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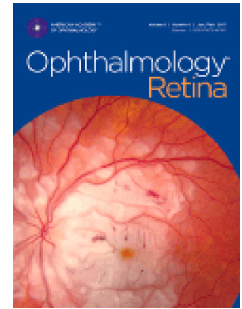
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# Journal Pre-proof

Improved structure and function in early detected second eye neovascular age-related macular degeneration; FASBAT/EDNA report 1

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1 Improved structure and function in early detected second eye  
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3 report 1  
4

5 **Running Title:**

6 FASBAT report 1; Improved structure and function in second eyes with nAMD.  
7

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54 and the FASBAT Study group

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56 Chakravarthy, McKibbin, Tunde Peto and the FASBAT Study group

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59

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80

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82 Early detection | Neovascular age-related macular degeneration | Fellow eyes | Atrophy |  
83 Hyperreflective material | Fibrosis | Intraretinal fluid | Subretinal fluid | Quality-of-life

84

85

86 **Abbreviations:**

---

|        |  |
|--------|--|
| AMD    | Age-related Macular Degeneration             |
| VA     | Visual Acuity                                |
| CFP    | Colour fundus photography                    |
| CNV    | Choroidal neovascularisation                 |
| ETDRS  | Early Treatment Diabetic Retinopathy Study   |
| IRF    | Intraretinal Fluid                           |
| nAMD   | Neovascular age-related macular degeneration |
| OCT    | Optical Coherence Tomography                 |
| SD-OCT | Spectral Domain Optical Coherence Tomography |
| SHRM   | Subretinal hyperreflective material          |
| SRF    | Subretinal Fluid                             |

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89 **Abstract**

90 **Purpose:** Visual Acuity (VA) and structural biomarker assessment before and at 24-months  
91 after early detection and routine treatment of second eye involvement with neovascular age-  
92 related macular degeneration (nAMD) and additional comparison with the first eye affected.

93 **Design:** Prospective, 22-centre observational study of participants with unilateral nAMD in  
94 the Early Detection of Neovascular AMD (EDNA) study, co-enrolled into the Observing  
95 fibrosis, macular atrophy and subretinal highly reflective material, before and after  
96 intervention with anti-VEGF treatment (FASBAT) study for an additional 2-year follow-up.

97 **Participants:** Older adults (>50 years) with new onset nAMD in the first eye.

98 **Methods:** Assessment of both eyes with optical coherence tomography (OCT), colour fundus  
99 photography (CFP), clinic-measured visual acuity (VA) and quality-of-life (QoL).

100 **Main Outcome Measures:** Prevalence of Atrophy, Subretinal Hyperreflective Material  
101 (SHRM), Intraretinal fluid (IRF), Subretinal fluid (SRF) and changes in VA over the study  
102 duration in both the first and second eyes affected with nAMD. Composite QoL scores over  
103 time.

104 **Results:** Of 431 participants recruited to the FASBAT study, the second eye converted to  
105 nAMD in 100 participants at a mean of 18.9 months. VA was 18 letters better at the time of  
106 early diagnosis in the second eye compared with conventional diagnosis in the first eye (72.9  
107 vs 55.6 letters). 24.9-months post-conversion in the second eye, VA was 69.5 letters  
108 compared with at a similar matched time point in the first eye (59.7 letters; 18.9 months). A  
109 greater proportion of participants had vision >70 letters in the second eye versus the first eye,  
110 24.9-months post-conversion (61 vs 38). Prevalence of SHRM and IRF was lower in the  
111 second eye compared with the first eye at 24.9-months post-conversion to nAMD. However,  
112 SRF prevalence was greater in the second eye at 24.9-months post-conversion. The  
113 development and progression of total area of atrophy appears similar in both eyes. Mean  
114 composite QoL scores increased over time, with a significant correlation between VA for the  
115 second eye only 24.9 months post-conversion.

116 **Conclusion:** This study has shown that early detection of exudative AMD in the second eye  
117 is associated with reduced prevalence of SHRM and IRF and greater visual acuity which is  
118 significantly correlated with maintained quality-of-life.

119

## 120 **Introduction**

121 Neovascular age-related macular degeneration (nAMD) remains the commonest cause of  
122 treatable severe vision loss developed countries, with projections estimating 288 million  
123 people affected globally by the year 2040 (1). Usually manifesting unilaterally, onset of  
124 nAMD in the fellow, unaffected eye typically occurs in 26-50% of patients within 3 years  
125 (2,3). Importantly, fellow eyes treated for nAMD generally show better visual function at  
126 diagnosis and over time compared with the first eye, if treatment is commenced promptly (4).

127 The relationship between morphological characteristics of the retina and change in visual  
128 function has identified several retinal biomarkers most pertinent to nAMD disease. It has  
129 been long established that atrophy and fibrosis within the fovea are the main drivers of visual  
130 loss in AMD (5). A recent systematic literature review has highlighted five key OCT  
131 biomarkers related to disease progression in nAMD; subretinal hyperreflective material  
132 (SHRM), drusen, intraretinal fluid (IRF), outer retinal tubulations (ORT) and hyperreflective  
133 foci, with IRF having the most significant impact on visual outcome (6).

134 In this study we compare the visual acuity outcomes and prevalence of twelve retinal  
135 biomarkers in a cohort of patients with first eye routinely presenting with nAMD and in their  
136 second, early detected eyes, up to 24-months post-conversion.

137

## 138 **Methods**

139 The observing fibrosis, macular atrophy and subretinal highly reflective material – before and  
140 after intervention with anti-VEGF treatment (FASBAT) study was a multicentre, prospective,  
141 observational study extending from the Early Detection of Neovascular Age-related macular  
142 degeneration (EDNA) study. The EDNA study compared the diagnostic accuracy of optical  
143 coherence tomography (OCT), self-monitoring with an Amsler grid, self-reported visual  
144 function, slit lamp examination and dye based angiography for early detection of nAMD in the  
145 second eye of those already undergoing routine care for nAMD in their first eye (3). The  
146 FASBAT study was conducted in twenty-two National Health Service (NHS) ophthalmology  
147 departments across the United Kingdom from December 2018 to February 2022. Ethical  
148 approval was granted by the NHS Research and Ethics Committee (IRAS: 197731). Written  
149 informed consent was obtained from all study participants, and the study followed the tenets



150 of the Declaration of Helsinki, Good Clinical Practice guidelines and International Council for  
151 Harmonization.

## 152 **Participants**

153 Participants were approached to co-enrol in the FASBAT study at the point of enrolment, at a  
154 subsequent date during enrolment or following their involvement in the EDNA study.

155 Participants had to meet the inclusion/exclusion criteria specified to join the EDNA study (3)  
156 and be willing to provide data for both eyes for an additional 2 years following their exit from  
157 the EDNA study, attending FASBAT study visits with appropriate imaging. In brief, EDNA  
158 inclusion/exclusion criteria stipulated that participants were required to have newly diagnosed  
159 nAMD in the first eye and an unaffected fellow eye confirmed to be free of nAMD by FFA  
160 and with a VA of  $\geq 68$  ETDRS letters with no confounding retinal pathology.

## 161 **Study Outcomes**

162 This prospective study was conducted to assess the prevalence of key retinal biomarkers  
163 (Table 1) pertinent to nAMD development up to 24-months post-conversion. Similar matched  
164 timepoints following conversion to nAMD in both eyes were analysed in order to compare  
165 the prevalence of key biomarkers in both the first and second eye. Visual acuity trajectories  
166 of both eyes were also studied.

167 In this study, the 'baseline' timepoint refers to the point of recruitment into the EDNA study,  
168 when the first eye had a diagnosis of nAMD. The point in which the second eye converted to  
169 nAMD is referred to as to the 'conversion' timepoint. Therefore, baseline for the first eye and  
170 conversion for the second eye represent a similar matched timepoint for development of  
171 nAMD. The point of conversion of the second eye was at a mean of 18.9 months. This  
172 timepoint was used to make similar comparisons of biomarkers in the first eye with the pre-  
173 planned 24-month conversion in the second eye.

174 Quality-of-life was assessed at each timepoint using the National Eye Institute Visual  
175 Functional Questionnaire (NEI VFQ) assessment. Composite scores were compared at  
176 matched timepoints and a Pearson correlation made between visual acuity in either the first or  
177 second eye.

178

## 179 **Assessments**

180 Participants were treated following NHS standard care which was defined by the treating  
181 physician and could have been a treat-and-extend, as required or fixed regimen. Study-related  
182 assessments were carried out at routine NHS standard care clinical visits coinciding with the  
183 key study milestone visits (baseline, conversion, post-conversion), for both eyes.

184 **Retinal Imaging.** Optical coherence tomography (OCT) and colour fundus  
185 photography (CFP) and fluorescence angiography (FA) were captured at each interval using  
186 local protocols. All images collected during the FASBAT study were analysed by the reading  
187 centre (Central Angiographic Resource Facility) in Belfast following a study-specific  
188 protocol. Definitions of the retinal biomarkers are listed in Table 1.

189 **Visual Acuity.** Clinic-measured visual acuity (VA) was measured as the number of  
190 letters read on an Early Treatment Diabetic Retinopathy Study (ETDRS) chart.

191 **Quality-of-Life (QoL).** National Eye Institute Visual Functional Questionnaire (NEI  
192 VFQ) assessed patient reported outcome measures at each time point.

193

## 194 **Statistical Analysis**

195 All analyses were completed using SPSS version 26 (IBM, Chicago, IL, USA) following a  
196 pre-defined statistical analysis plan.

197

## 198 **Results**

199 **Participant Characteristics.** Of 562 participants recruited to the EDNA study, 431  
200 participants co-enrolled into the FASBAT study for an additional 2-year observational period  
201 following completion of the EDNA study (Figure 1). All 431 participants were diagnosed  
202 with nAMD in the first eye with dry AMD in the second eye. Of the 431 FASBAT cohort, the  
203 second eye remained dry in 314 participants with 117 participants converting to nAMD in  
204 their second eye. A total of 56 participants withdrew from FASBAT; of these 17 participants  
205 had their second eye convert to nAMD and 38 participants whose second eye remained dry  
206 (Figure 1).

207 This report details characteristics of the 100 participants whose second eye converted  
208 to nAMD. Baseline characteristics of the 100 participants are shown in Table 2. The mean

209 time to conversion in the second eye was 18.9 months (mean: 567.1 days; SD: 309.5 days),  
210 ranging from 68-1221 days, with 52% (n=52) converting prior to the mean and 48% (n=48)  
211 converting after the mean (Figure 2).

212

### 213 **Retinal Biomarker Evaluation**

214 A summary of key retinal biomarkers evaluated in both the first and second eye at similar  
215 timepoints from diagnosis of nAMD in each eye can be found in Table 3. The OCT and CFP  
216 biomarkers most pertinent to nAMD (6) are discussed. The results of the FA assessment are  
217 not reported here.

218 **Subretinal Hyperreflective Material (SHRM).** The prevalence of SHRM in the first  
219 eye was 93.0% (n=93) at baseline and 92.4% (n=85) at 18.9 months post-conversion. In the  
220 second eye, SHRM prevalence was 77.2% (n=71) at conversion and 80.5% (n=70) at 24.9  
221 months post-conversion.

222 **Intraretinal Fluid (IRF).** The prevalence of IRF in the first eye 57.7% (n=56) at  
223 baseline and 46.5% (n=34) at 18.9 months post-conversion. In the second eye, the prevalence  
224 of IRF was 32.9% (n=24) at conversion and 34.1% (n=28) at 24.9 months post-conversion  
225 (Table 3).

226 **Subretinal Fluid (SRF).** The prevalence of SRF in the first eye was 59.8% (n=58) at  
227 baseline 25.4% (n=18) at 18.9 months post-conversion. In the second eye, the prevalence was  
228 35.6% (n=27) at conversion and 28.0% (n=23) at 24.9 months post-conversion (Table 3).

229 **Atrophy (CFP).** In the first eye, the prevalence of atrophy was 15.9% (n=14) at  
230 baseline and 42.9% (n=33) 18.9 months post-conversion. For the second eye, atrophy  
231 prevalence was 17.3% (n=13) at conversion to nAMD and 43.9% (n=25) 24.9 months post-  
232 conversion.

233 **Atrophy (OCT).** In the first eye, the prevalence of atrophy detected was greater at  
234 31.3% (n=31) at baseline and 55.3% (n=52) 18.9 months post-conversion. For the second  
235 eye, atrophy prevalence was 23.4% (n=22) at conversion and 53.5% (n=46) 24.9 months  
236 post-conversion.

237

## 238 **Visual Acuity**

239 Mean VA in the first eye was 55.6 (SD=15.7) ETDRS letters at the point of diagnosis  
240 (baseline), compared with 59.7 (SD=20.5) letters, a mean of 18.9 months post-conversion. In  
241 the second eye, the number of ETDRS letters was 72.9 (SD=8.1) at the point of conversion to  
242 nAMD and 69.5 (SD=14) letters 24.9 months post-conversion (Table 2). The number of  
243 participants gaining and/or losing 15 ETDRS letters in each eye are shown in Figure 3. The  
244 proportion of participants with a visual acuity >70 letters in the first eye at 18.9 months post-  
245 conversion was 36.5% (n=35) and 65.6% (n=61) in the second eye 24.9 months post-  
246 conversion.

247

## 248 **QoL**

249 Mean composite score at baseline, when the first eye was diagnosed with nAMD was 73.6  
250 (SD=27.5, n=85). At the point of conversion to nAMD in the second eye, the mean composite  
251 score was 70.0 (SD=27.2, n=68) increasing to 76.4 (SD=17.4, n=84) 24.9 months post-  
252 conversion in the second eye. A significant Pearson correlated emerged between composite  
253 scores and VA for the second eye only 24.9 months post-conversion (R=.429, p=.000, n=80).

254

## 255 **Discussion**

256 The FASBAT study reports on the prevalence of a number of key retinal biomarkers, visual  
257 acuity and quality-of-life in the first and second eyes of nAMD up to 24-months post-  
258 conversion of the second eye. In this observational study of real-world practice, biomarkers  
259 were compared at a mean of 18.9 months in the first eye and 24.9 months in the second eye.  
260 The FASBAT study was an extension to the EDNA study which evaluated diagnostic  
261 accuracy of tools used in the early diagnosis of second eyes.

262 Across the retinal biomarkers evaluated, it was demonstrated there was a lower prevalence of  
263 SHRM and IRF in the second eye compared with the first eye, whilst SRF prevalence was  
264 greater in the second eye. Atrophy prevalence was similar between the two eyes. We also  
265 reveal greater absolute visual acuity in the second eye of over 10 ETDRS letters at baseline  
266 that was maintained across all time points from conversion compared to the first eye. The  
267 findings from this study provide strong evidence to monitor the macula of the fellow eye with

268 OCT regularly to facilitate earlier diagnosis and treatment of nAMD in the second eye to  
269 prevent long-term, irreversible damage to retinal structure and function.

270 In line with previous research, VA in the first affected eye initially increased from 55.6 letters  
271 at baseline when the initial diagnosis of nAMD was made, to 59.7 letters at a mean of 18.9  
272 months post-conversion. Both the baseline VA and the +4 letter increase post-conversion is  
273 typical of real-world practice in the first eye (7,8). Conversely, at the point of conversion to  
274 nAMD in the second eye, VA decreased from 72.9 letters to 69.5 letters at a mean of 24.9  
275 months post-conversion. Whilst this differs to previous research which shows a significantly  
276 lower gain in VA in fellow eyes of  $0.37 \pm 14$  letters over 2 years (9), the reduction in VA in  
277 our cohort is driven by four individuals who showed reductions in vision  $>20$  letters.  
278 Nevertheless, despite the numerical decrease in VA in the second eye, visual performance  
279 was consistently better in the second eye compared to the first at approximately 2 years  
280 following diagnosis, supporting previous research at 12-months (10,11), 2 years (9), 3 years  
281 (4) and real-world datasets (7,8). The proportion of second eyes with good vision ( $>70$   
282 letters) 24-months post-conversion is also in line with previous research at almost double that  
283 of the first eye at 65.6% v 36.5%, respectively (9).

284 This FASBAT study has demonstrated better visual acuity in the second eye. Importantly this  
285 study has shown that visual acuity positively correlates with QoL at 24.9 months post-  
286 conversion. This underlies the importance of early diagnosis particularly in the second eye, to  
287 maintain QoL and prevent significant visual loss for patients with nAMD in the long-term.  
288 Economic modelling has also identified that earlier diagnosis of the second eye in nAMD  
289 with OCT is indeed cost-effective for patients with nAMD in the first eye (12).

290 The principal determinants of good visual acuity outcomes in patients with nAMD are the  
291 presence and extent of fibrosis, atrophy, IRF and SHRM.

292 Fibrosis is identifiable as highly reflective material often in the subretinal space (SHRM),  
293 although SHRM could also represent fibrin, haemorrhage, neovascular membrane,  
294 hyperpigmentation or exudate (6). This study demonstrates there is a lower prevalence of  
295 SHRM in the second eye compared with the first eye and this continues to be the case up to  
296 24 months post-diagnosis. We postulate that early diagnosis could therefore lead to less  
297 fibrosis, fibrin and identifiable neovascular membrane. It is important to note that Casalino et  
298 al. detected a lower prevalence of SHRM in  $\sim 66\%$  in their cohort at diagnosis (13), using the  
299 same definition (14), perhaps reflecting the inconsistency to grade this biomarker. Since the

300 commencement of this study there is now consensus nomenclature statement on the definition  
301 of SHRM on OCT, defined as ‘exudation in the subretinal space of material that is  
302 hyperreflective as compared with fluid’ (15) which should help with consistency in reporting.

303 The presence of persistent IRF is associated with worse visual acuity outcomes (6,16). It is  
304 pleasing to note that early diagnosis leads to not only less IRF at diagnosis but also out to 24  
305 months post-diagnosis. It is interesting to note that in this real-world setting, the prevalence  
306 of SRF at 24 months post-treatment is similar between the first and second eyes. However,  
307 persistent SRF, particularly if this is not changing in volume, appears to have less or no  
308 detrimental effect on visual acuity in the medium-term (16).

309 Atrophy was consistently more diagnosed with OCT compared with CFP. We believe this is  
310 a combination of the grading definitions used and the ability to detect atrophy on the different  
311 imaging modalities. Nonetheless, there appears to be little difference in the prevalence of  
312 atrophy diagnosed with either method at diagnosis in the first eye and the second eye and  
313 indeed the prevalence increases to a similar extent approximately 2 years post-diagnosis.  
314 Therefore, early diagnosis of nAMD does not influence the prevalence of atrophy.

315

### 316 **Study Strengths and Limitations**

317 Our study has multiple strengths. FASBAT was a prospective, multicentre study including 22  
318 NHS Trusts across 3 nations of the United Kingdom thus providing real-world evidence from  
319 a diverse and representative population of nAMD patients. All imaging data collected were  
320 evaluated following reading centre grading which is a further strength of the study.

321 Our study is not without its limitations. Firstly, due to the observational nature of this study,  
322 the matched timepoints for analysis of biomarkers between first and second eyes were not  
323 exact; being earlier in the first eye at approximately 18.9 months compared with 24.9 months  
324 in the second eye. This could lead to an under-representation of biomarker prevalence that  
325 may continue to develop in the first eye. Secondly, at 24.9 months post-conversion for the  
326 second eye there was a number of missing data points for between 7 and 41 participants.  
327 Unfortunately, for the majority of participants, this time point coincided with the lockdowns  
328 and restrictions imposed by the United Kingdom government in response to COVID-19.  
329 Thirdly, although FA was used to exclude nAMD in the fellow eye at baseline, multimodal  
330 imaging, including structural OCT and OCT-angiography, may reveal the possibility of

331 neovascularisation at baseline. The likelihood of this is low however, and as such we believe  
332 this would not fundamentally change the observed improved structural and functional  
333 outcomes with early detection in the second eye. Nevertheless, the FASBAT study still  
334 provides important evidence pertaining to retinal changes associated with the development of  
335 nAMD in the second eye both before and 2 years post-conversion. Finally, definitions of such  
336 biomarkers continue to evolve and there is now consensus nomenclature for many  
337 biomarkers, such as atrophy defined by the classification of atrophy meetings program group  
338 (17) and hyperreflective material defined by the consensus on neovascular age-related  
339 macular degeneration nomenclature study group (15).

340 In unilateral nAMD, the FASBAT study has shown that in the second eye there is a greater  
341 visual acuity and reduced prevalence of pertinent retinal biomarkers post-conversion to  
342 nAMD due to early detection of disease onset and after follow-up to 2 years. Currently, OCT  
343 is the best imaging modality in terms of diagnostic accuracy (3) of new nAMD and our study  
344 results substantiate the need for regular monitoring of fellow eyes of unilateral nAMD to  
345 prevent significant changes to retinal structure and function.

346

347

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- 416
- 417

418 **Table 1:** List of the key retinal imaging biomarkers evaluated in the FASBAT study and the  
 419 reading centre definitions.

| <b>Retinal Biomarker</b> | <b>Imaging Modality</b> | <b>Reading Centre Definition</b>   |
|--------------------------|-------------------------|--|
| SHRM                     | OCT                     | Any hyper-reflective material that obscures normal retinal anatomical features.  |
| IRF                      | OCT                     | Hypo-reflective spaces with a minimum vertical diameter of 50 microns.   |
| SRF                      | OCT                     | Areas of hypo reflectivity or moderate reflectivity between the neurosensory retina and RPE/BM.  |
| Atrophy                  | OCT                     | Increased signal transmission through the RPE/Bruch's complex; RPE band thinning or missing; Outer nuclear layer thinning, missing   |
|                          | CFP                     | An area of sharply defined drop out of RPE of at least 175 microns in diameter with two of the following identified; choroidal vessels exposed; well defined margins; scalloped edges. |

420 \*SHRM: Subretinal Hyperreflective Material; IRF: Intraretinal Fluid; SRF: Subretinal  
 421 Fluid; OCT: Optical Coherence Tomography; CFP: Colour Fundus Photography

422

423

424 **Table 2:** Baseline demographics of the 100 participants whose second eye converted to  
 425 nAMD

|                                     |             |
|-------------------------------------|-------------|
| Age (mean, SD)                      | 76,5        |
| Age range (years, months)           | 59,9 – 92,6 |
| Gender (n, %)                       |             |
| Male                                | 41 (41)     |
| Female                              | 59 (59)     |
| Mean VA (ETDRS letters)             |             |
| First eye at baseline               | 55.6        |
| Second eye (at point of conversion) | 72.9        |

426 \*SD: Standard Deviation; VA: Visual Acuity; ETDRS: Early Treatment Diabetic Retinopathy  
 427 Study

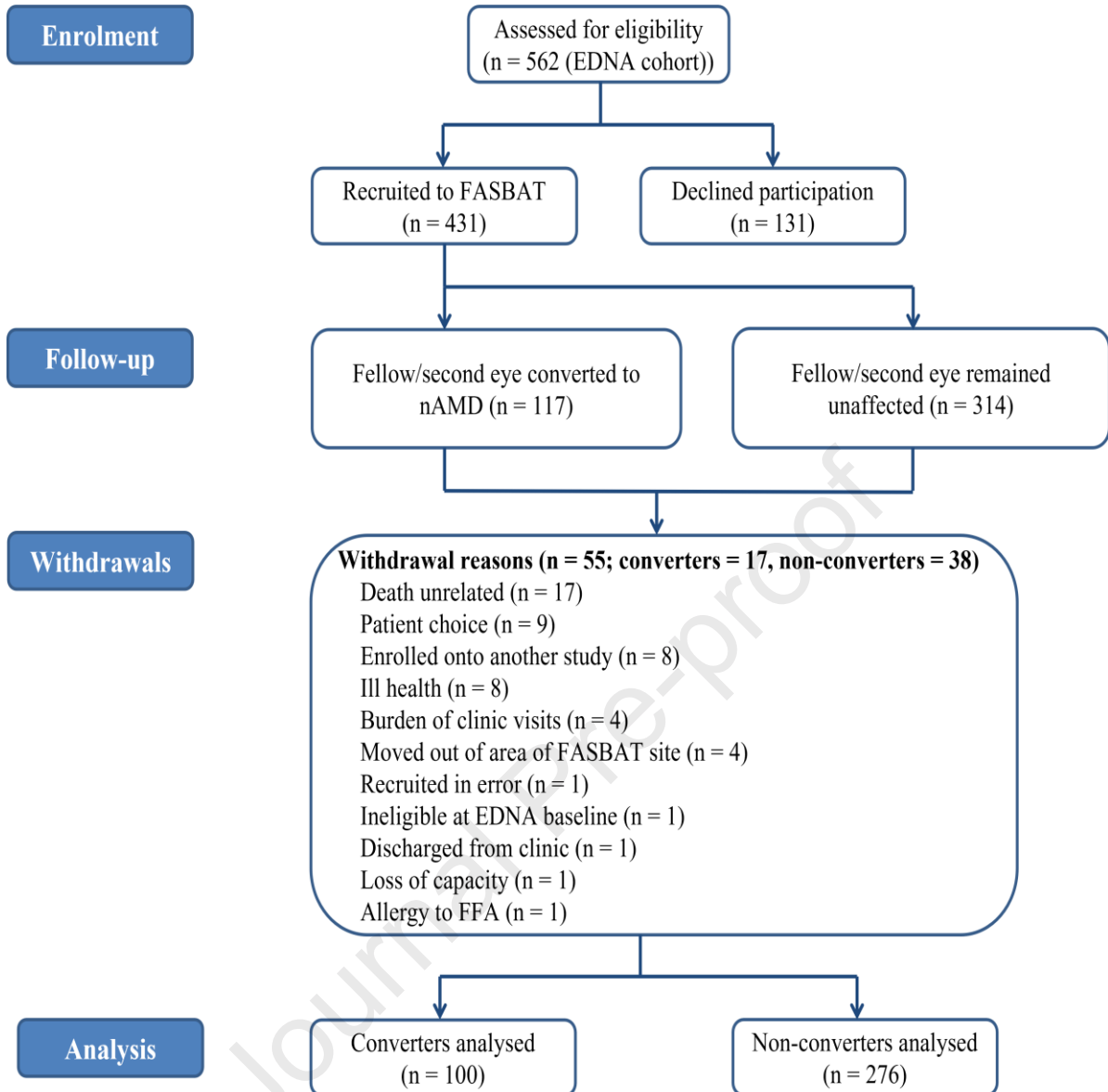
428 **Table 3:** Retinal biomarker evaluation of the 100 FASBAT participants whose second eye converted to nAMD.

|  | First Eye at diagnosis of nAMD (Baseline) | Second Eye at diagnosis of nAMD (Conversion) | First Eye a mean of 18.9 months post-conversion | Second Eye a mean of 24.9 months post-conversion |
|--|---|--|---|--|
| <b>Atrophy (CFP)</b>                         |   |  |   |  |
| No (n; %)                                    | 74 (84.1)                                 | 62 (82.7)                                    | 44 (57.1)                                       | 32 (56.1)  |
| Yes (n; %)                                   | 14 (15.9)                                 | 13 (17.3)                                    | 33 (42.9)                                       | 25 (43.9)  |
| Cannot Grade (n)                             | 0   | 0  | 0   | 2  |
| Missing data (n)                             | 12  | 25   | 23  | 41   |
| <b>Atrophy (OCT)</b>                         |   |  |   |  |
| No (n; %)                                    | 68 (68.7)                                 | 72 (76.6)                                    | 42 (44.7)                                       | 40 (46.5)  |
| Yes (n; %)                                   | 31 (31.3)                                 | 22 (23.4)                                    | 52 (55.3)                                       | 46 (53.5)  |
| Cannot Grade (n)                             | 1   | 0  | 0   | 1  |
| Missing data (n)                             | 0   | 6  | 6   | 13   |
| <b>SHRM (OCT)</b>                            |   |  |   |  |
| No (n; %)                                    | 7 (7)                                     | 21 (22.8)                                    | 7 (7.6)   | 17 (19.5)  |
| Yes (n; %)                                   | 93 (93)                                   | 71 (77.2)                                    | 85 (92.4)                                       | 70 (80.5)  |
| Cannot Grade (n)                             | 0   | 1  | 2   | 0  |
| Missing data (n)                             | 0   | 7  | 6   | 13   |
| <b>SRF (OCT)</b>                             |   |  |   |  |
| Mean Max Height ( $\mu\text{m}$ ; SD)        | 141.6 (125.7)                             | 87 (63.1)                                    | 61.8 (83.9)                                     | 64.1 (80.6)                                      |
| n (%)  | 58 (59.8)                                 | 27 (35.6)                                    | 18 (25.4)                                       | 23 (28)  |
| Mean Foveal Max Height ( $\mu\text{m}$ ; SD) | 98.1 (75.5)                               | 82.5 (73.6)                                  | 69.3 (23.1)                                     | 73.3 (42)  |
| n (%)  | 20 (20.6)                                 | 10 (13.7)                                    | 3 (4.2)   | 7 (8.5)  |
| <b>IRF (OCT)</b>                             |   |  |   |  |
| No (n; %)                                    | 42 (42.3)                                 | 50 (67.1)                                    | 38 (38.4)                                       | 55 (65.9)  |
| Yes (n; %)                                   | 56 (57.7)                                 | 24 (32.9)                                    | 34 (46.5)                                       | 28 (34.1)  |
| Cannot Grade (n)                             | 0   | 0  | 0   | 0  |
| Missing data (n)                             | 2   | 26   | 28  | 17   |

429 \*CFP: Colour Fundus Photography; OCT: Optical Coherence Tomography; SHRM: Subretinal Hyperreflective Material; SRF: Subretinal  
430 Fluid; IRF: Intraretinal Fluid.  $\mu\text{m}$ : Microns; SD: Standard Deviation

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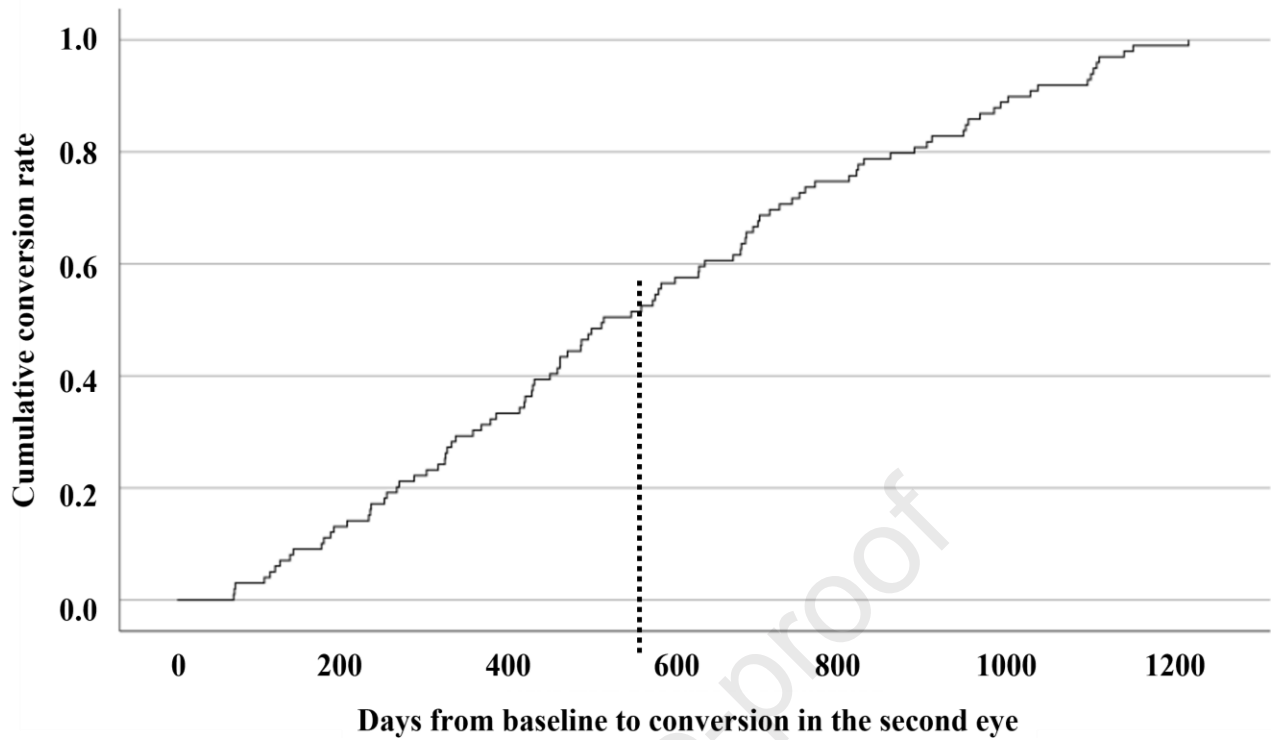


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434 **Figure 1: CONSORT diagram of participant flow through the FASBAT study**

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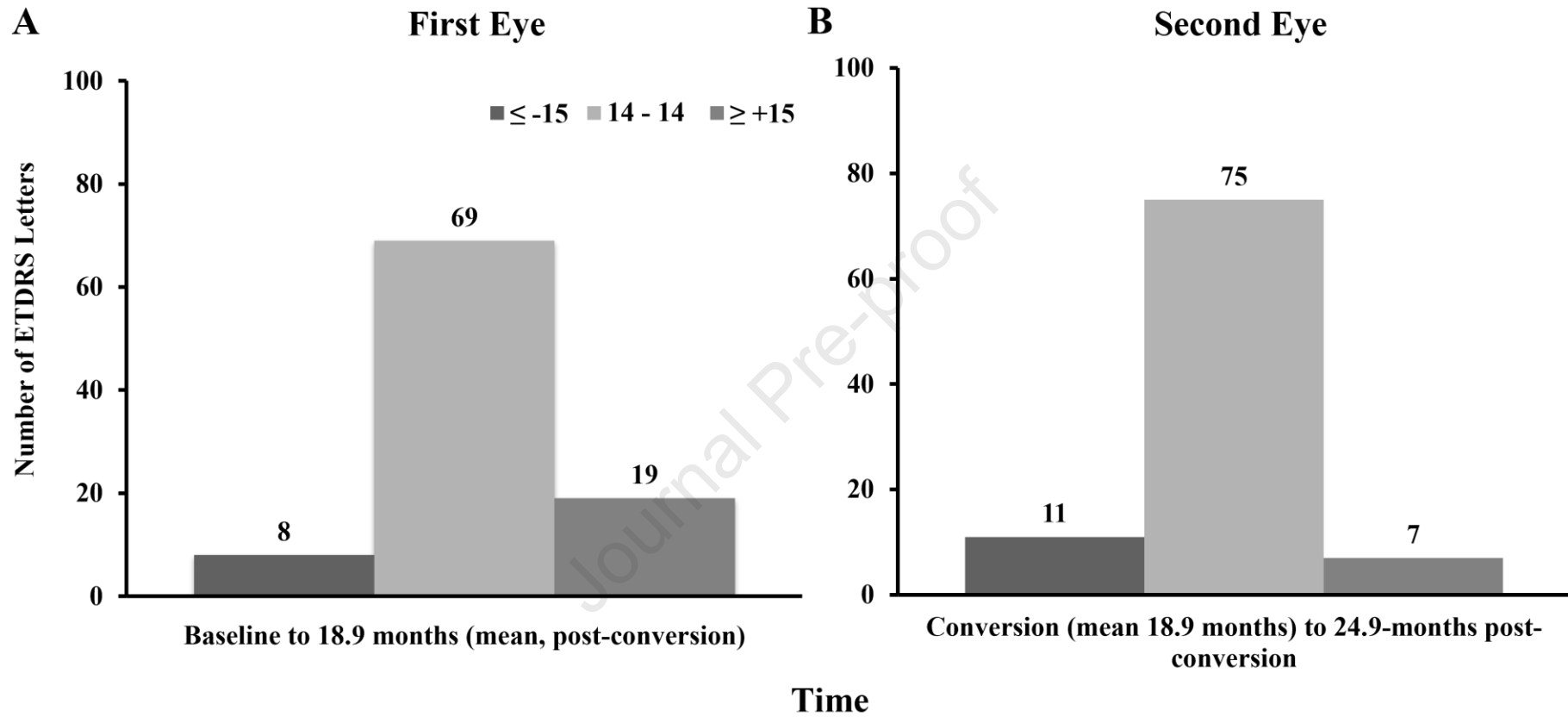
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438 **Figure 2:** Distribution of participants whose second eye converted to nAMD. The mean time  
 439 to conversion, indicated by the vertical dashed line, was 18.9 months (mean number of days  
 440 = 567.1;  $SD = 309.5$  days), ranging from 2.3 to 40.7 months (68 – 1221 days). There were  
 441 52% ( $n=52$ ) of participants who converted before this mean with 48% ( $n=48$ ) converting  
 442 after the mean.

443



444

445 **Figure 3:** The number of participants gaining or losing more than 15 ETDRS letters between baseline and 18.9 months mean, post-conversion in  
 446 the first eye (A) and between the point of conversion and 24.9 months post-conversion in the second eye (B).

**Table 1:** List of the key retinal imaging biomarkers evaluated in the FASBAT study and the reading centre definitions.

| <b>Retinal Biomarker</b> | <b>Imaging Modality</b> | <b>Reading Centre Definition</b>   |
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|                          | CFP                     | An area of sharply defined drop out of RPE of at least 175 microns in diameter with two of the following identified; choroidal vessels exposed; well defined margins; scalloped edges. |

*\*SHRM: Subretinal Hyperreflective Material; IRF: Intraretinal Fluid; SRF: Subretinal Fluid; OCT: Optical Coherence Tomography; CFP: Colour Fundus Photography*



**Table 2:** Baseline demographics of the 100 participants whose second eye converted to nAMD

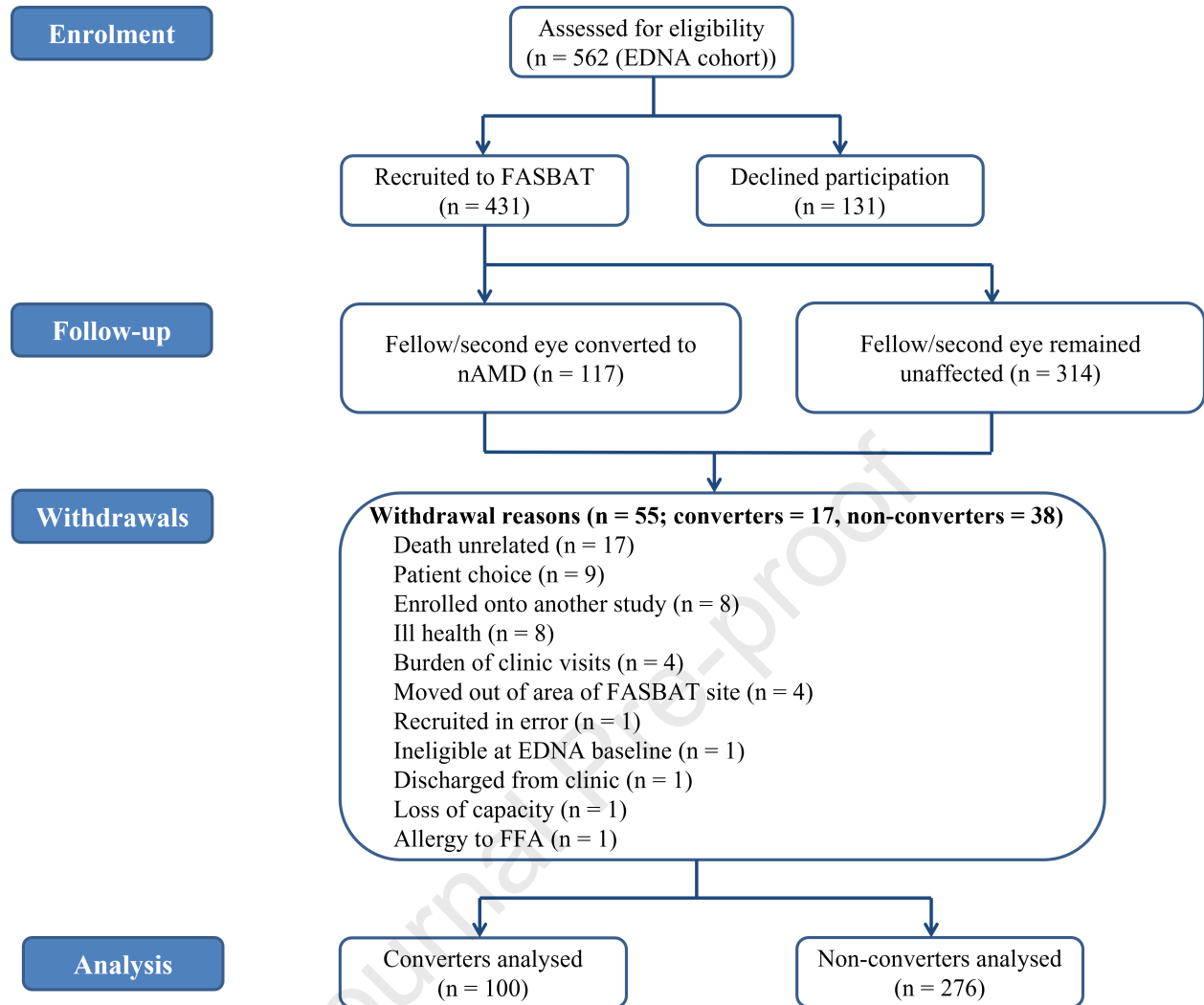
|                                     |             |
|-------------------------------------|-------------|
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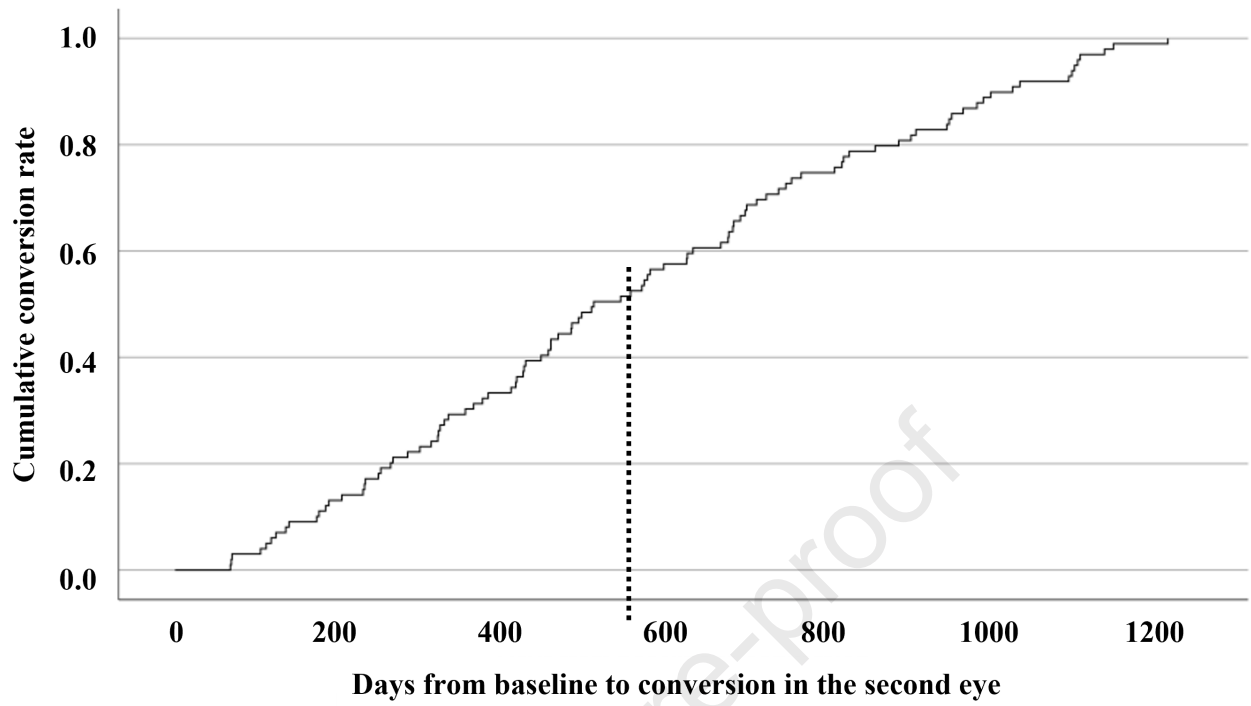
\*SD: Standard Deviation; VA: Visual Acuity; ETDRS: Early Treatment Diabetic Retinopathy Study

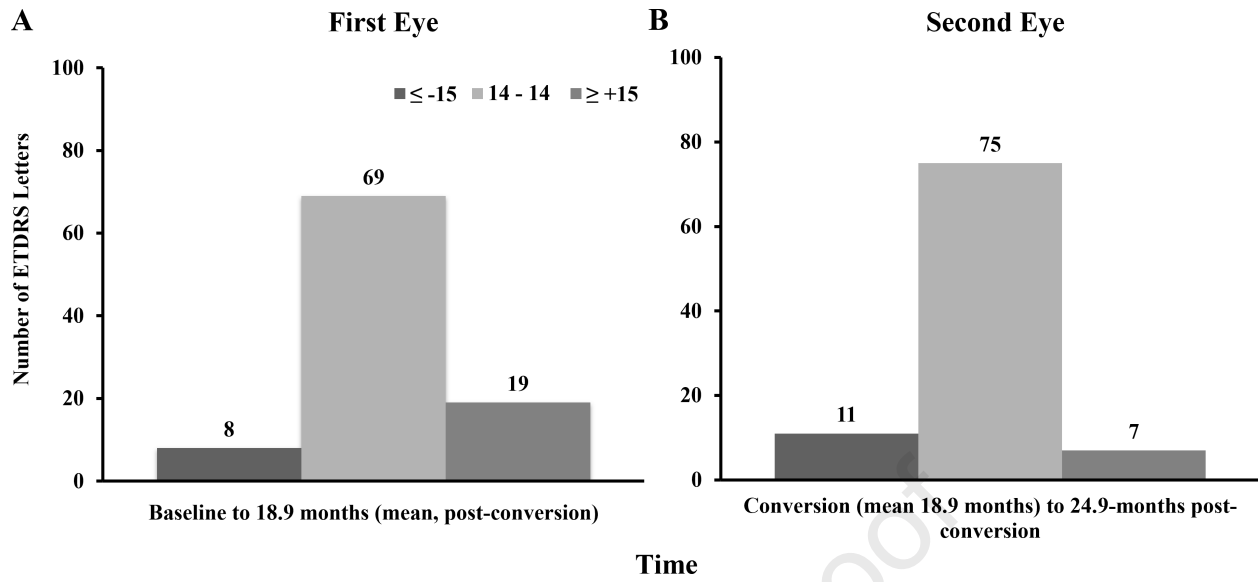
**Table 3:** Retinal biomarker evaluation of the 100 FASBAT participants whose second eye converted to nAMD.

|                      |  | First Eye at diagnosis of<br>nAMD (Baseline) | Second Eye at diagnosis<br>of nAMD (Conversion) | First Eye a mean of 18.9<br>months post-conversion | Second Eye a mean of 24.9<br>months post-conversion |
|----------------------|--|--|---|--|---|
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|                      | Yes (n; %)                                   | 31 (31.3)                                    | 22 (23.4)                                       | 52 (55.3)  | 46 (53.5)   |
|                      | Cannot Grade (n)                             | 1  | 0   | 0  | 1   |
|                      | Missing data (n)                             | 0  | 6   | 6  | 13  |
| <b>SHRM (OCT)</b>    |  |  |   |  |   |
|                      | No (n; %)                                    | 7 (7)  | 21 (22.8)                                       | 7 (7.6)  | 17 (19.5)   |
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| <b>IRF (OCT)</b>     |  |  |   |  |   |
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|                      | Yes (n; %)                                   | 56 (57.7)                                    | 24 (32.9)                                       | 34 (46.5)  | 28 (34.1)   |
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\*CFP: Colour Fundus Photography; OCT: Optical Coherence Tomography; SHRM: Subretinal Hyperreflective Material; SRF: Subretinal Fluid; IRF: Intraretinal Fluid.  $\mu\text{m}$ : Microns; SD: Standard Deviation







# Visual and structural outcomes of eyes with neovascular age-related macular degeneration: FASBAT report 1; An extension to EDNA

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## Precise

Early detection of neovascular age-related macular degeneration in the second eye is associated with greater visual acuity and reduced prevalence of pertinent retinal biomarkers up to 24-months post-conversion.

**ORET-D-23-00804 – Improved structure and function in early detected second eye neovascular age-related macular degeneration; FASBAT/EDNA report 1****FASBAT Study Group:**

Richard P. Gale, York and Scarborough Teaching Hospital (FASBAT Study Chair); Sohba Sivaprasad, Moorfields Eye Hospital; Martin McKibbin, St. James's University Hospital, Leeds; Nicola Hopkins, Colchester Hospital; Louise Downey, Hull Royal Infirmary; Geeta Menon, Frimley Park Hospital; Emily Fletcher, Gloucestershire Royal Hospital; Tunde Peto, Belfast City Hospital; Ben Burton, James Paget University Hospital; Mandeep Bindra, Stoke Mandeville Hospital; Sergio Pagliarini, University Hospitals Coventry & Warwickshire; Faruque Ghanchi, Bradford Royal Infirmary; Sarah MacKenzie, Harrogate District Hospital; Amy Stone, Manchester Royal Eye Hospital; Sheena George, The Hillingdon Hospital; Sanjiv Banerjee, University Hospital of Wales; Konidaris Vasileios, Leicester Royal Infirmary; Steven Dodds, Sunderland Royal Hospital; Savita Madhusudhan, Royal Liverpool University Hospital; Chris Brand, Royal Hallamshire Hospital; Andrew Lotery, Southampton General Hospital; Diane Whistance-Smith, New Cross Hospital; Theo Empeslidis, Leicester Royal Infirmary