9:30 AM

Vascularized Pigment Epithelial Detachment Treated With 0.5 mg versus 2 mg Ranibizumab: Analysis of Results Based on Lesion Subtypes

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- David Sarraf, MD
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- Colin A. McCannel, MD

OBJECTIVE

Analysis of outcomes based on lesions subtypes in eyes with vascularized pigment epithelial detachment (vPED) treated with 0.5 vs. 2.0 mg ranibizumab.

PURPOSE

1) Comparison of responses of serous vascularized pigmented epithelial detachment (svPED)(Grp1) with fibrovacsular pigment epithelial detachment (fvPED) (Grp2) to 0.5 vs. 2.0 mg ranibizumab injections (RI), and 2) Analysis of vision results for all study eyes with vs. without flattening of the pigment epithelial detachment (PED) due to AMD.

METHODS

RI groups in this ***prospective, randomized trial*** were:1) 0.5mg monthly (QM) x12 months(M), 2) 0.5mg QM x4M then PRN injections to12M, 3) 2.0mg QM x12M, 4) 2.0mg QM x4M then PRN injections to 12M. Primary outcome measures were pre-& post-RI(last visit),best corrected standardized vision (BCVA). Secondary measures were pre- & post central-1mm thickness (1mm); area (A^2), diameter (GLD),& heights of PED & choroidal neovascularization(CNV); subretinal fluid (SRF),cystoid macular edema (CME);complications.Results of svPED Grp1)vs.fvPED(Grp2) were compared. Vision results of with vs without resolved PED were compared. Statistics were 2 & 3-way analysis of variance (ANOVA) & nonparametric tests.

RESULTS

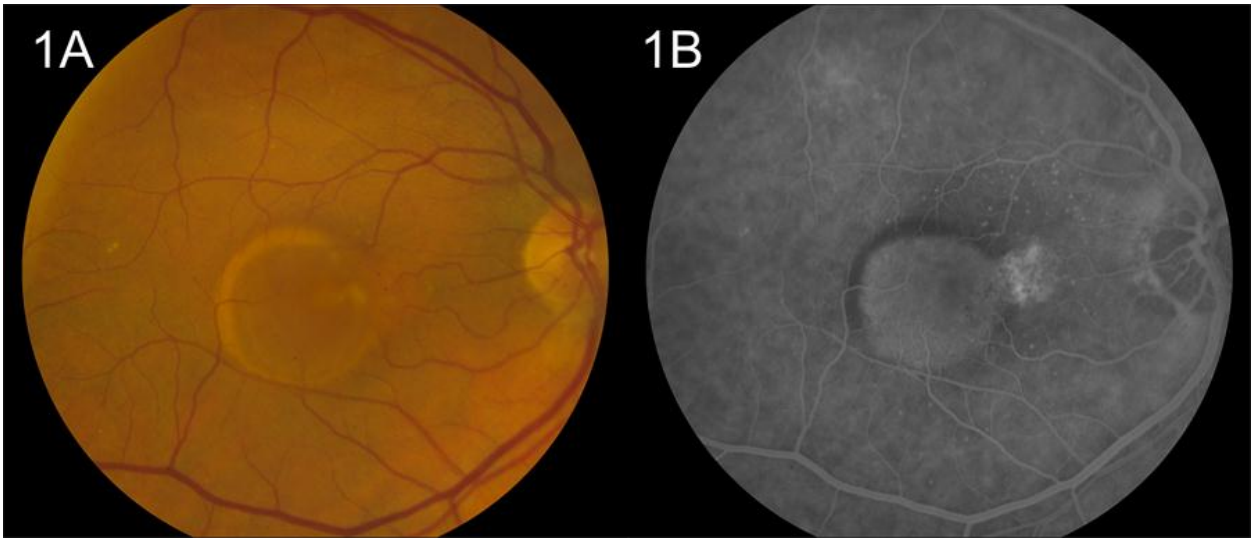
Of 36 eyes (10 men), 8 were in Grp1& 28 in Gp2 (Mean age: 78.6,&mean follow-up:11.8M).No differences were in baseline features between groups except $PEDA^2$ (Grp2>Grp1). 2-way ANOVA (pre/post,lesion type) showed less post-RI PED height, PED & $CNVA^2$ & GLD, 1mm, SRF, CME,& improved BCVA compared to baseline(all $p<0.03$).No differences were noted between groups except for slightly greater PED SA^2 &GLD in Grp2 vs Grp 1 eyes ($p<0.05$). 3-way ANOVA (pre/post, lesion type, dose) showed no differences in all variables, irrespective of dose (all $p>0.05$). There was a trend for more flattened PED in Grp1, but statistical significance was not reached (87.5%-Grp1[95%CI:64.5-100%]),53.6%-Grp2 [95%CI:35.1-72.1%],$p=0.08$).Similar % of retinochoroidal anastomoses (RAP) were in both groups (12.5-Grp1&17.9%-Grp2,$p=0.72$).Cataract worsening were similar for both groups. RPE tears were in 2 Grp1 eyes & 3 Grp2 eyes. Flattened PED yielded more frequent stable or Improved vision ($p=0.008$),&less vision loss ($p=0.03$).

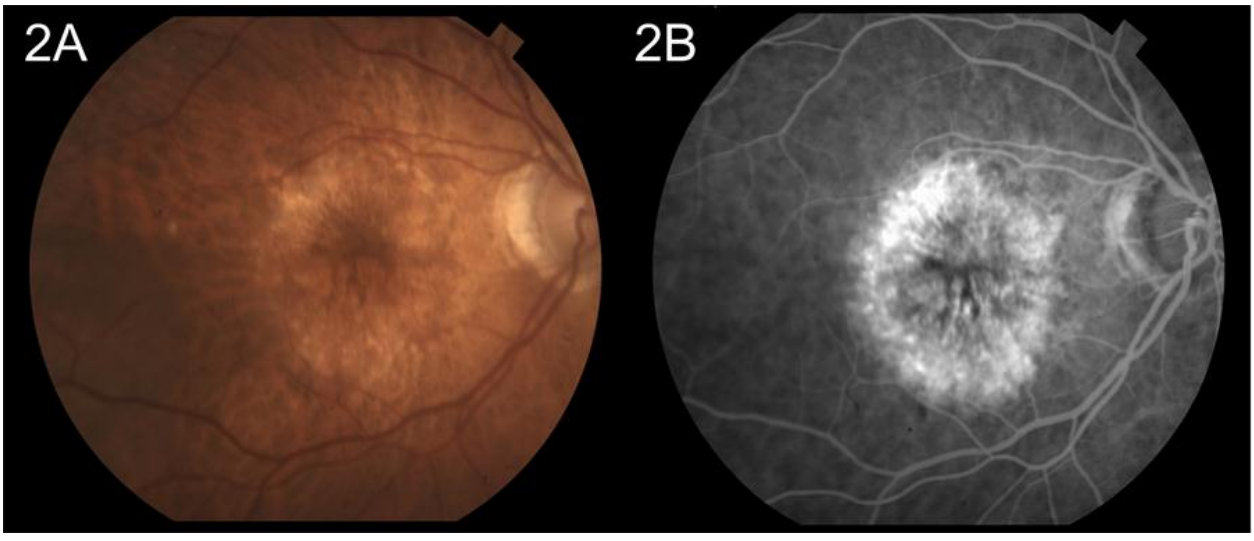
CONCLUSION

Irrespective of the 2 doses of ranibizumab, the outcome and safety profiles were similar for eyes with svPED and fvPED. Flattening of PED yielded greater chance of vision stabilization or improvement and reduced chance of vision loss.

TAKE HOME MESSAGE

This study shows similar efficacy and safety outcomes for vascularized serous PED and fibrovascular PED, 2 major subtypes of vascularized PED; and flattening of PED yielded better vision outcome.





9:34 AM

Juxtapapillary Retinal Pigment Epithelial Detachments in Asymptomatic Subjects Detected With Spectral Domain Optical Coherence Tomography

- Alexander Craig Walsh, MD
- Srinivas Reddy Sadda, MD
- Srinivas Reddy Sadda, MD
- Yanling Ouyang, MD
- Florian M Heussen, MD
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OBJECTIVE To determine the prevalence of juxtapapillary PEDs in asymptomatic individuals, investigate associations with other findings, and form a hypothesis as to their etiology.

PURPOSE This study used spectral domain optical coherence tomography (SD-OCT) to assess the prevalence of juxtapapillary retinal pigment epithelial detachments (jPED) in an asymptomatic population. Associations between jPEDs and findings such as drusen, peripapillary pigmentation and atrophy were also investigated.

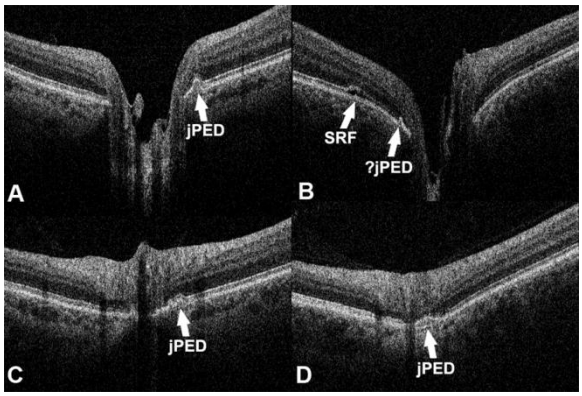
METHODS Asymptomatic subjects (i.e. patient companions) were prospectively recruited for this study over a six-month period from an eye clinic waiting room. Each subject

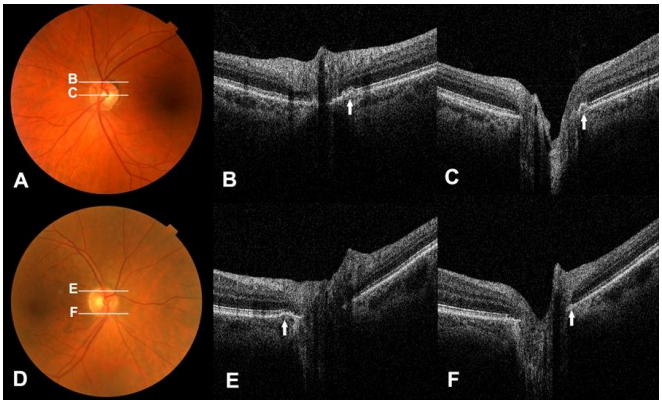
completed a questionnaire prior to the acquisition of two undilated 45° fundus images and four undilated raster SD-OCT scans (3x 512x128, 1x 1024x64) covering the macula and optic nerve of each eye using a Topcon 3D-OCT-1000 (Topcon Co, Tokyo). Fundus images were graded for the presence of peripapillary atrophy (PPA), peripapillary pigment (PPP), and drusen; while SD-OCT scans were assessed for the presence of both jPED and drusen (categorized as PED elsewhere = PEDe).

RESULTS 276 eyes from 138 participants were evaluated. The mean subject age was 37.7 years (range = 18-74). Sixty percent of participants were women. Fifty percent identified themselves as Hispanic, 18% as non-Hispanic white, 18% as Asian, and 4% as African-American. jPEDs were graded as definitely present in 40% of the subjects (26% of eyes) and questionably present in an additional 15% of subjects (15% of eyes). There was no statistically significant association between the presence of jPED and the presence of PPP or PPA on fundus imaging. The prevalence of both jPEDs and drusen increased statistically with age ($p<0.001$, respectively), while PPA ($P=0.846$) and PPP ($P=0.990$) remained unchanged with subject age. More jPEDs were found in the nasal and temporal quadrants than the superior and inferior quadrants. One subject had subretinal fluid adjacent to a jPED.

CONCLUSION In this study, 48% of asymptomatic subjects (34% of eyes) had definite or questionable jPEDs. PPP and PPA were not reliable surrogate markers for the presence of jPEDs. Like drusen, jPEDs were seen more commonly with age. Although jPEDs may be drusen-like deposits, they may also be aborted CNV since they are adjacent to a natural break in Bruch's membrane and may have associated subretinal fluid.

TAKE HOME MESSAGE Juxtapapillary PEDs are common and visible only with OCT. If jPEDs represent spontaneously aborted CNV, early detection of jPEDs may lead to beter understanding and treatment of peripapillary CNV.





9:42 AM

A Phase 1 Study Targeting Tissue Factor with a Single Dose of Intravitreal hI-con1 for Exudative Age-Related Macular Degeneration (AMD)

- Christine R. Gonzales, MD
- John A. Wells, MD, FACS
- Brian B. Berger, MD
- Victor Hugo Gonzalez, MD
- Brian D. Sippy, MD, PhD
- manju Soni, MD
- Kirk T. Dornbush, J.D. Boston Unversity School of Law
- David L. Johnson, MD

OBJECTIVE This phase 1 study evaluated the safety and tolerability of single ascending doses of intravitreous injections of hI-con1 in eyes with active neovascular AMD

PURPOSE Tissue factor is a potential therapeutic target as it is found on abnormal vascular endothelial cells. hI-con1 binds tissue factor triggering natural killer cells to selectively destroy pathologic blood vessels. This study evaluated the safety and tolerability of single ascending doses of intravitreous injection of hI-con1™ alone or with anti-VEGF therapy in eyes with active neovascular AMD.

METHODS This prospective, multi-center, dose-escalating clinical study evaluated the safety and tolerability of a single, intravitreous injection of 60µg, 150µg and 300µg of hI-con1 in 18 patients (6 per cohort) with neovascular AMD. Ocular inclusion criteria included active subfoveal choroidal neovascularization (CNV) in which at least 50% was actively leaking and best-corrected visual acuity by ETDRS of 20/63 – CF. Eyes with prior anti-VEGF therapy and treatment-naïve eyes were enrolled. Anti-VEGF therapy was allowed 2 weeks after the hI-con1 injection at the investigator's discretion.

RESULTS No ocular or systemic dose limiting toxicities were identified. Specifically, there were no retinal or choroidal vascular, inflammatory or hemorrhagic toxicities; and no drug related adverse systemic events. Overall, visual acuity improved +3.7 letters and OCT analysis revealed -103 microns change from baseline at 12 weeks. The high dose (300 µg) group demonstrated a +8.2 letter change in vision and -122 micron change in OCT thickness from baseline at 12 weeks. Fluorescein angiography revealed substantial neovascular regression in many of the patients.

CONCLUSION A single injection of hI-con1, alone or in combination with anti-VEGF agents, showed no ocular or systemic safety signals. Evidence of dose-related biologic activity with reduced OCT thickness, evidence of CNV regression, and gains in BCVA was observed in many of the treated eyes. Further investigation is planned.

TAKE HOME MESSAGE A single injection of hI-con1, alone or with anti-VEGF agents, showed no ocular or systemic safety signals. Evidence of dose-related biologic activity was observed in many of the treated eyes.

9:46 AM

Argon Laser With and Without Anti-Vascular Endothelial Growth Factor Therapy (VEGF) for Polypoidal Choroidal Vasculopathy

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- Choi Mun Chan, MBBS, MMed, FRCS
- Doric Wong
- Tien Yin Wong, MBBS, MMED, MPH, PhD, FRCSE, FRANZCO, FAFPHM, FAMS
- Xiang Li, BSc
- Gemmy chui ming Cheung, FRCOphth

OBJECTIVE To study the effect of thermal laser on polypoidal lesions and associated vascular networks in polypoidal choridal vasculopathy with or without anti-vascular endothelial growth factor

PURPOSE To describe the clinical characteristics and outcome of eyes with polypoidal choroidal vasculopathy (PCV) treated with argon laser, with or without anti-Vascular Endothelial Growth factor therapy.

METHODS A prospective study of the proportion of Asian patients with neovascular AMD and PCV. Eyes with extrafoveal PCV confirmed on indocynanine green angiography were treated with argon laser with and without anti-vascular endothelial growth factor therapy and followed-up over 12 months. Visual and angiographic outcome and additional therapy over 12-months was recorded.

RESULTS 158 eyes with neovascular AMD were included. PCV was identified in 93 eyes, of which 33 eyes (31 patients) were extrafoveal and treated with argon laser for PCV. 12 of these 33 eyes (36.4%) also received anti-VEGF injections (median 2.5 injections). Foveal involvement with fluid or blood at baseline was apparent in 23 eyes (69.7%)

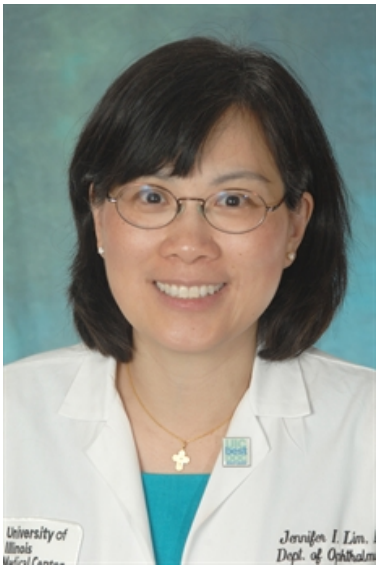
despite the extrafoveal location of polyp(s). Median visual acuity improved from 0.56 LogMAR (0.02-2.0, SD 0.50) at baseline to 0.48 LogMAR (0.02-2.0, SD 0.49) at month 3, and further to 0.41 LogMAR (0.00-2.0 SD 0.43) at month 12. The mean gain in visual acuity was 8.0 letters at month 12. The mean central subfield thickness improved from 292.7µm (185-758 µm, SD 104.1) to 225.6 µm (142-326 µm. SD 29.1) at month 3 and was maintained at 230.4 µm (167-296 µm, SD 29.1) at month 12. Stable or improved vision was achieved in 28 eyes (84.9%).

CONCLUSION Thermal laser with and without anti-VEGF therapy achieves stable or improved visual outcome in the majority of eyes with extrafoveal polyp, including eyes with fluid or blood affecting the fovea at presentation. Adjunct anti-VEGF injections may contribute to improved visual outcome by targeting leakage within the associated vascular network.

TAKE HOME MESSAGE Polypoidal Choridal Vasculopathy with extrafoveal polyps can be managed with focal thermal laser to obliterate the polyps. The addition of anti-VEGF therapy may have a role in these patients.

9:50 AM

Combination Therapy for Neovascular AMD Using PRN Ranibizumab and a Single Injection of Liquid-Sustained Release Intravitreal Triamcinolone Acetonide



- Jennifer I. Lim, MD
- Marcia Niec, BS MT
- Dean Hung, PhD
- Vernon Wong, MD

OBJECTIVE To determine whether combining a novel liquid sustained release system containing triamcinolone acetonide when combined with PRN ranibizumab is safe and lowers retreatment rates.

PURPOSE To determine evidence of safety and efficacy of a combination therapy of sustained release intravitreal triamcinolone acetonide and ranibizumab in eyes with neovascular AMD.

METHODS We performed a prospective pilot study of combination therapy for active, subfoveal, choroidal neovascularization (CNV) due to AMD. Patients underwent baseline ETDRS visual acuity, slit lamp and dilated fundus examinations, fluorescein angiography and spectral domain optical coherence tomography (OCT). Patients were randomly assigned to receive a single intravitreal injection of a sustained release liquid drug delivery system of 6.9 mg (25ml) or 13.8 mg (50ml) of triamcinolone acetonide. A ranibizumab intravitreal injection was given one week later. Patients were followed monthly with ETDRS and OCT tests and given ranibizumab as needed. Patients were monitored for adverse events.

RESULTS Ten patients ranged in age from 59 to 89 (median 73) years. Four patients were treatment naïve. The other six patients had received 4 to 16 prior injections (median 9). Baseline ETDRS visual acuity ranged from 81 to 25 letters (median 65). Baseline OCT ranged from 200 to 757 microns. Follow-up ranged from 60 to 360 days (median 285 days). At both days 30 and 60, one patient of 10 required retreatment with ranibizumab. At day 90, none of 9 patients required retreatment. At day 120, 4 of 7 patients and at day 180, 1 of 7 patients required retreatment. By 6 months, of 42 potential retreatments, 7 were required. By 12 months, of 74 potential retreatments, 14 were required. Adverse events included six patients with mild transient IOP elevations that responded to topical glaucoma therapy. There were no injection related events (endophthalmitis, retinal or vitreous hemorrhage, retinal tear or detachment). Visual acuity was stable or improved in 7 of the 8 patients at latest follow-up.

CONCLUSION Combination therapy using intravitreal ranibizumab and a single intravitreal injection of a liquid sustained release drug delivery system containing triamcinolone acetonide appears safe and may decreased the number of as needed ranibizumab retreatments.

TAKE HOME MESSAGE Combination therapy may be useful in reducing the number of anti-VEGF therapy required to control neovascular AMD.