PATIENT EFFICACY AND SAFETY OF BROLUCIZUMAB COMPARED WITH AFLIBERCEPT IN POLYPOIDAL CHOROIDAL VASCULOPATHY: 24-MONTH RESULTS FROM THE HAWK STUDY

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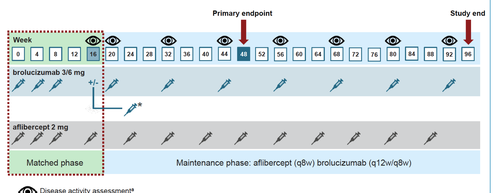
INTRODUCTION

- Polypoidal choroidal vasculopathy (PCV) is characterised by orange-red polyp-like structures diagnosed by Indocyanine green angiography (ICGA), which is considered the hallmark for PCV diagnosis.[1]
- PCV resembles neovascular age-related macular degeneration (nAMD) in its morphological features[1] and is more prevalent in Asian patients than in Caucasian patients.[2]
- Vascular endothelial growth factor (VEGF) is important for the pathophysiology of PCV, and anti-VEGF therapies reduce PCV exudation, decreases subretinal fluid and preserves vision.[1]
- Brolucizumab is a novel single-chain antibody fragment with potent anti-vascular endothelial growth factor attributes.[3]
- The innovative molecular structure and small size of brolucizumab enables concentrated molar dosing and may facilitate effective tissue penetration, for a longer-lasting effect.[3,4]
- This (descriptive) post-hoc analysis reports the results from Japanese PCV patients enrolled in HAWK (NCT02307682), a Phase III, prospective study assessing the efficacy and safety of brolucizumab versus aflibercept in nAMD.

METHODS

- Patients were randomised 1:1:1 to brolucizumab 3 mg (n=358), brolucizumab 6 mg (n=360) or aflibercept 2 mg (n=360), administered in one eye **(Figure 1)**.

Figure 1. Study design of HAWK



[a]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 dynamic functional and anatomical characteristics. Additional assessments and potential dosing interval adjustments occurred at Weeks 28, 40, 52, 64, 76, and 88 in Visual and anatomic assessments were made prior to injections at Week 16 and 48.

- ICGA was performed at screening on all patients in sites in Japan.
- After three monthly-loading doses, brolucizumab patients were treated every 12 weeks (q12w), with an option to adjust to 8-week dosing (q8w) based on disease activity assessments; aflibercept was dosed in a fixed q8w regimen.
- Spectral domain optical coherence tomography (SD-OCT) assessments were conducted at every monthly visit and were analysed by independent central reading centres.

RESULTS

Baseline characteristics

- Of the 154 Japanese patients in HAWK, PCV was present in 89 (58.6%, **Table 1**).

Table 1. Baseline characteristics of Japanese PCV patients in HAWK

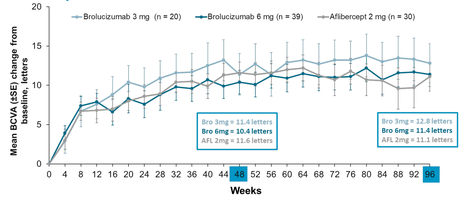
	Brolucizumab 3 mg (n = 20)	Brolucizumab 6 mg (n = 39)	Aflibercept 2 mg (n = 30)
BCVA, letters, mean (SD)	61.5 (15.9)	62.4 (13.9)	62.4 (10.8)
CSFT, µm, mean (SD)	446.9 (171.5)	392.8 (96.1)	444.8 (129.0)
Presence of SRF, n (%)	19 (95.0)	33 (84.6)	22 (73.3)
Presence of IRF, n (%)	7 (35.0)	15 (38.5)	12 (40.0)
Presence of sub-RPE fluid, n (%)	10 (50.0)	23 (59.0)	16 (53.3)
CNV-associated lesion area, mm², mean (SD)	4.8 (3.9)	4.4 (4.1)	4.9 (4.0)

BCVA, best-corrected visual acuity; CNV, choroidal neovascularization; CSFT, central subfield thickness; IRF, intraretinal fluid; PCV, polypoidal choroidal vasculopathy; RPE, retinal pigment epithelium; SD, standard deviation; SRF, subretinal fluid;

BCVA changes up to Week 96

- Robust and comparable best corrected visual acuity (BCVA) gains were observed in all treatment arms (**Figure 2**).

Figure 2. Mean BCVA change from baseline up to Week 96 for PCV patients

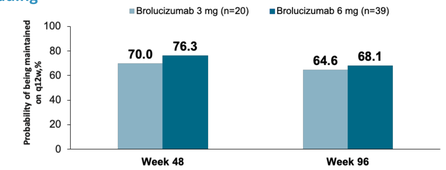


Full Analysis Set – LOCF. BCVA, best-corrected visual acuity; PCV, polypoidal choroidal vasculopathy; SE, standard error

Maintenance on q12w treatment interval at Week 48 and at Week 96

- A q12w dosing interval immediately following loading was maintained by up to 68% of 6 mg brolucizumab PCV patients up to Week 96 (**Figure 3**).

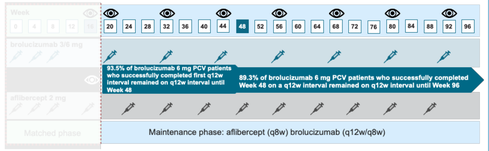
Figure 3. Proportion of brolucizumab PCV patients maintained on q12w dosing interval immediately following loading



Full analysis set, Estimated percentages from Kaplan Meier analysis with "Efficacy/Safety approach" : In case of missing / confounded data due to lack of efficacy and/or safety a 'q8-need' is allocated, otherwise censoring is applied. q12w, 12-week dosing interval; PCV, polypoidal choroidal vasculopathy

- **Figure 4** shows the probability of brolucizumab PCV patients remaining on a q12w interval after week 20

Figure 4. Probability of brolucizumab PCV patients remaining on a q12w interval after week 20

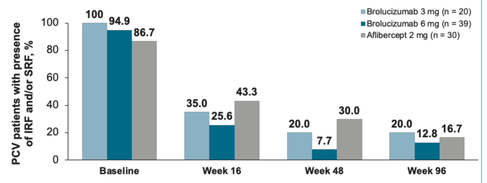


- Robust CST reductions were seen in all treatment arms and achieved with the majority of brolucizumab 6 mg patients maintained on a q12w dosing interval.

Effect on IRF, SRF and sub-RPE fluid at Week 48 and at Week 96

- Fewer brolucizumab 6 mg treated eyes had intraretinal and/or subretinal fluid compared to aflibercept treated patients at Weeks 16, 48 and 96 (**Figure 5**).

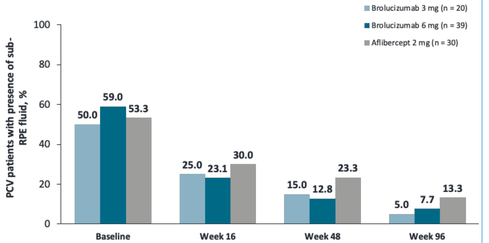
Figure 5. Proportion of PCV patients with presence of IRF and/or SRF



Full Analysis Set – LOCF. All patients had fluid at screening and were confirmed for eligibility by the Reading centre. IRF, intraretinal fluid; PCV, polypoidal choroidal vasculopathy; q12w, 12-week dosing interval; SRF, subretinal fluid.

- Similarly, fewer brolucizumab 6 mg patients had sub-RPE fluid compared to aflibercept patients despite the majority being on a q12 regimen (**Figure 6**).

Figure 6. Proportion of PCV patients with presence of sub-RPE fluid



Full Analysis Set – LOCF. All patients had fluid at screening and were confirmed for eligibility by the Reading centre.

Safety

- Brolucizumab exhibited an overall well-tolerated safety profile (**Table 2**).

Table 2. Overall safety

n (patients, %)	Brolucizumab 3 mg (n = 20)	Brolucizumab 6 mg (n = 39)	Aflibercept 2 mg (n = 30)
≥1 adverse event			
Ocular (study eye)	7 (35.0)	22 (56.4)	12 (40.0)
Non-ocular	17 (85.0)	34 (87.2)	24 (80.0)
≥1 serious adverse event			
Ocular (study eye)	0 (0.0)	1 (2.6)	1 (3.3)
Nonocular	6 (30.0)	7 (17.9)	7 (23.3)
≥1 nonocular arterial thromboembolic event, n (%)*	1 (5.0)	0 (0.0)	0 (0.0)
Death, n (%)	0 (0.0)	0 (0.0)	0 (0.0)

CONCLUSIONS

- Robust BCVA gains were observed in the PCV population, across all treatment arms.
- Anatomic outcomes favoured brolucizumab–treated patients over aflibercept–treated patients.
- 76% of brolucizumab 6 mg patients were successfully maintained on an exclusive q12w dosing immediately following the loading phase to Week 48, and 68% to Week 96.

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