Real-world outcomes with ranibizumab 0.5 mg treatment in French patients with visual impairment due to diabetic macular edema: 12-month results from the 36-month BOREAL-DME study

1915 – B0419

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INTRODUCTION

- Ranibizumab 0.5 mg has a well-established efficacy and safety profile for the treatment of diabetic macular edema (DME) based on several randomized clinical studies (RESTORE, RETAIN, REVEAL, RIDE-RISE, READ-2, DRCR.net).[1–7]
- However, as per randomized controlled trial methodology, these studies have stringent eligibility (inclusion/exclusion) criteria, and the selected patients' population may not necessarily be representative of the real-life setting,[8] especially with regard to diabetes control.
- Therefore, understanding the different treatment patterns, regimens, and response to treatment in a real-world scenario is an essential approach towards better management of patients with DME.[9,10]

PURPOSE

- The aim of the BOREAL DME study was to assess the effectiveness and safety of ranibizumab 0.5 mg under real-life conditions in the French population with visual impairment due to DME treated over a 36-month duration.
- Here, we present the 12-month follow-up results from this study.

METHODS

- This is a non interventional, multicenter, post-authorization, observational cohort study conducted in France.

Key eligibility criteria

- Patients with Type I or II diabetes aged ≥18 years who had a reduction in visual acuity (VA) due to DME and for whom ranibizumab therapy was initiated by the treating physician were included in the study.
- Patients refusing to participate, or residing outside metropolitan France or those who participated in an interventional study (for diabetes, hypertension, or ocular disease) were excluded from the study.

Objectives

- The primary endpoint was the mean change in best-corrected VA (BCVA) from baseline to Month 12.
- Key secondary endpoints include the proportion of patients with BCVA gain or loss of ≥5, ≥10, and ≥15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters at Month 12, mean change in central subfield thickness (CSFT) over 12-months, number of injections and monitoring visits, and ocular and non ocular adverse events (AEs) up to Month 12.
- A subgroup analysis was carried out to evaluate the impact of baseline BCVA, prior treatment exposure, and initial three monthly injections on the mean BCVA change at Month 12.
- A multivariate analysis was used to determine predictive factor associated with the final BCVA at Month 12.

RESULTS

- Between December 2013 and April 2015, a total of 344 patients were screened and 290 were enrolled in the study. Of those, 242 patients (83.4%) completed the 12-month follow-up.
- At baseline, the mean (standard deviation [SD]) age of the patients was 66.1 (11.0) years and 56.6% of patients were male (**Table 1**).
- The mean (SD) duration of diabetes was 17.4 (11.2) years and the mean HbA_{1c} level was 7.6 (1.4) mmol/mol (**Table 1**).

Table 1. Baseline demographics and disease characteristics (patients with 12 months follow-up)

Characteristics	Patients N=242
Demographics	
Age, years	n=242
Mean (SD) age, years	66.1 (11.0)
Gender, n (%)	n=242
Male	137 (56.6)
Disease characteristics	
Duration of diabetes, years	n=227
Mean (SD)	17.4 (11.2)
HbA_{1c} (≤3 month), mmol/mol	n=165
Mean (SD)	7.6 (1.4)

HbA_{1c}, glycated hemoglobin; SD, standard deviation

- The majority of the patients (67.8%) had nonproliferative diabetic retinopathy; time since the diagnosis of DME was more than 6 months in 43.8% patients and 66.5% patients presented bilateral DME (**Table 2**).
- The mean (SD) BCVA and CSFT at baseline were 59.2 (15.0) ETDRS letters and 457 (144) µm, respectively (**Table 2**).

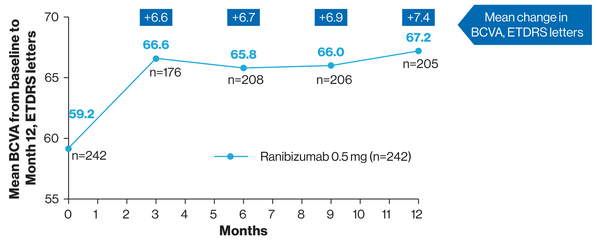
Table 2. Baseline DME characteristics (patients with 12 months follow-up)

Characteristics	Patients N=242
DME characteristics	
Diabetic retinopathy, n (%)	n=241
Absence of lesion	3 (1.2)
Non proliferative	164 (67.8)
Proliferative	25 (10.3)
Other	49 (20.2)
Time since diagnosis of DME, n (%)	n=231
<1 month	78 (32.2)
1 to 2 months	16 (6.6)
3 to 6 months	31 (12.8)
>6 months	106 (43.8)
DME involvement, n (%)	n=241
Bilateral	161 (66.5)
Ocular characteristics	
BCVA, ETDRS letters	n=242
Mean (SD)	59.2 (15.0)
BCVA at baseline, n (%)	n=242
>70 ETDRS letters	32 (13.2)
CSFT, µm	n=221
Mean (SD)	457 (144)

BCVA, best-corrected visual acuity; CSFT, central subfield thickness; DME, diabetic macular edema; ETDRS, Early Treatment Diabetic Retinopathy Study; SD, standard deviation

- At Month 12, the mean (SD) change in BCVA from baseline was +7.4 (14.4) letters (**Figure 1**).
- At Month 12, 36.8% patients had a BCVA of >70 letters compared with 13.2% patients at baseline.

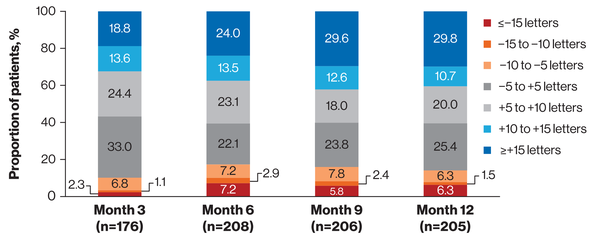
Figure 1. Mean change in BCVA from baseline to Month 12



BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study

- The proportion of patients with a BCVA gain of ≥5, ≥10, and ≥15 letters and those with a BCVA loss of ≥5, ≥10, and ≥15 letters at Month 12 are presented in **Figure 2**.

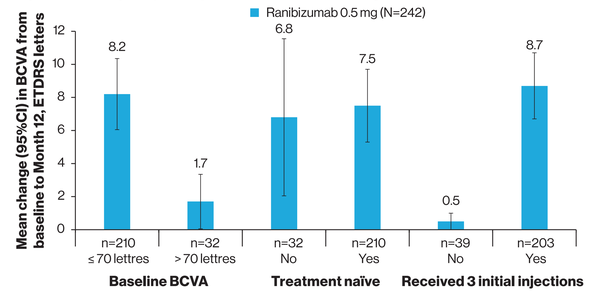
Figure 2. Categorized BCVA outcome



BCVA, best-corrected visual acuity

- The significant predictive factors associated with final BCVA gain at Month 12 were baseline BCVA and BCVA gain at Month 3 (both P<0.001).
- The subgroup analysis of the mean BCVA change at Month 12 (**Figure 3**), showed that:
  - Patients with a baseline BCVA >70 letters had lower BCVA gain compared with those with a baseline BCVA <70 letters
  - Patients who did not receive the initial three monthly injections had lower BCVA gain compared with those who received the initial three monthly injections.

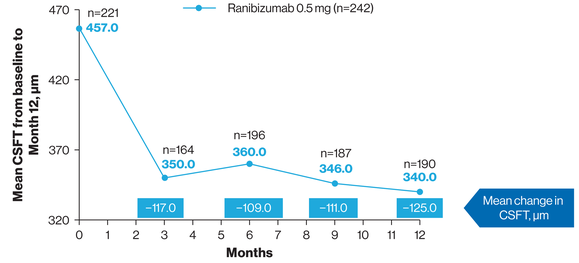
Figure 3. Subgroup analysis of the mean change in BCVA at Month 12



BCVA, best-corrected visual acuity; CI, confidence interval; ETDRS, Early Treatment Diabetic Retinopathy Study

- The mean (SD) change in CSFT from baseline at Month 12 was −125 (147) µm (**Figure 4**).

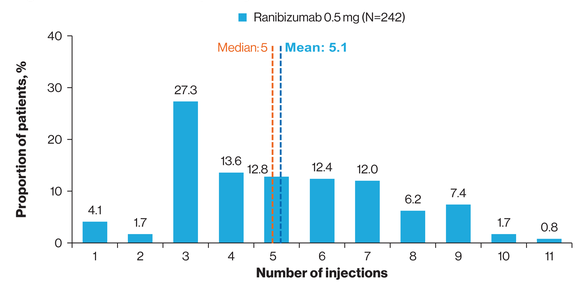
Figure 4. Mean change in CSFT from baseline to Month 12



CSFT, central subfield thickness

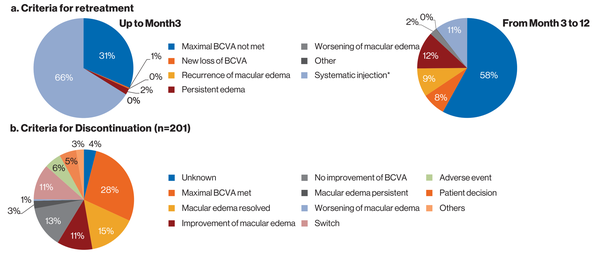
- Over the 12-month follow-up, patients received a mean (SD) of 5.1 (2.3) ranibizumab 0.5 mg injections (**Figure 5**) and the mean (SD) number of monitoring visits was 13.4 (5.2).
- The mean time (SD) between ranibizumab 0.5 mg injections up to Month 3 was 36.5 (27.8) days and that after Month 3 was 55.8 (41.6) days.

Figure 5. Treatment frequency



- At Month 3, patients received retreatment with ranibizumab 0.5 mg according to the treatment regimen (66.2%) or when the maximum BCVA was not achieved (31.4%; **Figure 6**).
- At Month 12, 83.1% eyes had at least one treatment discontinuation and the prominent reasons for discontinuation were maximum BCVA achieved, macular edema resolved, and no improvement in BCVA (**Figure 6**).

Figure 6. Criteria for retreatment and discontinuation



*Systematic injection refers either to the injection in the induction phase or treat and extend.
BCVA, best-corrected visual acuity

- Ranibizumab 0.5 mg was well-tolerated and no new safety findings were reported.
- Overall, 4.5% and 2.8% patients had at least one AE and serious AE related to ranibizumab 0.5 mg, respectively.
- Ocular SAEs related to ranibizumab 0.5 mg were reported in 0.7% patients and non ocular SAEs of cardiac and/or vascular nature were reported in 0.3% and 1.0% patients, respectively.

CONCLUSIONS

- Ranibizumab 0.5 mg treatment improved VA in patients with visual impairment due to DME in routine clinical practice, with fewer injections than that reported in previous clinical trials.
- The subgroup analysis of the mean BCVA change at Month 12 showed that lower baseline BCVA (<70 letters) and treatment with initial three monthly injections was associated with higher BCVA gains.
- Along with the BCVA gains, treatment with ranibizumab 0.5 mg led to reduction in CSFT.
- The safety profile of ranibizumab 0.5 mg was consistent with that reported in the previous studies in patients with DME.

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Financial disclosures

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Patrick Blin: Novartis: Code F (Financial Support).
BPE Team: Novartis Pharma SAS: Code F (Financial Support).

Acknowledgment

The authors received writing support for this poster from Lakshya Untwal and creative support from Maninder Reddy Karka (Scientific Services Practice, Novartis Healthcare Pvt. Ltd., Hyderabad, India).

Poster presented at the Annual Meeting of the Association for Research in Vision and Ophthalmology (ARVO), Baltimore, Maryland, USA, May 7–11, 2017.
This study was sponsored by Novartis Pharma SAS, France.

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