PRN Ranibizumab for exudative age-related macular degeneration: 5 years follow-up dropout rate

Elise Boulanger-Scemama (1), Giuseppe Querques (1), Nathalie Puche (1), Fredegonde About (2), Mayer Srour (1), Valerie Mane (1) , Nathalie Massamba (1), Florence Canoui-Poitrine (2), Eric H Souied (1)

(1) Retina Creteil, University Paris Est Creteil, Creteil, France; (2) Epidemiology-Public Health, University Paris Est Creteil, LIC, EA4393, F-94000, Creteil, France.

Purpose:

Visual prognosis in exudative age-related macular degeneration (AMD) has considerably improved since the advent of anti-vascular endothelial growth factor (VEGF) therapy. Although ranibizumab efficacy on visual and anatomic parameters has been demonstrated by the two studies MARINA and ANCHOR, the cost and burden of a monthly injection regimen has proved difficult for patients in real life practice. Whatever the treatment regimen, reports have all shown that long-term regular follow-up is crucial to obtaining and then preserving significant visual gain.

The aim of this study was to analyze the follow-up adherence over 5 years of patients treated by ranibizumab for exudative AMD with a PRN regimen in a tertiary health care center, under real-life setting. Our purpose was also to evaluate dropout rate at five years and investigate associated factors.

Methods:

Retrospective chart review of all consecutive patients with exudative AMD, who underwent their first ranibizumab intravitreal injection (IVT) at the Creteil University Hospital Eye Clinic between October 1, 2006 and March 31, 2007.

Patient clinical characteristics at baseline and at the last follow-up visit were recorded. (Table 1)

Patients who had not attended a follow-up visit for more than 6 months at the final observation were considered to be lost to follow-up.

A phone survey was conducted for patients lost to follow-up to establish their actual follow-up status and reasons for discontinuation.

Baseline characteristics of patients were compared according to the follow-up status of patients.

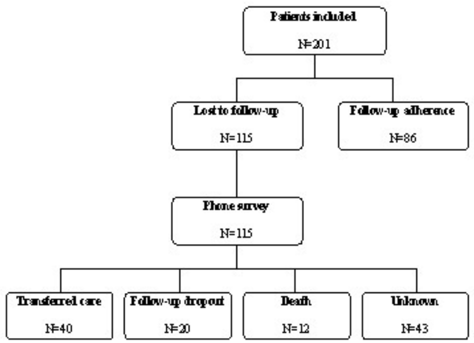

Figure 1. Flow chart showing the five years' follow-up of the 201 patients

Table 1. Demographic and clinical data of the 201 patients included

	Adherent n (%)	Lost to follow-up n (%)	Overall percentages (%)
Patients	86 (43)	115 (57)	
Mean follow-up time (years), mean (SD)	5.06 (0.18)	1,57 (1,37)	
Gender			
Men	29	46	(37)
Women	57	69	(63)
Age (years), mean (SD)	76.6 (6.4)	79.1 (7.1)	
Naive status	19	36	(27)
Opposite eye involvement	56	72	(64)
BCVA at baseline (letters), mean (SD)	51.0 (15.5)	44.8 (18.5)	
BCVA change at last visit (letters), mean (SD)	-4.0 (21)	-1.3 (20.7)	
Number of IVT, mean (SD)	14.5 (11.9)	5.4 (4.2)	
Number of visits, mean (SD)	32.9 (19)	8.4 (8.1)	
Distance home-hospital (kilometers), median (Q1-Q3)	18 (11-36)	40 (14-136)	

Data are expressed in n (%) for qualitative data and mean (SD) or median (Q1-Q3) for quantitative variables as appropriate
CNV= choroidal neovascularisation, BCVA= best-corrected visual acuity, IVT= intravitreal injection

Table 2. Associated factors with four follow-up status at five years: univariate and multivariate analyses

	Follow-up adherence (n=86)	Transferred care (n=40)	Follow-up dropout (n=20)	Unknown/ Deceased (n=55)	p*
Female gender, n(%)	57 (66.3)	27 (67.5)	14 (70)	28 (50.9)	0.20
Age at baseline (years), mean(SD)	76.6 (6.4)	76.6 (8.5)	78.7 (5.7)	82.0 (7.2)	< 0.001
Adjusted age at baseline (years), mean(SD) †	76.5 (6.5)†	76.5 (8.8)†	78.8 (5.9)†	82.2 (8.6)†**	< 0.001
Naive status, n(%)	18 (21.2)	9 (23.1)	6 (30)	20 (36.4)	0.23
Opposite eye involvement, n(%)	56 (65.1)	24 (60)	14 (70)	34 (61.8)	0.86
BCVA at baseline (letters), mean(SD)	51.0 (15.5)	45.9 (18.7)	42.5 (19.4)**	44.7 (18.3)**	0.069
Adjusted BCVA at baseline (letters), mean(SD) †	50.1 (15.9)†	45.9 (19.1)†	43.8 (18.3)†	45.4 (19.8)†	0.18
Distance home-hospital (kilometers), median(Q1-Q3)	18 (11-36)	38 (17-186)	105.5 (18-328)	40 (13-122)	0.0018
Adjusted distance home-hospital (kilometers), median(Q1-Q3) †	17.1 (11-36)†	38.5 (17-186)†**	132 (18-328)†**	40.4 (13-122)†**	0.007

*Global test: Pearson's chi-squared or Kruskal-Wallis test as appropriate
** Post-hoc tests 0.02: comparison between each category toward the reference group (follow-up adherence)
† mean or median were adjusted for age, BCVA and distance home-hospital by using linear regression or quantile regression models respectively
BCVA= best-corrected visual acuity

Results:

- Numbers of patients attending their follow-up visits were 149/201 (74%) at 1 year, 124/201 (62%) at 2 years, 108/201 (54%) at 3 years, 94/201 (47%) at 4 years and 86/201 (43%) at 5 years. (Figure 1)
- **The dropout rate after 5 years of follow-up at our hospital was 57%** (115/201), with a median time to dropout of 3.7 years. (Figure 1 and 2)
- The main reasons given by patients for follow-up discontinuation at our hospital were **long distance from home to hospital** (51.7%, 30/58), **subjective dissatisfaction with IVT benefit** (34.5%, 20/58), and **burden of periodic follow-up visits** (24.1%, 14/58). (Figure 3)
- **High age at baseline** (82.2 *vs.* 76.5 years, $p < 0.001$), **poor best corrected visual acuity (BCVA) at baseline** (42.5 *vs.* 51.0 letters, $p = 0.020$), and **long distance from home to hospital** (132 *vs.* 17.1 km, $p < 0.001$) were significantly associated with follow-up discontinuation. (Table 2)

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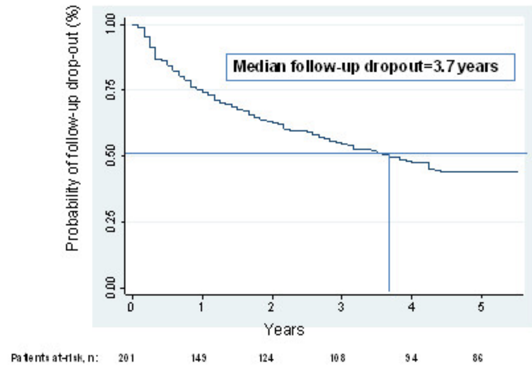

Figure 2. Kaplan-Meier curve: occurrence of follow-up dropout over five years in our tertiary center

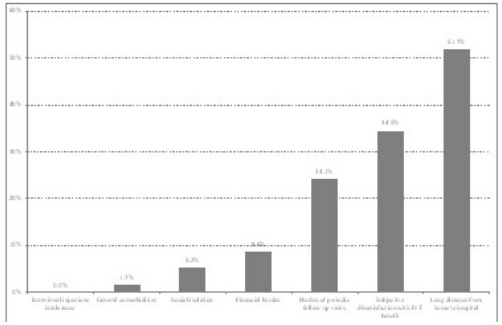

Figure 3. Phone survey answers (58 patients): reasons for failing to continue under follow-up in our tertiary center (7-item multiple-choice questionnaire)

Conclusion:

Although intravitreal ranibizumab therapy has considerably improved the visual prognosis in exudative AMD, the monthly visits required by the PRN regimen represent a high burden for patients.

In our tertiary referral center the dropout rate after 5 years' follow-up was high (57%).

Age, BCVA at baseline and distance from home to hospital were factors independently associated with long-term adherence.

This highlights the need for maintaining local access to ophthalmologic care for elderly AMD patients.