Effectiveness of ranibizumab intravitreal injections in visual impairment due to macular edema secondary to retinal vein occlusion: final results at 24 months from the French BOREAL Cohorts

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Abstract

Background: The French Health Technology Assessment agency requested information on the ranibizumab (RBZ) usage and impact in real-world setting **– Objectives:** To assess the effectiveness and patterns of use of RBZ intravitreal injections (IVI) for patients with visual impairment due to macular edema secondary to branch (B) or central (C) retinal vein occlusion (ME-RVO) for up to 24-month follow-up **– Methods:** This is a real-world, post-authorization, observational cohort study in adult patients with RBZ IVI initiation for best-corrected visual acuity (BCVA) loss due to ME-RVO, followed-up for up to 24 months by their ophthalmologist. The primary endpoint was BCVA evolution from baseline to Month 6. BCVA, central subfield thickness (CSFT) evolution from baseline to Month 24, treatment exposure to ranibizumab and safety were also assessed **– Results:** Between December 2013 and April 2015, for B/C cohorts, 226 / 196 patients were enrolled, and 162 / 139 (71.7 / 70.9%) completed the 24-month follow-up. Patient characteristics were: mean (SD) age of 70.9 (11.1) / 70.4 (14.3) years, 48.7 / 51.5% of men, mean baseline BCVA of 52.2 (18.7) / 40.4 (25.6) letters, mean CSFT of 550 (175) / 643 (217) µm. The BCVA mean change from baseline was +14.1 [11.7 to 16.5] / +9.5 [5.5 to 13.5] letters at 6 ± 1.5 months. The vision is maintained at Month 12 and 24 with a mean change in BCVA from baseline of +13.0 [10.2 to 15.9] / +9.2 [4.5 to 13.9] letters at 12 ± 1.5 months and +11.4 [7.7 to 15.2] / +8.3 [3.7 to 12.8] letters at 24 ± 1.5 months, with 53.1 / 38.9% of patients having a BCVA > 70 letters. The CSFT mean change was -223 [-254 to -192] / -267 [-314 to -220] µm at 6 ± 1.5 months, -225 [-260 to -191] / -284 [-334 to -233] µm at 12 ± 1.5 months and -211 [-251 to -170] / -305 [-356 to -255] µm at 24 ± 1.5 months. At the end of 24 months of follow-up, the mean number of IVI was 7.2 (4.3) / 7.1 (4.4) with 85.8 / 85.6% patients who had at least one interruption of RBZ IVI, 72.6 / 62.5% for improvement of the pathology and 15.2 / 26.7% for lack of efficiency. At 24 months, 69.8 / 62.6% of studied eyes received only ranibizumab and 30.2 / 37.4% received another intravitreal treatment. No new safety findings were identified **– Conclusions:** Effectiveness of RBZ in daily practice at 24 months is close to the results at 6 months, but limited compared to the results of the preregistration randomized clinical trial at 24 months, probably due to the fewer number of IVI.

Background

- **Macular edema (ME)**
  - A complication of **retinal vein occlusion (RVO)**
  - The most common cause of RVO-associated vision loss
  - Different RVO forms related to occlusion location:
    - Branch retinal vein occlusion (BRVO)
    - Hemiretinal vein occlusion (HRVO)
    - Central retinal vein occlusion (CRVO)
- **Ranibizumab** (Lucentis®)
  - **Anti-VEGF** administered by intravitreal injections (IVI)
  - Extent of market authorization for the treatment of visual impairment due to ME secondary to RVO in France in 2012
  - At that time: request from the French Health Technology Assessment agency (the HAS) for complementary data on the impact of ranibizumab on the change in visual activity
- The BOREAL ME-BRVO (BRVO) and ME-CRVO (CRVO) cohorts answer to this request

Objectives

- **Main objective:** To assess the change in visual activity at Month 6
- **Secondary objectives:** During the 24-month follow-up
  - To assess the change in visual activity
  - To assess the change in central subfield thickness
  - To describe patterns of ranibizumab use

Methods

- **Design:** real-world, post-authorization, observational cohort study in adult patients with ranibizumab IVI initiation for best-corrected visual acuity (BCVA) loss due to ME-RVO, followed-up for up to 24 months by their ophthalmologist.
- **Data sources:** Data collection from patient medical files at:
  - Inclusion: general characteristics, history of ME-RVO, previous treatments, ophthalmological workup
  - 3, 6, 9, 12, 18, 24 months: ophthalmological workup, ME-RVO treatments and follow-up modalities
- **Endpoints**
  - Primary endpoint : BCVA evolution from baseline to Month 6
  - Secondary endpoints : BCVA evolution, central subfield thickness evolution, description of ME-RVO treatments modalities, ophthalmological workup and adverse events during the follow-up
- **This presentation details** final results of BRVO and CRVO cohorts at **24 month of follow-up.**
- Patients with HRVO were included in BRVO cohort as in randomized controlled trial (RCT).

Declaration of interest

The study was performed at the request of the HAS and funded by Novartis.

Results

Study populations

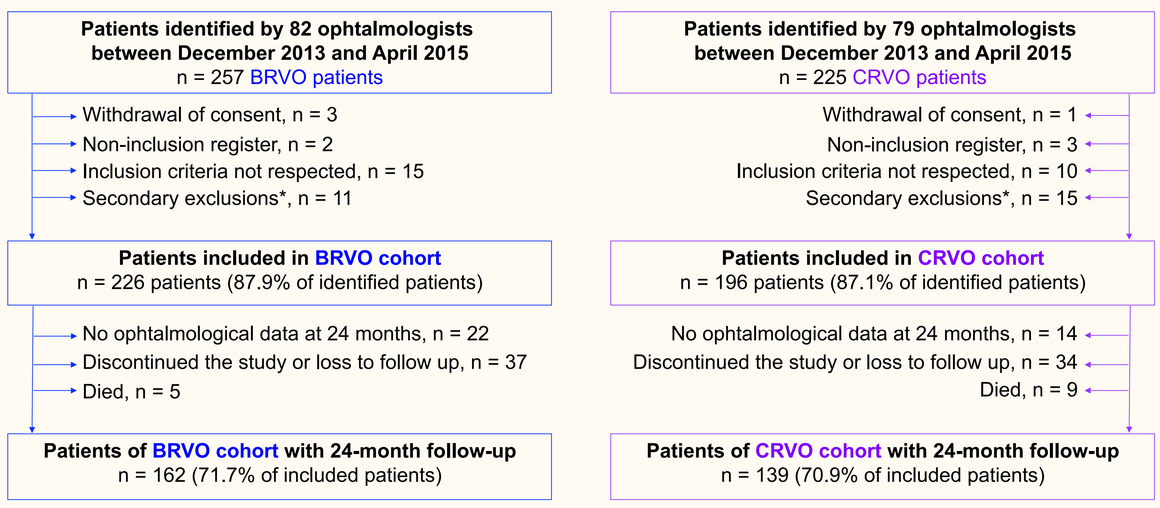

Figure 1: Flowchart of study populations in BRVO cohort and CRVO cohort

** On Scientific Committee decision: ranibizumab IVI not performed at baseline or not performed within 45 days of study initiation, lack of BVCA measurement at baseline.*

Baseline characteristics of patients at inclusion

Table 1: Patients characteristics at inclusion

	BRVO patients n = 226	CRVO patients n = 196
Male, n (%)	110 (48.7)	101 (51.5)
Mean age, year (± standard-deviation)	70.9 (11.1)	70.4 (14.3)
Mean BCVA, in ETDRS letter (± standard-deviation)	55.2 (18.7)	40.4 (25.6)
BCVA > 70 letters, n (%)	32 (14.2)	16 (8.2)
Mean central subfield thickness, in µm (± standard-deviation)	550 (175)	643 (217)

BCVA evolution

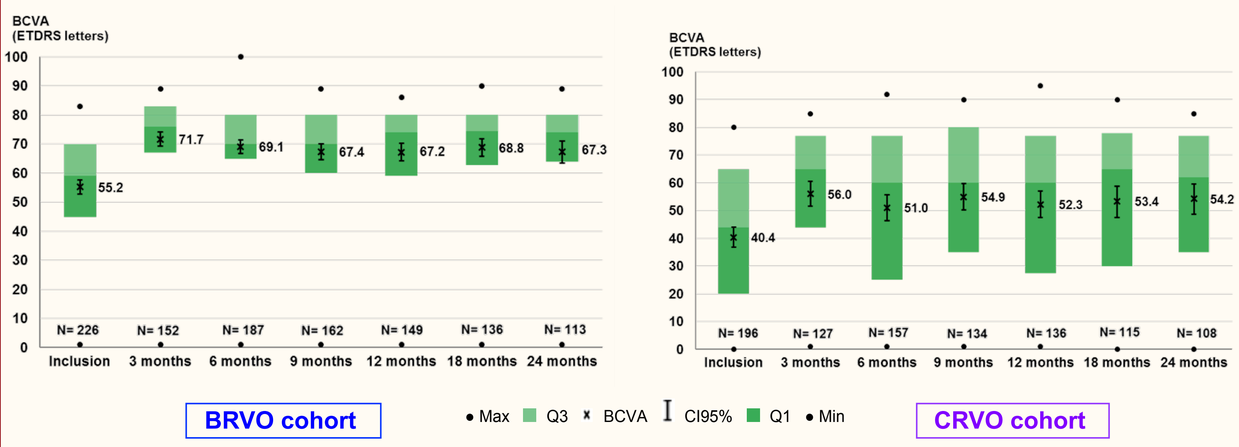

Figure 2: Evolution of mean BCVA during the follow-up (ETDRS letters) for studied eyes of followed patients in BRVO cohort and CRVO cohort

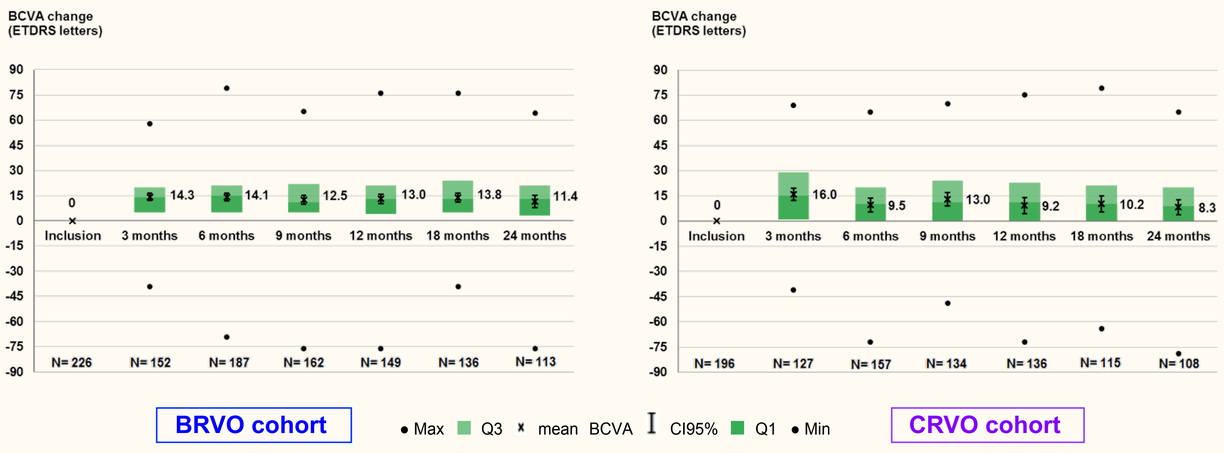

Figure 3: Evolution of mean BCVA change during the follow-up (ETDRS letters) for studied eyes of followed patients in BRVO cohort and CRVO cohort

Central subfield thickness evolution

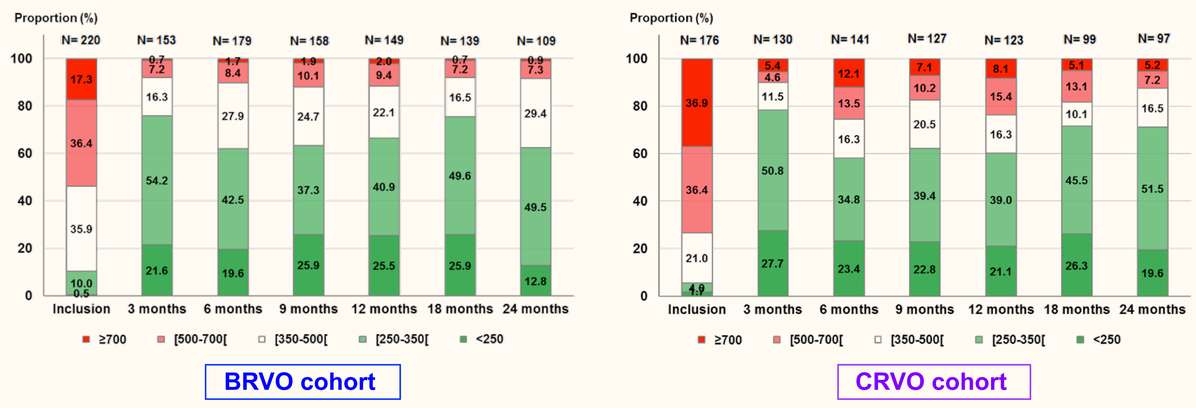

Figure 4: Evolution of patients distribution according to central subfield thickness (CSFT) measure during the follow-up for studied eyes of followed patients in BRVO cohort and CRVO cohort

Treatments modalities

Table 2: Intravitreal treatment and interruption details of ME-BRVO and ME-CRVO for studied eyes of followed patients in BRVO cohort and CRVO cohort at 24-month

	BRVO patients at 24-month n = 162	CRVO patients at 24-month n = 139
Mean number of IVI (± standard-deviation)	7.2 (4.3)	7.1 (4.4)
≥ 1 interruption of ranibizumab IVI, n (%)	139 (85.8)	119 (85.6)
Interruption for pathology improvement*	143 (72.6)	110 (62.5)
Interruption for lack of efficiency*	30 (15.2)	47 (26.7)
Ranibizumab IVI without switch to another treatment, n (%)	113 (69.8)	87 (62.6)
Switch to another IVI treatment, n (%)	49 (30.2)	52 (37.4)
Aflibercept	22 (13.6)	29 (20.9)
Dexamethasone	25 (15.4)	17 (12.2)
Bevacizumab	-	6 (4.3)
Triamcinolone	2 (1.2)	-

** Among total number of ranibizumab interruptions (BRVO = 197 ; CRVO = 176)*

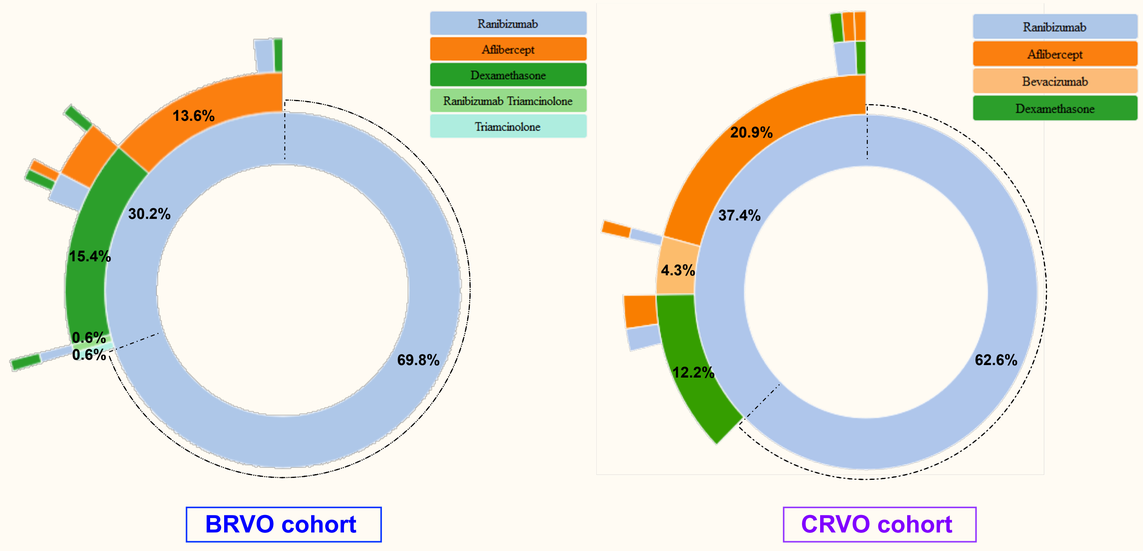

Figure 5: Intravitreal treatments modalities of ME-BRVO and ME-CRVO for studied eyes of followed patients in BRVO cohort and CRVO cohort at 24-month

Conclusion

This real-world study of patients with ranibizumab IVI initiation in ME-RVO **showed an improvement of BCVA and CSFT 6 months after initiation followed by a relative stability until 24-month.**

Mean BCVA change at 24-month **is lower in this study than in RCT but with less mean injections in real life:** 11.4 letters and 7.2 IVI in BRVO cohort compared to 15.5 letters and 11.4 IVI in BRIGHTER RCT, and 8.3 letters and 7.1 IVI in CRVO cohort compared to 12.1 letters and 13.1 IVI in CRYSTAL RCT.

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