# LOAD study:

## Effectiveness of Switching to Aflibercept 8 mg With Versus Without a LOAding Dose in Previously Treated Patients With Neovascular AMD Requiring Treatment Intervals of ≤8 Weeks




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# Financial Disclosures

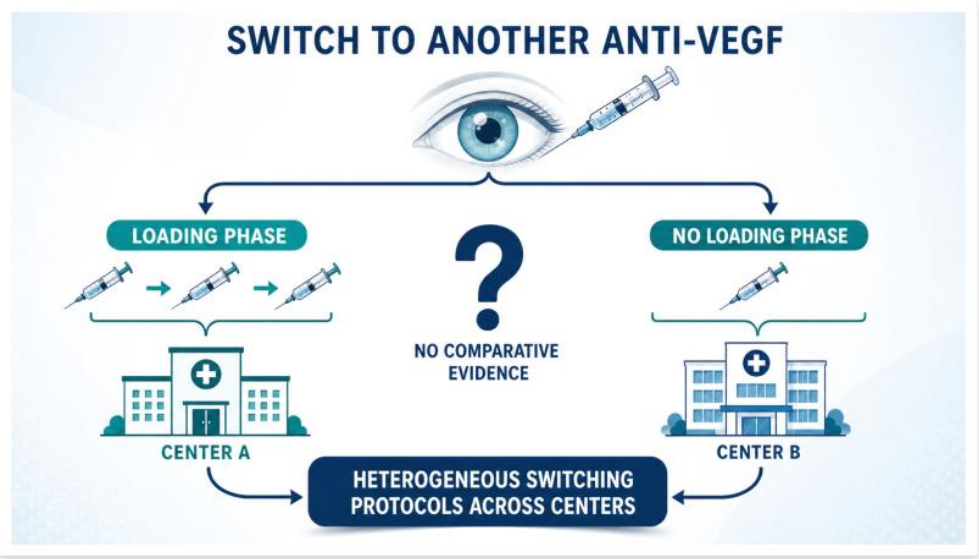
AbbVie, Alcon / Lumithera, Bayer, Celltrion, Horus / Alimera, KOL, Krys, Novartis, Roche, Théa



# Effectiveness of Switching to Aflibercept 8 mg **With** Versus **Without a Loading Phase** in Previously Treated Neovascular AMD Patients Requiring **Short Intervals (≤Q8)**

## Rationale

- **When switching previously treated patients, no study has ever evaluated whether a loading dose/phase* is beneficial or not.**
- **Consequently, switching protocols vary widely across centers.**




## Study design

**319** patients

**18** private & public centers

**6 mo** enrolment period

**≤32 wk** follow-up visits




- **Sponsor: Hospices Civils de Lyon, France**
- **Grant from Bayer****
- **FPFV: *5 May 2025***
- **LPLV: *13 May 2026***

***18 participating centers : thank you!***

*LD: Loading Dose or Phase of 3 monthly intravitreal injection, recommended for treatment-naïve patients.

**This study received financial support from Bayer Healthcare. **Bayer was not involved in the design or conduct of the study, nor in the analysis of the results.**

# LOAD STUDY — Study Design & Inclusion Criteria

OPHTALMO CROIX-ROUSSE TEAM

French | Multicenter | Ambispective* | Observational comparative cohort

**nAMD "poor responders"**
anti-VEGF intervals ≤ 8 weeks → switched to **aflibercept 8 mg**

**WITH loading dose****
3 monthly IVT, then extension

**WITHOUT loading dose**
Direct switch, then extension

**Allocation**
- Non-randomized
- Predefined center-level strategy
- Consecutive patients

**≥ 132**
**patients per arm**
α = 5% / power = 80%
Primary endpoint: interval extension at V4

## Inclusion criteria (all required)

| | | |
|---|---|---|
| ≥ 50 y | **Age** | Adults aged ≥ 50 years, men or women |
| 4–120 mo | **nAMD duration** | Documented nAMD diagnosed 4 to120 months before first aflibercept 8 mg injection |
| ≤ 8 wk | **"Poor responders"** | Previous anti-VEGF at injection intervals ≤ 8 weeks ranibizumab, aflibercept 2 mg, bevacizumab, brolucizumab, faricimab |
| 8 mg | **Switch** | Switch to aflibercept 8 mg planned or already initiated |
| > 1/10 | **Baseline VA** | VA > 1/10 (> 35 ETDRS letters, 20/200) |

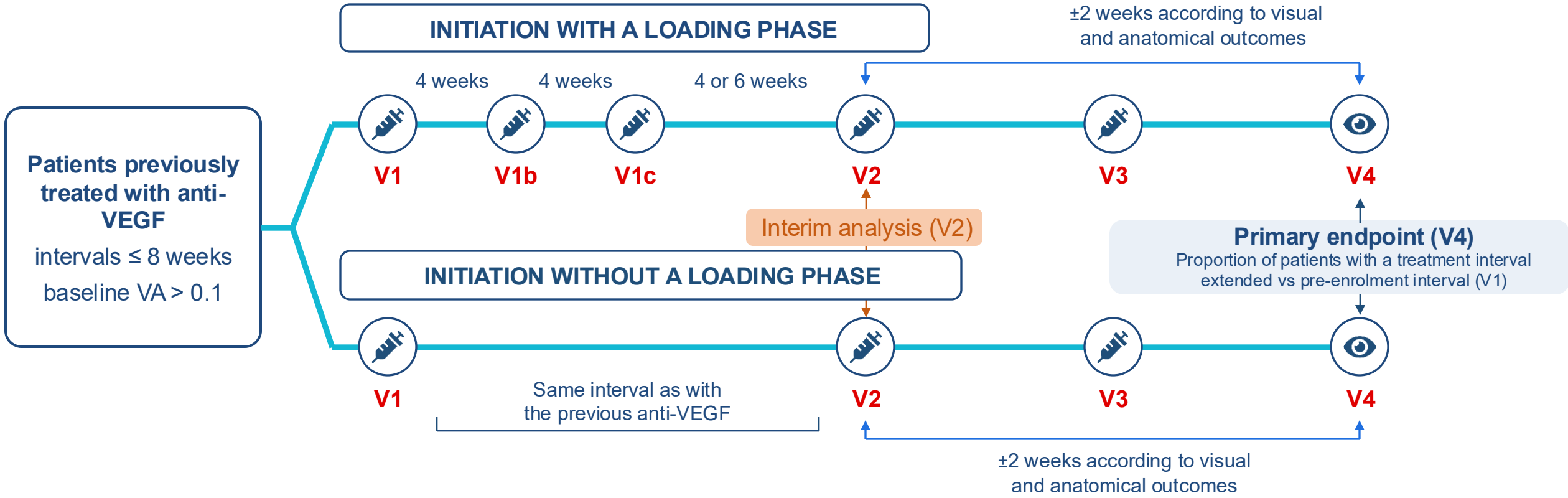
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*Retrospective and prospective data collection
** LD: loading dose = 3 monthly intravitreal injections (IVT)
nAMD: neovascular age-related macular degeneration; VA: visual acuity

Mateis | cnrs

# VISIT SCHEDULE

## Previously treated patients

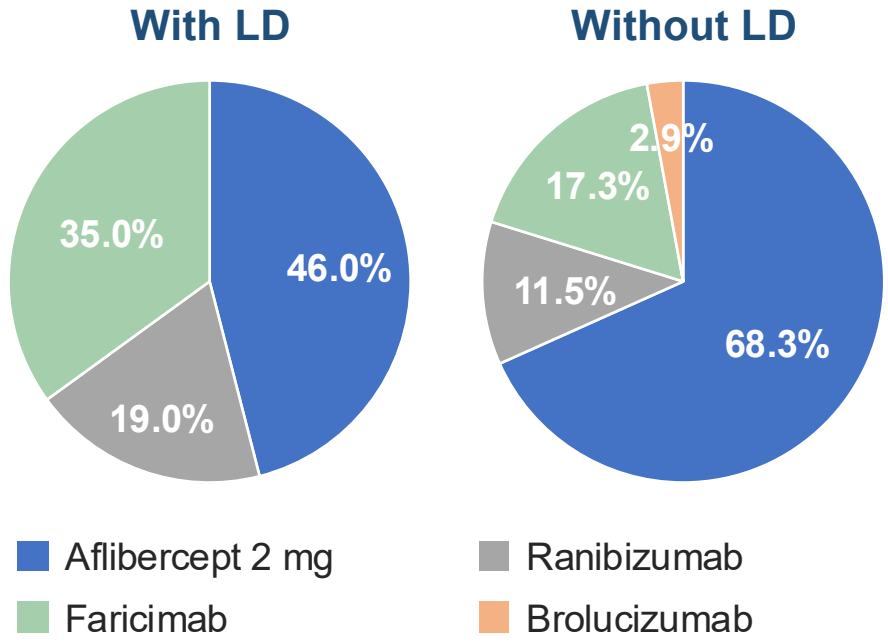



VA: visual acuity

# BASELINE CHARACTERISTICS

| Baseline characteristics | With LD n = 137 | Without LD n = 139 |
|---|---|---|
| Age, years, mean (SD) | 80.2 (6.5) | 80.7 (7.2) |
| Women, % | 56.9 | 62.6 |
| **Baseline VA, ETDRS letters** | **72.3** | **68.2** |
| Bilateral involvement, % | 49.6 | 41.0 |
| MNV type 1 / 2 / 3, % | 83.3 / 12.1 / 4.5 | 74.6 / 16.4 / 9.0 |
| **Last interval before switch, weeks (mean)** | **5.1** | **6.2** |
| **Anatomical parameters** | | |
| PED, % | 81.5 | 76.3 |
| **IRF, %** | **20.7** | **46.0** |
| SRF, % | 46.7 | 48.9 |
| IRF and/or SRF, % | 58.5 | 75.5 |
| CRT, µm | 295 | 291 |

## Previous anti-VEGF




LD: loading dose ; VA: visual acuity ; MNV: macular neovascularization ; PED: pigment epithelial detachment ; IRF / SRF: intraretinal / subretinal fluid ; CRT: central retinal thickness

# PRIMARY CRITERIA : POPULATION ANALYSIS

**Proportion of patients whose treatment interval at V4 was extended vs. the interval prior to enrolment (V1)**

**Full treatment population**
**n = 276**

**ITT-like**

All patients who received every scheduled injection: V1, (V1b, V1c), V2, V3, V4

**− 62 patients**

**included if:**

- Adherence o the pre-switch interval (both groups)
- Not immediate T&E in the group without LD

**Compliant population**
**n = 214**

**PP-like**

**Patients whose treatment followed the protocol-defined algorithm in both groups**

## Subgroups of the compliant population by previous anti-VEGF

**1st generation n = 151**
ranibizumab, aflibercept 2 mg, bevacizumab

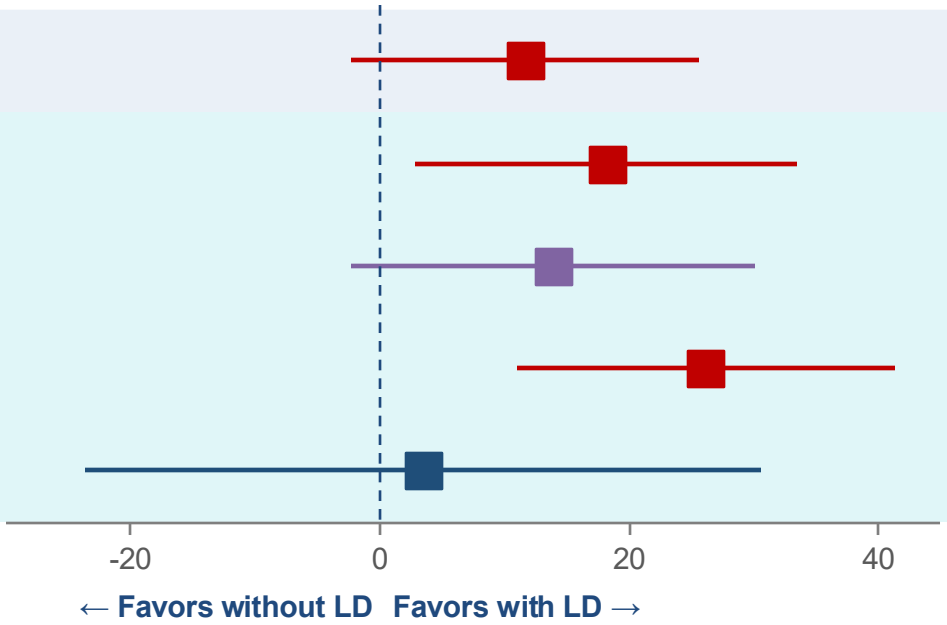
**2nd generation n = 62**
faricimab, brolucizumab

ITT: intention-to-treat ; PP: per-protocol ; LD: loading dose · T&E: treat-and-extend ; anti-VEGF: anti-vascular endothelial growth factor

# PRIMARY CRITERIA : POPULATION ANALYSIS

## Proportion of patients whose treatment interval at V4 was extended vs. the interval prior to enrolment (V1)

| Population | RD [95% CI] | p |
|---|---|---|
| **Full treatment population (n = 276)** *Primary analysis* | **11.7 [-2.3; 25.7]** | **0.10** |
| **Compliant population (n = 214)** *PP-like analysis* | **18.2 [2.9; 33.5]** | **0.02** |
| *Adjusted on prior interval** | 14.0 [-2.2; 30.2] | 0.09 |
| *Previous anti-VEGF 1st gen. (n = 151)* | **26.2 [11.0; 41.4]** | **< 0.001** |
| *Previous anti-VEGF 2nd gen. (n = 62)* | 3.5 [-23.6; 30.7] | 0.80 |




1. **Primary analysis (full treatment population) :** +11.7 points with LD, **not significant (p = 0.10)**
2. **Compliant population : LD associated with an 18% greater likelihood of extending the treatment interval** (p = 0.02)
3. **After adjustment for the initial interval:** directionally favorable to LD, but reduced magnitude, not significant (p = 0.09)

* Adjusted on the interval prior to enrolment
RD: Risk difference estimated from the adjusted g-computation model (adjusted for centre, age, sex and cataract surgery history). ; CI: confidence interval ; LD: loading dose

# Treatment interval at V4 Distribution and change

**'Full treatment' population** (n = 276) **mean follow-up 24.5 weeks**

## Change in interval, V1 → V4**

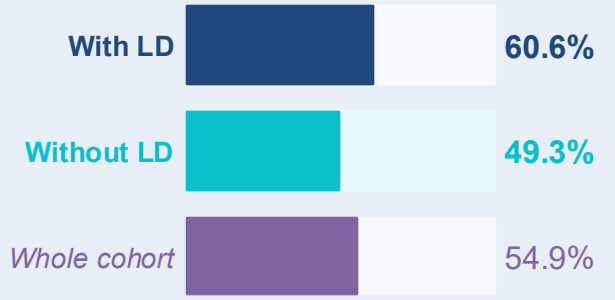
**With LD**
**+1.9 wk**
mean (SD 2.8)
median +2 (−5; +10)

**Without LD**
**+1.1 wk**
mean (SD 2.7)
median +0.5 (−4; +11)

**p = 0.006***

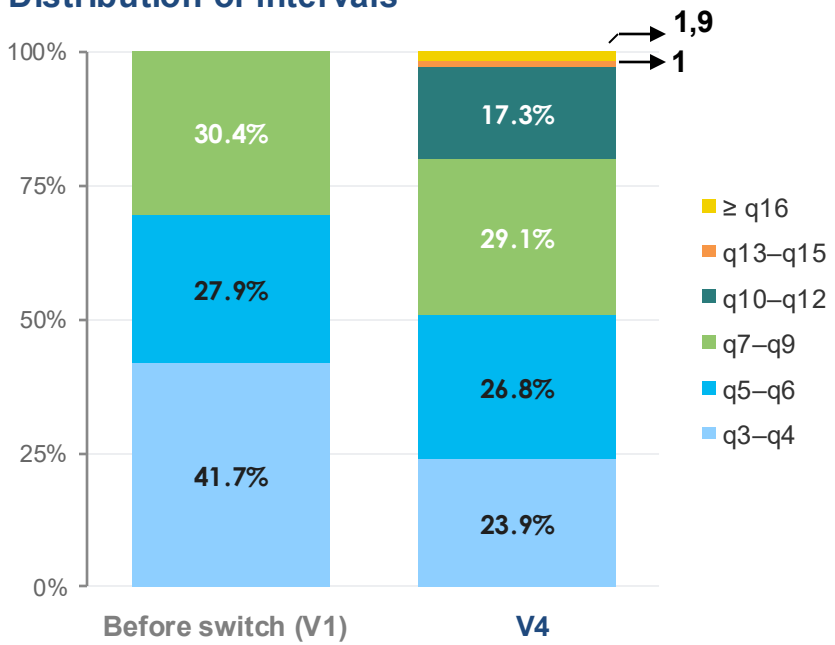
**Whole cohort: +1.5 wk** (median +1, −5; +11)

## Patients with an extended interval at V4




**Mean extension in these patients**
**+3.6 wk** with LD vs **+3.1 wk** without LD
*whole cohort +3.3 wk*

## Distribution of intervals




| ≥ 10 weeks | ≥ 7 weeks | ≤ 4 weeks |
|---|---|---|
| 0% → 20.2% | 30.4% → 49.3% | 41.7% → 23.9% |

**With LD: significantly greater mean extension (+1.9 vs +1.1 wk, p = 0.006)**

qX: one injection every X weeks; V1: interval prior to enrolment; V4: interval decided at V4; LD: loading dose. *Wilcoxon rank sum p-value. **Change (weeks) between the interval decided at V4 and the interval prior to enrolment (V1). Extended interval: interval at V4 > interval at V1.

# SAFETY & CONCLUSION

LOAD STUDY

OPHTALMO CROIX-ROUSSE TEAM

## Aflibercept 8 mg reduced treatment burden in "poor responders"

Patients on q3–q4 dosing: 42% → 24% · 20% extended to ≥ 10 weeks

## Loading phase: greater extension of the treatment interval at V4

+1.9 vs +1.1 weeks (p = 0.006) · patients extended: 61% vs 49% (primary analysis, p = 0.10)

**Protocol-defined algorithm followed: 18-point greater likelihood of extension (p = 0.02)**




**1,377** IVT injections
aflibercept 8 mg

**307** patients
safety population

**42** adverse events
in 28 patients (9.1%)

**No intraocular inflammation, vasculitis or vascular occlusion**
0 cases over 1,377 injections

**1 loss of light perception (0.07% of injections)**
Immediately after 1st IVT; resolved without AC paracentesis; no recurrence

**Other events: no new safety signal**
**Ocular:** floaters, subjective VA decrease, SCH, YAG. **Systemic (1 each):** stroke, HBP, heart failure, headache

**Real-world safety data for aflibercept 8 mg are reassuring**

IVT: intravitreal injection; AC: anterior chamber; VA: visual acuity; SCH: subconjunctival hemorrhage; HBP: high blood pressure; qX: one injection every X weeks; V4: third post-initiation visit (mean follow-up 24.5 weeks)

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