

# Macular Atrophy (MA) in the Phase 2 Ladder Trial

Glenn J. Jaffe, MD<sup>1</sup>

Giulio Barteselli, MD<sup>2</sup>; Chin-Yu Lin, PhD<sup>2</sup>; and Shamika Gune, PhD<sup>2</sup>

<sup>1</sup> Duke University, Durham, NC;

<sup>2</sup> Genentech, Inc., South San Francisco, CA



# Ladder Investigators

Aaberg Jr., Thomas	Chen, Sanford	Higgins, Patrick	McCannel, Colin	Singh, Rishi
Antoszyk, Andrew	Chittum, Mark	Hovland, Peter	Miller, Daniel	Suñer, Ivan
Awh, Carl C.	Clark, W. Lloyd	Howard, James	Mittra, Robert	Thompson, John
Baker, Carl	Dreyer, Richard	Johnson, Robert	Nielsen, Jared	Tosi, Joaquin
Berger, Brian	Dugel, Pravin	Katz, Randy	Pearlman, Joel	Wagner, Alan
Bhisitkul, Robert	Eichenbaum, David	Khanani, Arshad	Pieramici, Dante	Walker, Joseph
Brown, David M.	Engstrom, Bob	Kitchens, John	Pollack, John	Wieland, Mark
Callanan, David	Freeman, William	Lai, Michael	Rachitskaya, Aleksandra	Williams, David
Calzada, Jorge	Gordon, Alan	Lauer, Andreas	Regillo, Carl	Zilis, John
Campochiaro, Peter	Graff, Jordan	Marcus, Dennis	Rose, Steven	
Chang, Margaret	Gupta, Sunil	McCabe, Frank	Singer, Michael	

# Disclosures

## ► Financial disclosures

- GJJ: Consultant) Novartis, EyePoint, Neurotech, Iveric, Clearside.
- GB, CYL, SG: Employee) Genentech, Inc.

## ► Study disclosures

- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation
- Funding was provided by Genentech, Inc., a member of the Roche Group, for the study and third-party writing assistance, which was provided by Karlina J. Kauffman, PhD, of Envision Pharma Group

# Summary-Key Takeaways

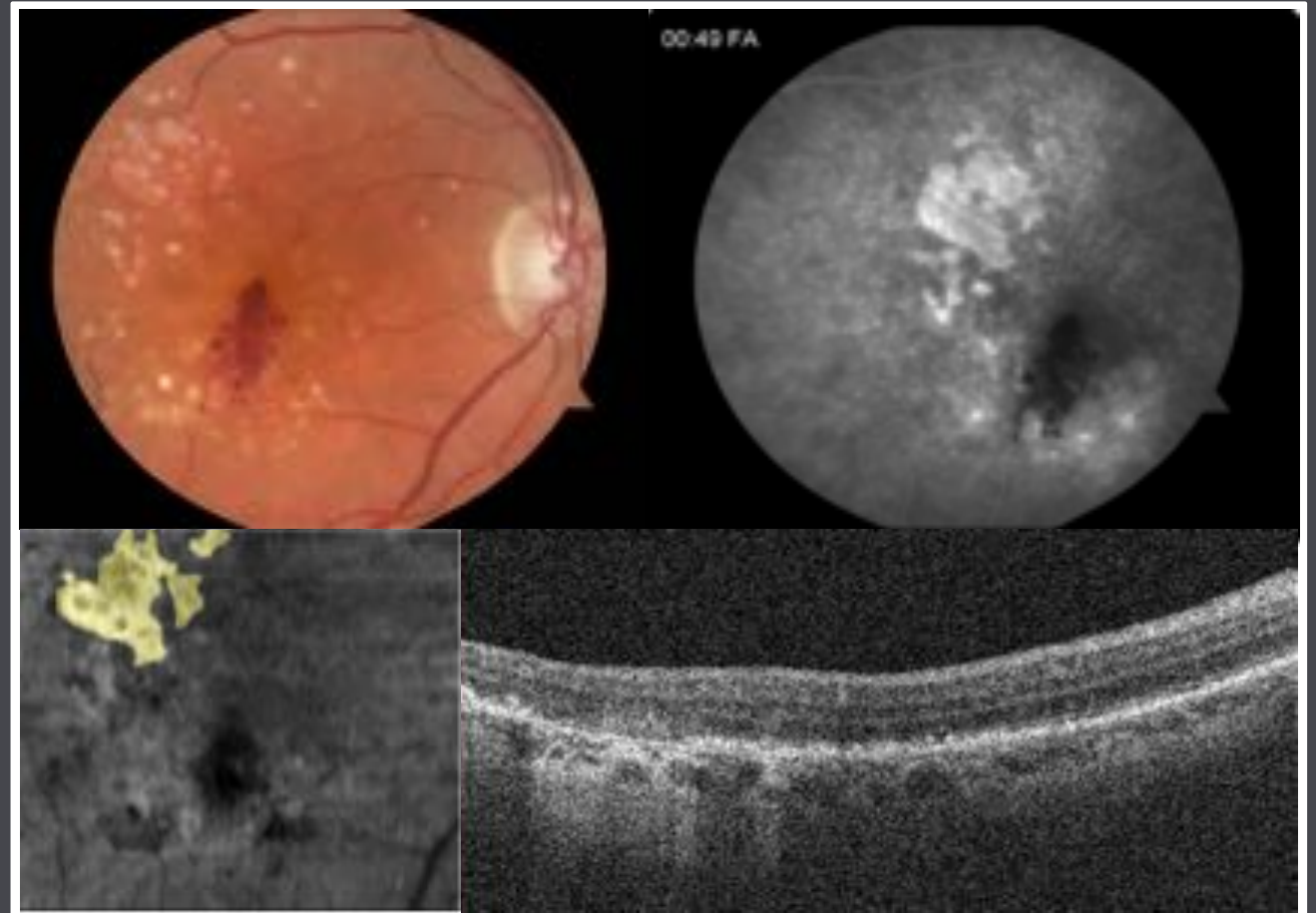
## Macular Atrophy (MA) in the Phase 2 Ladder Trial

- Continuous ranibizumab delivery via the PDS does not cause more atrophy than monthly injections
- Comparable rates of MA incidence, size, enlargement



# Macular Atrophy in Eyes With nAMD Receiving Anti-VEGF Treatment

- ▶ Macular atrophy definition<sup>1</sup>
- ▶ MA in IVAN,<sup>2</sup> CATT,<sup>3</sup> and HARBOR<sup>4</sup> trials
- ▶ What about continuous delivery?



1. Sadda SR et al. *Ophthalmology*. 2018;125(4):537-548. 2. Chakravarthy U et al. *Lancet*. 2013;382(9900):1258-1267. 3. Grunwald JE et al. *Ophthalmology*. 2014;121(1):150-161. 4. Sadda SR et al. *Ophthalmology*. 2018;125(6):878-886.



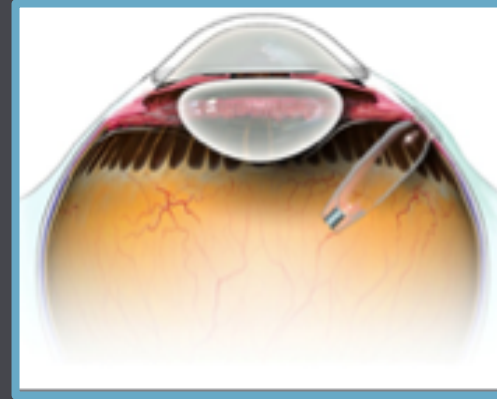
# Purpose

- ▶ Macular atrophy incidence, size, and enlargement in PDS vs monthly ranibizumab injections

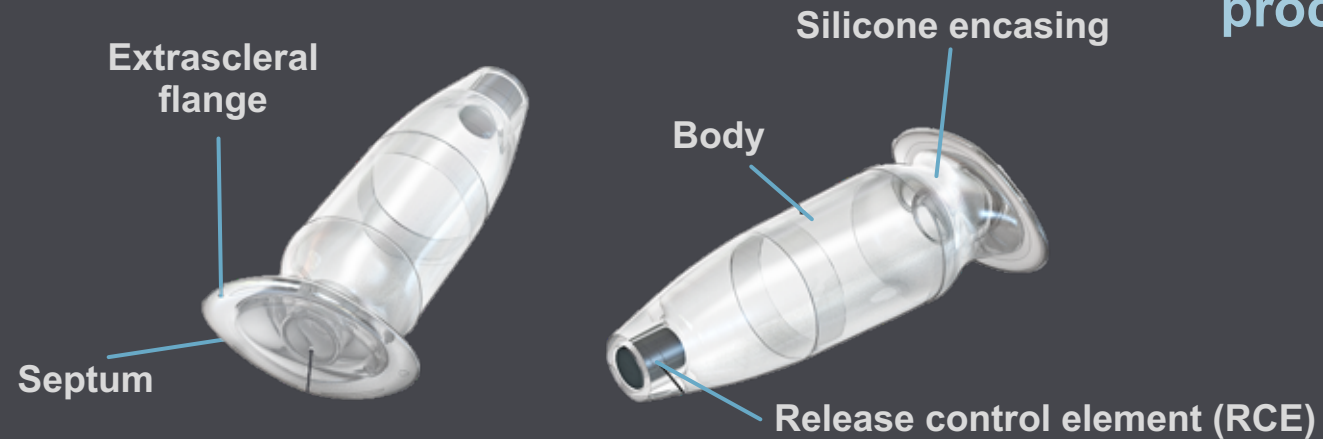


# The Port Delivery System With Ranibizumab (PDS)

- ▶ Continuous drug delivery system
  - Permanent, refillable intraocular implant
  - Customized ranibizumab formulation
  - Implant surgically placed at the pars plana
  - In office refill-exchange procedure



**OR-based insertion procedure**



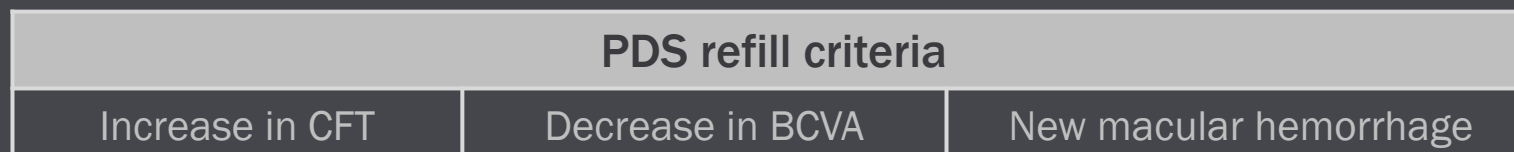
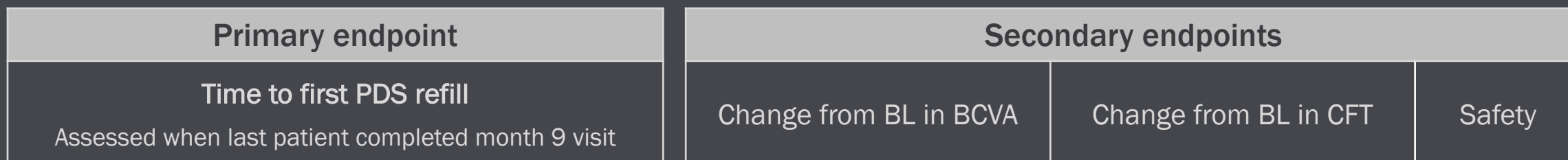
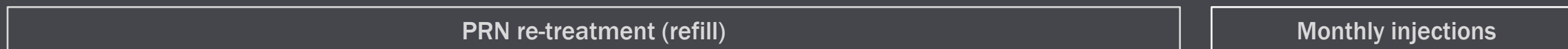
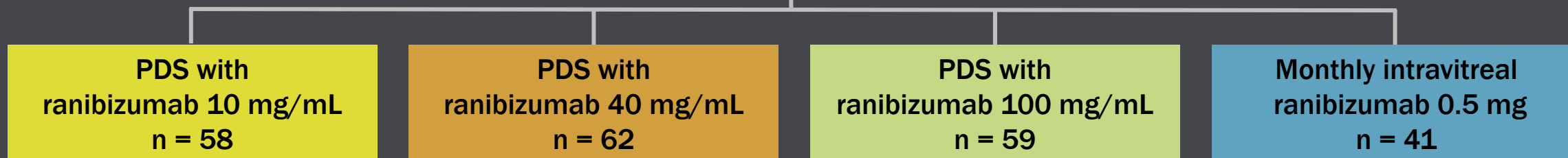
# Ladder Phase 2 Trial Design

## Characterize the Treatment Effect, Durability, and Safety of the PDS

Patients with nAMD responsive to  $\geq 2$  anti-VEGF injections of any type

N = 220

Randomized 3:3:3:2



Last assessment varied due to variable time on study (mean = 22.1 months for all PDS patients (range, 10.8–37.6 months))



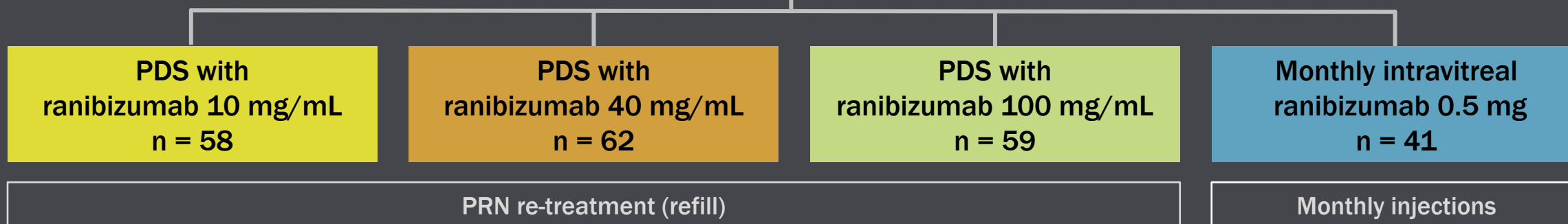
# Ladder Phase 2 Trial Design

## Characterize the Treatment Effect, Durability, and Safety of the PDS

Patients with nAMD responsive to  $\geq 2$  anti-VEGF injections of any type<sup>1</sup>

N = 220

Randomized 3:3:3:2

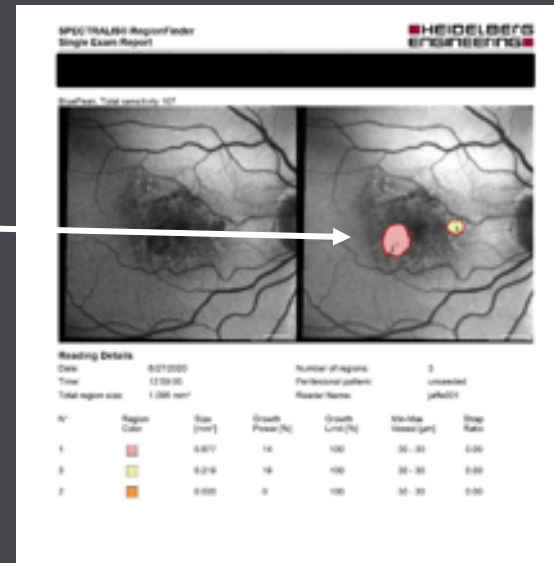
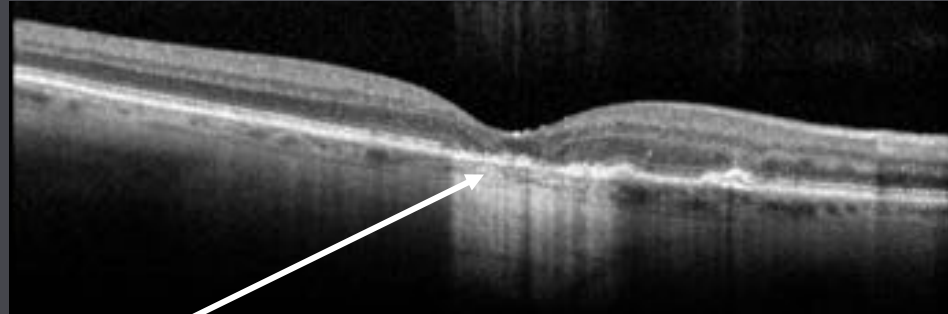


### Ladder phase 2 trial

- ▶ PDS 100 mg/mL vision and anatomic outcomes comparable with monthly ranibizumab
- ▶ PDS was generally well tolerated
- ▶ Supported evaluation in Archway phase 3 trial

# Macular Atrophy in Ladder Assessed at Screening, Months 4 and 9, and Last Assessment

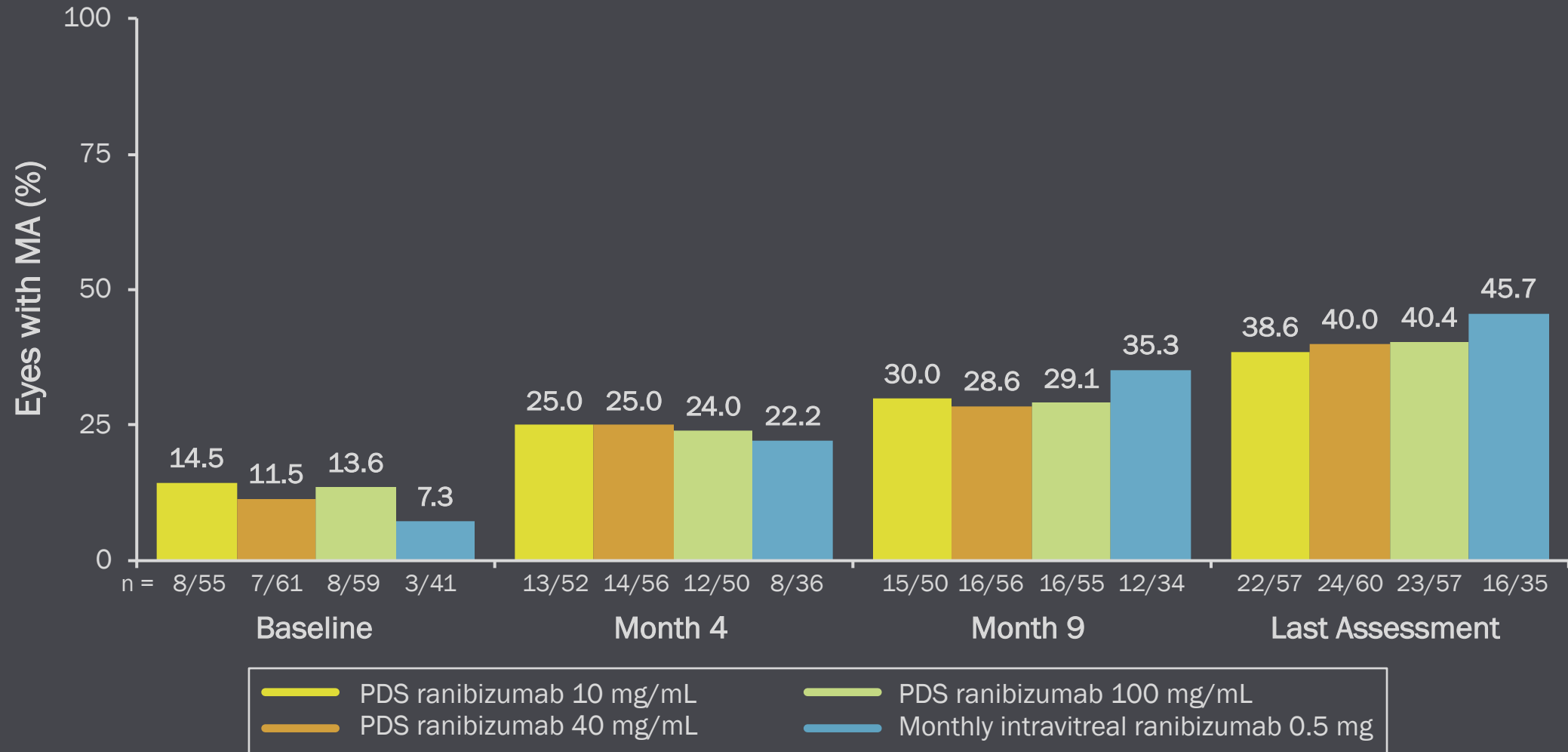
- ▶ DRC assessed MA
- ▶ Two readers assessed MA, MA area
  - Third reader arbitrated values that differed >10%
  - Areas differing by  $\leq 10\%$  were averaged
- ▶ SDOCT: MA presence according to CAM
- ▶ FAF: MA area
- ▶ The worst-observation-carried-forward approach was used to impute missing data



# RESULTS

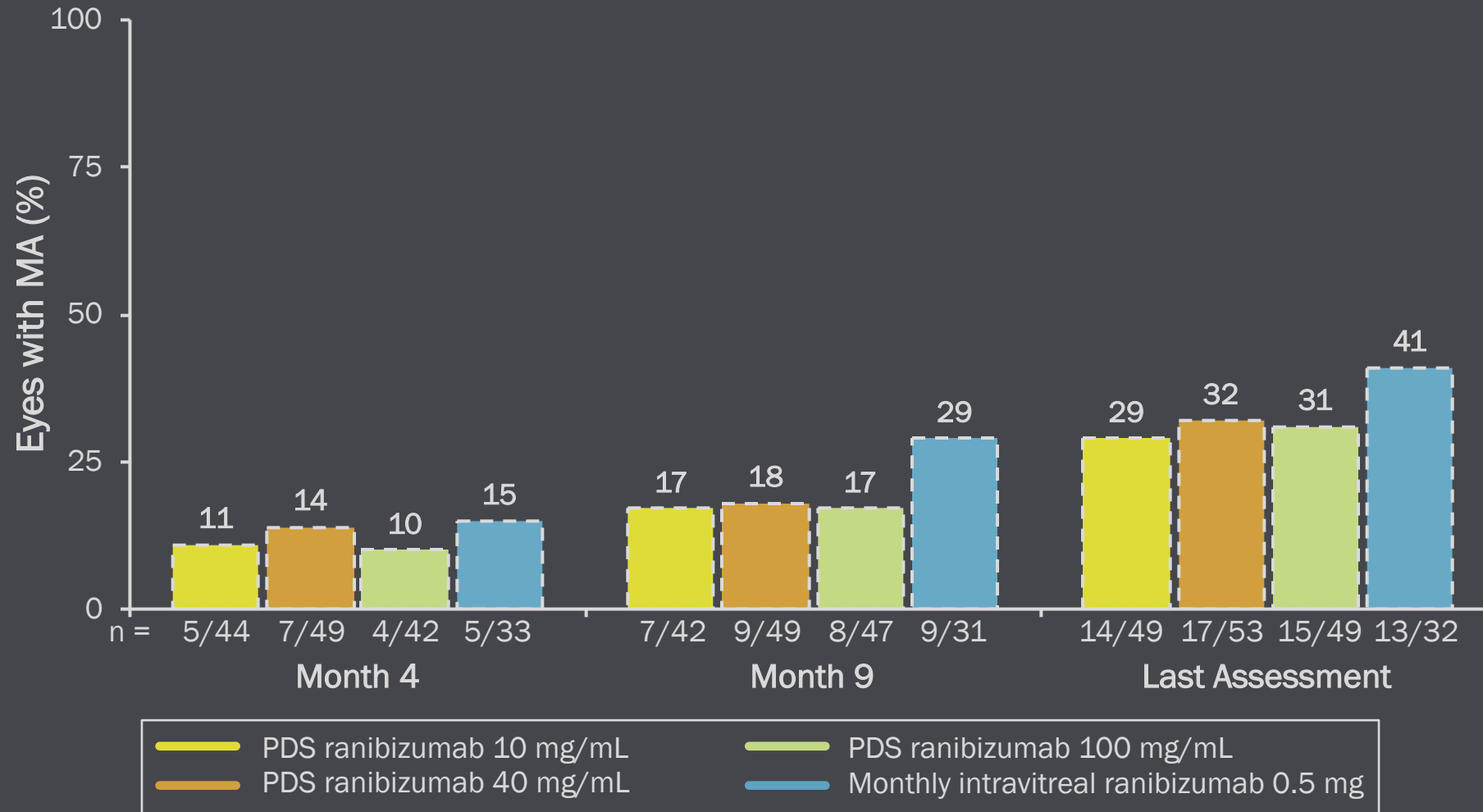


# % MA Throughout Ladder was Similar Across Treatment Arms

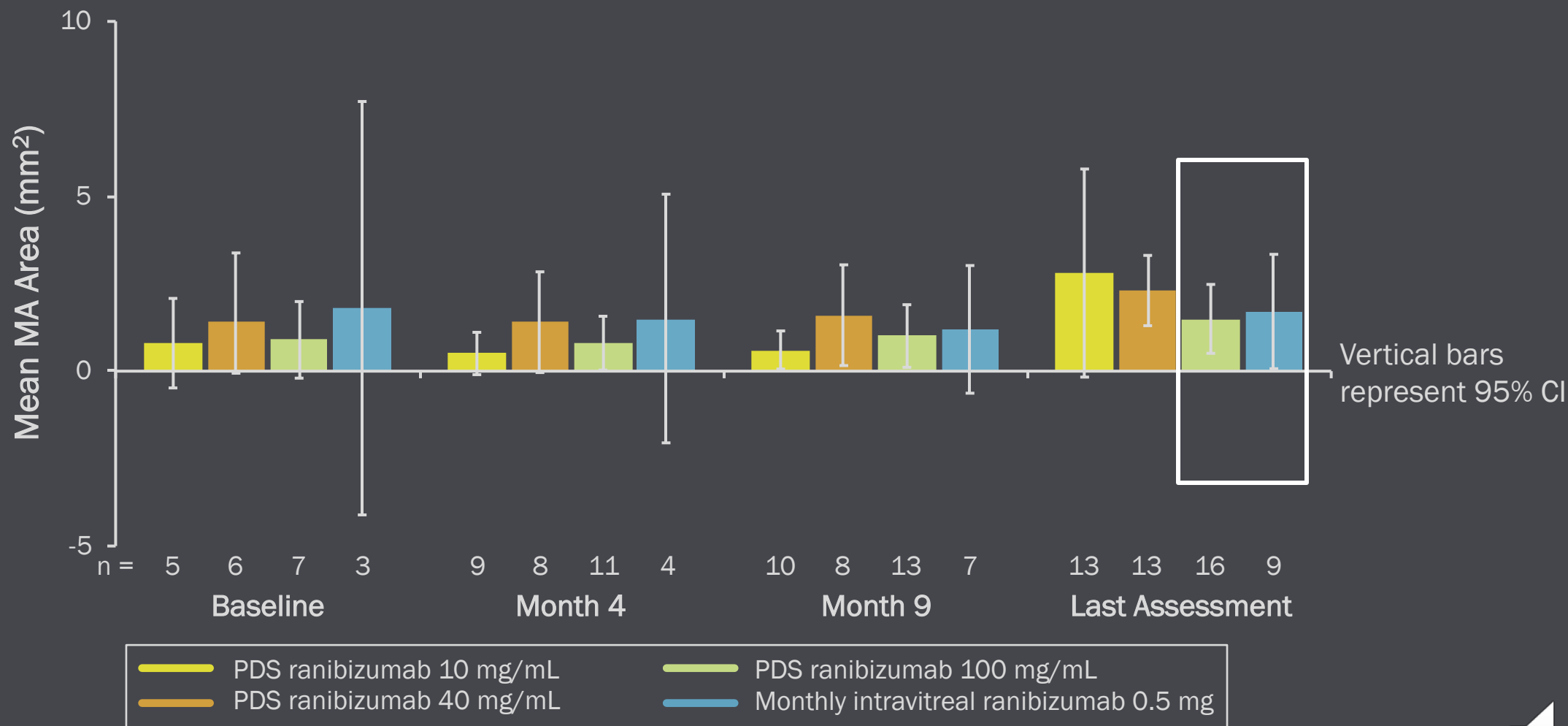


Ladder

# New MA Incidence Similar Across Treatment Arms in Patients Without MA at Baseline

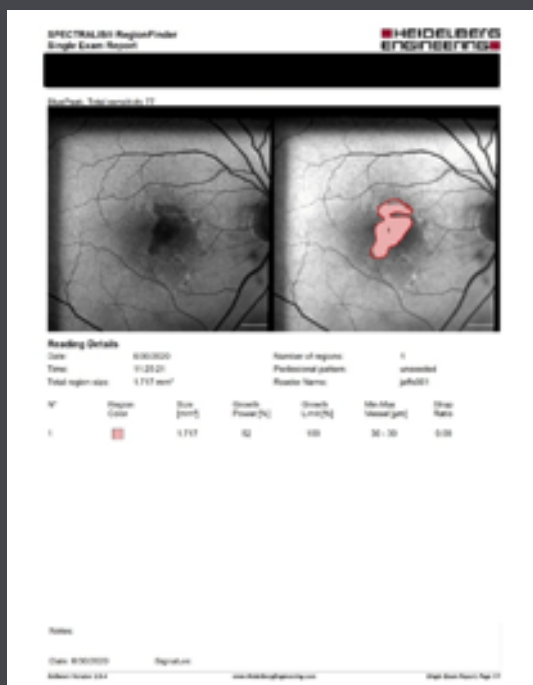


# PDS 100 mg/mL Mean MA Area Was Similar to Monthly Ranibizumab Injections Throughout Ladder



# PDS 100 mg/mL Mean MA Area Similar to Monthly Ranibizumab Injections Throughout Ladder

Monthly intravitreal  
ranibizumab



1.7 mm<sup>2</sup>

Port Delivery System  
with ranibizumab



1.7 mm<sup>2</sup>

# Example of Macular Atrophy Area Change Over Time

4/21/16



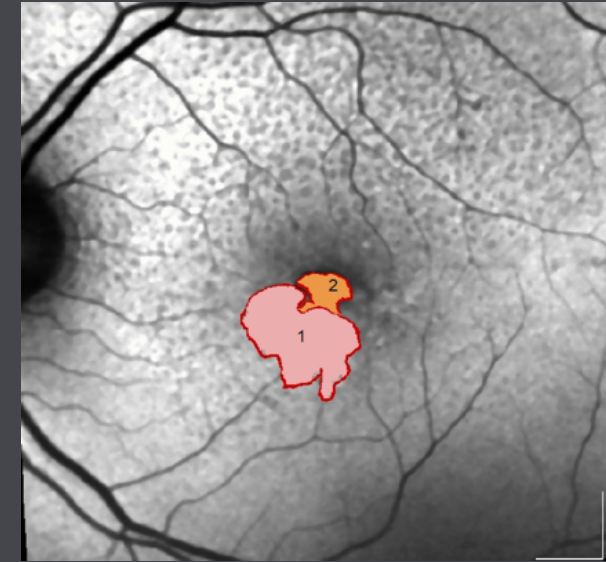
Baseline  
0.510 mm<sup>2</sup>

9/7/16



Month 4  
0.778 mm<sup>2</sup>

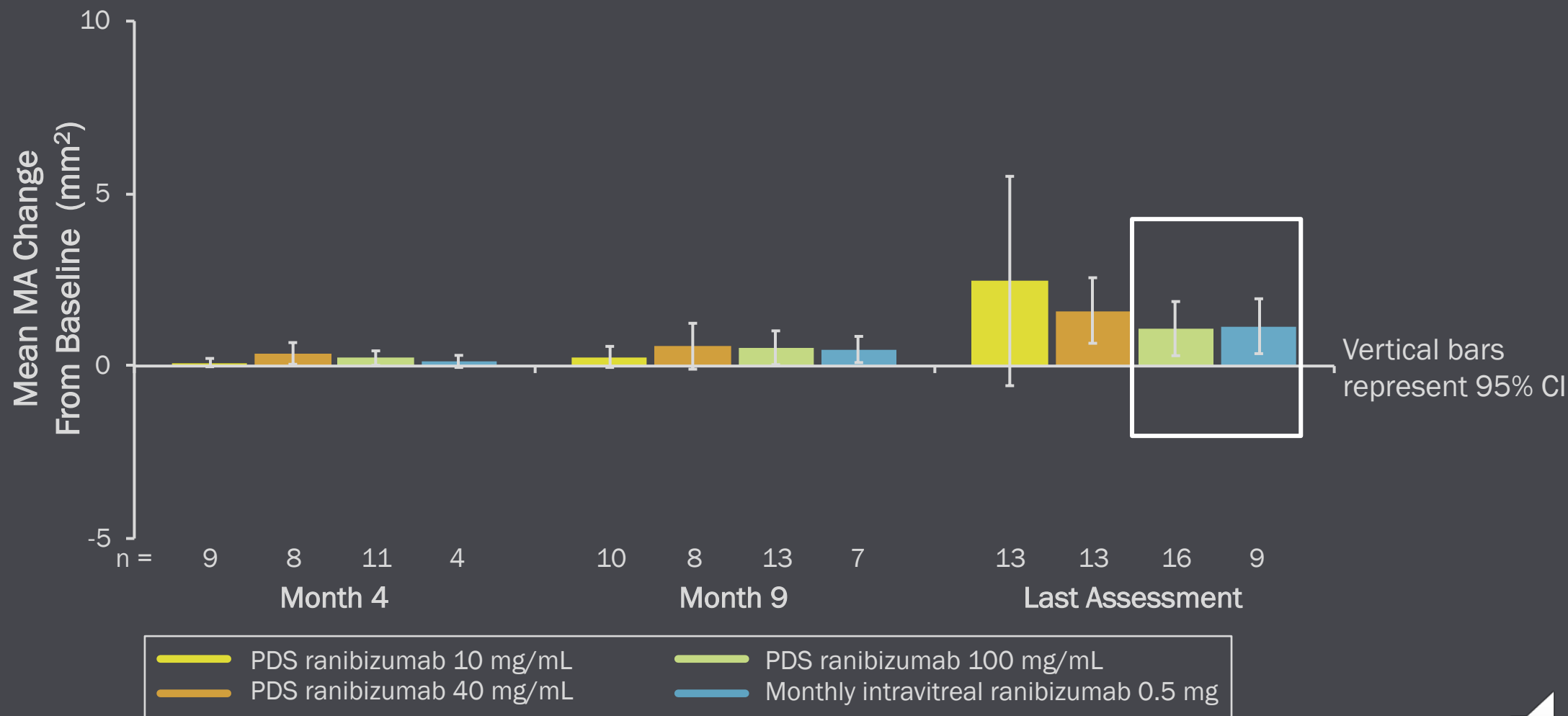
12/27/18



Last Assessment  
1.770 mm<sup>2</sup>



# PDS 100 mg/mL MA Area Change Is Similar to Monthly Ranibizumab Injections



# Conclusions

- Continuous ranibizumab delivery via the PDS does not cause more atrophy than monthly injections
- Comparable rates of MA incidence, size, enlargement