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

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Disclosures

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- **Peter Kaiser:** Consultant for 2020 On-site, AbbVie/Allergan, Alexion, Alzheon, Annexon Biosciences, Aviceda Therapeutics, Bausch + Lomb, Bayer, Biogen, Bionic Vision Technologies, Carl Zeiss Meditec, Chengdu Kanghong Pharmaceutical Group, Coherus, Complement Therapeutics, Galimedix Therapeutics, Genentech/Roche, Innovent Biologics, iRenix Medical, jCyte, Kanaph Therapeutics, Kera Therapeutics, Kriya Therapeutics, Nanoscope Therapeutics, Novartis, Ocugenix, Ocular Therapeutix, Oculis, REGENXBIO, RetinaAI, Retinal Sciences, Samsung Bioepis, Stealth BioTherapeutics, Stuart Therapeutics, Sustained Nano Systems, Takeda, Théa Pharma, and Unity Biotechnology; Stock options for Ocular Therapeutix. **MS:** Consultant for Bayer, Biogen, and Revana. **PL:** Consultant for Aerie Pharmaceuticals, Allergan, Annexon, Apellis, Bausch + Lomb, Bayer, Biogen, Boehringer Ingelheim, Eyepoint Pharmaceuticals, Genentech, I-Care, Novartis, Ocular Therapeutix, Outlook Therapeutics, and Roche. **JFK:** Consultant for AbbVie, Apellis, Bayer, Carl Zeiss Meditec AG, Janssen, Nano Retina, Roche, and Théa Pharmaceuticals; member of the data safety monitoring board or advisory board for Alexion, Novo Nordisk, and Oxular. **TM:** Employee of Bayer AG. **XZ and SL:** Employees of Bayer Consumer Care AG.
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- This study includes research conducted on human patients. Institutional Review Board approval was obtained prior to study initiation
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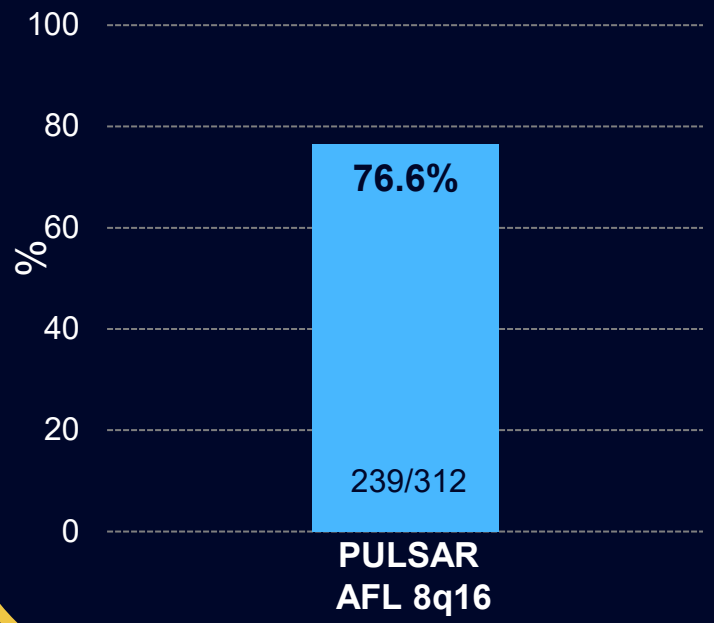
Background and Aims

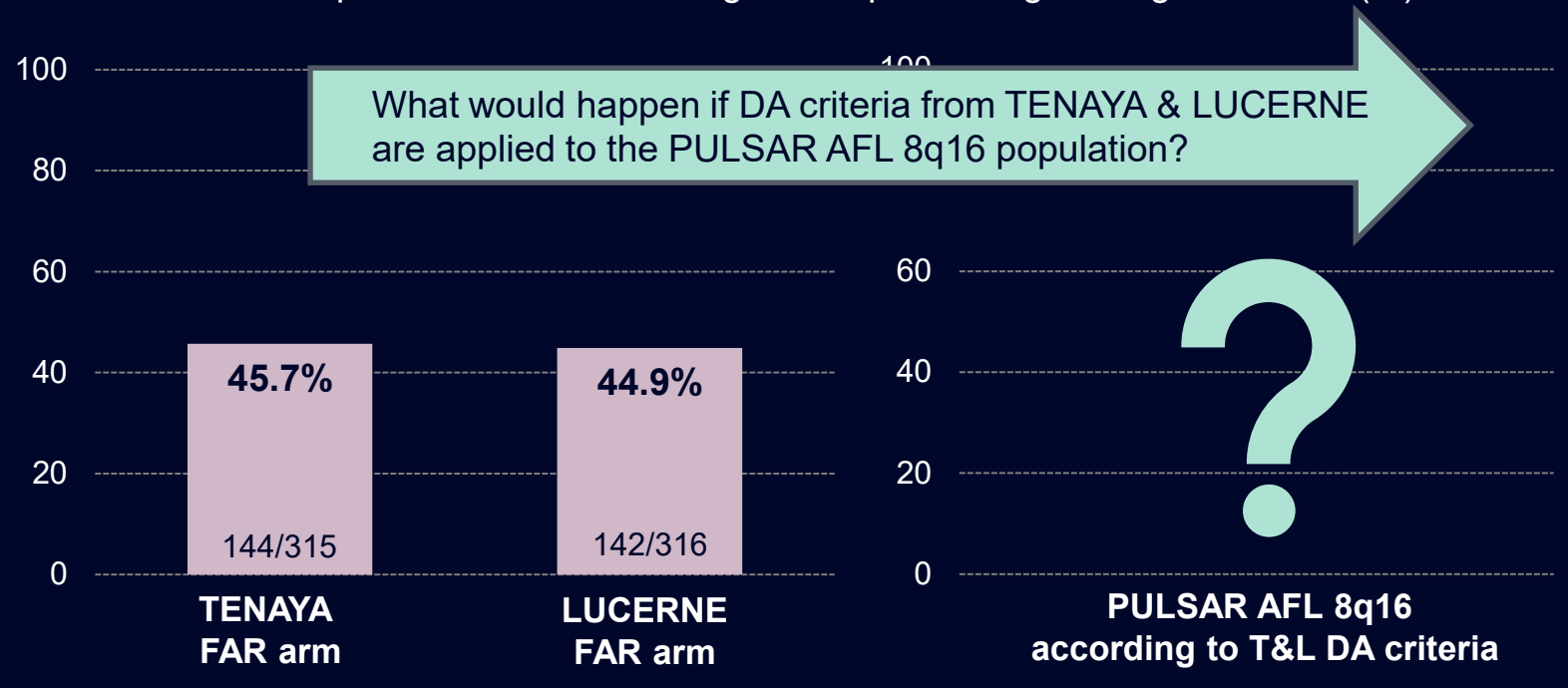
PULSAR, and **TENAYA & LUCERNE**, were studies using anti-VEGF therapies with **presumed different** durability, and with **different** treatment algorithms and criteria for interval modification

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

pulsar nAMD

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]

or

≥5 letters (vs average BCVA over previous 2 scheduled visits)

or

≥10 letters (vs highest BCVA at either of previous 2 scheduled visits)

or

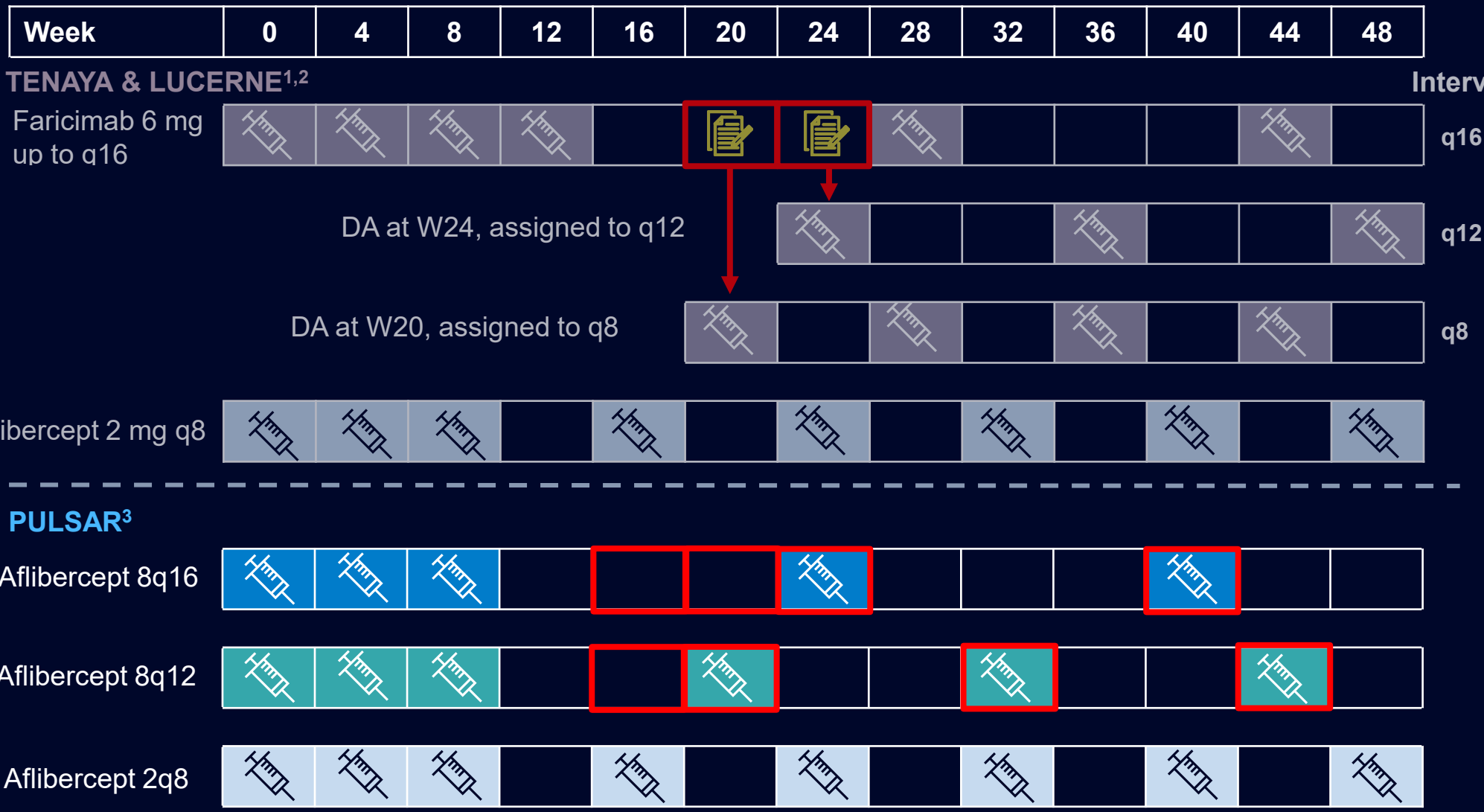
New macular hemorrhage (per the investigator and attributable to nAMD)

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

pulsar nAMD

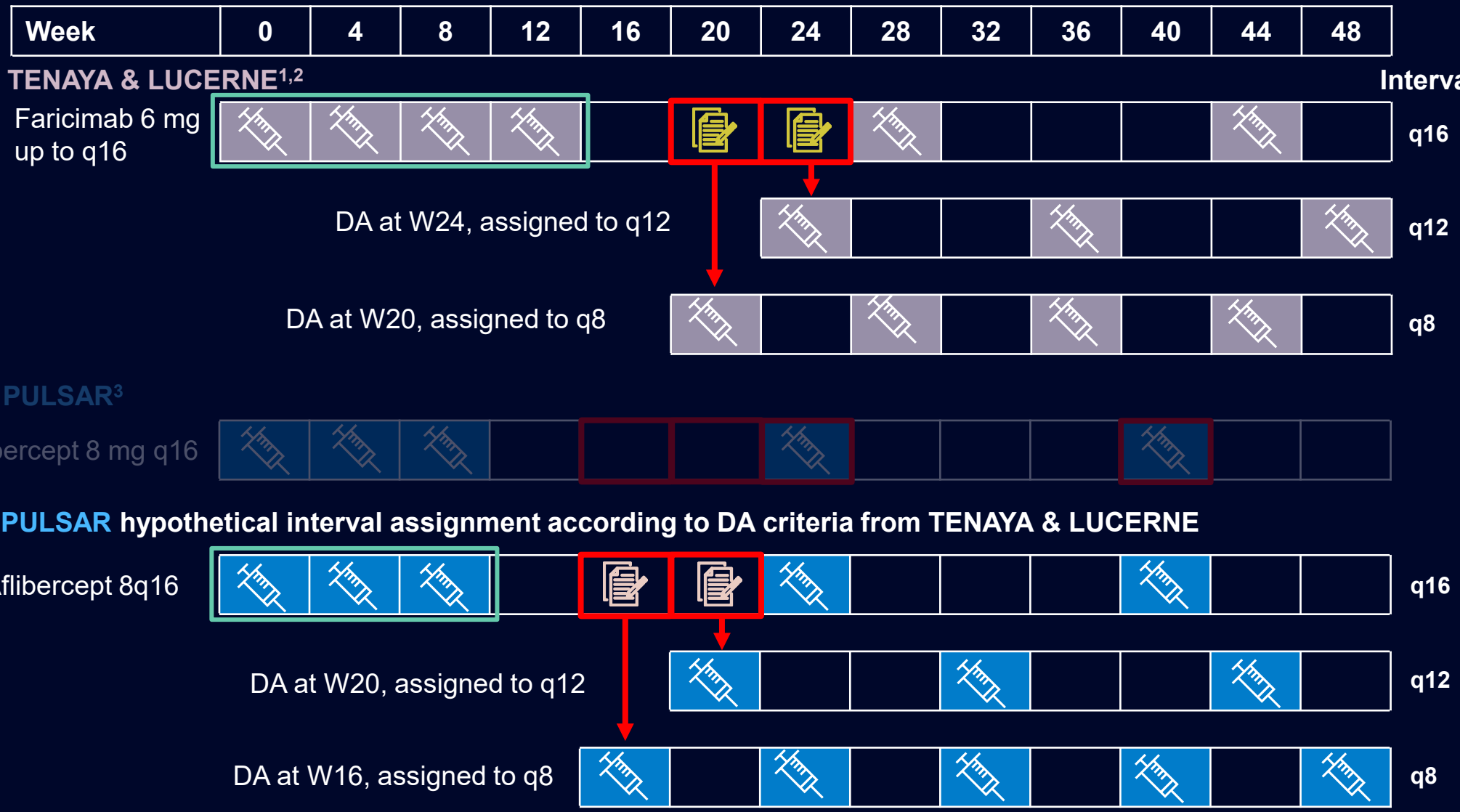


Note: Difference in the number of opportunities for interval adjustment

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

pulsar nAMD



Injection of study drug

Opportunity for interval adjustment

Prespecified DA assessment

DA assessment based on T&L criteria

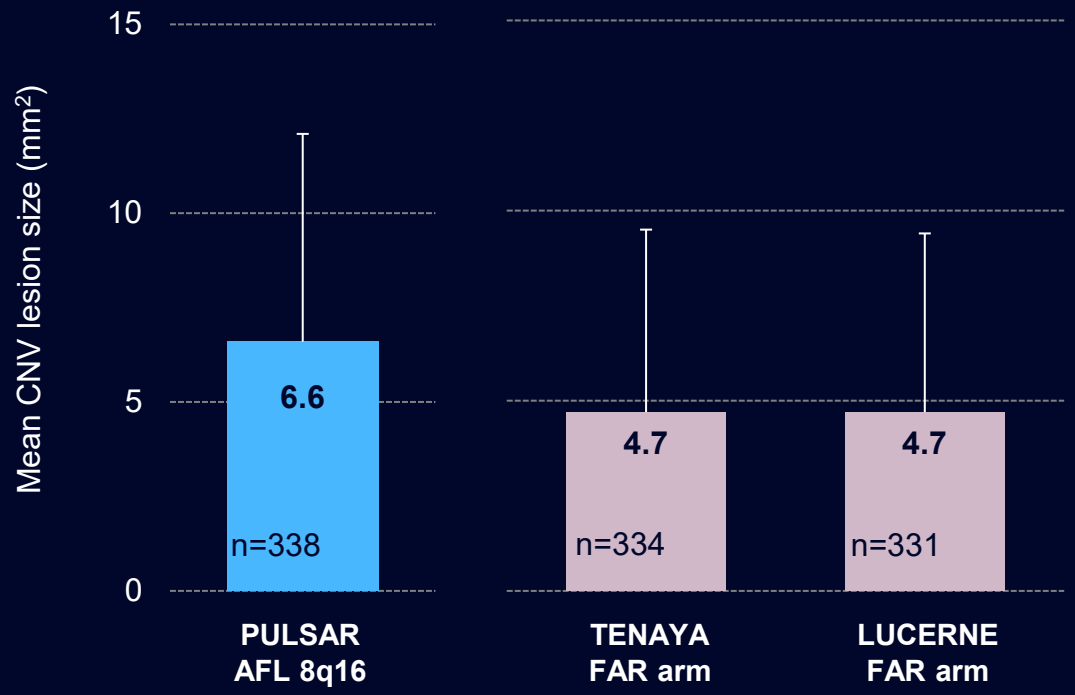
Note: Difference in the number of initial monthly injections

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.

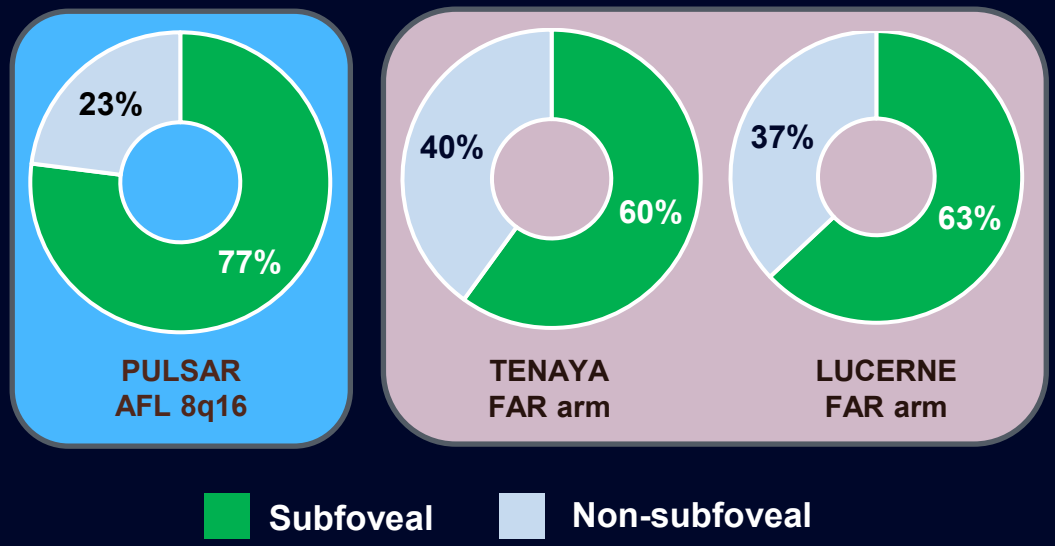
Baseline Characteristics of Patients in PULSAR[1] and TENAYA & LUCERNE[2]

pulsar nAMD

Baseline CNV lesion size



CNV Location (%)



A conservative approach was used in this analysis

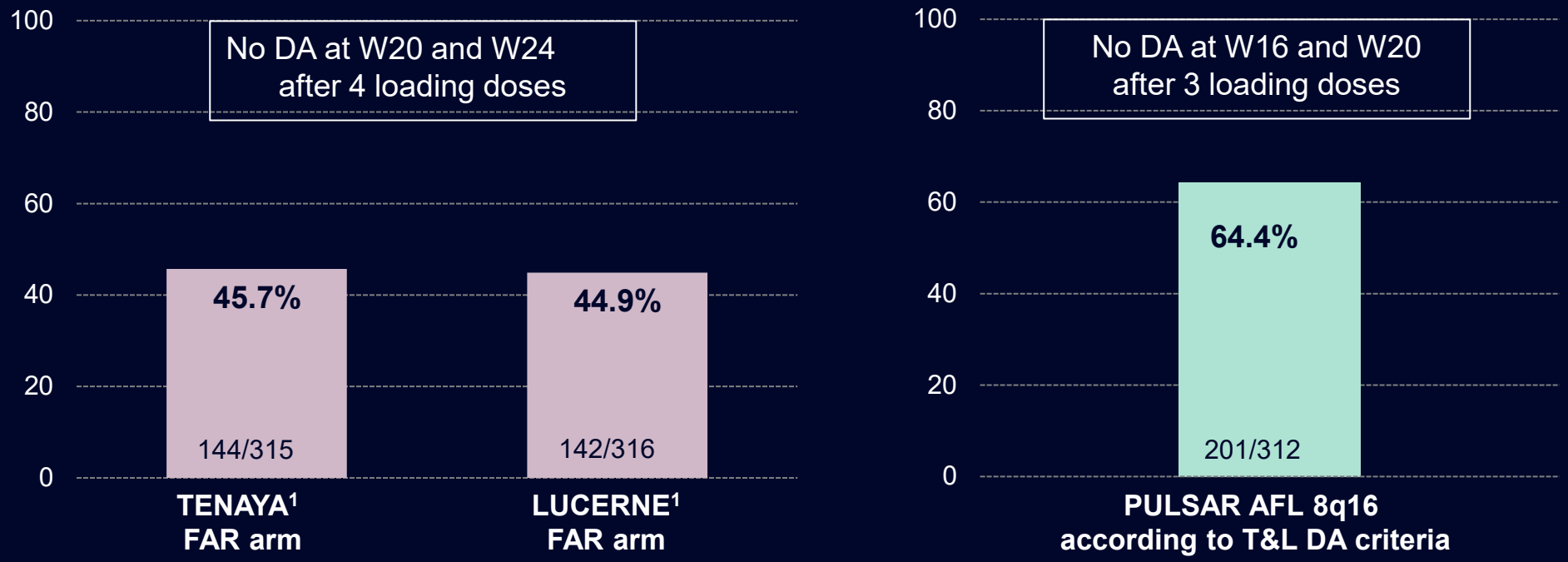
- Different magnitude of disease activity at baseline was observed in different studies
- No adjustments were made to compensate for **fewer initial monthly doses**, **larger lesion size**, or **higher proportion of subfoveal CNV** in **PULSAR**, even though these could increase the difficulty for **aflibercept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

pulsar nAMD

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



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

Conclusions

pulsar
nAMD

Findings from this *post-hoc* analysis support earlier control of disease activity with aflibercept 8 mg in PULSAR (64% at W16/W20) than that reported for faricimab in TENAYA and LUCERNE (45% at W20/W24),[1] using similar DA assessment criteria

Inter-trial assessments should be interpreted with caution due to various **limitations**, such as **differences in magnitude of baseline DA and impact of DA criteria on study protocols**

In this *post-hoc* analysis, limitations include the **differences in the number of initial monthly injections and baseline disease activity between PULSAR and TENAYA & LUCERNE**

Despite the **conservative approach** applied, these results should be **interpreted with caution**

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