Darren

Synthetic control arm paper

Two files are linked by the study number

We are interested in treatment == avastin arm

Vast0= visit at 0 weeks (baseline), Vast1= week 1 visit

avastintrt

= number of avastin treatments actually given to week 54

**Analysis Plan**

**Select out patients with avastin treatment only**

**Match the following variables for each avastin treated patient to all possible matches treated with Eylea (aflibercept) for the first 54+ weeks of treatment in the EMR dataset. Aflibercpet patient myst have>=7 and a second study of >=8 treatment in 54 weeks**

Mactch 1

**Baseline VA**

**Age**

**OCT thickness if available**

**PED if available ( presence or absence\_**

**( see paper 1 – for tolerance of match )**

**Generate CI by bootstrapping al lthe matching patients without replacement**

**Analysis**

**Mean change in VA over time**

**Time to 5/15 letter loss or gain (KM plots)**

**Match 2**

**Visual acuity change at 12 weeks – match with (XX – tolerance )**

**(see paper 2)**

Paper 1

**Baseline Predictors for One-Year Visual Outcomes with Ranibizumab or Bevacizumab for Neovascular Age-related Macular Degeneration**

**Gui-shuang Ying, PhD,1,2,3 Jiayan Huang, MS,1,2 Maureen G. Maguire, PhD,1,2,3 Glenn J. Jaffe, MD,4 Juan E. Grunwald, MD,1,2 Cynthia Toth, MD,4 Ebenezer Daniel, MBBS, MS, MPH,1,2 Michael Klein, MD,5 Dante Pieramici, MD,6 John Wells, MD,7 Daniel F. Martin, MD,8 on behalf of the Comparison of Age-related Macular Degeneration Treatments Trials Research Group\***

**Objective: To determine the baseline predictors of visual acuity (VA) outcomes 1 year after treatment with ranibizumab or bevacizumab for neovascular age-related macular degeneration (AMD). Design: Cohort study within the Comparison of Age-related Macular Degeneration Treatments Trials (CATT). Participants: A total of 1105 participants with neovascular AMD, baseline VA 20/25 to 20/320, and VA measured at 1 year. Methods: Participants were randomly assigned to ranibizumab or bevacizumab on a monthly or as-needed schedule. Masked readers evaluated fundus morphology and features on optical coherence tomography (OCT). Visual acuity was measured using electronic VA testing. Independent predictors were identified using regression techniques. Main Outcome Measures: The VA score, VA score change from baseline, and ⱖ3-line gain at 1 year. Results: At 1 year, the mean VA score was 68 letters, mean improvement from baseline was 7 letters, and**

**28% of participants gained ⱖ3 lines. Older age, larger area of choroidal neovascularization (CNV), and elevation of retinal pigment epithelium (RPE) were associated with worse VA (all P ⬍ 0.005), less gain in VA (all P ⬍ 0.02), and a lower proportion gaining ⱖ3 lines (all P ⬍ 0.04). Better baseline VA was associated with better VA at 1 year, less gain in VA, and a lower proportion gaining ⱖ3 lines (all P ⬍ 0.0001). Predominantly or minimally classic lesions were associated with worse VA than occult lesions (66 vs. 69 letters; P⫽0.0003). Retinal angiomatous proliferans (RAP) lesions were associated with more gain in VA (10 vs. 7 letters; P⫽0.03) and a higher proportion gaining ⱖ3 lines (odds ratio, 1.9; 95% confidence interval, 1.2–3.1). Geographic atrophy (GA) was associated with worse VA (64 vs. 68 letters; P⫽0.02). Eyes with total foveal thickness in the second quartile (325–425 ␮m) had the best VA (P⫽0.01) and were most likely to gain ⱖ3 lines (P⫽0.004). Predictors did not vary by treatment group.**

**Conclusions: For all treatment groups, older age, better baseline VA, larger CNV area, predominantly or minimally classic lesion, absence of RAP lesion, presence of GA, greater total fovea thickness, and RPE elevation on optical coherence tomography were independently associated with less improvement in VA at 1 year. Financial Disclosure(s): The author(s) have no proprietary or commercial interest in any materials discussed**

**in this article. Ophthalmology 2013;120:122–129 © 2013 by the American Academy of Ophthalmology.**

**Paper 2**

**Association of Baseline Characteristics and**

**Early Vision Response with 2-Year Vision Outcomes in the Comparison of AMD Treatments Trials (CATT)**

**Gui-shuang Ying, PhD,1 Maureen G. Maguire, PhD,1 Ebenezer Daniel, MBBS, PhD,1 Frederick L. Ferris, MD,2 Glenn J. Jaffe, MD,3 Juan E. Grunwald, MD,1 Cynthia A. Toth, MD,3 Jiayan Huang, MS,1 Daniel F. Martin, MD,4 on behalf of the Comparison of Age-Related Macular Degeneration Treatments Trials (CATT) Research Group\***

**Purpose: To evaluate the association of baseline characteristics and early visual acuity (VA) response with**

**visual outcomes at years 1 or 2 in the Comparison of Age-Related Macular Degeneration (AMD) Treatments Trials (CATT).**

**Design: Secondary analysis of CATT. Participants: The 1185 CATT participants with baseline VA of 20/25 to 20/320. Methods: Participants were assigned to ranibizumab or bevacizumab and to 1 of 3 dosing regimens.**

**Associations of baseline characteristics and early VA response (week 4 or 12) with VA response at years 1 or 2 were assessed by R2 from linear regression analyses. Patients who had a poor initial response (VA 20/ 40 or worse with persistent fluid and without 1-line VA gain) were defined as candidates for changing treatment. Main Outcome Measures: Visual acuity change from baseline. Results: Statistically significant (P < 0.05) baseline predictors for less VA gain at year 2 were older age, VA of**

**20/40 or better, larger choroidal neovascularization area, presence of geographic atrophy, total foveal thickness 325 mmor 425 mm, and elevation of retinal pigment epithelium. Among 176 eyes gaining 3 lines at week 12, 78% had a 3-line gain at year 2, whereas among 113 eyes losing 1 line at week 12, 27% improved to a 1-line gain at year 2. Visual acuity response at week 12 was more predictive of VA response at year 2 (R2 ¼ 0.30) than VA response at week 4 (R2 ¼ 0.17) and baseline predictors (R2 ¼ 0.13; P < 0.0001). Among 126 candidates for changing treatment drug at week 12, mean VA improved by 2.8 letters (P ¼ 0.050), mean total retinal thickness decreased 53 mm(P < 0.0001), and fluid resolved in 33% (P < 0.0001) between week 12 and year 1 with continued use of the same drug and regimen. Similar improvements were observed among 83 candidates for changing drugs at week 24. Conclusions: Visual acuity response at week 12 is more predictive of 2-year vision outcomes than either**

**several baseline characteristics or week 4 response. Eyes with poor initial response may benefit from continued treatment without switching to another drug. Ophthalmology 2015;122:2523-2531 ª 2015 by the American Academy of Ophthalmology.**