A PULSAR Phase 3 Trial *Post-hoc* Analysis: Evaluating the Timing and Magnitude of Control of Disease Activity with Aflibercept 8 mg and Faricimab, Applying Similar Disease Activity Criteria Across Different Pivotal Phase 3 Trials for nAMD

Michael W. Stewart,[1] Paolo Lanzetta,[2] Jean-François Korobelnik,[3] Tobias Machewitz,[4] Xin Zhang,[5] and Sergio Leal,[5] on behalf of the PULSAR investigators

[1]Mayo Clinic College of Medicine and Science, Department of Ophthalmology, Mayo Clinic, Jacksonville, FL, USA; [2]Department of Medicine – Ophthalmology, University of Udine, Udine, Italy and Istituto Europeo di Microchirgugia Oculare – IEMO, Udine, Italy; [3]Service d'Ophtalmologie, CHU Bordeaux, Bordeaux, France and Bordeaux Population Health Research Center, INSERM, UMR1219, F-33000, University of Bordeaux, Bordeaux, France; [4]Bayer AG, Berlin, Germany; [5]Bayer Consumer Care AG, Basel, Switzerland

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Disclosures and acknowledgments

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Disclosures

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- **PL:** Consultant: Aerie, Allergan, Apellis, Bausch + Lomb, Bayer, Biogen, Boehringer Ingelheim, I-Care, Genentech, Novartis, Ocular Therapeutix, Outlook Therapeutics, and Roche. **J-FK:** Consulting fees: AbbVie, Apellis, Bayer, Carl Zeiss Meditec, EyePoint Pharma, Ocuphire, Roche, and Thea Pharmaceuticals; Member of data and safety monitoring boards or advisory boards for Alexion, Novo Nordisk, and Opthea. **TM:** Employee of Bayer AG. **SL** and **XZ**: Employees of Bayer Consumer Care AG

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Background and Aims

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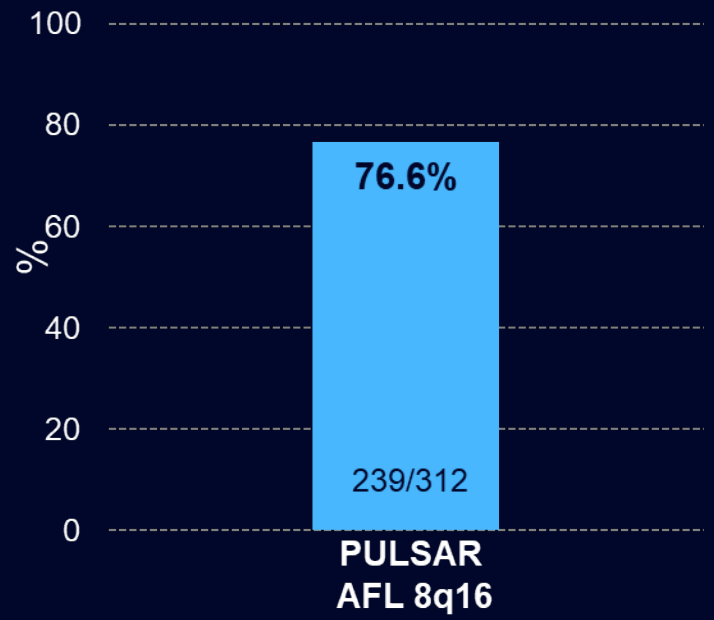
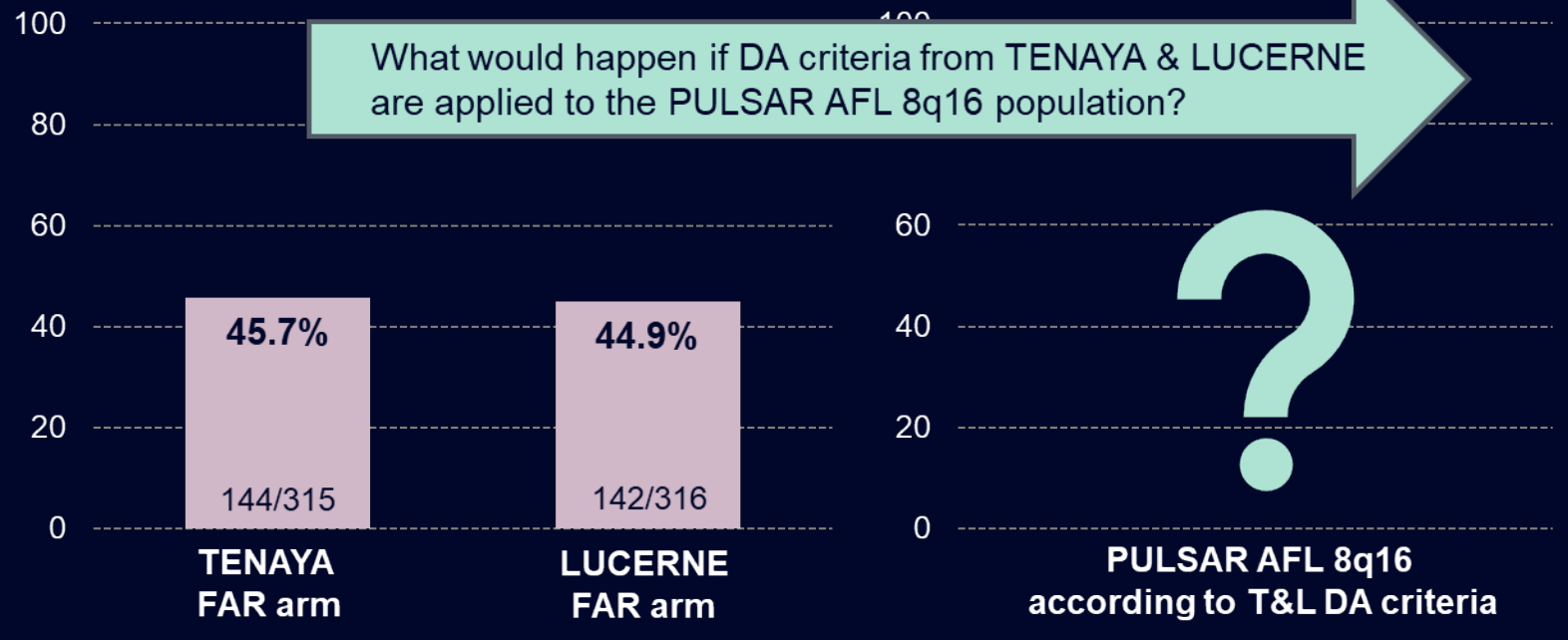
- **PULSAR**, and **TENAYA & LUCERNE**, were studies using anti-VEGF therapies with **presumed different** durability, and with **different** treatment algorithms and criteria for interval modification

PULSAR N=1009	Aflibercept 8 mg (8q12/8q16) vs aflibercept 2 mg (2q8) for treatment-naïve nAMD[1]
TENAYA & LUCERNE N=1329	Faricimab 6 mg (up to q16) vs aflibercept 2 mg (2q8) for treatment-naïve nAMD[2]

Proportion of **Patients** Maintaining q16 Dosing Through Week 48 (%)[1]



Proportion of **Patients** assigned to q16 Dosing Through Week 48 (%)[2]



2q8, aflibercept 2 mg every 8 weeks; **8q12/8q16**, aflibercept 8 mg every 12/16 weeks; AFL, aflibercept; **anti-VEGF**, anti-vascular endothelial growth factor; **DA**, disease activity; **FAR**, faricimab; **nAMD**, neovascular age-related macular degeneration; **q16**, every 16 weeks; T&L, TENAYA & LUCERNE. 1. Lanzetta P, et al. Lancet. 2024;403:1141–1152. 2. Heier J et al. Lancet. 2022;399:729–740.

TENAYA & LUCERNE Study Design

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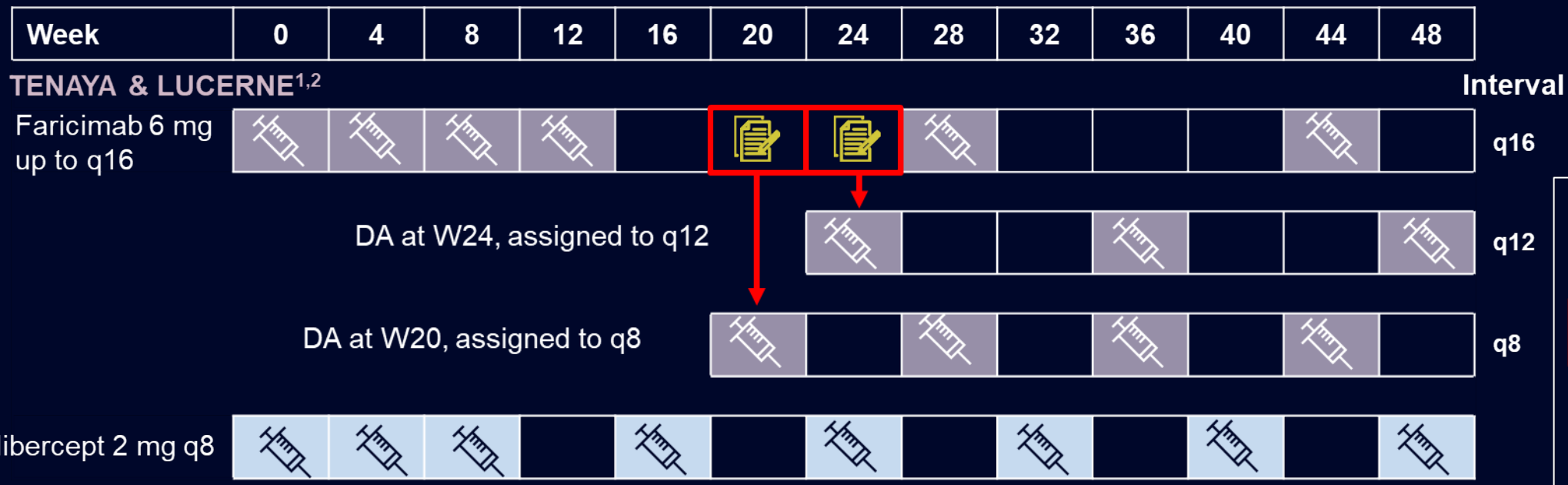

Prespecified DA assessment

CST increase

- **>50 µm** (vs average CST over previous 2 scheduled visits)
- or **≥75 µm** (vs lowest CST at either of previous 2 scheduled visits)

BCVA loss[a]

- **≥5 letters** (vs average BCVA over previous 2 scheduled visits)
- or **≥10 letters** (vs highest BCVA at either of previous 2 scheduled visits)
- or **New macular hemorrhage** (per the investigator and attributable to nAMD)

Representations of study design have been simplified, please refer to original publications for more information. In TENAYA & LUCERNE, sham injections given to mask treatment intervals (i.e., at every visit if not receiving study treatment). [a]Owing to nAMD DA. **BCVA,** best-corrected visual acuity; **CST**, central subfield thickness; **q8/q12/q16,** every 8/12/16 weeks.

1. Khanani A. et al. Ophthalmol Sci. 2021:17;100076. 2. Heier J. et al. Lancet. 2022;399:729–740.

TENAYA & LUCERNE, and PULSAR, Study Design

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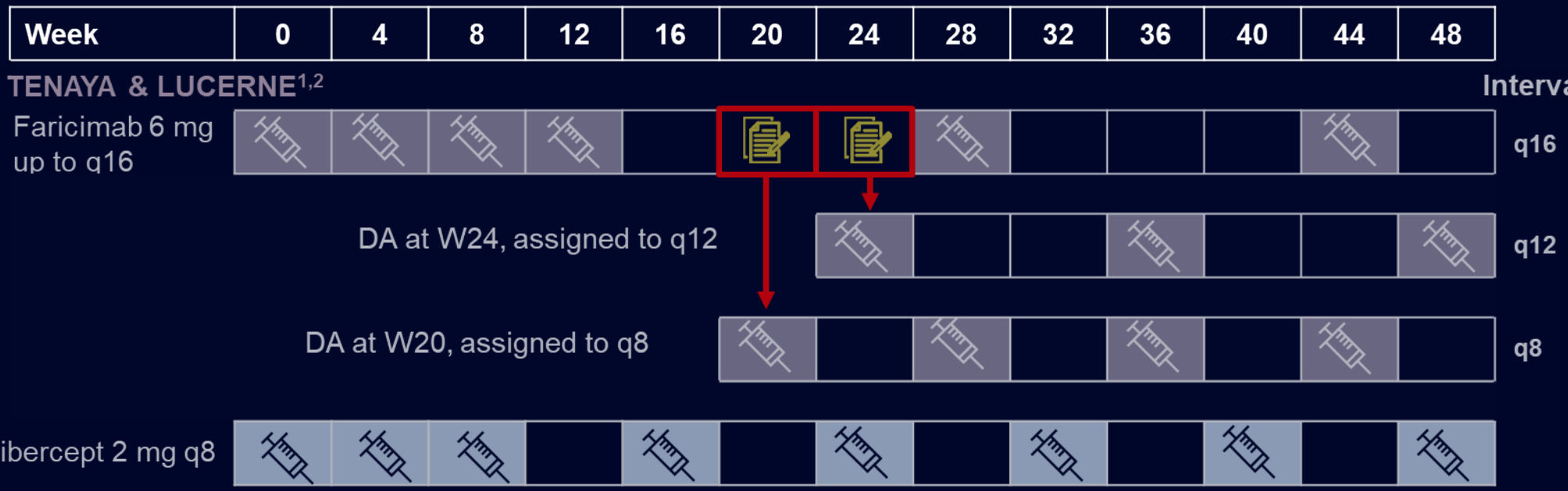

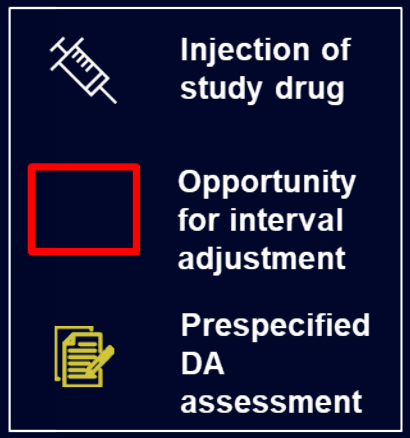

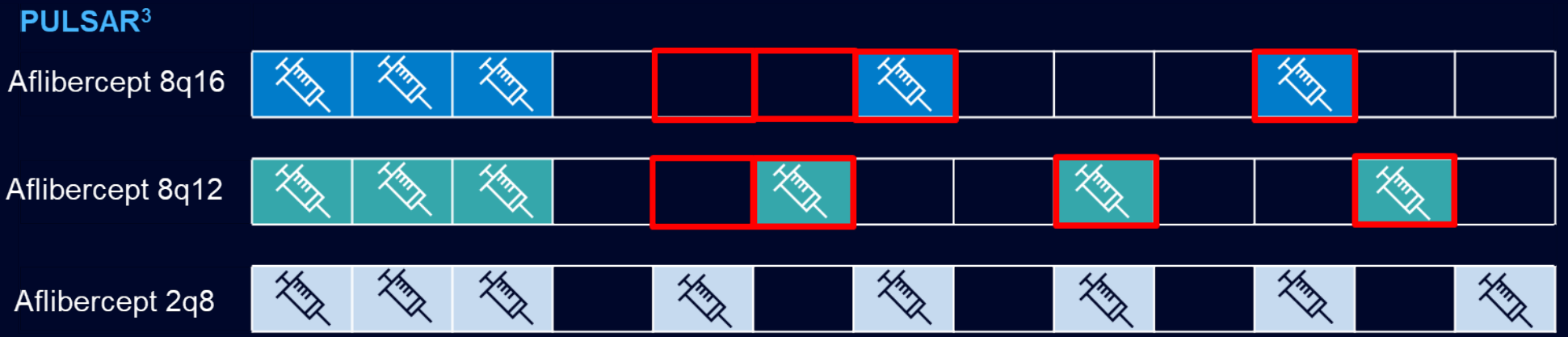

Note: Difference in the number of opportunities for interval adjustment

Representations of study designs have been simplified, please refer to original publications for more information. In PULSAR and in TENAYA & LUCERNE, sham injections given to mask treatment intervals (i.e., at every visit if not receiving study treatment). 1. Khanani A. et al. Ophthalmol Sci. 2021:17;100076. 2. Heier J. et al. Lancet. 2022;399:729–740. 3. Lanzetta P, et al. Lancet. 2024;403:1141–1152.

Application of TENAYA & LUCERNE DA Criteria to PULSAR 8q16 Population

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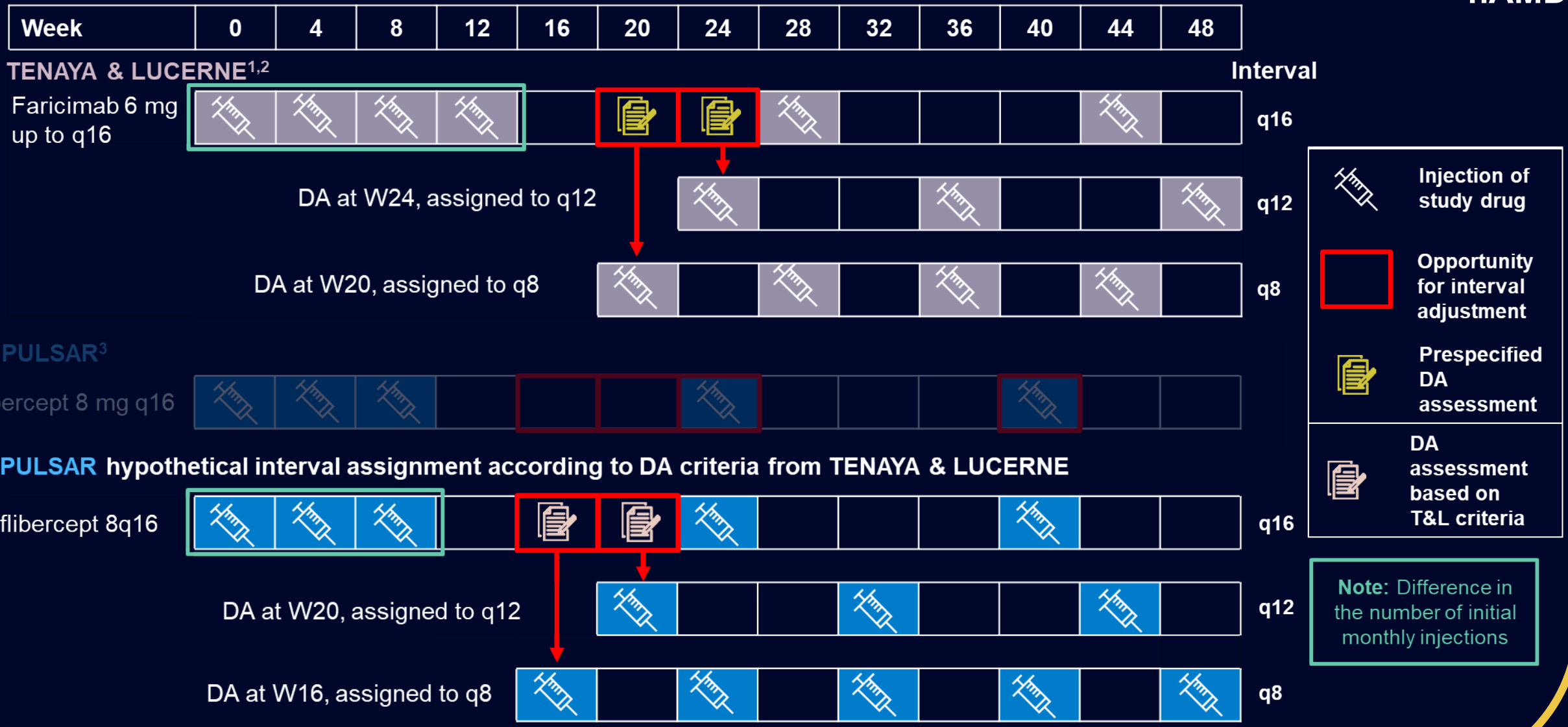

Note: Difference in the number of initial monthly injections

Representations of study designs have been simplified, please refer to original publications for more information. In PULSAR and in TENAYA & LUCERNE, sham injections given to mask treatment intervals (i.e., at every visit if not receiving study treatment). 1. Khanani A. et al. Ophthalmol Sci. 2021:17;100076. 2. Heier J. et al. Lancet. 2022;399:729–740. 3. Lanzetta P, et al. Lancet. 2024;403:1141–1152.

Baseline Characteristics of Patients in PULSAR[1] and TENAYA & LUCERNE[2]

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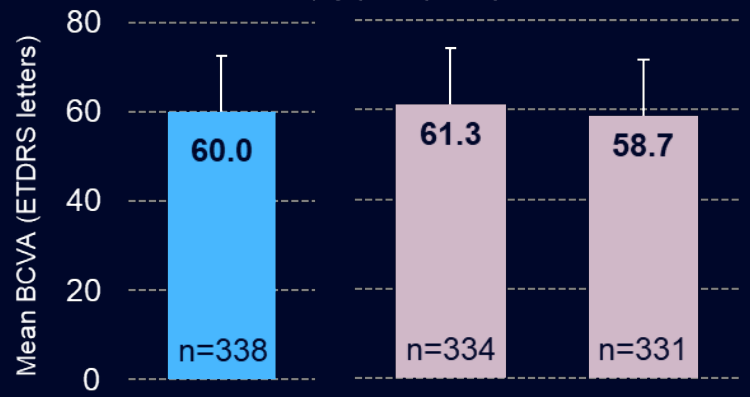
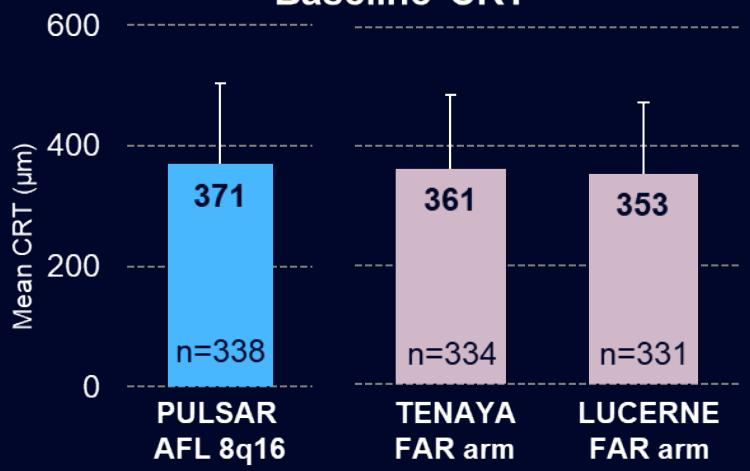
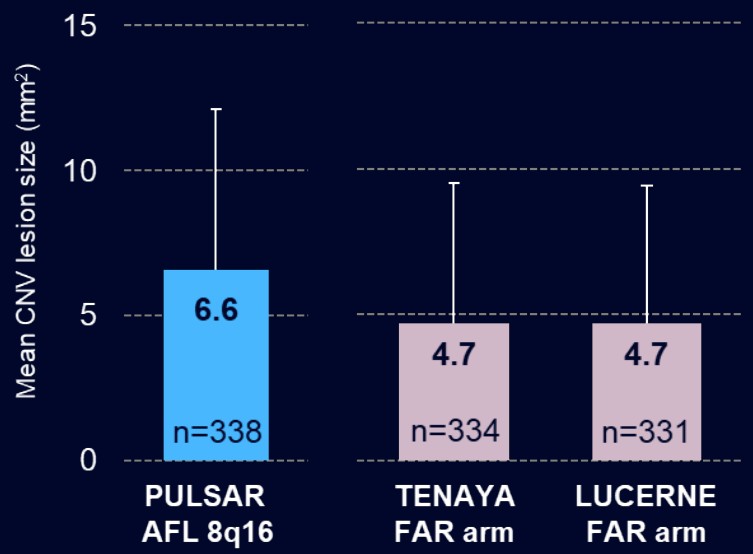
Baseline BCVA



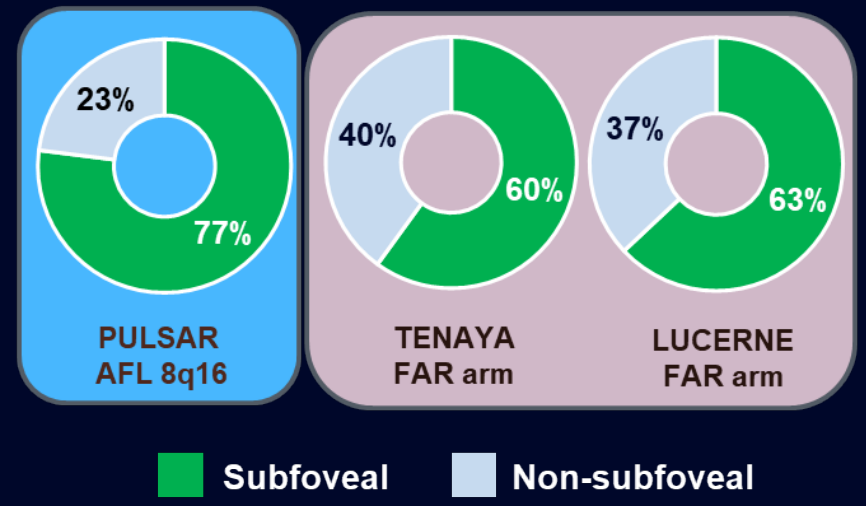
Baseline CRT



Baseline CNV lesion size



CNV Location (%)



A conservative approach was used in this analysis

- Different magnitude of disease activity at baseline was observed in different studies
- No adjustments were made to compensate for **fewer initial monthly doses**, **larger lesion size**, or **higher proportion of subfoveal CNV** in **PULSAR**, even though these could increase the difficulty for **aflibercept 8mg** to achieve control of disease activity

Error bars indicate SD. **CNV**, choroidal neovascularization; **CRT**, central retinal subfield thickness; **ETDRS**, Early Treatment Diabetic Retinopathy Score; **SD**, standard deviation. 1. Lanzetta P, et al. Lancet. 2024;403:1141–1152. 2. Heier J. et al. Lancet. 2022;399:729–740.

Proportion of Patients Assigned to Aflibercept 8q16 Treatment Through W48 should TENAYA & LUCERNE DA Criteria be Applied

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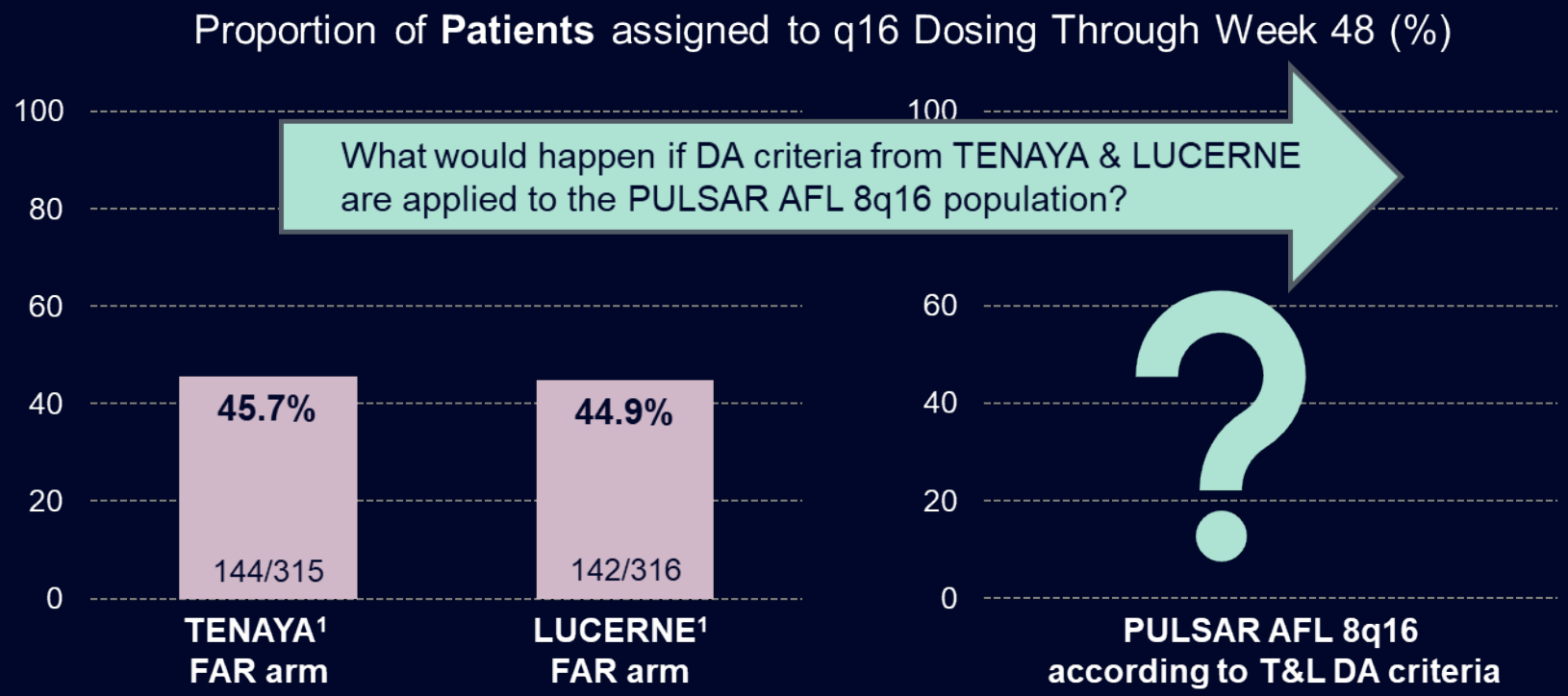

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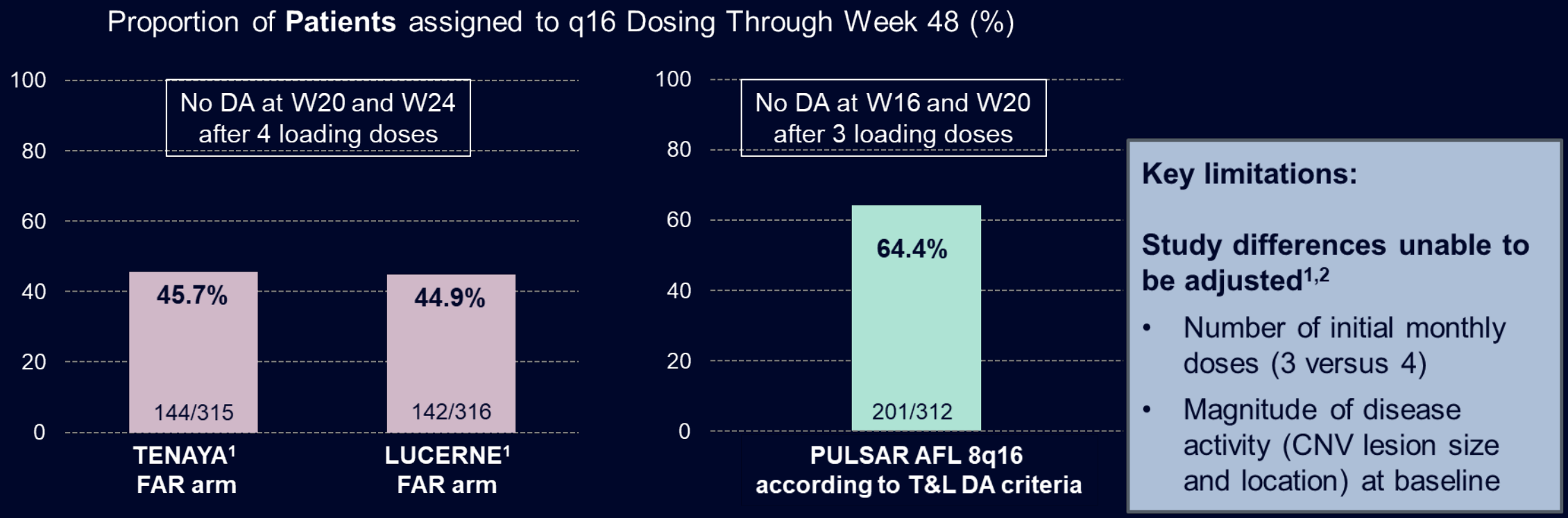

Key limitations:

Study differences unable to be adjusted[1,2]

- Number of initial monthly doses (3 versus 4)
- Magnitude of disease activity (CNV lesion size and location) at baseline

When DA criteria from TENAYA & LUCERNE are applied:

- **64%** of patients in the **aflibercept 8q16 group in PULSAR** are predicted to have no DA at W16 or W20 (and thus would be assigned to q16 dosing intervals through W48)
- This compares to **~45%** of patient receiving **faricimab** in **TENAYA & LUCERNE**, with no DA at W20 and W24

1. Heier J. et al. Lancet. 2022;399:729–740. 2. Lanzetta P, et al. Lancet. 2024;403:1141–1152.

Conclusions

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Findings from this *post-hoc* analysis support earlier control of disease activity with aflibercept 8 mg in PULSAR than that reported for faricimab in TENAYA and LUCERNE

- Despite patients in the **aflibercept 8q16 group in** PULSAR having **fewer initial monthly doses and more severe disease at baseline**, a higher proportion of patients in this group **(64%)** achieved control of DA compared with **faricimab** in TENAYA & LUCERNE **(~45%)**,[1] and at an earlier time point (W16/W20 vs W20/24), using similar DA assessment criteria

Inter-trial assessments should be interpreted with caution due to various limitations

- Different magnitude of baseline disease activity are observed in different studies
- DA criteria in clinical trials can have a substantial effect on the determination of dosing intervals
- Limitations in this *post-hoc* analysis include the differences in initial monthly injection number and baseline disease activity between PULSAR and TENAYA & LUCERNE
- Despite the **conservative approach** applied, the results of this analysis should be **interpreted with caution**

1. Heier J. et al. Lancet. 2022;399:729–740.