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**ANTI-VEGF MEDICATION IN
THE TREATMENT OF WET
AGE-RELATED MACULAR
DEGENERATION (AMD)**

Treatment of Wet AMD at Retina Associates of Florida

- ① Treat to maximum improvement
 - Give monthly injections usually for a year
- ① Prevent recurrences
 - Usually every six weeks after maximum benefit is achieved
- ① Treatment is for life

History of Macular Degeneration treatment

⦿ Thermal laser

- Could only treat patients whose disease was outside the area of central vision
- 50% recurrence rate at 5 years

⦿ PDT (Visudyne)

- Could treat under the center but 5% lost vision with treatment and didn't get it back
- 90% recurrence

History of Anti-VEGF medication

⦿ Macugen

- First approved medication for the eye
- 2002
- Not very effective, but better than natural course
- Fewer people went blind
- Not used any more

History of Anti-VEGF medication

⦿ Avastin

- Not approved for intraocular use
- Approved for use as adjuvant treatment for colon cancer
- Mouse antibody against VEGF
- Before Lucentis was approved was tried for macular degeneration and it showed efficacy in small, uncontrolled studies
- Problems with ocular inflammation
- Not manufactured to standards that are required for intraocular use

History of Anti-VEGF medication

◎ Lucentis

- Approved June 30th, 2006
- Revolutionized treatment of wet macular degeneration
- Good, long-term studies
- High response rate
- Manufactured to higher standards for intra-ocular use
- Drug stays in eye for 5 days and has biologic activity for one month

MARINA Study

- Minimally classic subretinal membranes were compared to a non-treated control group that were given sham injections
- 90% did not lose three lines of vision compared to 53% in the control group
- 33% gained three lines of vision compared to 4% in the control group
- 69% gained vision compared to 22% in the control group

ANCHOR Study

- Treatment with PDT (best treatment at the time) compared to monthly Lucentis
- 90% did not lose 3 lines of vision compared to 66% in the PDT group
- 41% gained three lines of vision compared to 6% in the PDT treated group
- 76% gained some vision compared to 27% in the PDT treated group

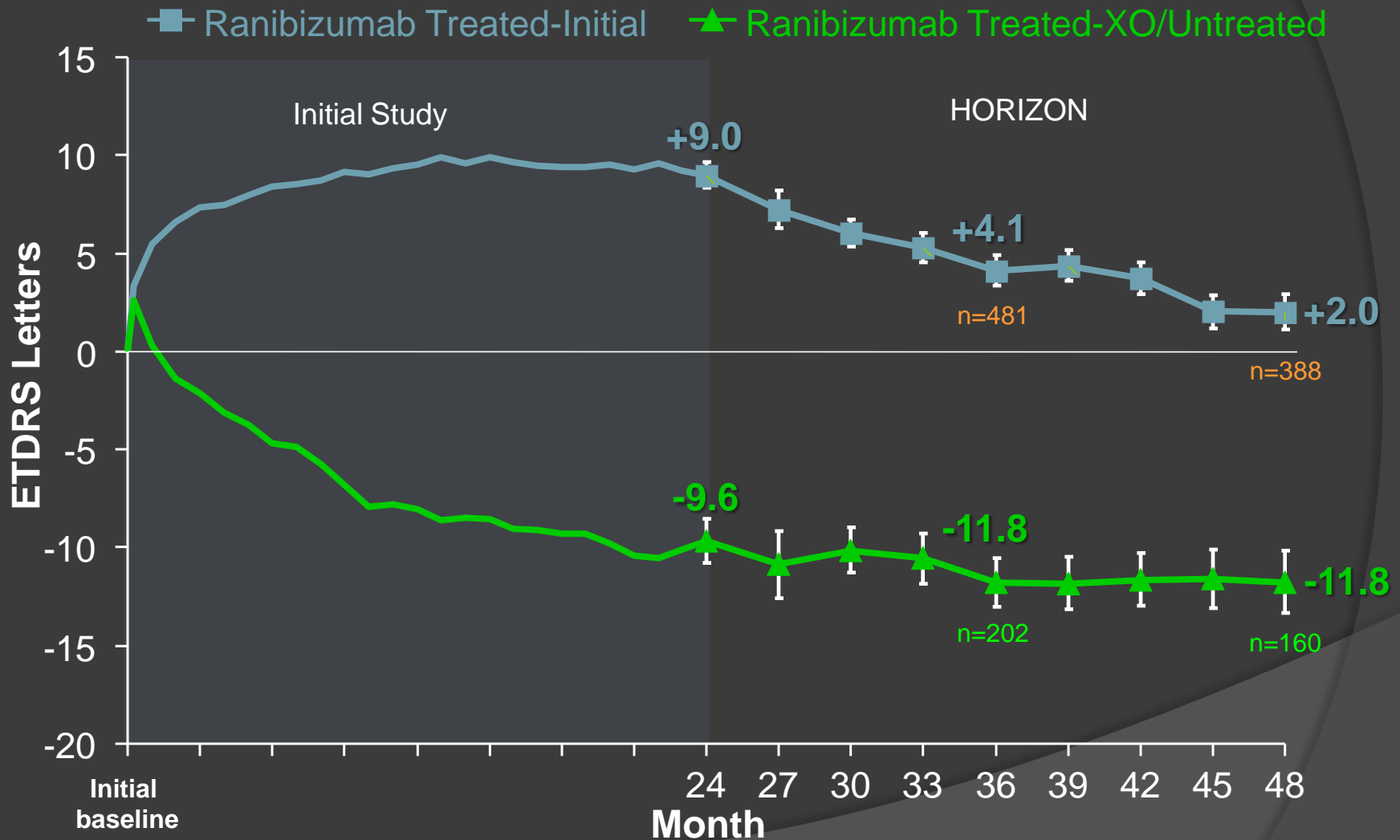
Different type of responders

- 32% were rapid responders
- 47% were gradual responders
- 19% were delayed responders
- 2% were non-responders

PIER Study

- Three months initial treatment with Lucentis followed by treatment every three months
- After initial favorable response, patient's vision returned to base line with every three month dosing

Mean Change in Visual Acuity from Initial Baseline

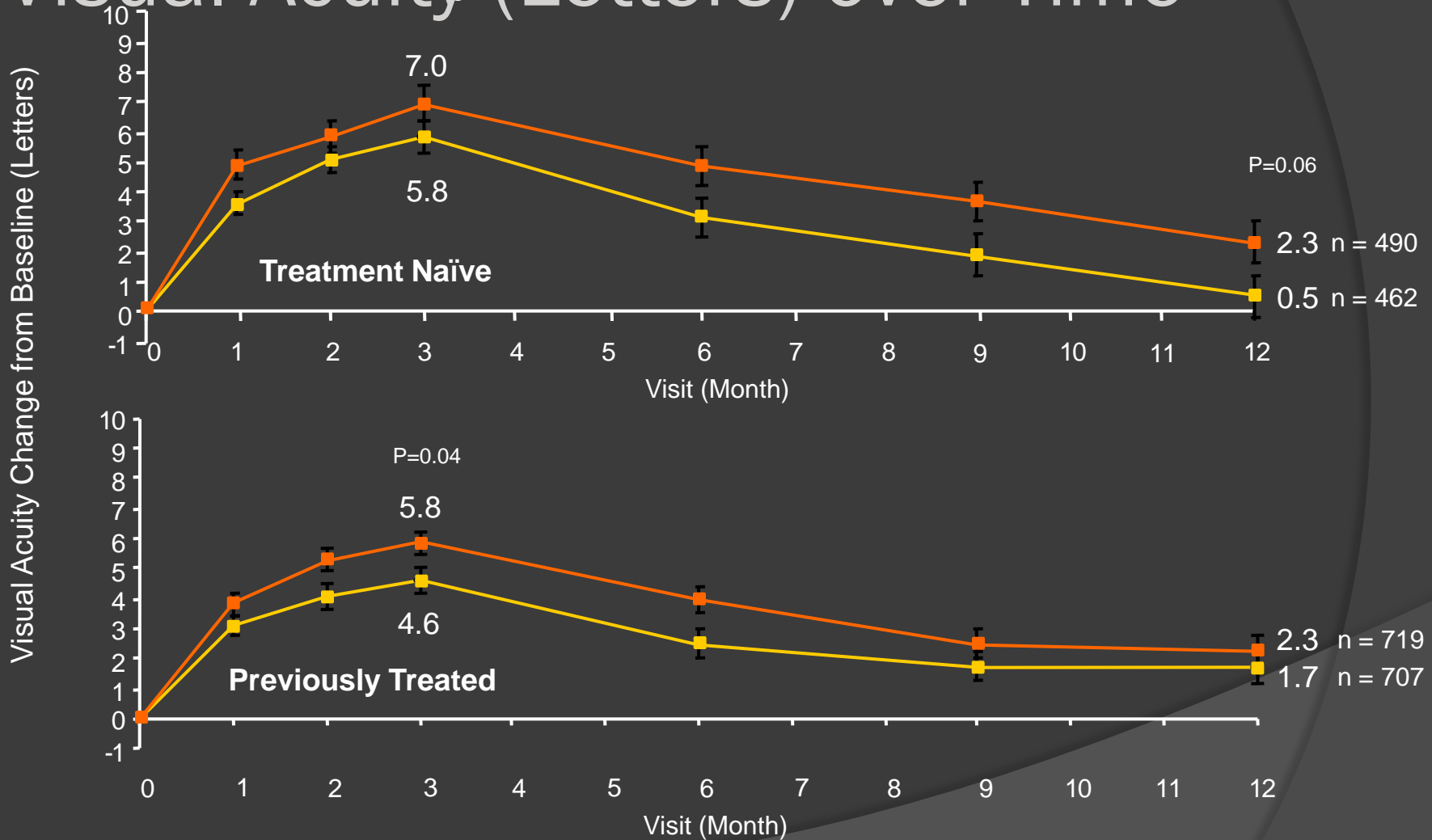


Vertical bars are \pm one standard error of the mean. All observed data through 2 years in HORIZON. Month 27 had fewer samples. Ranibizumab Untreated=never received ranibizumab. Benz M. AAO, 2009.

SAILOR Study

- Safety study and free-access study to allow patients to get Lucentis for free while the FDA took its time in approving Lucentis
- Patients got three monthly injections and then were placed on PRN dosing
- After initial response, patients lost vision when put on PRN dosing

Mean Change in Visual Acuity (Letters) over Time*

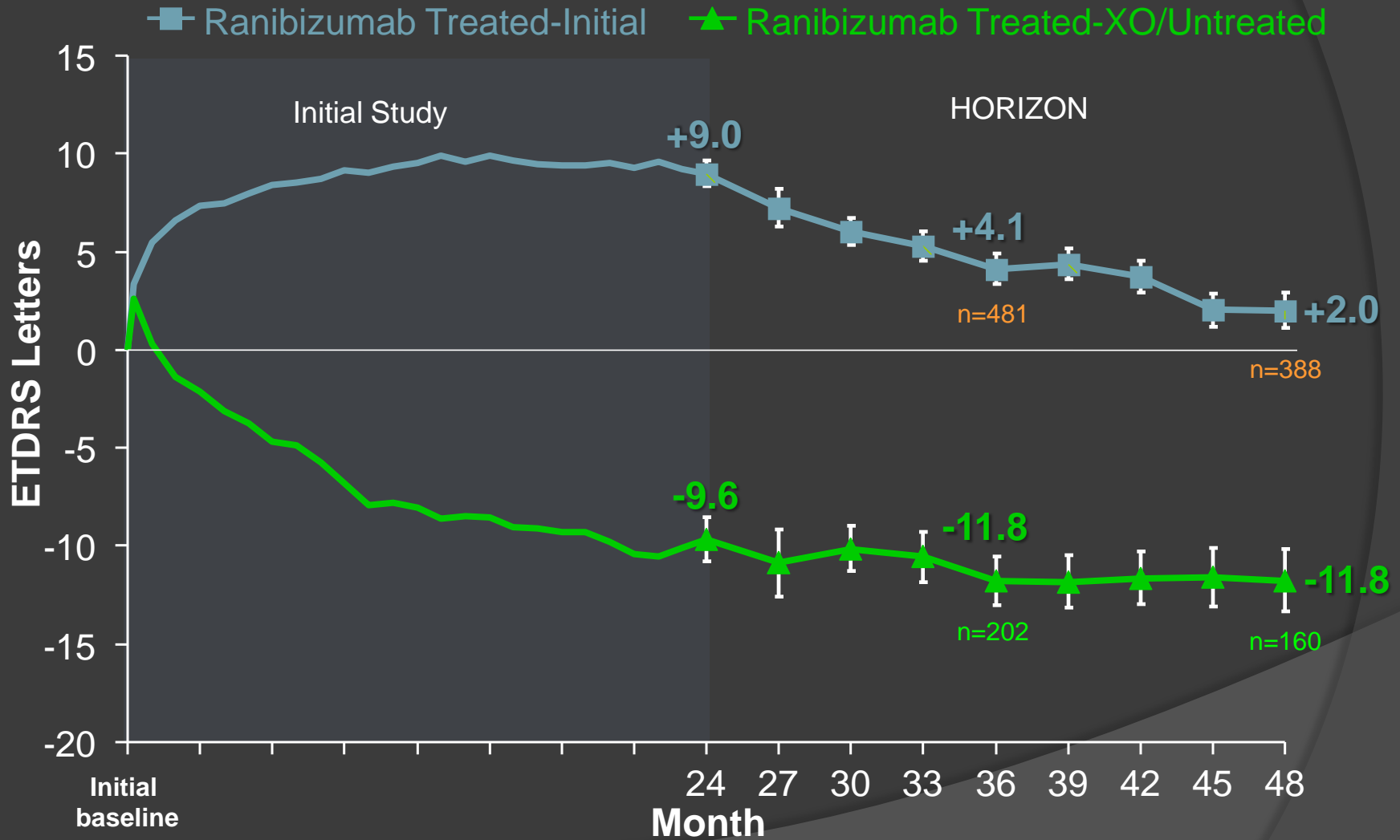


*Results are reported using the last observation carried forward (LOCF) to account for missing data and early dropouts.
 Boyer DS. Bascom Palmer Angiogenesis Conference, 2008.

HORIZON Study

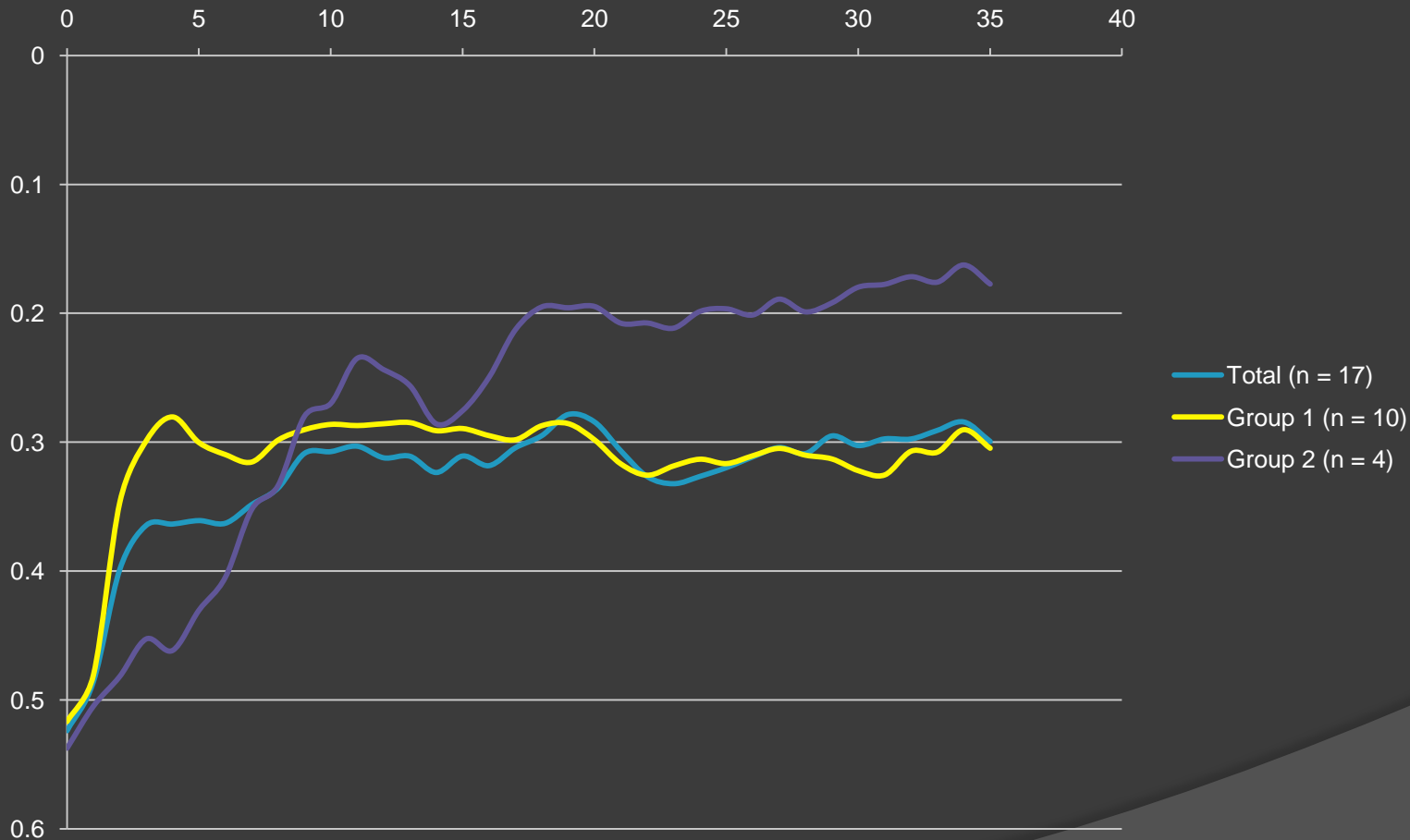
- Four year follow-up of patients who were initially in the MARINA and ANCHOR trials
- Patients continued to improve for the first two years while they received monthly dosing
- At two years patients were placed on PRN dosing and lost vision back to base line

Mean Change in Visual Acuity from Initial Baseline



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RAF data on continuing regular treatment continuously



The whole Lucentis story

