# Brolucizumab for the treatment of visual impairment due to diabetic macular edema: 52-week results from the KESTREL and KITE PHASE III studies


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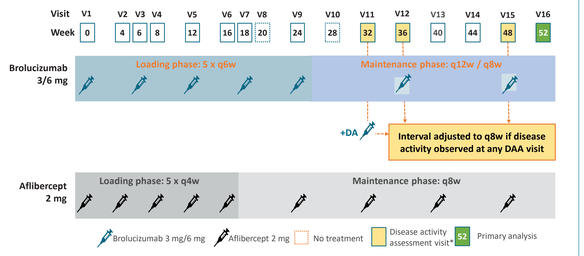
## INTRODUCTION

- KESTREL and KITE are two-year, double-masked, Phase III multicentre trials evaluating the efficacy and safety of brolucizumab for the treatment of patients with visual impairment due to diabetic macular edema (DME).
- The aim of this study was to evaluate KESTREL and KITE efficacy and safety data up to Week 52.

## METHODS

- In KESTREL, patients were randomised 1:1:1 to brolucizumab 3 mg, 6 mg or aflibercept 2 mg (**Figure 1**).
- In KITE, 1:1 randomisation to brolucizumab 6 mg or aflibercept 2 mg.
- Brolucizumab groups received 5 loading doses every 6 weeks followed by q12w dosing, with an option to adjust to q8w if disease activity was identified (**Figure 1**).
- Aflibercept groups received 5 loading doses every 4 weeks followed by eight weekly (q8w) dosing (**Figure 1**).
- The primary endpoint was mean change in best-corrected visual acuity (BCVA) from baseline at Week 52.
- The secondary endpoints included the proportion of brolucizumab patients maintained at every 12 week (q12w) dosing up to Week 52 and the change in central subfield thickness (CSFT) from baseline.

### Figure 1. KESTREL and KITE study design up to Week 52




*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. Sham injections were administered to maintain masking. Aflibercept was administered as per current label at the time of the study. Visual and anatomic assessments were made prior to all injections.
DA, disease activity; q8w, 8-week dosing interval; q12w, 12-week dosing interval.

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## RESULTS

### Baseline characteristics

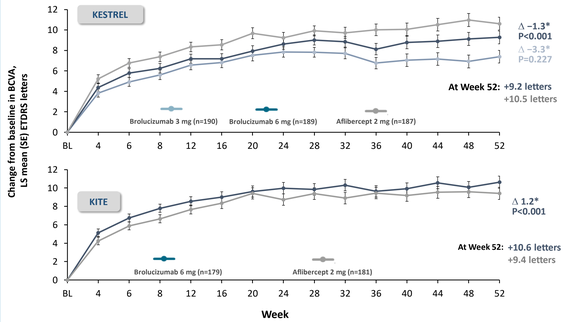
#### Table 1. Baseline characteristics were balanced across the treatment arms

| Baseline Characteristics | KESTREL | | | KITE | |
|---|---|---|---|---|---|
| | Brolucizumab 3 mg (n=190) | Brolucizumab 6 mg (n=189) | Aflibercept 2 mg (n=187) | Brolucizumab 6 mg (n=179) | Aflibercept 2 mg (n=181) |
| Age, Mean (SD), Years | 64.4 (9.76) | 62.4 (10.14) | 63.9 (10.09) | 62.3 (10.55) | 62.2 (9.48) |
| Males, n (%) | 119 (62.6) | 110 (58.2) | 126 (67.4) | 120 (67.0) | 115 (63.5) |
| Race, n (%) | | | | | |
| White | 151 (79.5) | 158 (83.6) | 152 (81.3) | 133 (74.3) | 132 (72.9) |
| Asian | 25 (13.2) | 25 (13.2) | 26 (13.9) | 43 (24.0) | 48 (26.5) |
| BCVA, Mean (SD), Letters | 65.7 (11.09) | 66.6 (9.67) | 65.2 (12.38) | 66.0 (10.77) | 63.7 (11.70) |
| ≤65 Letters | 78 (41.1) | 74 (39.2) | 64 (34.2) | 65 (36.3) | 91 (50.3) |
| >65 Letters | 112 (58.9) | 115 (60.8) | 123 (65.8) | 114 (63.7) | 90 (49.7) |
| CSFT, Mean (SD), µm | 456.0 (118.04) | 453.1 (123.42) | 475.6 (135.84) | 481.1 (132.46) | 483.8 (134.39) |
| <450 µm | 111 (58.4) | 107 (56.6) | 96 (51.3) | 85 (47.5) | 83 (45.9) |
| ≥450 – <650 µm | 64 (33.7) | 70 (37.0) | 71 (38.0) | 74 (41.3) | 79 (43.6) |
| ≥650 µm | 15 (7.9) | 12 (6.3) | 20 (10.7) | 20 (11.2) | 19 (10.5) |
| IRF Present, n(%) | 190 (100) | 189 (100) | 184 (98.4) | 176 (98.3) | 179 (98.9) |
| SRF Present, (n%) | 60 (31.6) | 62 (32.8) | 61 (32.6) | 56 (31.3) | 67 (37.0) |

BCVA, best-corrected visual acuity; CNV, choroidal neovascularization; CSFT, central subfield thickness; DME, diabetic macular edema; IRF, intraretinal fluid; SD, standard deviation; SRF, subretinal fluid

### Primary endpoint: BCVA at Week 52

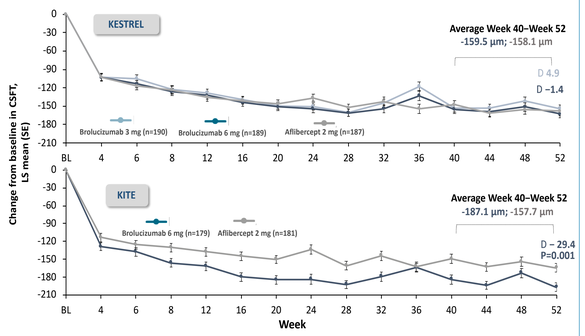
#### Figure 2. Primary endpoint met in KESTREL & KITE: Brolucizumab 6 mg non-inferior to aflibercept in change from baseline in BCVA at Week 52




Full analysis set LOCF. Mean differences in BCVA (brolucizumab–aflibercept, Δ). ª Non-inferiority margin = 4 letters. One-sided P-value for non-inferiority. Analysed using ANOVA model with baseline BCVA categories (≤65, >65 letters), age categories (<65,≥65 years) and treatment as fixed effect factors. * Δ (95% CI) in KESTREL: -1.3 (-2.9, 0.3) for brolucizumab 6 mg vs aflibercept 2 mg and -3.3 (-5.1, -1.4) for brolucizumab 3 mg vs aflibercept 2 mg ; * Δ (95% CI) in KITE: 1.2 (-0.6, 3.1) for brolucizumab 6 mg vs aflibercept 2 mg. BCVA, best corrected visual acuity; LS, least squares; SE, standard error

### Secondary endpoint: CSFT at Week 52

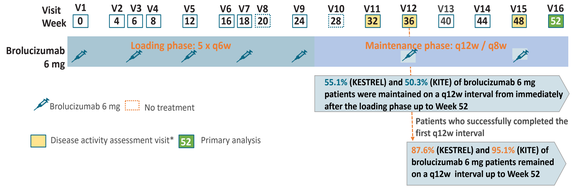
#### Figure 3. Robust improvement in CSFT from baseline with brolucizumab 6 mg in both studies; superior reduction achieved with brolucizumab 6 mg compared to aflibercept 2 mg in KITE




Full analysis set LOCF. Mean differences analysed using ANOVA model with baseline CSFT categories (<450 µm, ≥450 µm, <650 µm; ≥650 µm), age categories (<65,≥65 years) and treatment as fixed effect factors. One-sided P-value for superiority testing of brolucizumab vs aflibercept. CSFT, central subfield thickness; LS, least squares; SE, standard error

### Maintenance until Week 52

#### Figure 4. ≥87% of brolucizumab 6 mg patients who successfully completed the first q12w interval remained on a q12w interval until Week 52




DA, disease activity; q8w, 8-week dosing interval; q12w, 12-week dosing interval.

### Safety

#### Table 2. Safety profile

| Adverse Events | KESTREL | | | KITE | |
|---|---|---|---|---|---|
| | Brolucizumab 3 mg (n=190) | Brolucizumab 6 mg (n=189) | Aflibercept 2 mg (n=187) | Brolucizumab 6 mg (n=179) | Aflibercept 2 mg (n=181) |
| Patients with ≥1 AE, n (%)* | | | | | |
| Ocular (study eye) | 81 (42.6) | 76 (40.2) | 73 (39.0) | 53 (29.6) | 52 (28.7) |
| Nonocular | 122 (64.2) | 128 (67.7) | 122 (65.2) | 108 (60.3) | 127 (70.2) |
| Patients with ≥1 serious AE, n (%)* | | | | | |
| Ocular (study eye) | 7 (3.7) | 2 (1.1) | 4 (2.1) | 4 (2.2) | 3 (1.7) |
| Nonocular | 23 (12.1) | 35 (18.5) | 37 (19.8) | 30 (16.8) | 37 (20.4) |
| Patients with ≥15 letter loss from baseline at Week 52, %† | 1.6 | 0.0 | 0.5 | 1.1 | 1.7 |
| Death, n (%) | 1 (0.5) | 5 (2.6) | 2 (1.1) | 3 (1.7) | 2 (1.1) |
| AEs of special interest (study eye), n (%) | | | | | |
| Endophthalmitis | 2 (1.1) | – | 1 (0.5) | 1 (0.6) | 1 (0.6) |
| Intraocular inflammation§ | 9 (4.7) | 7 (3.7) | 1 (0.5) | 3 (1.7) | 3 (1.7) |
| - including Retinal vasculitis§ | 3 (1.6) | 1 (0.5) | – | – | – |
| Retinal vascular occlusion# | 2 (1.1) | 1 (0.5) | – | 1 (0.6) | 1 (0.6) |

Medical Dictionary for Regulatory Activities Version 23.0 (KITE) and 23.1 (KESTREL) used for the reporting of adverse events. Safety Analysis Set. AE with a start date on or after the date of first study treatment administration were counted. *A patient with multiple occurrences of an AE for a preferred term or system organ class was counted only once in each specific category. †Full Analysis Set-LOCF. Neither case in KITE was associated with intraocular inflammation. §Percentages of subjects with intraocular inflammation and percentages of subjects with retinal vasculitis cannot be added up; all cases of vasculitis are considered in the intraocular inflammation events. #Includes reported cases of retinal vascular occlusion, retinal artery occlusion, and retinal vein thrombosis Neither case in KITE was associated with intraocular inflammation. AE, adverse event; LOCF, last observation carried forward.

## CONCLUSIONS

- Baseline characteristics were balanced across the KESTREL and KITE trials (**Table 1**).
- Brolucizumab 6 mg was non-inferior to aflibercept in mean change in BCVA at Week 52 with fewer injections (**Figure 2**).
- Significant improvement in mean CSFT from baseline over the period of week 40- week 52 with brolucizumab 6mg was seen in both studies and a superior reduction vs aflibercept in KITE (**Figure 3**).
- More than 50% of brolucizumab 6 mg patients were maintained on q12w dosing interval through Week 52, immediately after the loading phase (**Figure 4**).
- An overall favourable benefit/risk profile was demonstrated with brolucizumab (**Table 2**).


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