

5-Year Outcomes after Initiating Anti-VEGF Therapy for Neovascular AMD in the Comparison of AMD Treatments Trials (CATT)



- Daniel F. Martin, MD

OBJECTIVE To describe outcomes 5 years after initiating treatment with anti-VEGF therapy in patients with neovascular age-related macular degeneration (AMD).

PURPOSE To describe outcomes 5 years after initiating treatment with bevacizumab or ranibizumab for neovascular age-related macular degeneration (AMD).

METHODS Patients enrolled in the Comparison of AMD Treatments Trials (CATT) were assigned randomly to ranibizumab or bevacizumab and to 1 of 3 dosing regimens. After 2 years, patients were released from the clinical trial protocol. At 5 years, patients were recalled for examination. Best corrected ETDRS visual acuity, OCT, color photos, FA, and treatment history in the three-year interim were obtained. The mean number of examinations for AMD care after the clinical trial ended was 25.3, and the mean number of treatments was 15.4. Most patients (60%) were treated 1 time or more with a drug other than their assigned drug during the three year follow-up period.

RESULTS Visual acuity was obtained for 647 of 914 (71%) living patients with average follow-up of 5.5 years. At the 5-year visit, 50% of eyes were 20/40 or better and 20% were 20/200 or worse. Mean change in VA was -3 letters from baseline and -11 letters

from 2 years. Among 467 eyes with fluorescein angiography, mean total lesion area was 12.9 mm², 4.8 mm² larger than at 2 years. Geographic atrophy was present in 213 of 515 (41%) gradable eyes and was subfoveal in 85 eyes (17%). Among 555 eyes with spectral-domain optical coherence tomography, 83% had persistent fluid. Mean foveal total thickness was 278 um, a decrease of 182 um from baseline and 20 um from 2 years. The retina was abnormally thin (<120 um) in 36% of eyes. Between 2 and 5 years, the group originally assigned to ranibizumab for 2 years lost more VA than the bevacizumab group (-4 letters; P=0.008). Otherwise, there were no statistically significant differences in VA or morphologic outcomes between drug or regimen groups.

CONCLUSION Vision gains during the first 2 years were not maintained at 5 years. However, 50% of eyes had VA of 20/40 or better, confirming anti-VEGF therapy as a major long-term therapeutic advance for neovascular AMD.

TAKE HOME MESSAGE Vision gains during the first 2 years were not maintained at 5 years. However, 50% of eyes had VA of 20/40 or better, confirming anti-VEGF therapy as a major long-term therapeutic advance for neovascular AMD.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

Ocular Hypertension after Intravitreal Dexamethasone Sustained-Release Implant



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OBJECTIVE To evaluate the risk and likelihood of ocular hypertension (OHT) after intravitreal dexamethasone sustained-release implant injection(s).

PURPOSE To evaluate ocular hypertension (OHT) after intravitreal dexamethasone sustained-release implant injection to determine the incidence of OHT, therapy of OHT, and any associative factors such as diagnosis, underlying glaucoma and therapy, or sequential intravitreal dexamethasone sustained-release implant injection(s).

METHODS Retrospective consecutive case series with patients receiving one or more intravitreal intravitreal dexamethasone sustained-release implant implantations at a tertiary care academic center.

RESULTS Ninety-four injections in 52 patients (59 eyes) were reviewed. Forty eyes received a single injection, and 19 eyes received multiple injections. OHT developed in 14 patients (26.9%). IOP was elevated ≥ 10 mmHg from baseline in 14 instances (14.9%) and ≥ 30 mmHg in ten instances (10.6%). Thirteen patients (25%) had pre-existing

glaucoma or glaucoma suspicion, and six of these developed OHT. Glaucoma eye drops were initiated following 13 injections (13.8%). Invasive glaucoma surgery was required in three patients (3.2%): all had glaucoma or glaucoma suspicion. There was no difference in relative IOP increase between single versus multiple intravitreal dexamethasone sustained-release implant injections ($P = 0.883$).

CONCLUSION 26.9% patients who received intravitreal dexamethasone sustained-release implant developed OHT. Glaucoma or glaucoma suspicion factors were present in all patients who required invasive glaucoma surgery. A greater proportion of patients who received multiple injections had an IOP elevation, but the relative IOP increase was not significant.

TAKE HOME MESSAGE 26.9% patients who received intravitreal dexamethasone sustained-release implant developed OHT. A greater proportion of patients who received multiple injections had an IOP elevation, but the relative IOP increase was not significant.

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IRB Approval Status: Approved by institutional review board

Pneumatic Vitreolysis for Effective Treatment of Vitreomacular Traction Syndrome



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OBJECTIVE To study the benefits and risks of pneumatic vitreolysis with C₃F₈ gas in the treatment of vitreomacular traction syndrome.

PURPOSE To assess perfluoropropane (C₃F₈) gas injection for treating symptomatic vitreomacular traction (VMT) with or without a stage-2 macular hole (MH).

METHODS We conducted a retrospective study of eyes with focal VMT treated with 0.3 mL of intravitreal C₃F₈ gas injection. Treated patients avoided the supine position until gas resolution. Patients with stage-2 MH maintained partial face-down positioning.

RESULTS There were 48 consecutive patients (50 eyes) with symptomatic VMT who underwent pneumatic vitreolysis (PVL) with C₃F₈ gas between 2010 and 2016. VMT release developed in 43 eyes (86.0%), at a median of 3.0 weeks after gas injection. VMT release was achieved in 29 of 36 eyes (80.6%) with VMT only and all 15 eyes (100%) with a small stage-2 MH. MH closure occurred in 10 of 15 eyes (66.7%). Median baseline and last best spectacle-corrected visual acuity (BSCVA) was 20/50 and 20/40, respectively ($P=0.000082$). Mean follow-up time was 11.7 months. Rate of VMT release was reduced with broad VMT (>2 disc areas) (25%) and with thick cellophane membrane (50%). One eye with VMT only formed a MH, and one with VMT only developed a

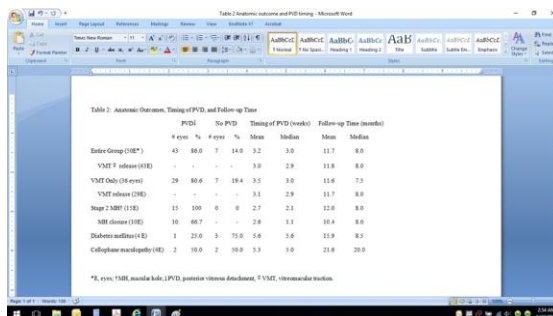
retinal detachment. Both responded to vitrectomy with latest VA of 20/30 and 20/70, respectively.

CONCLUSION PVL with C3F8 gas and limited face-down position was highly effective in releasing focal VMT in 86% of the treated eyes with narrow vitreoretinal adhesion. It was also capable of closing in 67% of treated eyes with small stage-2 macular holes. There were few associated adverse events. More studies are needed to elucidate its indications, benefits and risks.

TAKE HOME MESSAGE Pneumatic Vitreolysis with C3F8 gas is highly effective in resolving vitreomacular traction (VMT), as VMT release is achieved in 86% of treated eyes and highly significant visual recovery is attained.

	Baseline BCVA*			Last BCVA			p-value		
	Mean	Median		Mean	Median				
Entire Group (18E)	0.4022	20/30	0.3979	20/30	0.2770	20/18	0.3010	20/40	0.00082
VMT* release (18E)	0.3828	20/40	0.3979	20/30	0.2249	20/34	0.1761	20/30	0.00082
VMT Only (18E)	0.3739	20/40	0.3979	20/30	0.3010	20/40	0.3010	20/40	0.021
VMT release (18E)	0.3466	20/44	0.3683	20/43	0.2497	20/36	0.3010	20/40	0.018
Stage 2 MRF (18E)	0.4764	20/19	0.4771	20/40	0.3023	20/32	0.1761	20/30	0.0017
MRF closure (18E)	0.4762	20/40	0.5104	20/70	0.3894	20/30	0.1761	20/30	0.013
Diabetic maculopathy (18E)	0.4886	20/62	0.5296	20/39	0.4688	20/29	0.5000	20/43	0.87
Collophane maculopathy (18E)	0.4930	20/82	0.4375	20/33	0.2318	20/34	0.1761	20/30	0.014

*BCVA, best spectacle corrected visual acuity; 18E, eyes; 18M, macula hole; VMT, vitreomacular traction.



	PVD		Timing of PVD (weeks)		Follow-up Time (months)			
	# eyes	%	# eyes	%	Mean	Median		
Entire Group (18E*)	43	88.0	7	14.0	3.2	3.0	11.7	8.0
VMT* release (18E)	-	-	-	-	3.0	2.8	11.8	8.0
VMT Only (18E)	29	80.6	7	19.4	3.5	3.0	11.6	7.3
VMT release (18E)	-	-	-	-	3.1	2.8	11.7	8.0
Stage 2 MRF (18E)	15	100	0	0	2.7	2.1	12.0	8.0
MRF closure (18E)	10	66.7	-	-	2.8	1.1	10.4	8.0
Diabetic maculopathy (18E)	1	25.0	3	75.0	5.6	5.6	11.9	8.5
Collophane maculopathy (18E)	2	10.0	2	10.0	3.3	3.0	21.8	20.0

*E, eyes; 18M, macula hole; PVD, posterior vitreous detachment; VMT, vitreomacular traction.

HUMAN RESEARCH This study involves human research.

IRB Approval Status: Exempt from approval

Safety and efficacy of Razumab (Ranibizumab) - the new biosimilar in India : Our experience



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OBJECTIVE To evaluate the safety and efficacy of biosimilar intravitreal ranibizumab (Razumab) for the treatment of macular disorders at an affordable price

PURPOSE To evaluate the safety and efficacy of biosimilar intravitreal ranibizumab (Razumab) for the treatment of neovascular Age Related Macular Degeneration(AMD),Macular oedema secondary to Retinal vein occlusions(RVO) and Diabetic Macular Oedema (DME)

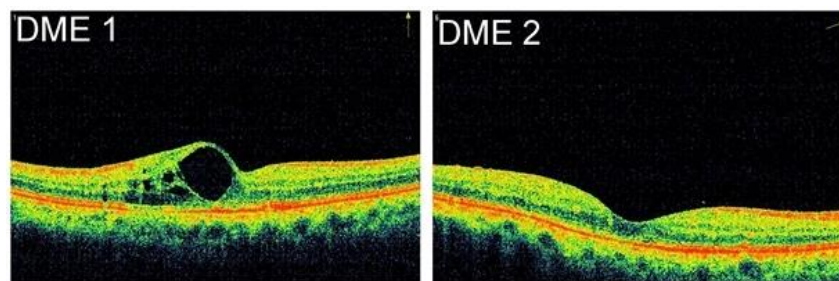
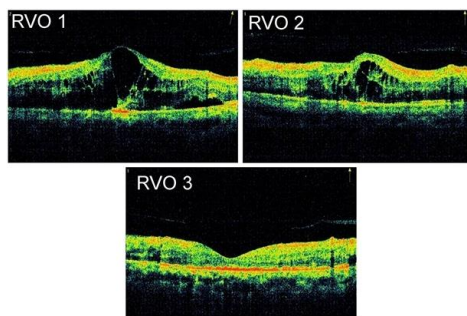
METHODS A prospective analysis was performed on consented patients with neovascular AMD (Group 1),Macular oedema secondary to RVO (Group2) and DME (Group3) receiving intravitreal Razumab therapy. All patients received intravitreal Razumab at baseline. A routine Snellen visual acuity assessment, Anterior segment, Fundus evaluation Optical coherence tomography (OCT) imaging was done at Day 0,1,7 and 30. ERG was performed at baseline and Day 30(23 eyes who could afford this investigation).Primary outcome measures were safety parameters that included signs of clinical and ERG toxicity. Secondary outcome measures included changes in best-corrected visual acuity (BCVA)and central macular thickness(CMT)

RESULTS 119 eyes of 95 patients received Razumab injection between November 2015 and May 2016. No serious drug-related ocular adverse events were identified. There were

no significant differences in implicit times, "a" and "b" wave amplitudes, or b/a ratios at 1 month when compared with baseline ($P = 0.706$). Multifocal ERG (7 affordable patients) showed generalised depression with no significant change from the baseline. Mean pre-treatment best corrected visual acuity (BCVA) was 0.59 ± 0.43 logMAR with CMT $345.90 \pm 128.84 \mu\text{m}$ and post injection BCVA at day 30 was 0.50 ± 0.37 logMAR with CMT reducing to $287.65 \pm 90.29 \mu\text{m}$ indicating statistical significance ($p=0.0467$) and ($p<0.0001$) respectively for all groups.

CONCLUSION Off-label intravitreal Razumab for neovascular AMD, Macular oedema secondary to RVO and DME was tolerated over a month with improvements in BCVA & CMT without detectable ocular & systemic toxicity. While the long-term safety and efficacy remain unknown, these short-term results suggest that Razumab could become a safe, low-cost therapy for macular diseases in developing countries

TAKE HOME MESSAGE Razumab could become a safe, low-cost therapy for macular diseases



HUMAN RESEARCH This study involves human research.
 IRB Approval Status: Approved by institutional review board