Real-world outcomes with ranibizumab 0.5 mg treatment in French patients with visual impairment due to macular edema secondary to central retinal vein occlusion: 6-month results from the 24-month BOREAL-CRVO study

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INTRODUCTION

- Central retinal vein occlusion (CRVO) is a common vision-threatening disorder affecting about 1 in 1000 persons. Macular edema secondary to CRVO is a major complication and can lead to legal blindness, if untreated.[1–3]
- The efficacy and safety of an anti-VEGF, ranibizumab 0.5 mg, is well-established for improving visual outcomes in patients with visual impairment due to macular edema secondary to retinal vein occlusion (RVO), based on various randomized controlled trials.[4–9]
- However, the treatment patterns and treatment response still need to be defined in a real-life setting to optimize the management of patients with visual impairment due to macular edema secondary to CRVO.

PURPOSE

- The aim of the study was to assess the effectiveness and safety of ranibizumab 0.5 mg in French patients with visual impairment due to macular edema secondary to CRVO with a total follow-up of 24 months.
- Here, we present the first 6-month follow-up results from this study.

METHODS

- BOREAL CRVO was a 24-month, non-interventional, multicenter, post-authorization, observational cohort study in a real-life setting conducted in France.
- Consented adult patients (aged ≥18 years) with a confirmed diagnosis of CRVO 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 were excluded from the study.

Endpoints

- The primary endpoint was the mean change in best-corrected visual acuity (BCVA) from baseline to Month 6.
- **Key secondary endpoints:**
  - Mean change in central subfield thickness (CSFT) at Month 6.
  - Proportion of patients with a BCVA gain or loss of ≥5, ≥10, and ≥15 letters at Months 3 and 6.
  - Proportion of patients who gained >70 letters at Month 6 versus baseline.
  - Treatment exposure to ranibizumab up to Month 6.
  - Incidence of adverse events (AEs) and serious AEs (SAEs) up to Month 6.
- A multivariate analysis was used to determine predictive factors associated with the final BCVA at Month 6.

RESULTS

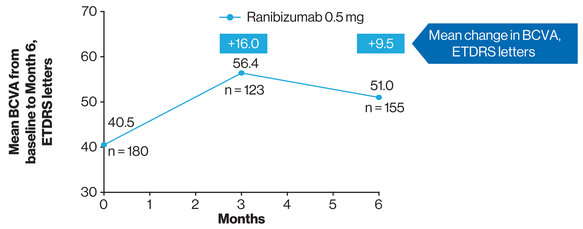
- Between December 2013 and April 2015, a total of 225 patients were screened and 196 were enrolled in the study. Of those, 180 (91.8%) completed the 6-month follow-up.
- The mean (SD) age of the patients was 70.5 (14.4) years, approximately half of the patient population were male (50.6%), and the mean (SD) baseline BCVA and CSFT were 40.5 (25.7) letters and 649 (216.0) µm, respectively (**Table 1**).
- Other ocular and disease characteristics and comorbidities are presented in **Table 1**.
- The mean (SD) change in BCVA from baseline to Month 3 was 16.0 (21.4) letters and at Month 6 was 9.5 (25.3) letters (**Figure 1**). A total of 30.6% of patients had a BCVA of >70 letters at Month 6 compared with 8.3% at baseline.
- The predictive factors associated with the final BCVA change at Month 6 were the age of the patients at inclusion, BCVA at baseline, and absolute BCVA variation at 3 months.
- The mean (SD) change in CSFT from baseline to Month 3 was −323.0 (256) µm and at Month 6 was −264 (270) µm (**Figure 2**).
- The proportion of patients with a gain or loss of ≥5, ≥10, and ≥15 letters in BCVA at Month 6 is shown in **Figure 3**. At Months 3 and 6, 55.3% and 42.6% of the patients gained ≥15 letters, respectively (**Figure 3**).

Table 1. Baseline demographics, ocular, and disease characteristics

Characteristics	CRVO (N = 180)
Mean (SD) age, years	70.5 (14.4)
Gender, male, n (%)	91 (50.6)
Patients with bilateral CRVO, n (%)	5 (2.8)
Mean (SD) BCVA, ETDRS letters	40.5 (25.7)
BCVA > 70 letters, n (%)	15 (8.3)
Mean (SD) CSFT, µm	649 (216)
Ocular comorbidities, (> 19%), n (%)	
At least one	112 (62.2)
Non-operated Cataract	51 (28.3)
Cataract surgery	35 (19.4)
Glaucoma and ocular hypertension	41 (22.8)
At least one systemic anterior treatment received for the visual loss due to CRVO, n (%)	5 (2.8)
Hemodilution	1 (20.0)
Platelet anti-aggregant (s)	4 (66.7)
Rheology corrector (s)	2 (33.3)

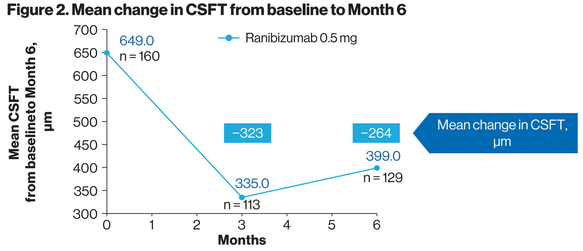
BCVA, best-corrected visual acuity; CRVO, central retinal vein occlusion; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; SD, standard deviation

Figure 1. Mean change in BCVA from baseline to Month 6



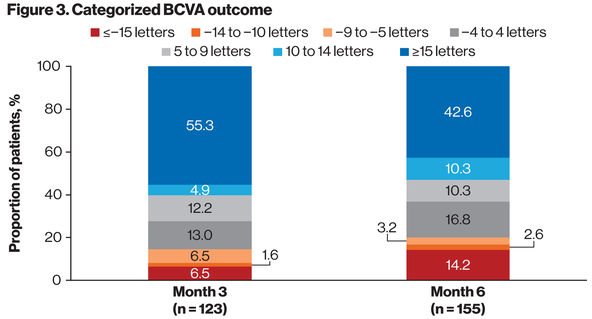
BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study

Figure 2. Mean change in CSFT from baseline to Month 6



CSFT, central subfield thickness

Figure 3. Categorized BCVA outcome



BCVA, best corrected visual acuity

Treatment exposure:

- Over 6 months, patients had a mean (SD) of 7.3 (2.3) visits during which they received a mean (SD) of 3.6 (1.2) ranibizumab injections (**Figure 4**).
- At Month 3, 76.1 % of patients received 3 injections.
- The mean (SD) time between the first three ranibizumab injections at Months 3 was 31.2 (5.3) days.
- At Month 6, 56.1% patients 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 5**).

Figure 4. Treatment frequency

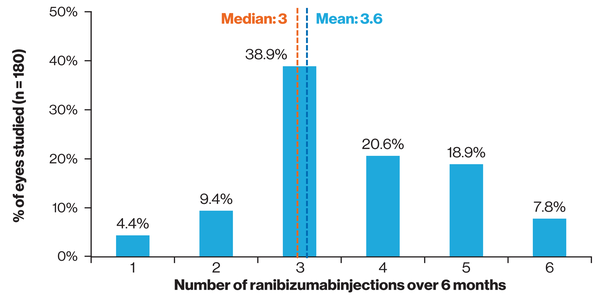
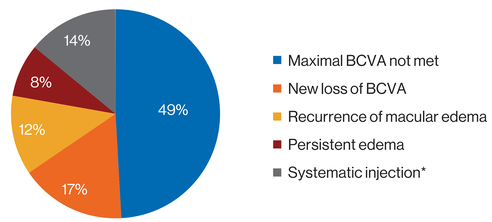
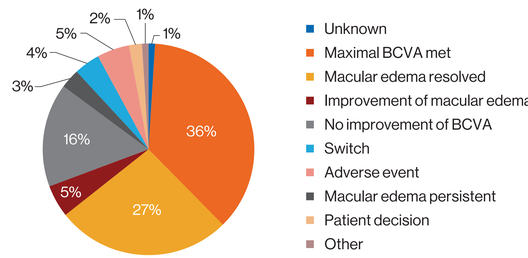


Figure 5. Criteria for retreatment and discontinuation

Criteria for retreatment



Criteria for discontinuation (n = 101)



*Refers either to the injection in the induction phase or treat and extend phase
BCVA, best corrected visual acuity

Safety

- Overall, 3.1% and 1.0% of patients had at least one AE and SAE related to ranibizumab 0.5 mg, respectively.
- Ocular AEs and SAEs related to ranibizumab 0.5 mg were reported in 0.5% and 2.6% of patients, and 0.5% of patients experienced nervous system disorders (transient ischemic attack).

CONCLUSIONS

- Ranibizumab 0.5 mg treatment improved functional and anatomical parameters in patients with visual impairment due to macular edema secondary to CRVO in routine clinical practice.
- The mean BCVA improved at Month 3 with ranibizumab treatment in patients with CRVO in a real-life setting.
- With ranibizumab 0.5 mg treatment, the improvement (decrease) in CSFT observed at Month 3 was grossly maintained at Month 6.
- At Month 6, mean gain in BCVA was lower in BOREAL-CRVO compared with CRUISE (9.5 letters vs 14.9 letters). However, this was achieved with lower number of ranibizumab injections in BOREAL-CRVO than in the CRUISE study (3.6 in BOREAL-CRVO versus 5.8 in CRUISE, respectively).[6]
- Concurrently, the BCVA at baseline was lower in BOREAL-CRVO than in CRUISE (40.1 vs 48.1).
- This suggests that in real-life setting, patients might be undertreated after the first three monthly injections and might explain the decrease in VA between Month 3 and Month 6.
- The safety profile of ranibizumab in BOREAL-CRVO was consistent with previously reported CRVO studies.

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Disclosures

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