Outcomes of Anti-VEGF Therapy for Neovascular Age-Related Macular Degeneration in Routine Clinical Practice

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- Consulting: Regeneron, Genentech, Allergan, Visunex, Valeant, Spark
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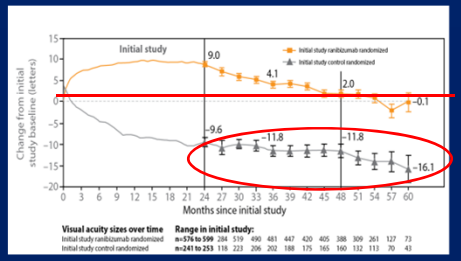
Dosing Approaches in Clinical Trials are Varied

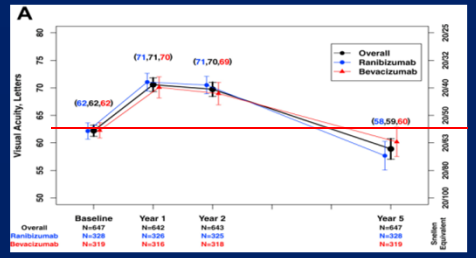
Quarterly	PRN[11,12]	Treat-and-Extend[11,12]	Monthly	Bimonthly
• PIER[8]	• HARBOR[3]	• LUCAS[17]	• ANCHOR[1]	• VIEW 1/2[6]
• SAILOR[9]	• CATT[4]	• TREX[18]	• MARINA[2]	• VISTA/VIVID[7]
• EXCITE[10]	• RESOLVE[13]		• HARBOR[3]	
	• RESTORE[14]		• CATT[4]	
	• Protocol I[15]		• RISE/RIDE[5]	
	• Protocol T[16]		• VIEW 1/2[6]	
			• VISTA/VIVID[7]	

1. Brown DM et al. *N Engl J Med*. 2006;355(14):1432-1444. 2. Rosenfeld PJ et al. *N Engl J Med*. 2006;355(14):1419-1431. 3. CATT Research Group. *N Engl J Med*. 2011;364(20):1897-1908. 4. Heier JS et al. *Ophthalmology*. 2012;119(12):2537-2548. 5. Nguyen QD et al. *Ophthalmology*. 2012;119(4):789-801. 6. Busbee BG et al. *Ophthalmology*. 2013;120(5):1046-1056. 7. Korobelnik J-F et al. *Ophthalmology*. 2014;121(11):2247-2254. 8. Wykoff C et al. *Ophthalmology*. 2015;122(12):2514-2522. 9. Regillo CD et al. *Am J Ophthalmol*. 2008;145(2):239-248.e5. 10. Schmidt-Erfurth U et al. *Ophthalmology*. 2011;118(5):831-839. 11. Freund KB et al. *Retina*. 2015;35(8):1489-1506. 12. Mantel I. *Transl Vis Sci Technol*. 2015;4(3):6. 13. Boyer DS et al. *Ophthalmology*. 2009; 116(9):1731-1739. 14. Massin P et al. *Diabetes Care*. 2010;33(11):2399-2405. 15. Diabetic Retinopathy Clinical Research Network. *Ophthalmology*. 2010;117(6):1064-1077. 16. Mitchell P et al. *Ophthalmology*. 2011;118(4):615-625. 17. Diabetic Retinopathy Clinical Research Network. *N Engl J Med*. 2015;372(13):1193-1203. 18. Berg K et al. *Ophthalmology*. 2015;122(1):146-152.

Long-term Trials in AMD Demonstrated that …..

Deviations from Consistent Dosing Resulted in Deterioration of Visual Gains Over Time



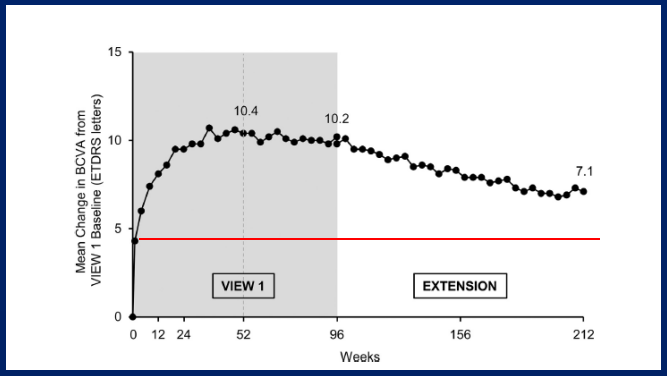


HORIZON	
Dosing Regimen in Extension Phase	PRN
Mean Number of Injections	
Year 3	2.2**
Year 4	2.0**

CATT	
Dosing Regimen in Extension Phase	Investigator Determined
Mean Number of Injections	
Year 3	4.8
Year 4	4.5
Year 5	4.0

**Calculated from the cumulative injection total

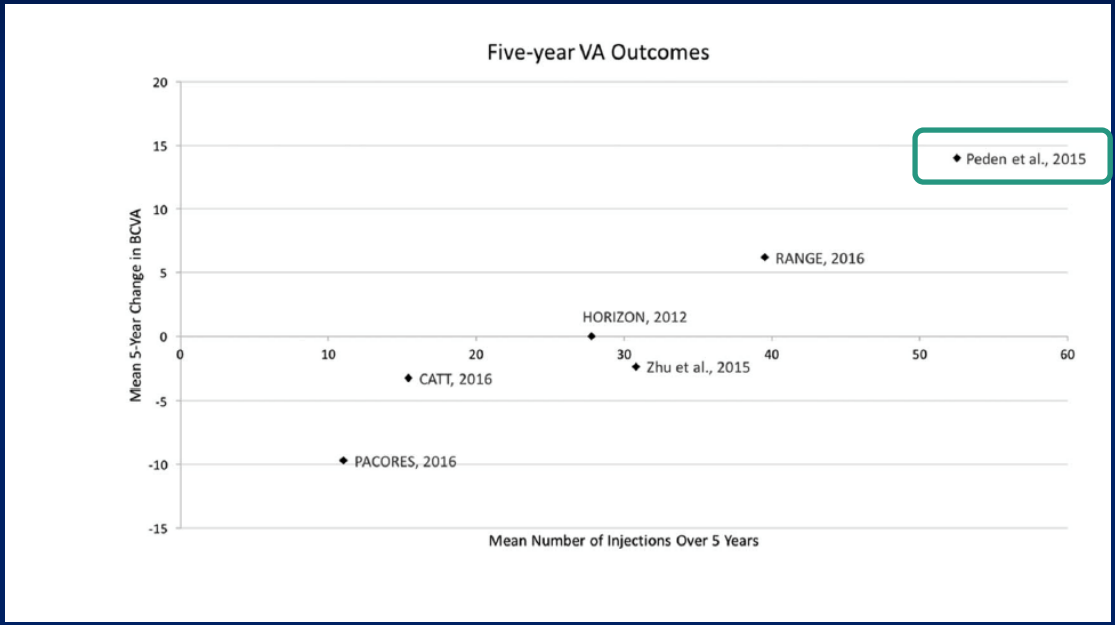
And Vision Could Largely be Maintained When Patients with Wet AMD Were Treated Consistently



VIEW 1 Extension	
Dosing Regimen in Extension Phase	Modified Quarterly*
Mean Number of Injections	
Year 3	6.0
Year 4	5.5

All patients received IAI 2 mg on a modified quarterly dosing schedule until the amendment in June 2012 mandated q8 dosing
*Mandatory dosing at least every 12 weeks, up to monthly injections possible

Five Year Visual Acuity Outcomes vs Injection Frequency in wAMD



Fixed q4/q8 weeks (10.5 injs/year)

"The body of evidence to date regarding long-term anti-VEGF treatment indicates a variable course at greater than 36 months follow-up and seems to be dependent on the treatment protocol. Consistent dosing with fluid-free interval is suggested to maintain VA gains in patients with exudative age-related macular degeneration."

OUTCOMES OF PATIENTS WITH EXUDATIVE AGE-RELATED MACULAR DEGENERATION TREATED WITH ANTIVASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY FOR THREE OR MORE YEARS: A Review of Current Outcomes.
Qin VL, Young J, Silva FQ, Conti FF, Singh RP. Retina. 2017 Jun 30. doi: 10.1097/IAE.0000000000001753. [Epub ahead of print]

Analysis of Outcomes in Routine Clinical Practice

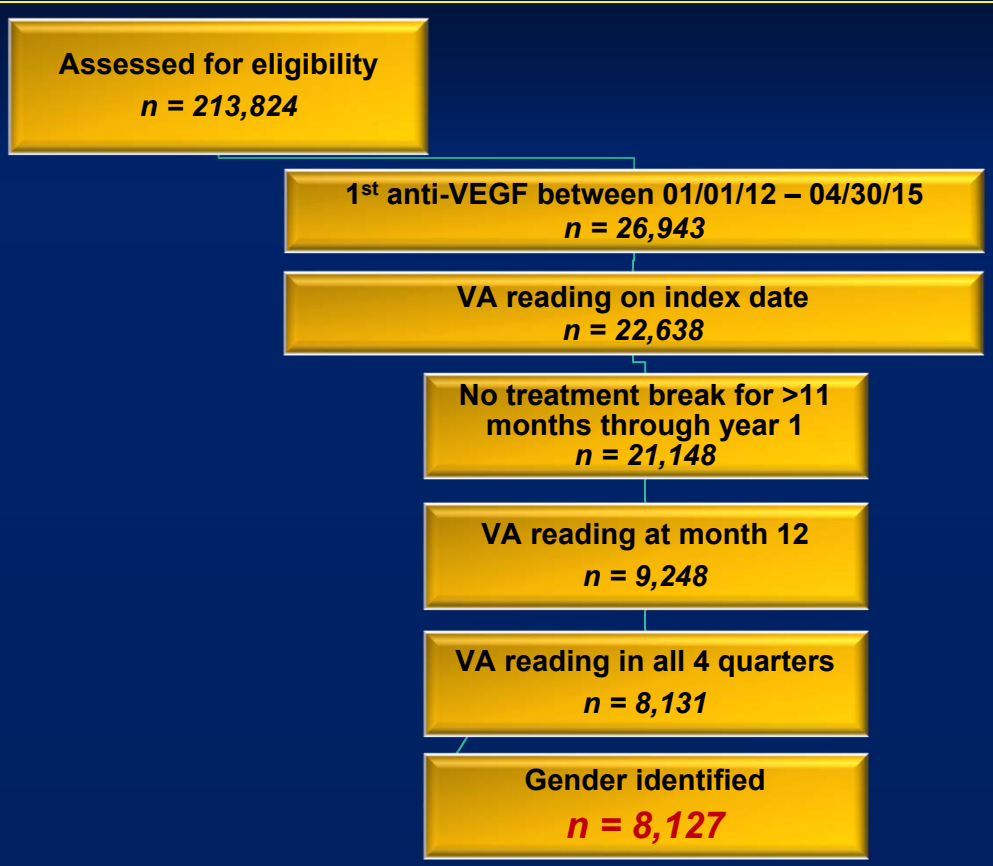
Study Design

- **Objective**
  - To evaluate visual acuity outcomes following treatment neovascular AMD with intravitreal anti-VEGF agents in routine clinical practice through 2 years

- **Methods**
  - Electronic medical record data* collected from 251 Retina Specialists for patients with –
    - *Neovascular age-related macular degeneration*
  - Anti-VEGF treatment naïve eyes
    - 1st anti-VEGF injection between January 1st, 2012 and April 30th, 2015
  - Two subgroups evaluated –
    - *Group 1: ≤6 injections/year*
    - *Group 2: ≥7 injections/year*

*Source: Vestrum Database

Patient Selection
Year 1



Baseline Characteristics

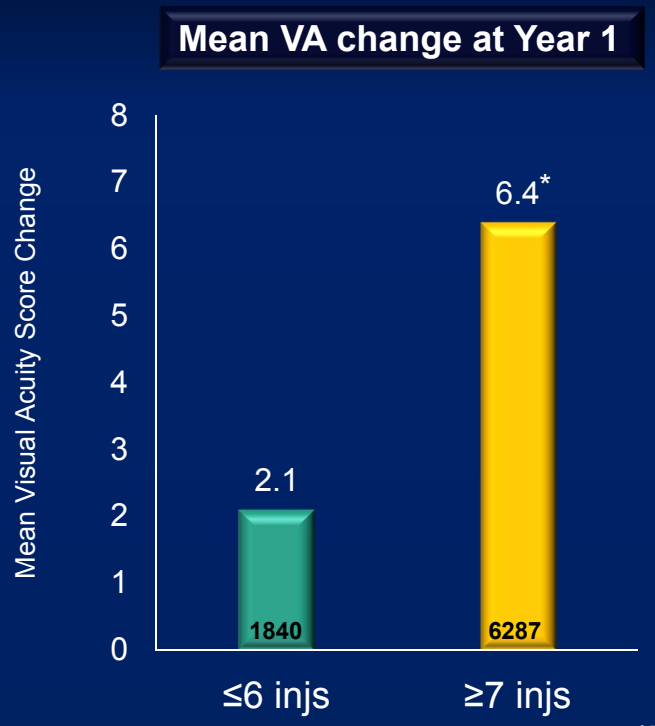
	Total *(n=8127)*	≤6 injections *(n=1840)*	≥7 injections *(n=6287)*
Mean Age, years	80	80	80
Female, %	64%	63%	65%
Mean VA, letters	65	61	66
Median VA, letters	74	72	74
VA Subgroups			
≥20/40	22%	23%	21%
<20/40 – 20/100	47%	39%	49%
<20/100 – 20/200	15%	13%	15%
<20/200	17%	24%	15%

Patients included in Year 1 analysis

Mean Visual Acuity Change By Injection Subgroups (*Year 1*)

Subgroup	Mean BSL VA
≤6 injs *(n=1840)*	61
≥7 injs *(n=6287)*	66

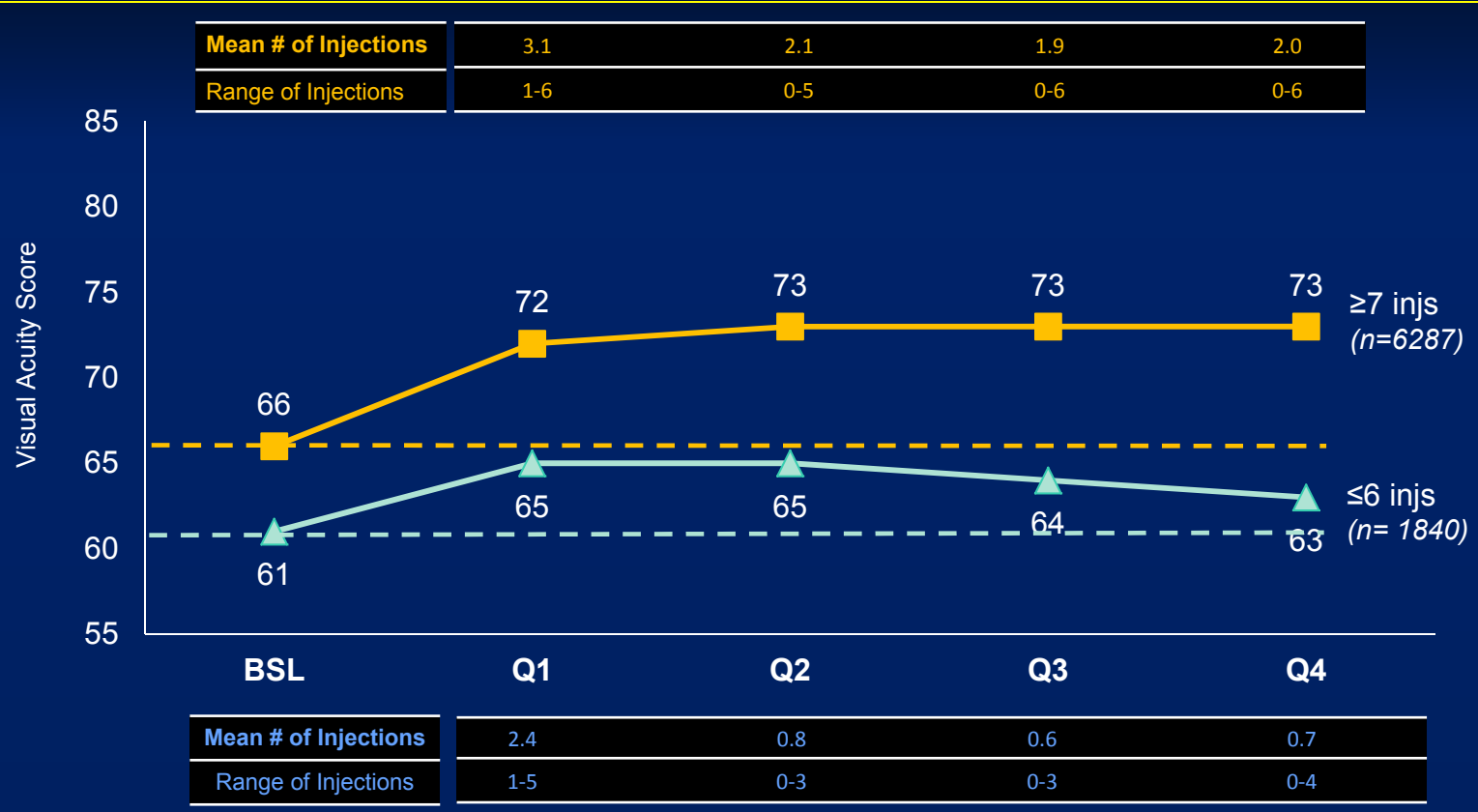
Subgroup	Mean Number of Injections
≤6 injs *(n=1840)*	4.5
≥7 injs *(n=6287)*	9.1



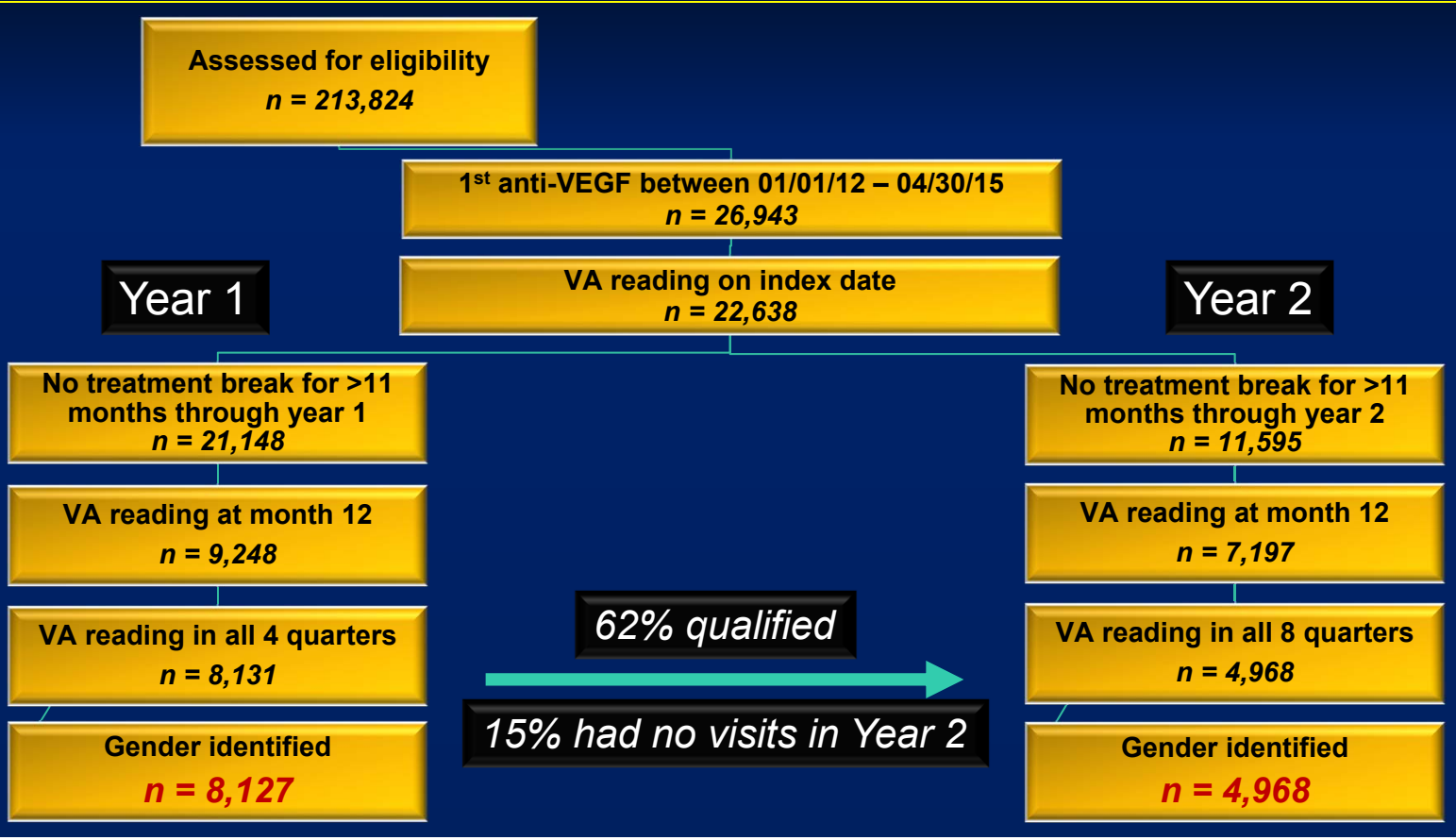
P < 0.001 compared with ≤6 injs

Visual acuity is reported in visual acuity score (VAS)

Mean Visual Acuity by Injection Subgroups (*Year 1)*

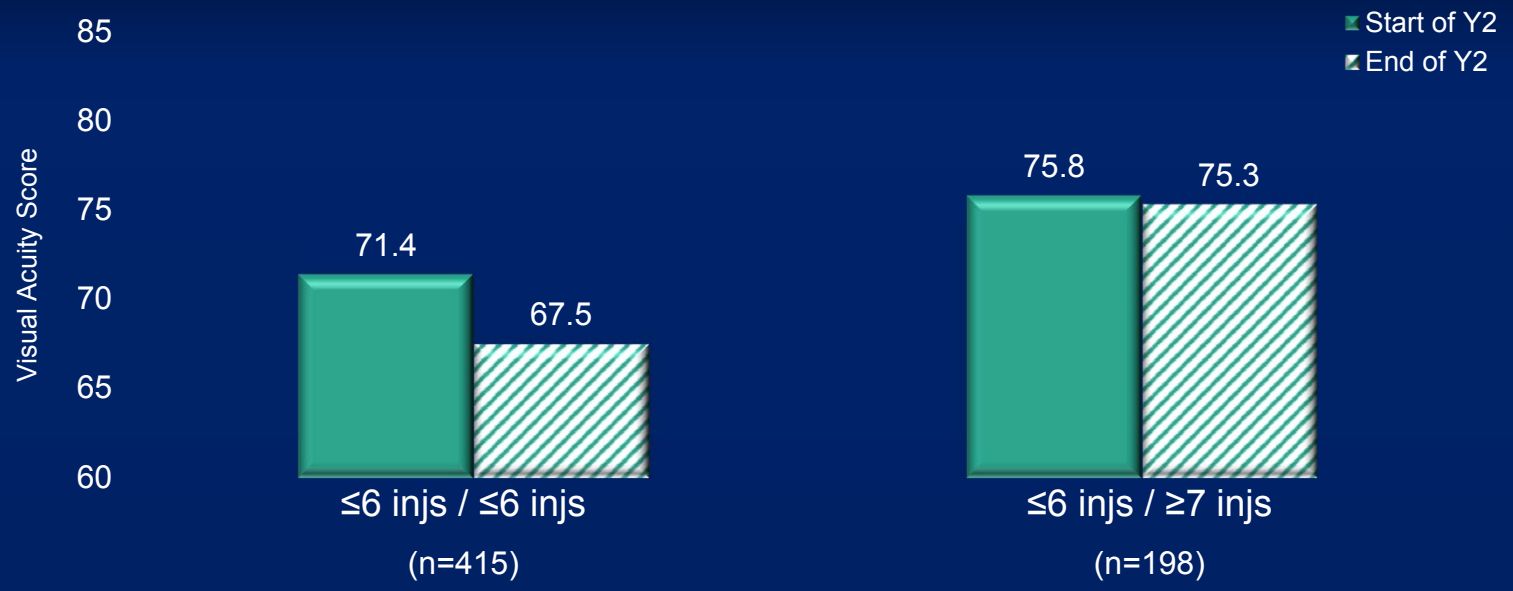


Patient Selection
Year 2



Mean Visual Acuity by Injection Subgroups *(Year 2)*

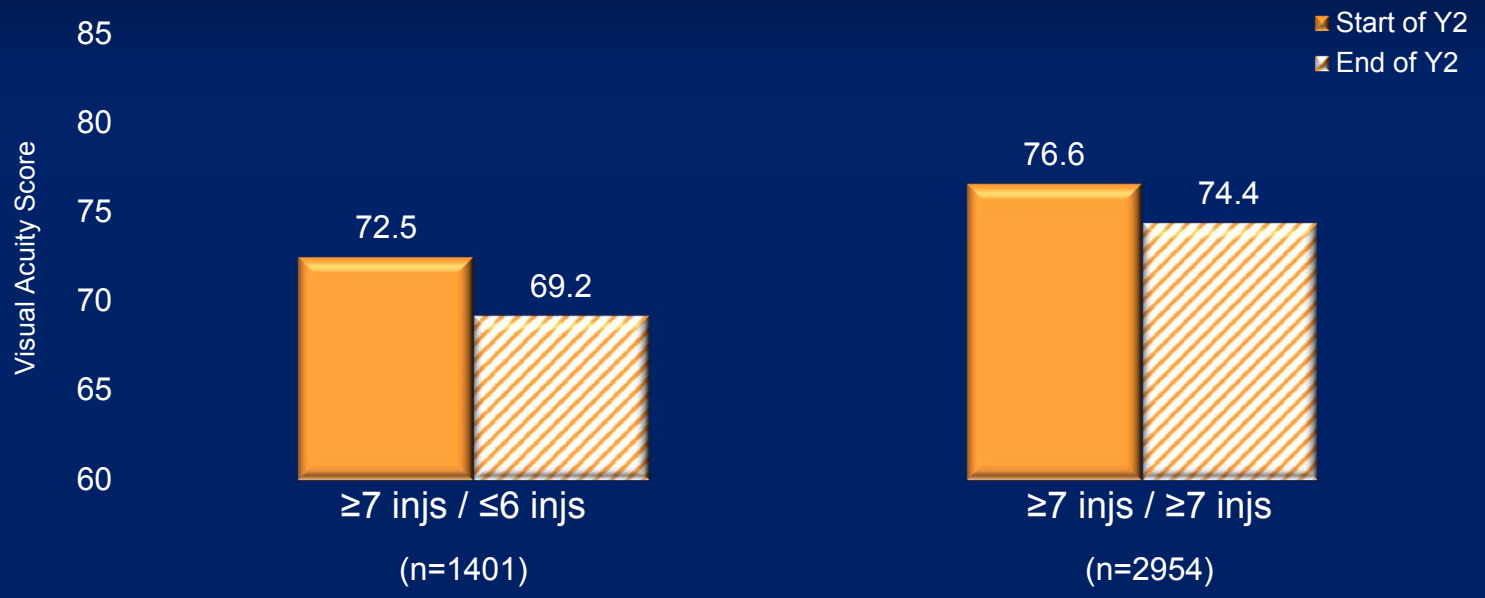
Patients Receiving ≤6 injections in Year 1



Mean number of injections		
Year 1	*5.2*	*5.3*
Year 2	*4.4*	*8.2*

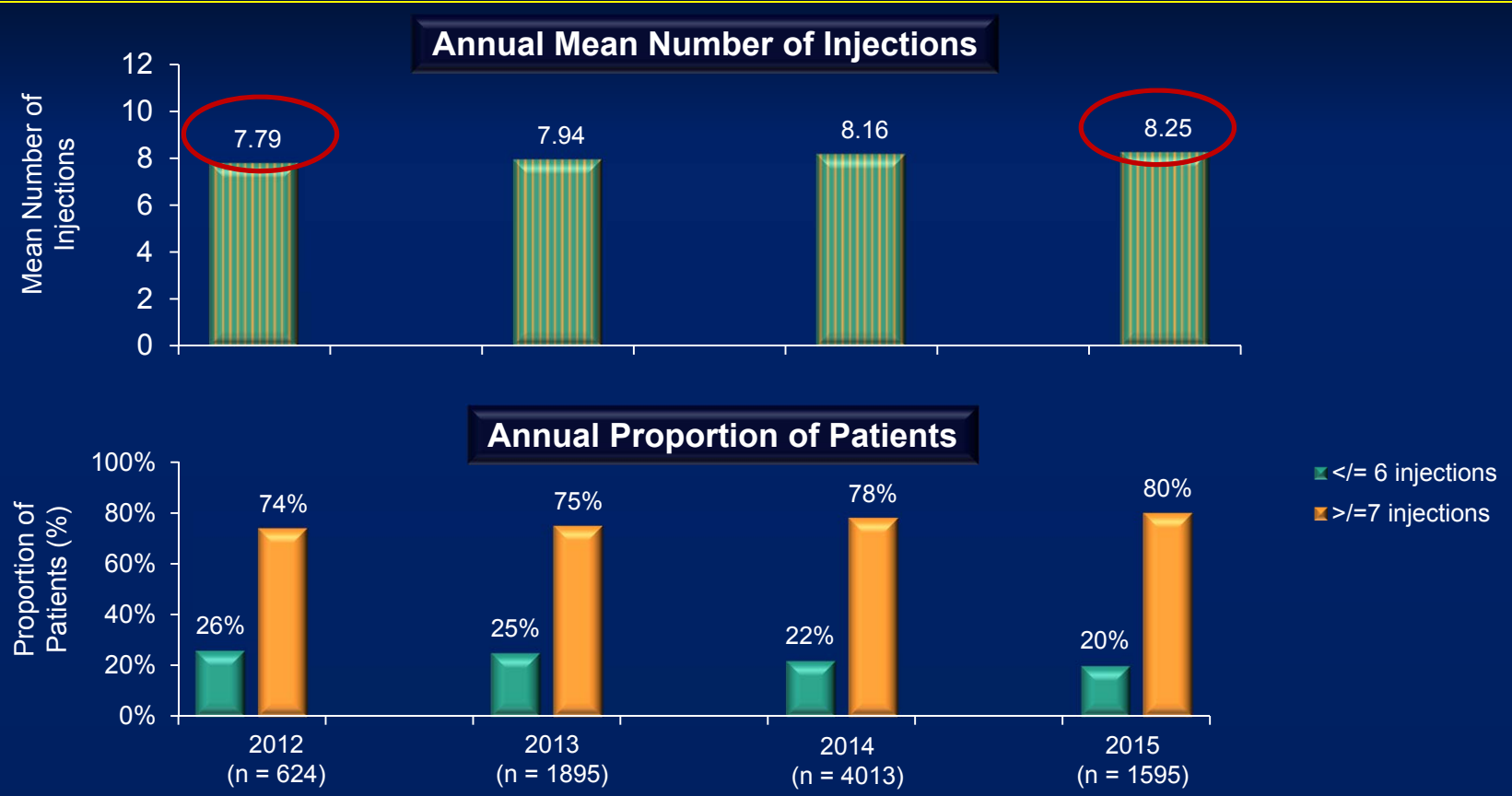
Mean Visual Acuity by Injection Subgroups (Year 2)

Patients Receiving ≥7 injections in Year 1



Mean number of injections		
Year 1	*8.5*	*9.7*
Year 2	*5.0*	*9.1*

Change Over Time in Injection Frequency During Year 1 of Treatment



Summary

- Consistent with results of clinical trials, in routine clinical practice, maintenance of visual gains was associated with more frequent anti-VEGF injections in patients with neovascular AMD
- Patients with neovascular AMD were more likely to receive more frequent injections (≥7) rather than fewer injections (≤6) during the first year of treatment
  - Annually, a trend towards more injections during the first year of treatment was observed in the neovascular AMD cohort

Thank You

Back-Up

Overview of Trials
Neovascular Age-related Macular Degeneration

Trial	Treatment Groups	Mean Change in BCVA at Year 1	Long-Term Follow-up	Mean Change in BCVA (As compared to enrollment in original study)
MARINA	RBZ 0.5mg monthly	+7.2	HORIZON** (PRN) Annual: 2.0 -2.2 injs	Year 2: +9.0
	sham	-10.4		Year 3: +4.0
ANCHOR	RBZ 0.5mg monthly	+11.3		Year 4: +2.0
	PDT	-9.6		Year 5: -0.1
VIEW 1	IAI 2mg monthly	+10.9	VIEW 1 Extension (Modified Quarterly/ Bimonthly) Annual: 5.5-6 injs	Week 96: +10.2
	IAI 2mg bi-monthly*	+7.9		Week 212: + 7.1
	RBZ 0.5mg monthly	+8.1		
CATT	RBZ 0.5mg monthly	+8.5	Extension (Variable) Annual: 4.0-4.8 injs	Year 2: +8#
	RBZ 0.5mg PRN	+6.8		
	BVZ 1.25mg monthly	+8.0		Year 5: -11#
	BVZ 1.25mg PRN	+5.9		

RBZ=ranibizumab, IAI=intravitreal aflibercept injection, BVZ=bevacizumab
**following 3 initial monthly doses*
*** Also Included patients from the FOCUS study*
#Calculated mean change