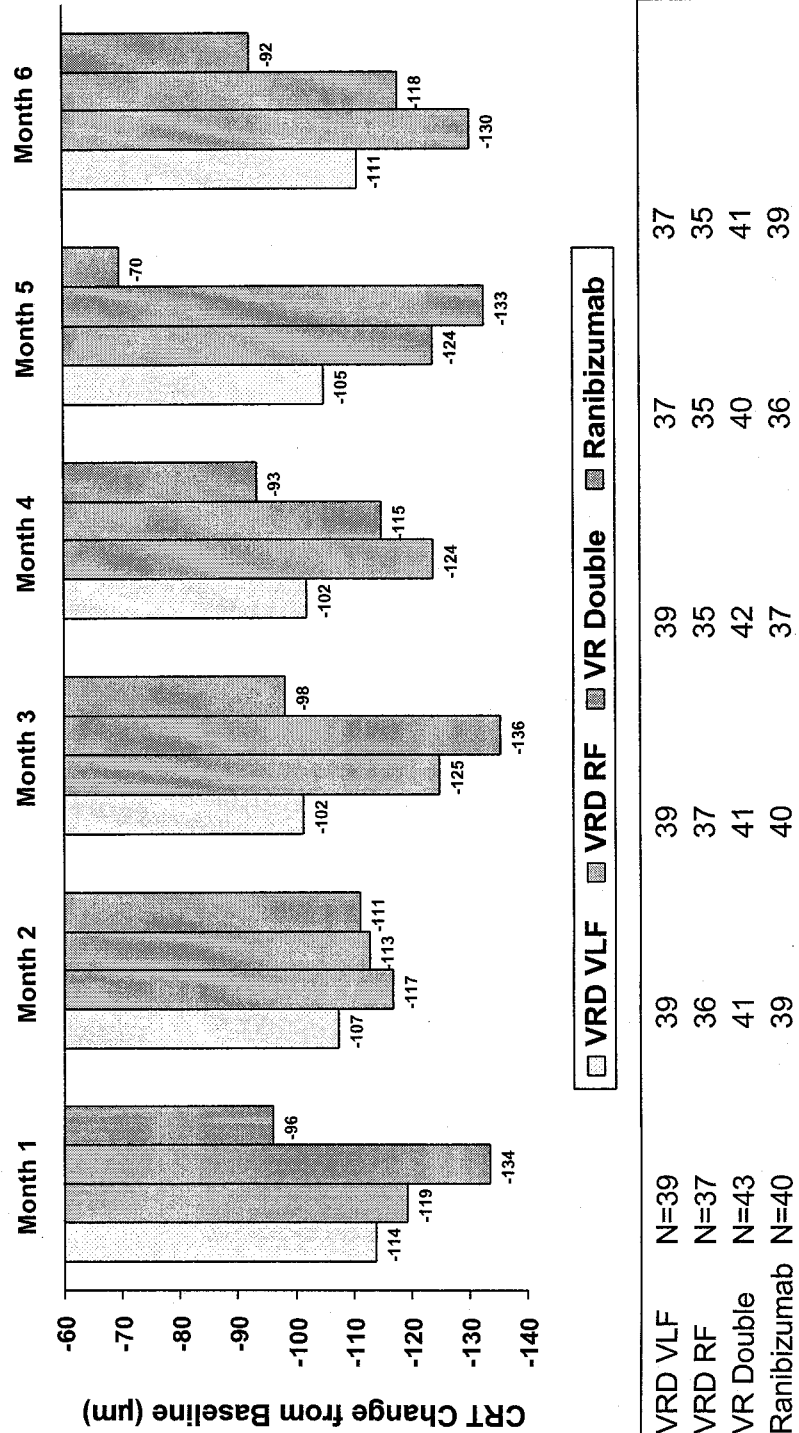


Figure 12
Cumulative Number of Retreatments
Based on Either OCT or FA

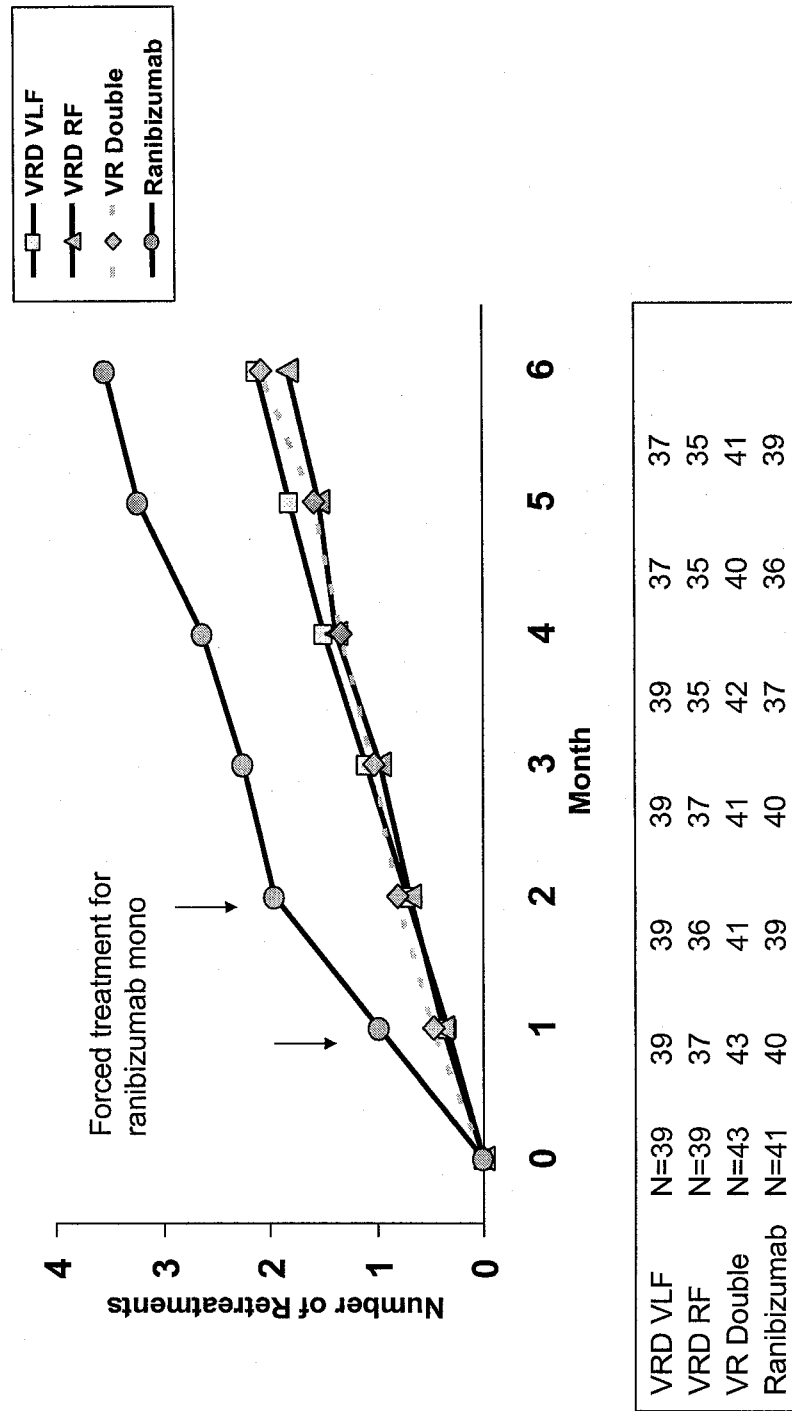


Figure 13
Cumulative Number of Retreatments
Based on Meeting OCT Criteria

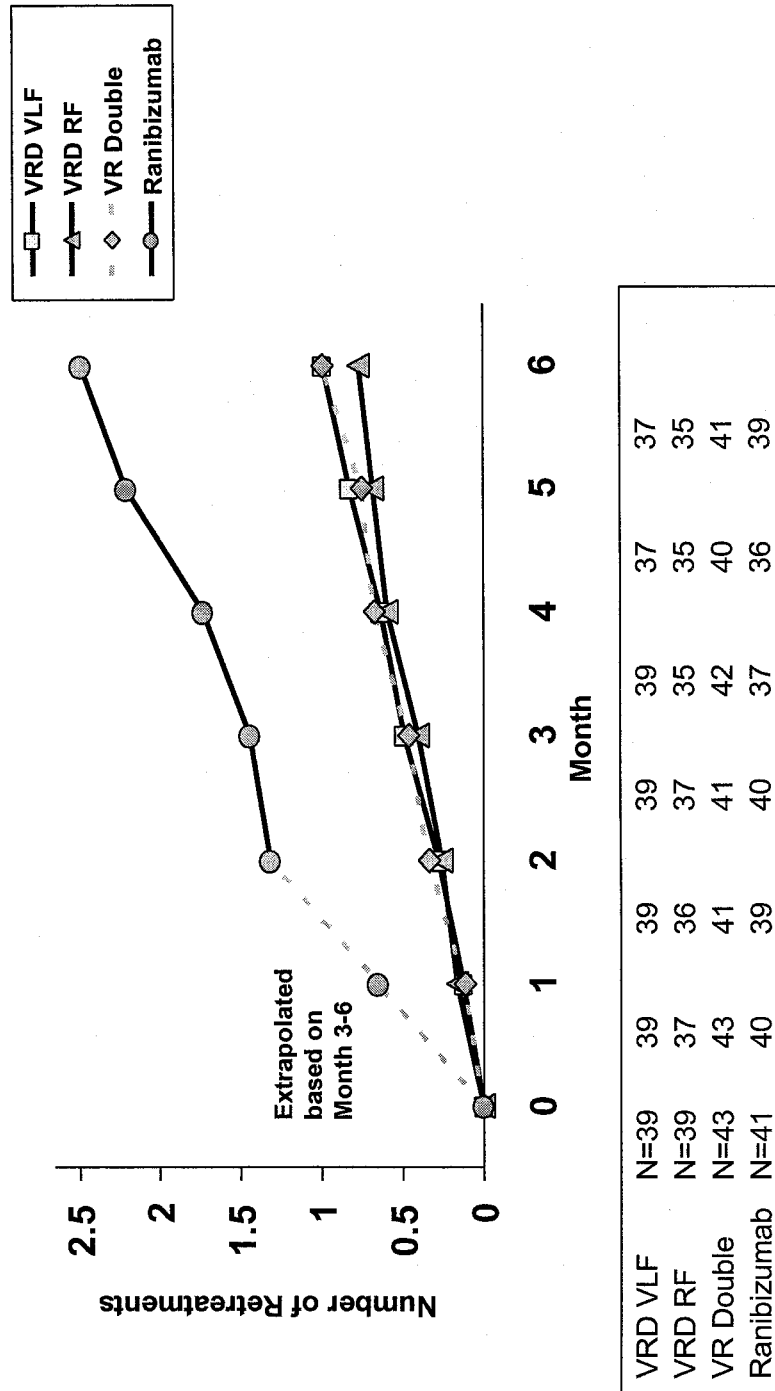


Figure 14
Cumulative Number of Retreatments
Based on Meeting FA Criteria

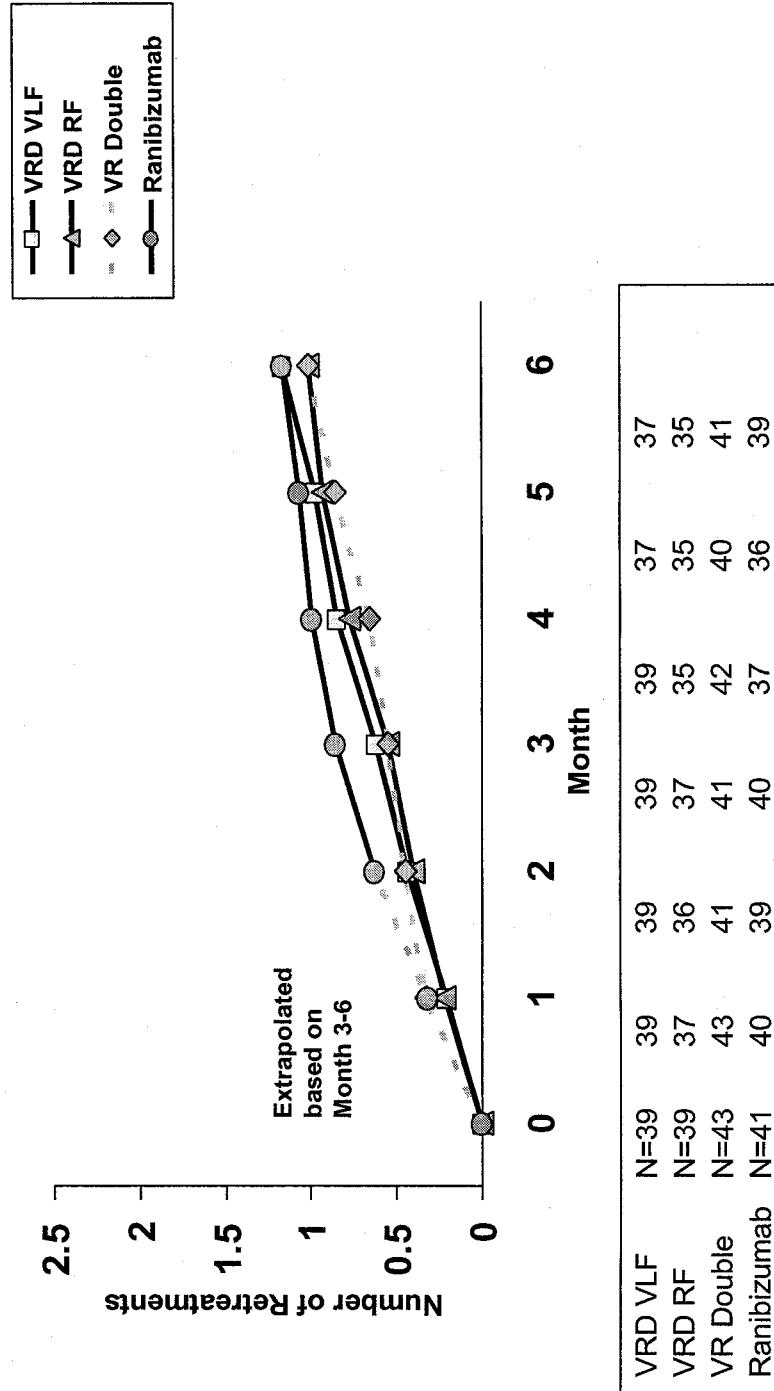
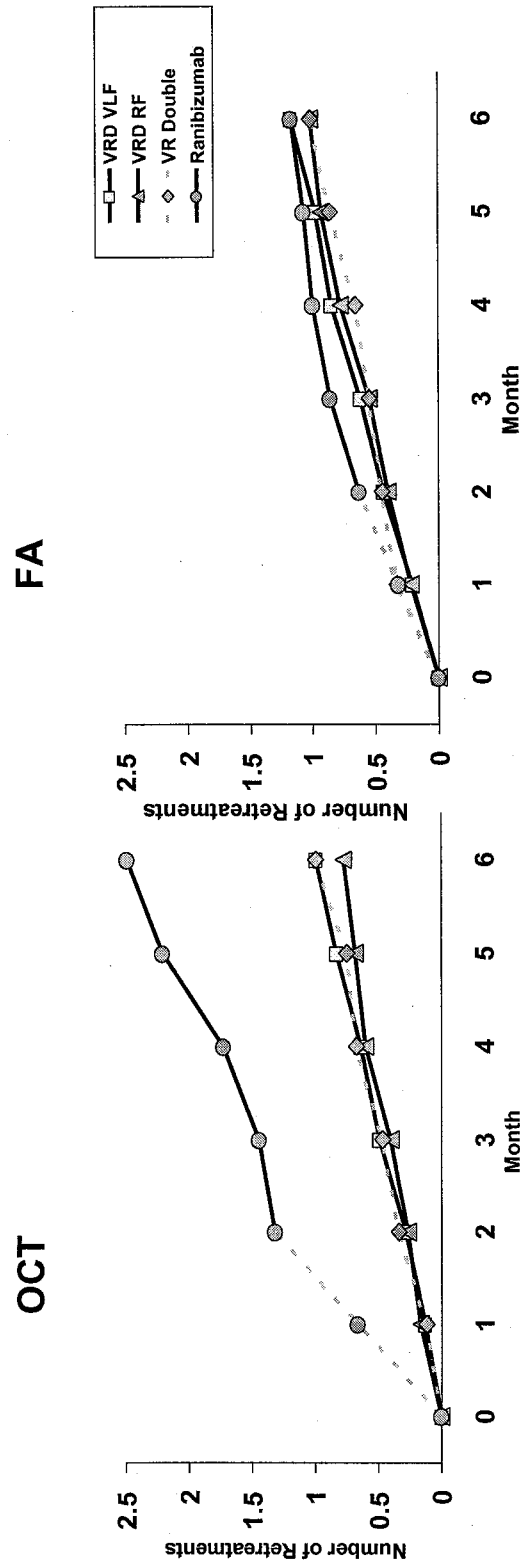


Figure 15
Cumulative Number of Retreatments
Based on Meeting OCT vs FA Criteria



Lucentis Month 1 and 2 extrapolated based on Month 3-6

Figure 16
Summary of Adverse Events (AEs)

	VRD VLF (N=39)	VRD RF (N=39)	Double (N=43)	Ranibizumab (N=41)
All AEs	28 (71.8%)	35 (89.7%)	33 (76.7%)	34 (82.9%)
All Associated AEs	13 (33.3%)	14 (35.9%)	17 (39.5%)	9 (22.0%)
All Study Eye Ocular AE	18 (46.2%)	19 (48.7%)	22 (51.2%)	20 (48.8%)
All Associated Ocular AEs	11 (28.2%)	11 (28.2%)	11 (25.6%)	9 (22.0%)
All SAEs	4 (10.3%)	10 (25.6%)	8 (18.6%)	8 (19.5%)
All Associated SAEs	1 (2.6%)	2 (5.1%)	0	0
All Associated Ocular SAEs	1 (2.6%)	2 (5.1%)	0	0

Figure 17
Ocular AEs Related to Treatment

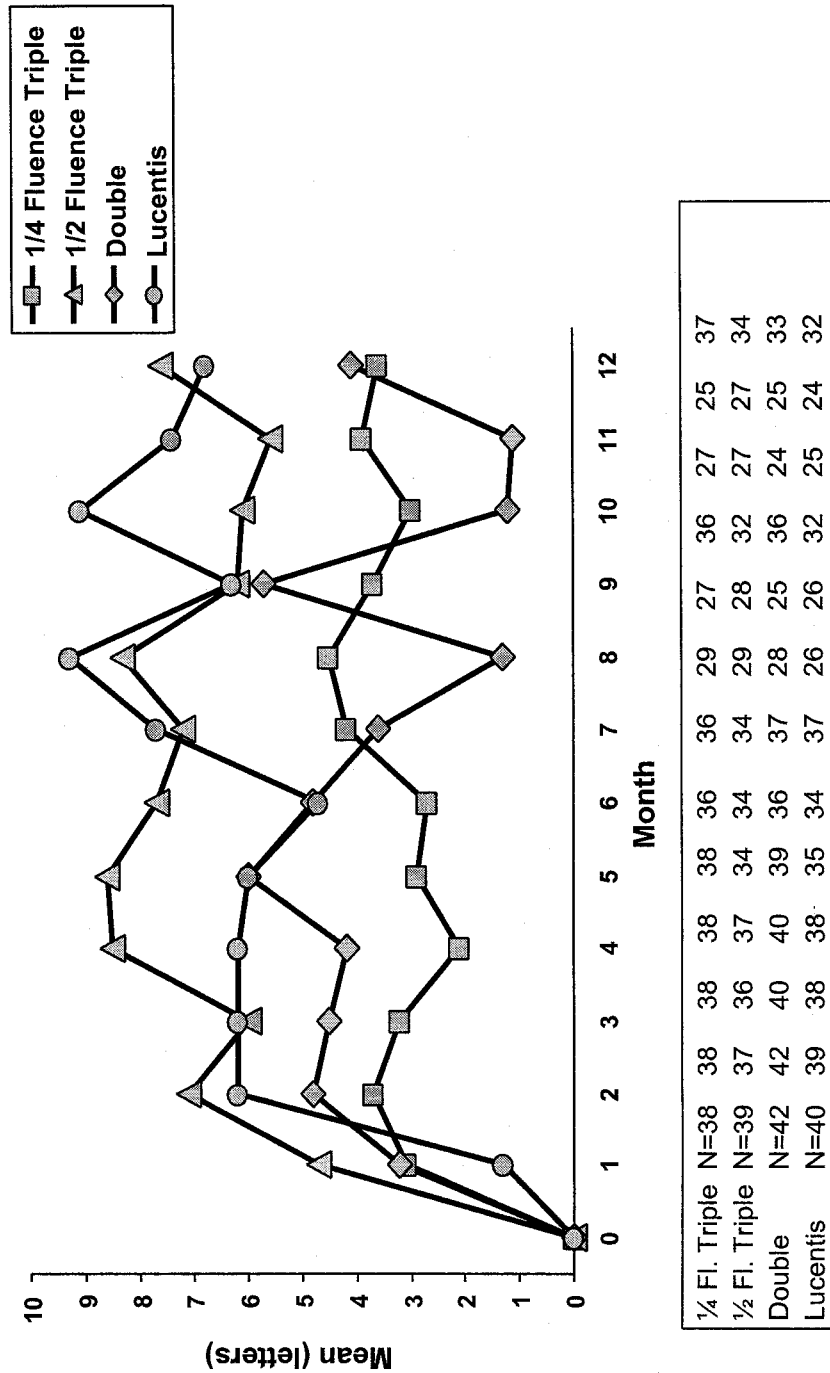
	VRD VLF (N=39)	VRD RF (N=39)	Double (N=43)	Ranibizumab (N=41)
All Associated Ocular AEs	11 (28.2%)	11 (28.2%)	11 (25.6%)	9 (22.0%)
Cataract	0	1 (2.6%)	3 (7.0%)	0
Choroidal hypoperfusion	0	0	2 (4.7%)	0
Glaucoma	0	0	1 (2.3%)	0
Increased IOP	1 (2.6%)	5 (12.8%)	3 (7.0%)	5 (12.2%)
Retinal disorder	3 (7.7%)	2 (5.2%)	0	0
Vision abnormal	4 (10.3%)	1 (2.6%)	6 (14.0%)	3 (7.3%)
Vision decreased	4 (10.3%)	3 (7.7%)	5 (11.6%)	0
Visual field defect	3 (7.7%)	1 (2.6%)	2 (4.7%)	1 (2.4%)

Figure 18

BSL Lesion Composition

Lesion Composition	VLD VLF (N=39)	VLD HF (N=39)	Double (N=43)	Lucentis (N=41)
Minimally classic	6 (15%)	4 (10%)	9 (21%)	8 (20%)
Occult	10 (26%)	16 (41%)	20 (47%)	18 (44%)
Predominantly classic	23 (59%)	19 (49%)	14 (33%)	15 (37%)

Figure 19
VA Change From Baseline over 12 months



1/4 Fl. Triple	N=38	38	38	38	38	36	29	27	36	27	25	37
1/2 Fl. Triple	N=39	37	36	37	34	34	29	28	32	27	27	34
Double	N=42	42	40	40	39	36	37	28	36	24	25	33
Lucentis	N=40	39	38	38	35	34	37	26	32	25	24	32

Figure 20
 VA Change From Baseline: Subjects
 Who Lost <15 Letters

	$\frac{1}{4}$ Fluence		$\frac{1}{2}$ Fluence		Double		Lucentis	
	Triple	n %	Triple	n %	Double	n %	Double	n %
Month 3	38	92%	37	97%	40	100%	38	97%
Month 6	36	92%	34	100%	37	97%	37	89%
Month 9	36	83%	32	91%	36	92%	32	88%
Month 12	37	86%	34	91%	33	91%	32	91%

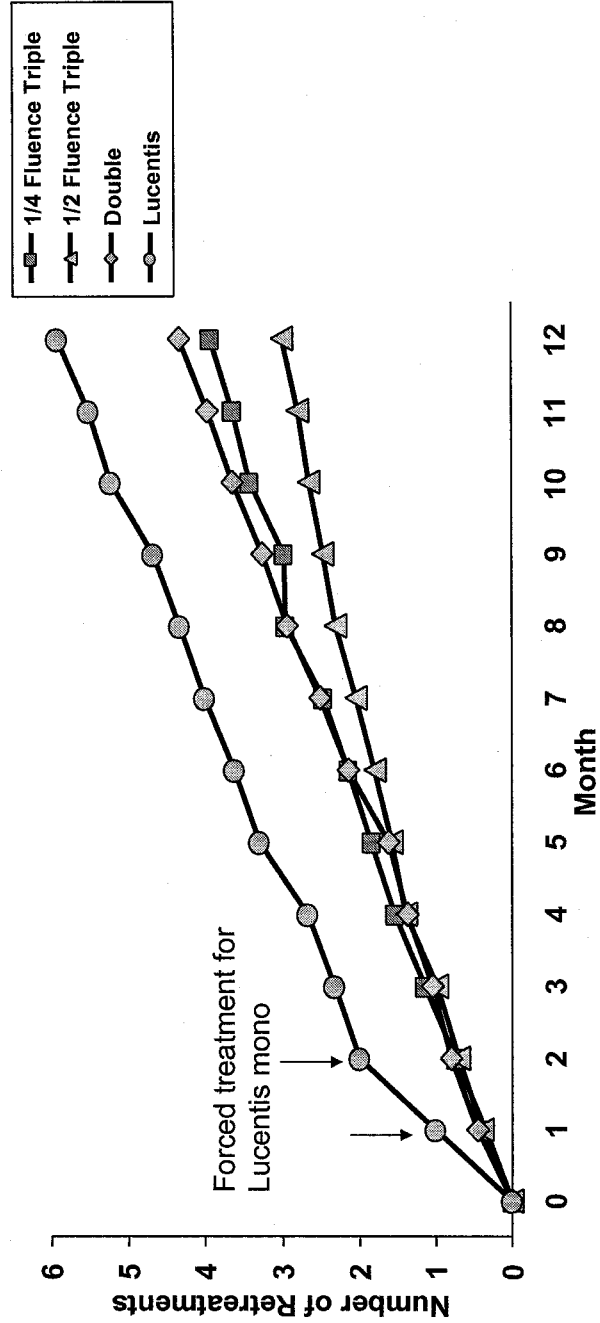
Figure 21
 VA Change From Baseline: Subjects
 Who Gained ≥ 15 Letters

	$\frac{1}{4}$ Fluence		$\frac{1}{2}$ Fluence		Double		Lucentis	
	Triple		Triple		n %		n %	
	n	%	n	%	n	%	n	%
Month 3	38	11%	37	19%	40	18%	38	21%
Month 6	36	22%	34	24%	37	16%	37	19%
Month 9	36	19%	32	28%	36	19%	32	31%
Month 12	37	27%	34	35%	33	24%	32	22%

Figure 22
 Central Retinal Thickness (µm)
 Mean Change from Baseline

	$\frac{1}{4}$ Fluence Triple				$\frac{1}{2}$ Fluence Triple				Double				Lucentis			
	N	mean	diff		N	mean	diff		N	mean	diff		N	mean	diff	
Day 0	38	314.6			39	337.3			42	341.3			40	313.2		
Month 3	38	216.8	-98		37	209.7	-125		40	207.0	-138		38	210.9	-104	
Month 6	36	210.9	-108		34	205.9	-130		37	223.5	-123		37	220.9	-94	
Month 9	36	198.0	-110		32	206.8	-116		36	199.1	-144		33	208.5	-97	
Month 12	37	200.6	-112		34	199.8	-133		33	201.2	-123		32	207.5	-109	

Figure 23
Cumulative Number of Retreatments
Based on Either OCT or FA at 12 months



1/4 Fl. Triple	N=38	38	38	38	38	38	38	38	37	36	37	36	37	37
1/2 Fl. Triple	N=39	37	36	37	34	34	34	34	35	35	32	34	34	34
Double	N=42	42	40	40	39	36	37	37	36	36	33	34	34	33
Lucentis	N=40	39	38	38	36	34	37	34	35	33	31	33	33	32

Figure 24
Summary of AEs at 12 months (Subjects Level)

	¼ Fluence Triple (N=39)	½ Fluence Triple (N=39)	Double (N=43)	Lucentis (N=41)
All AEs	35 (89.7%)	35 (89.7%)	35 (81.4%)	37 (90.2%)
All Associated AEs	17 (43.6%)	16 (41.0%)	21 (48.8%)	11 (26.8%)
All Study Eye Ocular AEs	21 (53.8%)	23 (59.0%)	25 (58.1%)	23 (56.1%)
All Associated Ocular AEs	13 (33.3%)	13 (33.3%)	14 (32.6%)	11 (26.8%)
All SAEs	7 (17.9%)	11 (28.2%)	13 (30.2%)	14 (34.1%)
All Associated SAEs	2 (5.1%)	2 (5.1%)	1 (2.3%)	0
All Associated Ocular SAEs	2 (5.1%)	2 (5.1%)	1 (2.3%)	0

Figure 25
Associated Treatment Site Ocular AEs by Subject and Event at 12 months

	$\frac{1}{4}$ Fluence Triple		$\frac{1}{2}$ Fluence Triple		Double		Lucentis	
	Sub.	Event	Sub.	Event	Sub.	Event	Sub.	Event
Vision abnormal	4 (10.3%)	5	2 (5.1%)	2	2 (4.7%)	3	0	0
Vision decrease	3 (7.7%)	3	3 (7.7%)	3	2 (4.7%)	2	0	0
Visual field defect	4 (10.3%)	4	0	0	2 (4.7%)	2	2 (4.9%)	2
Retinal detachment	0	0	0	0	1 (2.3%)	1	0	0
Retinal disorder	0	0	0	0	1 (2.3%)	1	0	0
Retinal tear	1 (2.6%)	1	0	0	0	0	0	0
Increased IOP	0	0	4 (10.3%)	8	3 (7.0%)	3	0	0