Columbus-AMD: Efficacy and Safety of FYB201, a Proposed Biosimilar to Ranibizumab, in Neovascular Age-Related Macular Degeneration

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Presenter

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Background

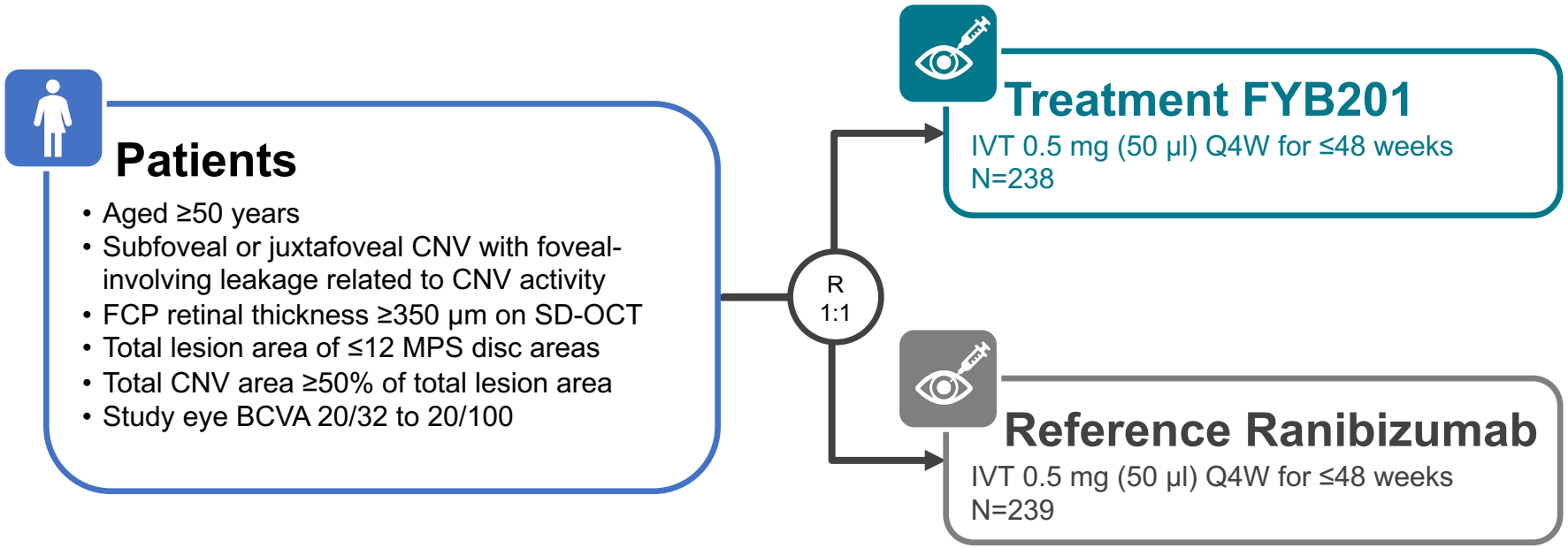
- nAMD is responsible for >90% of AMD-related severe visual loss[1,2]
  - Patients with nAMD experience impairment of daily activities and poor quality of life
- Intravitreal injection of ranibizumab, a VEGF-A–inhibiting biologic, is a well-established first-line treatment for patients with nAMD[3-5]
  - The high cost and treatment burden of monthly ranibizumab injections may limit real-world treatment outcomes[6,7]
- Biosimilars are high-quality, cost-effective alternatives to approved reference products
  - Biosimilars undergo comprehensive comparative studies to demonstrate high similarity in all critical quality attributes, including physical, chemical, and biological properties[8-11]
  - Biosimilars are not generic medications
- FYB201 is a ranibizumab biosimilar candidate with the same composition, formulation, strength, route of administration, dose, and storage conditions as reference ranibizumab[12]

AMD, age-related macular degeneration; nAMD, neovascular age-related macular degeneration; VEGF-A, vascular endothelial growth factor A.

1. Prokofyeva E, Zrenner E. *Ophthalmic Res*. 2012;47(4):171-88. 2. Jaffe DH et al. *J Comp Eff Res*. 2018;7(11):1125-32. 3. Rosenfeld PJ et al. *N Engl J Med*. 2006;355(14):1419-31. 4. Mavija M et al. *Med Arch*. 2014;68:204-8. 5. Ferrara N et al. *Retina*. 2006;26(8):859-70. 6. Kim LN et al. *Retina*. 2016;36(8):1418-31. 7. Holz FG et al. *Br J Ophthalmol*. 2015;99:220-26. 8. Sharma A et al. *Br J Ophthalmol*. 2020;104:2-7. 9. Giuliani J, Bonetti A. *Anticancer Res*. 2019;39(7):3971-3. 10. Aladul MI et al. *BioDrugs*. 2017;31(6):533-44. 11. Smolen JS et al. *RMD Open*. 2019;5:e000900. 12. Holz FG et al. *Ophthalmology*. 2021 May 3;S0161-6420(21)00325-0. doi: 10.1016/j.ophtha.2021.04.031.

The COLUMBUS-AMD Study Design

- The COLUMBUS-AMD study investigated the similarity of the biosimilar candidate FYB201 and reference ranibizumab in patients with nAMD
- The COLUMBUS-AMD study (NCT02611778) was a prospective 48-week, masked, parallel-group, global, multicenter, randomized phase 3 study in patients with treatment-naive, subfoveal CNV due to nAMD
- Patient characteristics were well balanced between study arms



BCVA, best corrected visual acuity; CNV, choroidal neovascularization; FCP, foveal center point; IVT, intravitreal; MPS, macular photocoagulation study; nAMD, neovascular age-related macular degeneration; Q4W, every 4 weeks; R, randomized; SD-OCT, spectral domain optical coherence tomography.

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The COLUMBUS-AMD Study Design

- The primary endpoint of the COLUMBUS-AMD study was change from baseline in BCVA by ETDRS letters after 8 weeks of treatment. The biosimilarity of FYB201 to its originator was assessed via a 2-sided equivalence test, with an equivalence margin in BCVA of 3 ETDRS letters
- Change from baseline in BCVA at 48 weeks, change from baseline in FCP retinal thickness at 48 weeks, safety, and immunogenicity were key secondary endpoints

Endpoints

- **Primary**
  Change from baseline in BCVA by ETDRS letters after 8 weeks

- **Key Secondary**
  Change from baseline in BCVA at 48 weeks, change from baseline in FCP retinal thickness at 48 weeks, safety, and immunogenicity

BCVA, best corrected visual acuity; CNV, choroidal neovascularization; ETDRS, Early Treatment Diabetic Retinopathy Study; FCP, foveal center point; IVT, intravitreal; MPS, macular photocoagulation study; nAMD, neovascular age-related macular degeneration; Q4W, every 4 weeks; R, randomized; SD-OCT, spectral domain optical coherence tomography.

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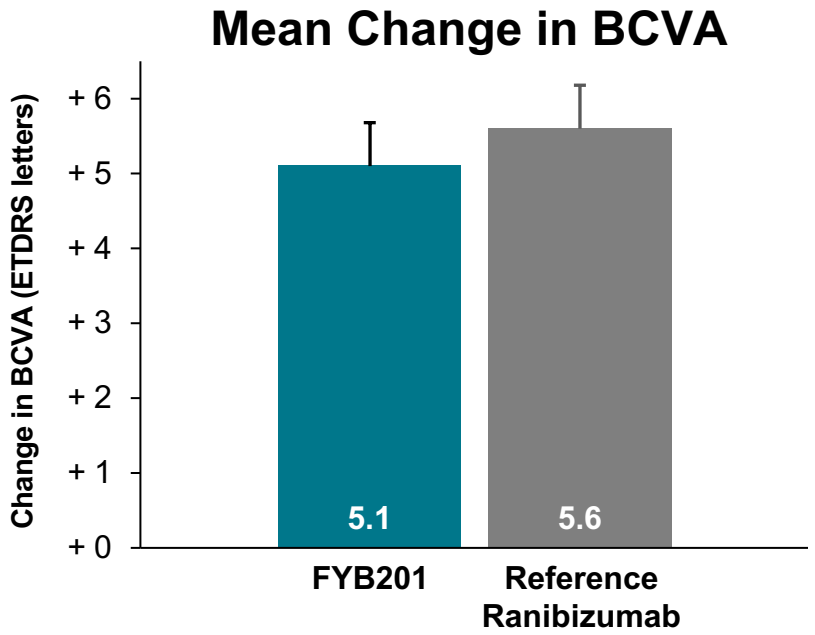
Primary Endpoint: Change in BCVA After 8 Weeks

- The primary endpoint (change from baseline in BCVA by ETDRS letters after 8 weeks) was met, as the 90% CI (–1.6 to 0.9) was within the predefined non-inferiority equivalence margin (–3.5 to 3.5)
- On average, patients who received FYB201 and reference ranibizumab saw ~5 more letters after 8 weeks of treatment



BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study.

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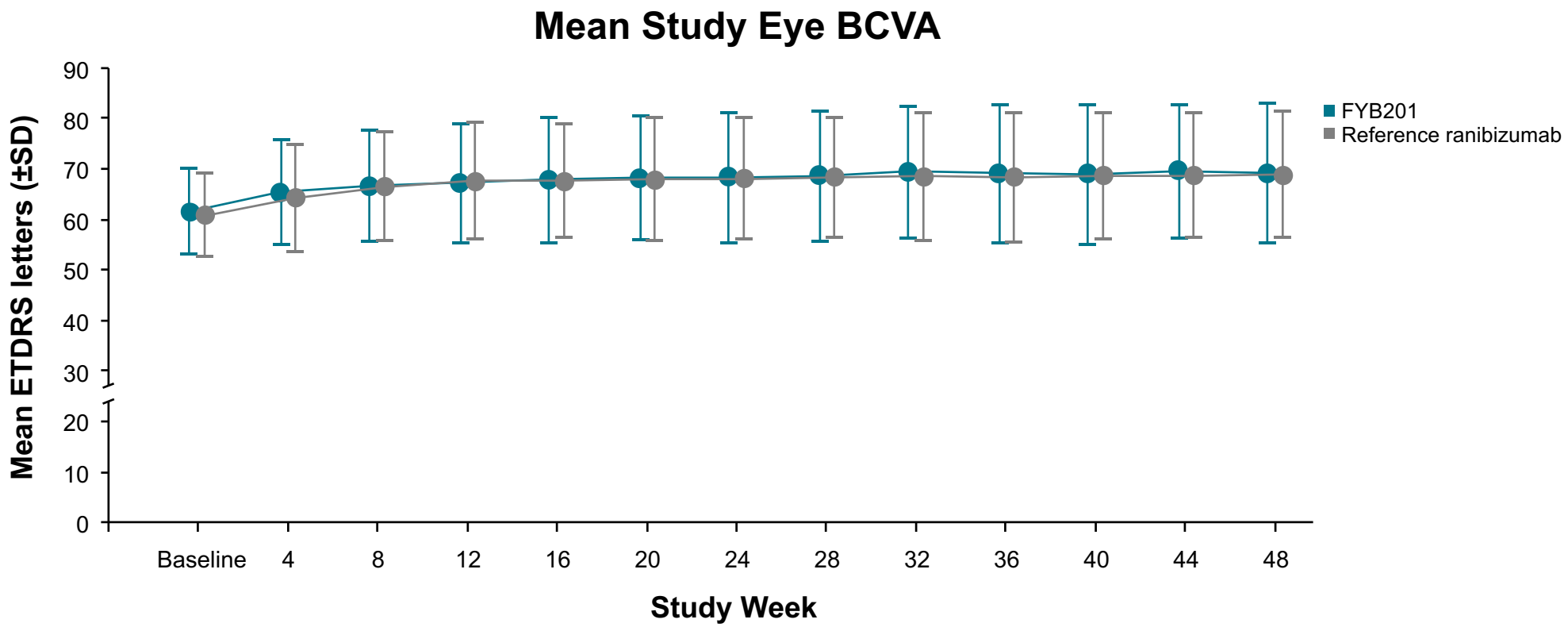
Secondary Endpoints: BCVA

- Mean (SD) study eye BCVA was highly similar between FYB201 and reference ranibizumab over the course of the study



BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; SD, standard deviation.

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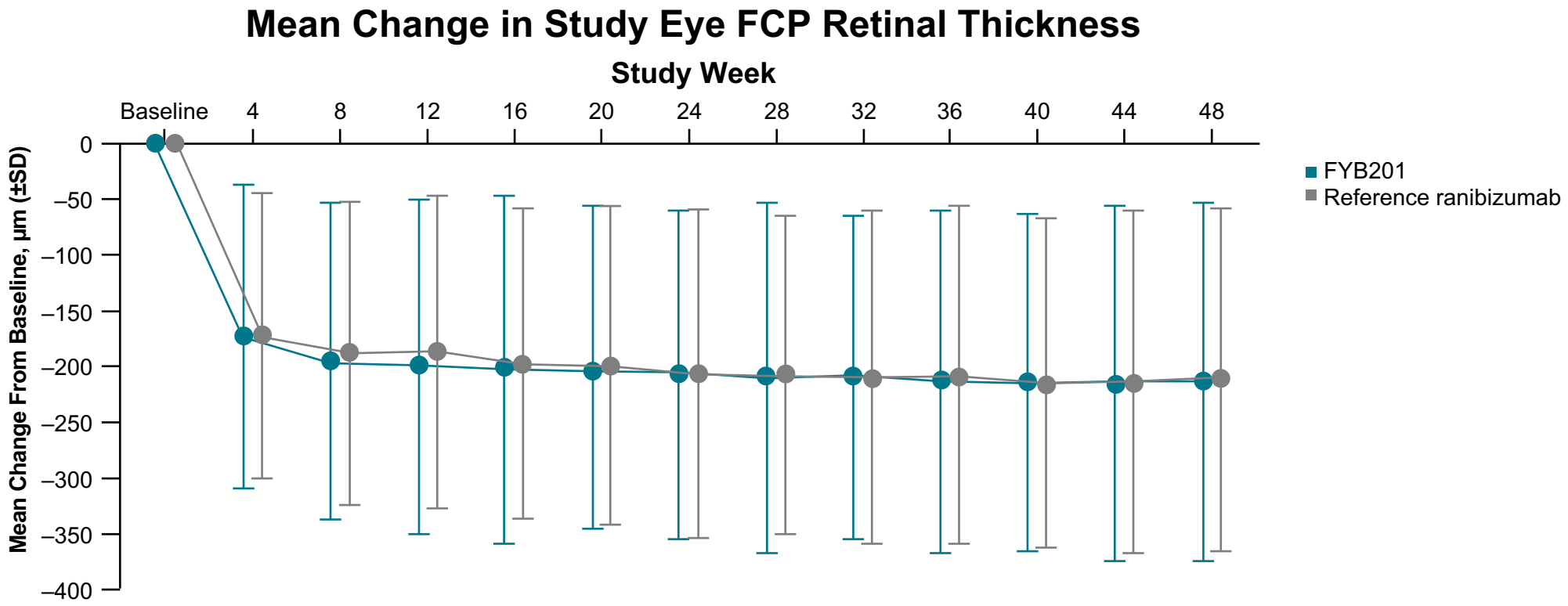
Secondary Endpoints: FCP Retinal Thickness

- Mean (SD) change in study eye FCP retinal thickness was highly similar between FYB201 and reference ranibizumab over the course of the study



BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; FCP, foveal center point; SD, standard deviation.

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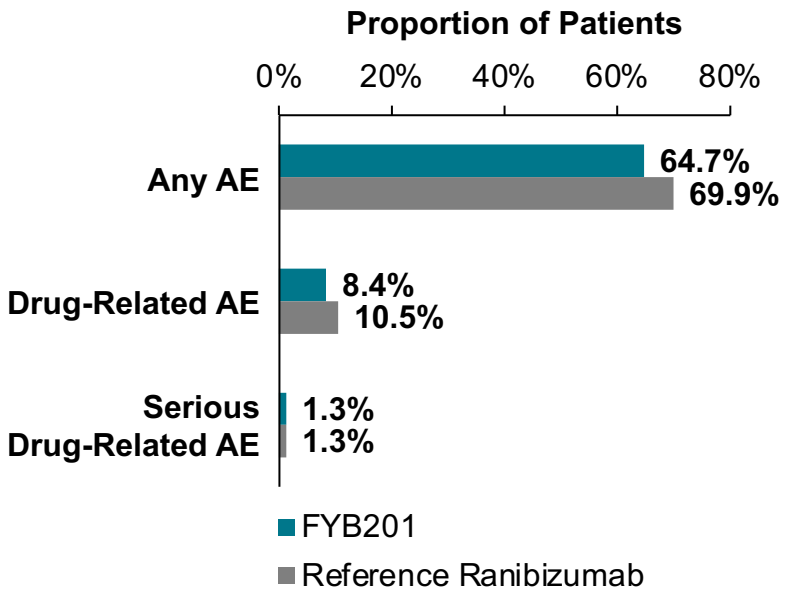
Overall Safety Profile and Ocular Adverse Events

- The overall safety profile of FYB201 and reference ranibizumab was highly similar



AE, adverse event; IMP, investigational medicinal product; nAb, neutralizing antibody; TEAE, treatment-emergent adverse event.
[a]MedDRA preferred terms associated with intraocular inflammation. [b]FYB201: iridocyclitis (n = 1) and conjunctivitis (n = 1); reference ranibizumab: punctate keratitis (n = 2).

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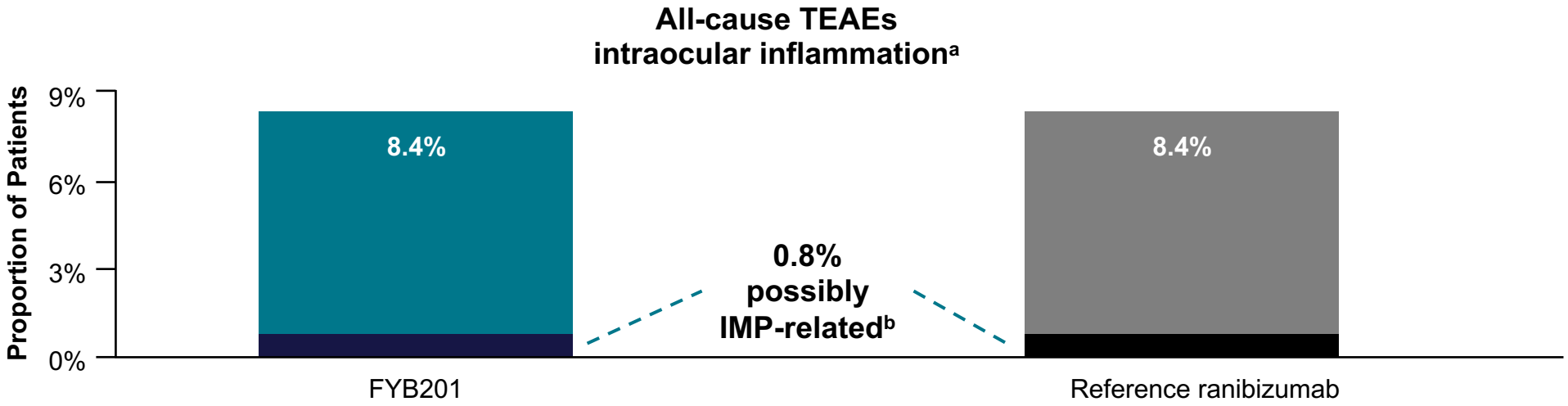
Overall Safety Profile and Ocular Adverse Events

- The prevalence of the TEAE “intraocular inflammation” was common and comparable between treatment groups



- Overall, the frequency and type of ocular AEs were comparable between the treatment groups
  - Most AEs were of mild or moderate intensity
  - No clinically relevant differences were identified between the treatment groups

AE, adverse event; IMP, investigational medicinal product; nAb, neutralizing antibody; TEAE, treatment-emergent adverse event.
[a]MedDRA preferred terms associated with intraocular inflammation. [b]FYB201: iridocyclitis (n = 1) and conjunctivitis (n = 1); reference ranibizumab: punctate keratitis (n = 2).
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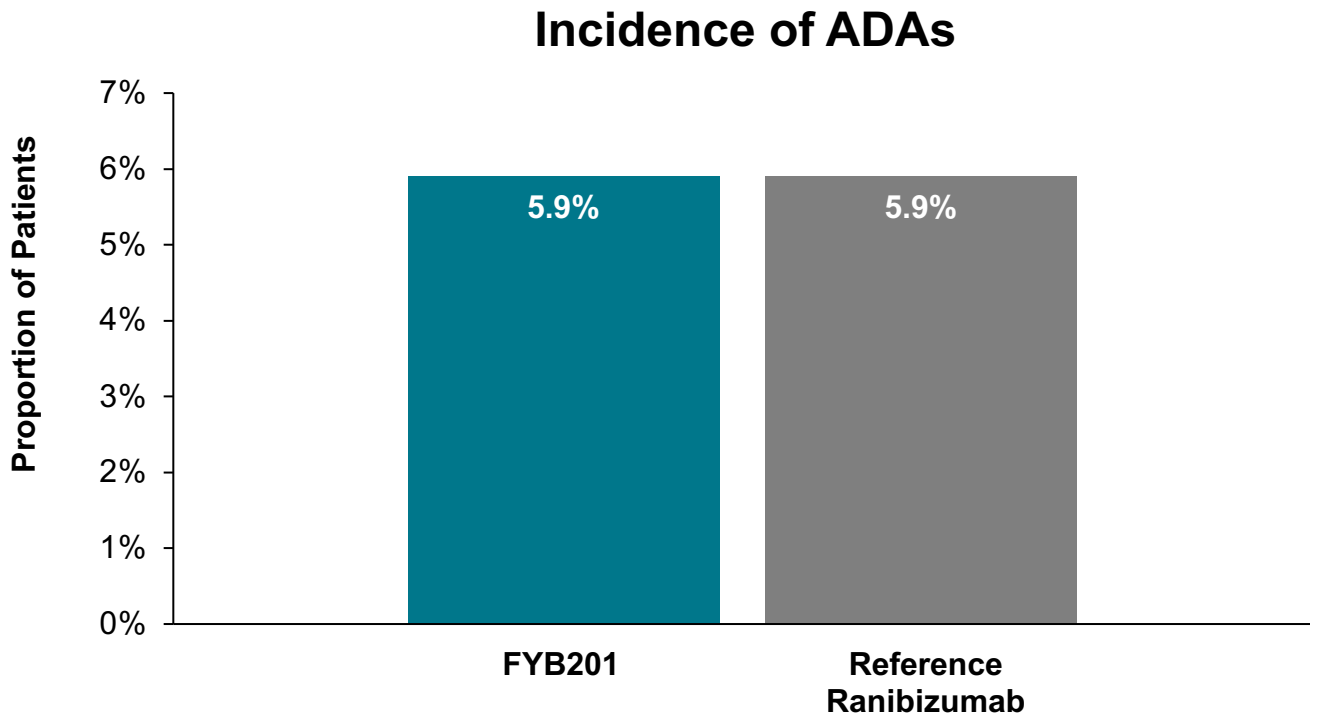
Immunogenicity

- FYB201 and reference ranibizumab had comparable immunogenicity profiles. Few patients developed ADAs during the study and had similar levels of ADA titers across treatment arms
- No NAbs were detected up to week 24. One patient tested positive for NAbs up to week 48 (FYB201 arm)



ADA, antidrug antibody; nAb, neutralizing antibody.

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Conclusion

- The COLUMBUS-AMD study demonstrated similarity of FYB201 and reference ranibizumab in terms of clinical efficacy, safety (local and systemic), and immunogenicity in patients with newly diagnosed subfoveal nAMD
- Biosimilar ranibizumab may offer a new, high-value treatment option for patients

nAMD, neovascular age-related macular degeneration.

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