A comparison of the efficacy of brolucizumab and aflibercept in eyes with early persistent retinal fluid: 96–week results from the HAWK and HARRIER studies

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The aim of current analysis is to compare the outcomes of brolucizumab 6 mg and aflibercept 2 mg treatment on best-corrected visual acuity (BCVA) and central subfield thickness (CST) in patients with early persistent retinal fluid from HAWK and HARRIER.

The reduction of retinal fluid is a hallmark of anti–vascular endothelial growth factor (VEGF) treatment for patients with neovascular age related macular degeneration (nAMD).

A subgroup of patients have persistent retinal fluid despite monthly treatment with anti-VEGF injections.
Disease activity assessments were conducted at pre-specified visits by the masked investigator. Presence of disease activity was determined at the discretion of the masked investigator and supported by protocol guidance based on functional and anatomical characteristics. OCT images and BCVA were collected monthly at all visits. Additional assessments and potential dosing interval adjustments occurred at Weeks 28, 40, 52, 64, 76, and 88 in HARRIER only. Sham injections were administered to maintain masking. Visual and anatomic assessments were made prior to injections at Weeks 16 and 48. DA, disease activity; IVT, intravitreal; q8w, 8-week dosing interval; q12w, 12-week dosing interval.

The subgroups for current analysis were defined post randomization based on patient response to treatment (IVT – Brolucizumab/Aflibercept) at baseline, Week 4 and Week 8 and monitoring visit at Week 12.
Early persistent retinal fluid was defined as presence of Sub-Retinal Fluid (SRF) and/or Intra-Retinal Fluid (IRF) at Baseline, Week 4, Week 8 and Week 12.

Differences in BCVA and CST outcomes between brolucizumab 6 mg and aflibercept 2 mg patients from the pooled HAWK and HARRIER data were analyzed using ANOVA model with baseline BCVA/CST and age categories as covariates.

BCVA, best corrected visual acuity; CST, central subfield thickness
Population and baseline characteristics of patients with early persistent retinal fluid

Baseline characteristics of patients with early persistent retinal fluid were well balanced in both groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Brolucizumab 6 mg</th>
<th>Aflibercept 2 mg</th>
</tr>
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<tbody>
<tr>
<td>Number of patients, n</td>
<td>91</td>
<td>149</td>
</tr>
<tr>
<td>Mean age, years</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (%)</td>
<td>49.5 %</td>
<td>44.3 %</td>
</tr>
<tr>
<td>Mean baseline BCVA, ETDRS letters</td>
<td>54.0</td>
<td>58.7</td>
</tr>
<tr>
<td>Mean CST, µm</td>
<td>527.4</td>
<td>483.1</td>
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</tbody>
</table>

These subgroups (patients with early persistent retinal fluid) are defined post randomization based on patients’ response to treatment (IVT – brolucizumab/aflibercept) at baseline, Week 4 and Week 8 and monitoring visit at Week 12.

BCVA, best corrected visual acuity; BL, baseline; CST, central subfield thickness; EDTRS, Early Treatment Diabetic Retinopathy Study; IVT, intravitreal
In patients with early persistent fluid numerically greater BCVA gains were observed with brolucizumab compared with aflibercept.

Full Analysis Set, LOCF. Analyzed using ANOVA model with baseline BCVA categories (<=55, 56-70, >=71 letters), age categories (<75, ≥75 years) and treatment as fixed effect factors. These subgroups (patients with early persistent retinal fluid) are defined post randomization based on patients’ response to treatment (IVT – brolucizumab/aflibercept) at baseline, Week 4 and Week 8 and monitoring visit at Week 12.

BCVA, best corrected visual acuity; BL, baseline; EDTRS, Early Treatment Diabetic Retinopathy Study; IVT, intravitreal; LOCF, last observation carried forward; LS, least squares; SE, standard error.
Higher proportion of these patients achieved ≥ 15 letters with brolucizumab compared with aflibercept

<table>
<thead>
<tr>
<th>Week 16</th>
<th>Week 48</th>
<th>Week 96</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brolucizumab (n = 91)</td>
<td>Aflibercept (n = 149)</td>
<td>Brolucizumab (n = 91)</td>
</tr>
<tr>
<td>15.7</td>
<td>14.6</td>
<td>28.6</td>
</tr>
<tr>
<td>8 %*</td>
<td>48 %*</td>
<td>31.7</td>
</tr>
<tr>
<td>20</td>
<td>59 %*</td>
<td></td>
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</tbody>
</table>
In patients with early persistent fluid brolucizumab achieved greater CST reduction from baseline versus aflibercept
A lower proportion of brolucizumab patients had early persistent retinal fluid compared with aflibercept.

Patients with early persistent retinal fluid had numerically better BCVA outcomes observed with brolucizumab compared with aflibercept.

A higher proportion of these patients gained ≥ 15 letters with brolucizumab compared with aflibercept.

Patients with early persistent retinal fluid had greater CST reductions with brolucizumab compared with aflibercept.

Brolucizumab may achieve greater disease control in nAMD patients with early persistent retinal fluid than aflibercept.