Visual and anatomical outcomes by q12w/q8w status in the HAWK and HARRIER studies of brolucizumab versus aflibercept in neovascular age-related macular degeneration

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Purpose:
The Phase III HAWK (NCT02307682) and HARRIER (NCT02434328) studies demonstrated that brolucizumab (6mg/3mg in HAWK; 6mg in HARRIER) was non-inferior to aflibercept (2mg) in visual acuity at Week 48 (primary endpoint); >50% eyes treated with brolucizumab 6mg were maintained on q12w dosing. Here, a subgroup analysis describes visual and anatomical outcomes for eyes treated with brolucizumab 6mg by treatment frequency (q12w/q8w) compared with fixed-dose q8w aflibercept.

Methods:
Following three monthly loading injections, brolucizumab was injected q12w unless disease activity was identified resulting in permanent adjustment to q8w; aflibercept was dosed q8w as per label at study initiation. Eyes with at least one disease activity assessment were included in the subgroup analysis. Pooled study data are presented as least squares mean (SE).

Results:
There was a clear differentiation in BCVA change from baseline to Week 48 among eyes treated with brolucizumab q12w (n=315), brolucizumab q8w (n=392), and aflibercept q8w (n=701) at 9.2 (0.62), 4.5 (0.69), and 7.4 (0.46) EDTRS letters, respectively. However, in brolucizumab (n=161) and aflibercept (n=226) eyes with disease activity at Week 16 (therefore, brolucizumab eyes allocated to q8w treatment at week 16) there was a comparable change in BCVA by visit from baseline to Week 96. Similarly, there was a comparable change in BCVA by visit from Weeks 12 to 96 for brolucizumab (n=448) and aflibercept (n=454) eyes without disease activity at Weeks 16 and 20. There were greater CST reductions from baseline to Week 96 for brolucizumab versus aflibercept-treated eyes both with and without disease activity.

Conclusions:
The separation in mean BCVA change at Week 48 suggests that brolucizumab q12w and q8w subgroups represent disease profiles with lesser/greater treatment need. A more relevant comparison of brolucizumab and aflibercept eyes with disease activity at Week 16 showed similar BCVA outcomes between treatments through Week 96, although the imbalance in patient numbers between treatment groups indicates a higher overall proportion of aflibercept patients with disease activity. Comparable BCVA outcomes at Week 96 for brolucizumab q12w and aflibercept q8w patients with lesser treatment need reflects non-inferiority in BCVA for brolucizumab seen in the primary analysis.