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Effectiveness of ranibizumab intravitreal injections in visual impairment due to diabetic macular edema from the French BOREAL cohort

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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 diabetic macular edema (DME) for up to 36-month follow-up.
Methods: This is a real-world, post-authorization, observational cohort study in adult patients with RBZ intravitreal injections initiation for best-corrected visual acuity (BVCA) loss due to DME, followed-up for up to 36 months by their ophthalmologist. The primary endpoint was BCVA evolution from baseline to Month 12.
Results: Between December 2013 and April 2015, 290 patients were enrolled and 242 (83.4%) completed the 12-month follow-up. Patient characteristics were: mean (SD) age of 66.1 (11.0) years, 56.6% of men, 43.8% with a DME duration ≥ 6 months, 13.2% previously treated for DME (8.3% macular laser, 4.5% intravitreal corticosteroids; 2.5% other anti-VEGF), 66.5% with bilateral DME, mean baseline BCVA of 59.2 (15.0) letters, 13.2% with a BCVA > 70 letters, mean central subfield thickness (CSFT) of 457 (144) µm. During the first three months, 83.9% of patients received the 3 recommended ranibizumab IVI. At the end of 12 months of follow-up, the mean number of IVI was 5.1 (2.3) with 83.1% patients who had at least one interruption of RBZ IVI, 45.4% for improvement of the pathology and 27.7% for lack of efficiency. After 12 ± 1.5 months of follow-up, the BCVA mean [95%CI] change from baseline was 7.4 [5.4 to 9.4] letters, with 36.8% of patients having a BCVA > 70 letters. The CSFT mean change was -125 [-146 to 103] µm.
Conclusions: This study showed a effectiveness of RBZ in daily practice close to the results of the preregistration randomized clinical trial, with fewer number of IVI.

Background

- **Diabetic macular edema (DME)** is a retinal complication of diabetes that may affect visual acuity and lead to vision loss. The overall prevalence of DME is estimated at 4.8% among patients with diabetes.
- **Ranibizumab** (Lucentis®) is an **anti-VEGF** administered by intravitreal injections (IVI). Ranibizumab had an extent of market authorization for the treatment of visual impairment due to DME in France in June 2011. At that time, the French Health Technology Assessment agency requested complementary data on the impact of ranibizumab on the change in visual activity.
- The BOREAL DME cohorts was conducted in order to answer to the request of the French Health Technology Assessment agency.

Conflict of Interest Statement

The study was performed at the request of the HAS, the French Health Technology Assessment agency and funded by Novartis.

Objectives

- **Main objective:** To assess the change in visual activity at Month 12.
- **Secondary objectives:** during the 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:** This is a real-world, post-authorization, observational cohort study in adult patients with ranibizumab IVI initiation for best-corrected visual acuity (BVCA) loss due to DME, followed-up for up to 36 months by their retinal specialist ophthalmologist.
- **Data sources:** data collection from patient medical files at inclusion (general characteristics, history of DME, previous treatments, ophthalmological workup) and at 3, 6, 9, 12, 18, 24, 30 and 36 months (ophthalmological workup, DME treatments and follow-up modalities).
- **Endpoints:**
  - ✓ Primary endpoint: BVCA evolution from baseline to Month 12 (304 patients expected in order to have a precision of ± 1 letter),
  - ✓ Secondary endpoints: BVCA evolution, central subfield thickness evolution, description of ME-RVO treatments modalities, and ophthalmological workup during the follow-up.
- **This presentation details** results of DME cohort with **12 months of follow-up.**

Results

- **Study population**

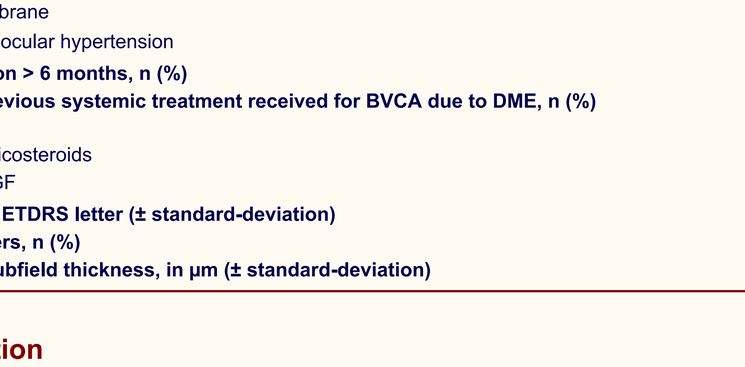

Figure 1 : Flowchart of study population in DME Cohort.
** On Scientific Committee decision: ranibizumab IVI not performed at baseline or not performed within 45 days of study initiation, lack of BVCA measurement at baseline.*

- **Baseline characteristics of patients at inclusion**

Table 1. Patients characteristics at inclusion

	DME Patients n = 242
Male, n (%)	137 (56.6)
Mean age, year (± standard-deviation)	66.1 (11.0)
Bilateral DME, n (%)	161 (66.5)
Diabetic retinopathy, n (%)	
No lesion	3 (1.2)
Non proliferative	164 (67.8)
Proliferative	25 (10.3)
PPR inactivated	49 (20.2)
At least one ophthalmic comorbidity, n (%)	183 (75.6)
Unoperated cataract	101 (41.7)
Pseudophakia	75 (31.0)
Epiretinal membrane	22 (9.1)
Glaucoma and ocular hypertension	18 (7.4)
Diabetic duration > 6 months, n (%)	106 (43.8)
At least one previous systemic treatment received for BVCA due to DME, n (%)	32 (13.2)
Macular laser	20 (8.3)
Intravitreal corticosteroids	11 (4.5)
Other Anti-VEGF	6 (2.5)
Mean BVCA, in ETDRS letter (± standard-deviation)	59.2 (15.0)
BVCA > 70 letters, n (%)	32 (13.2)
Mean central subfield thickness, in µm (± standard-deviation)	457 (144)

- **BVCA evolution**

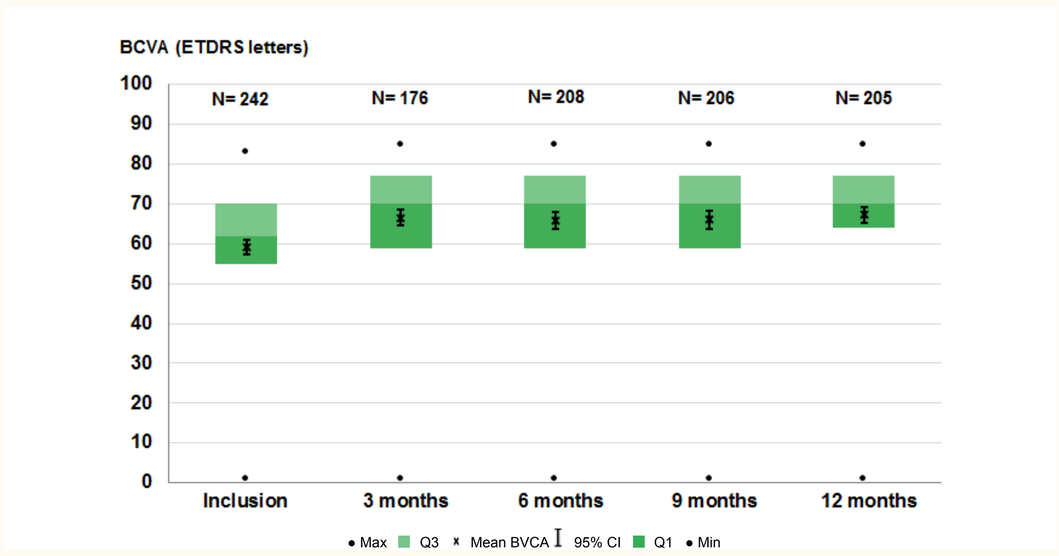

Figure 2 : Evolution of mean BVCA during the follow-up (ETDRS letters) in DME Cohort.

- ✓ Overall improvement in BVCA was observed observed from 3-month follow-up, then mean BVCA remains stable at 6, 9, and 12 months with high variability in patients (Figure 2).
- ✓ During the follow-up, the mean BVCA change from baseline was:
  - + 6.6 (± 10.7) letters ([95% CI] : [5.0; 8.2]) at 3-month follow-up (± 0.5),
  - + 6.7 (± 14.1) letters ([95% CI] : [4.8; 8.7]) at 6-month follow-up (± 1.5),
  - + 6.9 (± 14.5) letters ([95% CI] : [4.9; 8.9]) at 9-month follow-up (± 1.5),
  - **+ 7.4 (± 14.4) letters ([95% CI] : [5.4; 9.4]) at 12-month follow-up (± 1.5).**
- ✓ At 12-month follow-up, 36.8% of patients had BVCA above 70 letters (Figure 3).

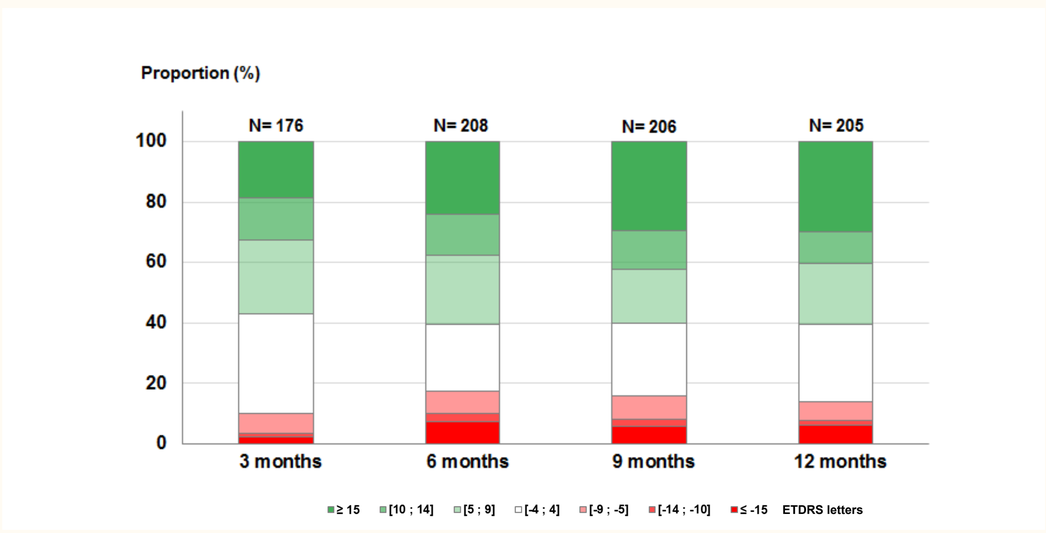

Figure 3 : Evolution of proportion of patients with BVCA gains or losses in EDTRS letters from baseline during the follow-up in DME Cohort.

- **Central subfield thickness evolution**

Table 2. Mean central subfield thickness (CSFT) evolution during the 12-month follow-up

	DME patients n = 242
At 3-month (± 0.5) follow-up, n	152
Mean CSFT variation [95% CI]	- 117 [-135 à -98]
At 6-month (± 1.5) follow-up, n	181
Mean CSFT variation [95% CI]	-109 [-127 à -91]
At 9-month (± 1.5) follow-up, n	175
Mean CSFT variation [95% CI]	- 111 [-133 à -89]
At 12-month (± 1.5) follow-up, n	176
Mean CSFT variation [95% CI]	- 125 [-146 à -103]

- **Treatments modalities**
  - ✓ During the first 3 months of follow-up, nearly 83.9% of received the initial three recommended ranibizumab injections (induction IVI).
  - ✓ At the end of 12-month follow-up, the mean number of IVI was 5.1 (± 2.3) for studied eye and 83.1% of patients had at least one interruption of ranibizumab IVI:
    - 45.4 % for pathology improvement,
    - 27.7% for lack of efficiency.

Conclusion

This real-world study of patients with ranibizumab IVI treatment initiation in DME **showed an improvement of visual acuity close to the results of the preregistration randomized clinical trial** (7.4 letters *vs* RESTORE: 6.8 letters) **with a fewer frequency of ranibizumab IVI in real-world** (5.1 in BOREAL *vs* 7 injections in RESTORE at 12 months).