Maximum consecutive fluid free months and its association with visual and anatomical outcomes in nAMD: A *post hoc* analysis of the 96-week data from HAWK and HARRIER

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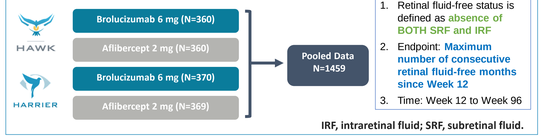
INTRODUCTION

- Retinal fluid is one of the parameters used to measure disease activity in neovascular age-related macular degeneration (nAMD).[1–3]
- However, limited evidence exists regarding the impact of fluid free status on visual and anatomic outcomes in patients with nAMD following anti-vascular endothelial growth factor (VEGF) treatment.
- The HAWK and HARRIER trials compared treatment with the anti-VEGF inhibitor, brolucizumab, with aflibercept for the treatment of nAMD.[4]
- This *post hoc* analysis of the HAWK and HARRIER trials assessed the impact of absolute retinal fluid-free duration and its association with visual and anatomic outcomes of nAMD patients.

METHODS

- In the HAWK and HARRIER trials, patients (aged ≥50 years, treatment-naïve, choroidal neovascularization lesions secondary to nAMD with presence of subfoveal fluid, best-corrected visual acuity of 78–23 Early Treatment Diabetic Retinopathy Study letters) were randomised 1:1:1 to brolucizumab 3 mg, brolucizumab 6 mg or aflibercept 2 mg, administered in one eye.[4]
- This post-hoc analysis, included pooled patient-level data from the brolucizumab 6 mg and aflibercept 2 mg groups of the Phase III HAWK and HARRIER studies (**Figure 1**).

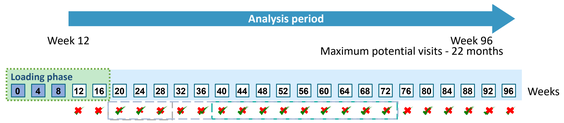
Figure 1. Cohorts for *post hoc* analysis



IRF, intraretinal fluid; SRF, subretinal fluid.

- Patients were categorised based on the maximum consecutive number of months they remained fluid free (FFM) after loading (Week 12 to 96), FFM defined as the absence of sub-retinal fluid (SRF) and intraretinal fluid (IRF).
- The categories were: category 1: 0 FFM ('never dry'); category 2: 1–3 FFMs; category 3: 4–9 FFMs; category 4: 10–21 FFMs ('dry for a long period of time'); category 5: 22 FFMs (always dry), with category 1 used as a reference for statistical comparison purposes (**Figure 2**).

Figure 2. Defining maximum consecutive fluid-free months



0 fluid-free months – Never dry– Category 1	n=80
1-3 Max consecutive fluid-free months – Category 2	n=357
4-9 Max consecutive fluid-free months – Category 3	n=371
10-21 Max consecutive fluid-free months – Category 4	n=443
22 Max consecutive fluid-free months – Always dry – Category 5	n=182

RESULTS

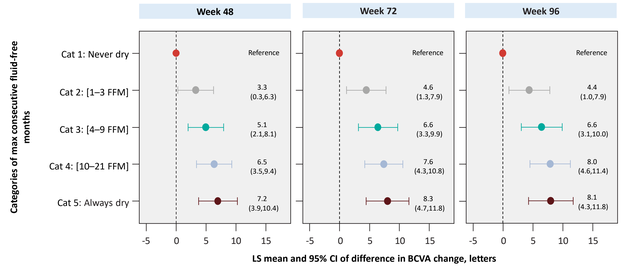
Baseline characteristics

- The best corrected visual acuity (BCVA) and central subfield thickness (CSFT) changes were corrected for baseline BCVA and CSFT differences.

BCVA changes up to Week 96

- At Week 96, patients in categories 4 and 5 had a least square mean difference in BCVA change of 8.0 and 8.1 letters respectively, compared with patients in category 'never dry' (**Figure 3**).

Figure 3. Longer fluid-free intervals (Category 4 and 5) were associated with better BCVA gains

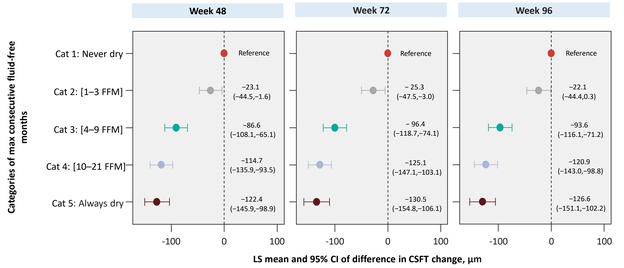


*LSM (+/-SE) with covariate adjustment. BCVA, best-corrected visual acuity; CI, confidence interval; ETDRS, Early Treatment Diabetic Retinopathy Study; FFM, fluid-free months; LSM, least square mean; n, number of patients; SE, standard error.

CSFT changes up to Week 96

- At Week 96, the least square mean difference in CSFT change of patients in categories 4 and 5 were -120.9 µm and -126.6 µm, respectively, compared with patients in category 1 'never dry' (**Figure 4**).

Figure 4. Longer fluid-free intervals (Category 4 and 5) were associated with greater CSFT reductions

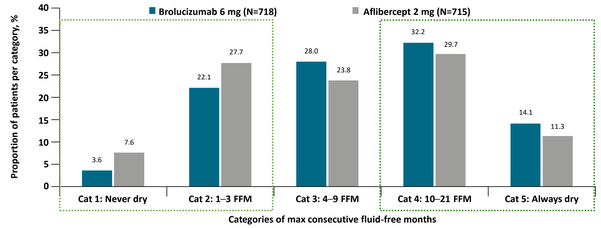


*LSM (+/-SE) with covariate adjustment.
CI, confidence interval; CSFT, central subfield thickness; FFM, fluid-free months; LSM, least square mean; n, number of patients; SE, standard error.

Patients with consecutive fluid-free months

- A lower proportion of patients who received brolucizumab were 'never dry' or 'dry for shorter periods (3.6% and 22.1%, respectively) compared with patients who received aflibercept (7.6% and 27.7%, respectively; **Figure 5**).
- A higher proportion of patients receiving brolucizumab were 'always dry' or 'dry for longer periods' compared with patients receiving aflibercept (32.2% vs 29.7% and 14.1% vs 11.3%, respectively; **Figure 5**).

Figure 5. A lower proportion of brolucizumab patients were 'never dry' (Category 1) or 'dry for shorter periods' (Category 2) compared with aflibercept



FFM, fluid-free months; N, total number of patients.

CONCLUSIONS

- In this treatment agnostic analysis, nAMD patients who were 'always dry' or 'dry for longer periods' had better vision and greater reduction of the CSFT compared to patients who were 'never dry'.
- These findings suggest that longer absolute fluid-free periods have a positive impact on visual and anatomic outcomes in nAMD patients.
- In a *treatment-specific analysis*, a **higher proportion** of patients receiving brolucizumab were **'always dry' or 'dry for longer periods'** compared with aflibercept patients.
- A **lower proportion** of patients receiving brolucizumab were **'never dry' or 'dry for shorter periods'** compared with aflibercept patients.

References

1. Wykoff CC et al. *J Manag Care Spec Pharm.* 2018;24(2-a):S3–S15.
2. Arnold JJ et al. *BMC Ophthalmol* 2016;16:31.
3. Clark WL et al. *Retina Today/New Retina MD* 2017;1–12.
4. Dugal PU et al. *Opthalmology* 2020;127:72–84.

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