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## **Off-label use of biologics for the treatment of refractory and/or relapsing granulomatosis with polyangiitis**

C. Mettler, Ca. Durel, P. Guilpain, B. Bonnotte, F. Cohen-Aubart, M. Hamidou, Jc. Lega, V. Le Guern, F. Lifermann, V. Poindron, et al.

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1 **Concise report**

2 **Off-label use of biologics for the treatment of refractory and/or relapsing**  
3 **granulomatosis with polyangiitis**

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30 **Ethical approval information and data sharing statement:** Study was approved by Local  
31 Institutional Review Board (Cochin Hospital).

32 **Abstract**

33 **Objective.** To describe the efficacy and safety of off-label use of biologics for refractory  
34 and/or relapsing granulomatosis with polyangiitis (GPA).

35 **Methods.** We conducted a French retrospective study including GPA patients who received  
36 off-label biologics for refractory and/or relapsing disease after failure of conventional  
37 immunosuppressive regimens.

38 **Results.** Among 26 patients included, 18 received infliximab (IFX), 2 adalimumab (ADA)  
39 and 6 abatacept (ABA). Biologics were initiated in median as 4<sup>th</sup>-line therapy (IQR 3-6) for  
40 relapsing and/or refractory disease in 23 (88%) and/or significant glucocorticoid-dependency  
41 in 8 cases (31%). At biologics initiation, median (IQR) BVAS and prednisone dose in anti-  
42 TNF- $\alpha$  and ABA recipients were 7 (3-8) and 2 (1-6), and 20 (13-30) mg/day and 20 (15-25)  
43 mg/day, respectively. Clinical manifestations requiring biologics were mainly pulmonary and  
44 ENT manifestations in 58% each. Anti-TNF- $\alpha$  and ABA were continued for a median  
45 duration of 8 months (IQR 6-13) and 11 months (IQR 6-18) respectively. Anti-TNF- $\alpha$   
46 recipients showed remission, partial response and treatment failure in 10%, 30% and 60% at 6  
47 months, and 25%, 20% and 55% at 12 months, respectively. ABA recipients showed  
48 remission, partial response and treatment failure in 17%, 33% and 50% at 6 months and 17%,  
49 33% and 50% at 12 months. One patient treated with IFX experienced life-threatening  
50 reaction while one patient treated with ABA experienced a severe infection.

51 **Conclusion.** This real-life study suggests that off-label use of anti-TNF- $\alpha$  and abatacept  
52 shows efficacy in less than 50% of refractory and/or relapsing GPA.

53

54 **Introduction**

55 Granulomatosis with polyangiitis (GPA) is an antineutrophil cytoplasmic antibody (ANCA)-  
56 associated vasculitis (AAVs), characterized by granulomatous necrotizing vasculitis of small  
57 vessels (1). Standard of care is based on a combination of glucocorticoids (GCs) and  
58 immunosuppressive agents (2). For remission-induction of organ-threatening or life-  
59 threatening GPA, European League Against Rheumatism (EULAR) and French guidelines  
60 recommend the use of GCs in combination with either cyclophosphamide (CYC) or rituximab  
61 (RTX) (2,3). Maintenance therapy is indicated in all cases of GPA because of the increased  
62 risk of relapse and is based on low-dose GCs and RTX (2,3). However, relapses remain  
63 frequent (4) and refractory manifestations may occur, especially subglottic stenosis and  
64 orbital mass (5). Case reports and non-randomized open-label studies have suggested that  
65 biologics (other than rituximab) could be a therapeutic option in relapsing and/or refractory  
66 GPA (6). A prospective open-label study suggested that the addition of adalimumab (ADA), a  
67 tumor necrosis factor-alpha (TNF- $\alpha$ ) blocking agent, to CYC for the treatment of severe AAV  
68 could be associated with increased response rates and reduced exposure to GCs when  
69 compared to historical cohorts (8). However, etanercept, a fully human soluble TNF- $\alpha$   
70 receptor fusion protein, showed negative results in the randomized controlled WGET trial (7).  
71 Also, Langford et al. provided promising open-label data supporting the therapeutic efficacy  
72 of abatacept (ABA) in non-severe relapsing GPA (9).

73 In the present study, we analyzed the off-label use of biologics for the treatment of  
74 refractory and/or relapsing GPA after failure of conventional immunosuppressive regimens.

75

76 **Patients and methods**

77 **Study design**

78 We performed a nationwide retrospective multicenter study in French departments involved  
79 within the French Vasculitis Study Group (FVSG) network between 1<sup>st</sup> January 2018 and 31<sup>st</sup>  
80 December 2020. Physicians from Internal Medicine, Nephrology, Pulmonology and  
81 Rheumatology departments were invited to participate in this retrospective study by e-mails.  
82 Patients fulfilling ACR 1990 criteria for GPA and receiving off-label biologics were included.  
83 The study was approved by Local Institutional Review Board (Cochin Hospital).

#### 84 **Clinical and laboratory assessment**

85 Clinical and biological data were retrospectively collected by practitioners in charge of the  
86 patients using a standardized form and reviewed by CM and BT. Collected data included age,  
87 gender, manifestations at diagnosis and during follow-up, previous drug history, biologics  
88 use, clinical and biological situation at the initiation of biologics and during the follow-up.  
89 Biological assessment included serum C-reactive protein (CRP), serum creatinine level,  
90 ANCA titers and specificity, proteinuria and hematuria. The Birmingham Vasculitis Activity  
91 Score version 2003 (BVAS) was used to assess disease activity at baseline and during follow-  
92 up. **Assessment of GPA activity**

93 Evolution of GPA-related manifestations was evaluated at 6 and 12 months, whatever the  
94 immunosuppressive or immunomodulatory agents used. In the absence of data available  
95 specifically at 6 and 12 months, the latest information available in the follow-up was used.  
96 Remission was defined by the absence of active manifestations of vasculitis (BVAS=0) and a  
97 dose of GCs  $\leq 5$  mg per day. Partial remission was defined by a BVAS=0 and GCs dose  
98 between 6 and 10 mg per day. Therapeutic failure was defined by refractory disease with  
99 persistent active manifestations of vasculitis despite treatment (BVAS>0), or inability to  
100 achieve GCs dose <10 mg/day, or relapse on therapy. Side effects related to the use of  
101 biologics was also collected and analyzed.

#### 102 **Statistical analyses**

103 Data are presented as medians with interquartile (IQR), as appropriate for continuous  
104 variables, and number with proportion (%) for qualitative variables.

105

## 106 **Results**

### 107 **Patients' characteristics**

108 Twenty-six patients with GPA were included, with a median age of 44.5 years (IQR 36-64).  
109 ANCA were present in 81%, with PR3-ANCA specificity in 91%. Patients' characteristics  
110 and previous treatments are summarized in **Table 1**. Previous treatments were oral GCs  
111 (100%), intravenous CYC (92%), methotrexate (54%), oral CYC (46%), azathioprine (46%),  
112 pulses of methylprednisolone (38%), RTX (35%), intravenous immunoglobulins (23%),  
113 mycophenolate mofetil (15%) and plasma exchanges (15%). Biologics were used in median  
114 in 4<sup>th</sup>-line (IQR 3-6) and mostly before 2010 (median 2007, IQR 2004-2014).

115 Twenty patients received TNF- $\alpha$  blockers, including infliximab (IFX) in 18 cases at a dose  
116 between 3 and 10 mg/kg, mainly with initial infusions at weeks 0, 2, and 6 followed by a  
117 maintenance regimen every 4 weeks, and ADA in two cases at 40 mg every 2 weeks. Six  
118 patients received ABA at a dose of 10 mg/kg every 4 weeks in 5 patients and every 6 weeks  
119 for one patient.

### 120 **GPA manifestations requiring biologics initiation**

121 **Table 2** summarizes patients' characteristics at biologics initiation in TNF- $\alpha$  blockers and  
122 ABA recipients. Clinical manifestations requiring biologics were relapsing and/or refractory  
123 disease in 23 (88%) and/or significant GCs-dependency in 8 cases (31%). Pulmonary and ear,  
124 nose and throat (ENT) diseases were present in 58% each. Tracheobronchial stenosis and  
125 ocular manifestations were present in 6 cases (23%) and 3 cases (12%), respectively. At  
126 biologics initiation, median (IQR) BVAS and prednisone dose in TNF- $\alpha$  blockers and ABA

127 recipients were 7 (3-8) and 2 (1-6), and 20 (13-30) mg/day and 20 (15-25) mg/day,  
128 respectively.

### 129 **Follow-up**

130 Median duration of biologics was 8 months (IQR 6-13) for anti-TNF- $\alpha$ -treated patients and 11  
131 months (IQR 6-18) in ABA-treated patients.

132 In anti-TNF- $\alpha$ -treated patients, median prednisone dose decreased from 20 (IQR 13-30,  
133 missing n=7) mg/day to 10 (IQR 5-10, missing n=11) mg/day at 6 months and 5 (IQR 0-6,  
134 missing n=12) mg/day at 12 months (**Figure 1A**). Remission, partial response and treatment  
135 failure in anti-TNF- $\alpha$ -treated patients were achieved in 10%, 30% and 60% at 6 months and  
136 25%, 20% and 55% at 12 months (**Figure 1B and Figure 2**). In ABA-treated patients, median  
137 prednisone dose decreased from 20 (IQR 15-25, missing n=1) mg/day to 10 (IQR 6-15,  
138 missing n=1) mg/day at 6 months and 8 (6-9, missing n=3) mg/day at 12 months (**Figure 1A**).  
139 In ABA-treated patients, remission, partial response and treatment failure were reached in  
140 17%, 33% and 50% at 6 months and 17%, 33% and 50% at 12 months (**Figure 1C and**  
141 **Figure 2**).

### 142 **Safety of biologics**

143 Anti-TNF- $\alpha$ -treated patients experienced minor reaction after infusion in 3 (16%) patients,  
144 one (5%) severe allergic life-threatening reaction and 3 (16%) other adverse events, including  
145 pulmonary infection, asthmatiform dyspnea and depressive state in one case each. ABA-  
146 treated patients experienced one (17%) minor reaction after infusion and one (17%) other  
147 adverse event, including pyogenic sinusitis and aspergillosis.

148

### 149 **Discussion**

150 Despite major breakthroughs during the last decade in the field of AAV, the  
151 management of refractory and/or relapsing GPA remains challenging. In the present study, we

152 describe the off-label use of TNF- $\alpha$  blockers and ABA for the management of refractory  
153 and/or relapsing GPA.

154         Biologics have revolutionized the treatment of inflammatory diseases, especially AAV  
155 (6). In AAV, rituximab is the only biological agent validated so far for remission induction  
156 and maintenance therapy (2). In GPA and MPA, two randomized controlled trials, RAVE (10)  
157 and RITUXVAS (11), showed that RTX was noninferior to CYC to induce remission of the  
158 disease, with comparable rates of adverse events. MAINRITSAN and RITAZAREM trials  
159 showed that RTX was superior to AZA to maintain remission (12,13). In our study, patients  
160 were mainly treated before the results of the RAVE study in 2010, explaining the low  
161 proportion of prior RTX treatment. However, among the 9 patients treated after 2010, 8  
162 received prior RTX treatment before considering alternative biological agents.

163         In contrast, TNF- $\alpha$  blockers are so far not recommended for remission induction nor  
164 maintenance therapy in AAV. In our study, majority of patients received IFX while only two  
165 patients received ADA. At 6 and 12 months, 60% and 55% of patients did not achieve any  
166 response, i.e., remission or partial response, suggesting that even if TNF- $\alpha$  blockers could be  
167 discussed in rare cases, it shows disappointing results.

168         Six patients were treated with ABA, with only 50% of patients showing remission or  
169 partial response at 6 and 12 months, with no severe adverse event. These data dampen the  
170 findings from the open-label study on ABA which showed a high frequency of disease  
171 remission and prednisone discontinuation (9). However, this study on ABA included 20  
172 patients with non-severe relapsing GPA, mainly with ENT and musculoskeletal  
173 manifestations. The patients treated in our study presented more severe and challenging  
174 manifestations than in the study by Langford *et al.*, since 67% had refractory diseases with  
175 severe and systemic manifestations, mainly tracheobronchial stenosis in half cases and/or  
176 central nervous involvement. Based on these findings, we could hypothesize that ABA may

177 be effective on non-severe GPA relapses, as presented by Langford et *al.*, but probably not on  
178 severe and/or refractory manifestations such as tracheobronchial stenosis, as presented here.

179         Importantly, the small sample size and uncontrolled design represent some limitations.  
180 Study objective was analysis of biologics use, so we did not have exhaustive information  
181 concerning the immunosuppressive agent used after stopping biologics. Moreover, data on the  
182 evolution of BVAS was frequently lacking during follow-up, explaining why we were not  
183 able to accurately analyze its evolution. Indication bias and confounding factors cannot be  
184 ruled out, but these data, even descriptive, provide some preliminary data for discussion  
185 managing severe and refractory patients. The ongoing phase 3 ABROGATE trial on the  
186 treatment of relapsing, non-severe GPA (NCT02108860) will provide some important data for  
187 non-severe relapses, but not for severe and refractory patients like in our study.

188         In conclusion, our data suggest that TNF- $\alpha$  blockers and abatacept may show some  
189 efficacy in refractory and/or relapsing GPA but in less than 50% of cases. Further studies with  
190 larger numbers of patients will provide some data on non-severe relapsing patients but  
191 probably not in severe refractory patients.

192 **Disclosure statement**

193 **C. Mettler** reports no conflicts of interest.

194 **CA. Durel** is VIFOR FRANCE board membership.

195 **P. Guilpain** is a medical expert for LFB (Laboratoire Français du Biofractionnement) and has  
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198 **B. Bonnotte** has been board membership for AMGEN, ROCHE-CHUGAI and reports  
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263 **Figure legends**

264 **Figure 1. Patients' outcome with off-label use of biologics.**

265 **Panel A** presents evolution of median of glucocorticoids dose during treatment by TNF- $\alpha$   
266 blockers and ABA at baseline, 6 months, and 12 months. **Panel B**, Sankey diagrams presents  
267 overall response to therapy at 6 months (M6) and 12 months (M12) after TNF- $\alpha$  blockers  
268 initiation. **Panel C**, Sankey diagrams presents overall response to therapy at 6 months (M6)  
269 and 12 months (M12) after ABA initiation.

270 *Footnote: ABA: Abatacept, TNF- $\alpha$ : tumor necrosis factor alpha, F: Failure, PR: Partial*  
271 *response, R: Remission.*

272

273 **Figure 2. Patients' follow up with off-label use of biologics.**

274 Each row stands for a patient, the first column shows the biologic used, the second column  
275 details the delay between the GPA diagnosis and the biologic's initiation. Columns named 1  
276 to 24 represent the months of follow-up. The last column presents the immunosuppressive  
277 agent use in association with the biologic. At 6 and 12 months, the GPA activity is rated (i.e.,  
278 failure, partial remission and remission) whatever the immunosuppressive or  
279 immunomodulatory agents used. In the absence of data available specifically at 6 and 12  
280 months, the latest information available in the follow-up was used. Shaded boxes represent  
281 months in which biologic therapy is used, dotted patterns represent months in which the  
282 associated immunosuppressant is used. Black boxes represent period without information  
283 about patient evolution.

284 *Abbreviations: AZA, Azathioprine; F, Failure; IS, Immunosuppressive drug; MTX,*  
285 *Methotrexate; oralCYC, oral Cyclophosphamide; PR, Partial remission; R, Remission.*

## **Tables**

**Table 1. Patients' characteristics before the off-label use of biologics.**

**Table 2. Patients' characteristics at the initiation of biologics.**

## Tables

**Table 1. Patients' characteristics before the off-label use of biologics.**

	All (n=26)	Anti-TNF- $\alpha$		ABA (n=6)
		IFX (n=18)	ADA (n=2)	
<b>Patients' characteristics at GPA diagnosis</b>				
Age, median (IQR)	45 (36-64)	50 (39-68)	40 (38-42)	37 (33-49)
Female, n (%)	17 (65%)	11 (61%)	2 (100%)	4 (67%)
Histological evidence of vasculitis, n (%)	13 (50%)	10 (56%)	1 (50%)	2 (33%)
<b>Clinical characteristics at diagnosis</b>				
ENT involvement, n (%)	20 (77%)	13 (72%)	2 (100%)	5 (83%)
Pulmonary involvement, n (%)	19 (73%)	14 (78%)	1 (50%)	4 (67%)
Constitutive symptoms, n (%)	12 (46%)	9 (50%)	1 (50%)	2 (33%)
Arthralgia/arthritis, n (%)	12 (46%)	7 (39%)	2 (100%)	3 (50%)
Glomerulonephritis, n (%)	10 (39%)	7 (39%)	2 (100%)	1 (17%)
Ocular manifestations, n (%)	8 (31%)	5 (28%)	1 (50%)	2 (33%)
Peripheral neuropathy, n (%)	7 (27%)	4 (22%)	1 (50%)	2 (33%)
Cutaneous involvement, n (%)	5 (19%)	3 (17%)	1 (50%)	1 (17%)
Central nervous system, n (%)	2 (8%)	1 (6%)	0	1 (17%)
Gastrointestinal involvement, n (%)	1 (4%)	1 (6%)	0	0
BVAS, median (IQR)	11 (6.5-22.0)	8.5 (5-15)	22 (21-23)	11 (6.5-21.5)
<b>Laboratory findings at diagnosis</b>				
Positive ANCA, n (%)	21 (81%)	15 (83%)	2 (100%)	4 (67%)
PR3-ANCA, n	19	14	2	3
MPO-ANCA, n	2	1	0	1
CRP, median (IQR), mg/l	113 (20-231)	125 (32-231)	20*	151 (2-300)
Serum creatinine, median (IQR), $\mu$ mol/L	69 (56-78)	76.5 (61-100)	40*	66 (53-70)
<b>Treatments prior to biologics</b>				
Oral glucocorticoids, n (%)	26 (100%)	18 (100%)	2 (100%)	6 (100%)
IV cyclophosphamide, n (%)	24 (92%)	18 (100%)	1 (50%)	5 (83%)
Methotrexate, n (%)	14 (54%)	8 (44%)	1 (50%)	5 (83%)
Azathioprine, n (%)	12 (46%)	7 (39%)	1 (50%)	4 (67%)
Oral cyclophosphamide, n (%)	12 (46%)	9 (50%)	0	3 (50%)
Pulse methylprednisolone, n (%)	10 (38%)	8 (44%)	0	2 (33%)
Rituximab <sup>a</sup> , n (%)	9 (35%)	3 (17%)	1 (50%)	5 (83%)
Cotrimoxazole, n (%)	9 (35%)	3 (17%)	2 (100%)	4 (67%)
IV immunoglobulins, n (%)	6 (23%)	4 (22%)	0	2 (33%)
Mycophenolate mofetil, n (%)	4 (15%)	4 (22%)	0	0
Plasma exchanges, n (%)	4 (15%)	3 (17%)	1 (50%)	0

\* Data from only one patient, <sup>a</sup> Rituximab was used in 1/17 patients treated before 2010 (1 in ABA group) and in 8/9 patients treated after 2010 (3 in IFX group, 4 in ABA group, and 1 ADA group).

Abbreviations: ABA: Abatacept; ADA: Adalimumab; ANCA: Antineutrophil cytoplasmic antibodies; Anti-TNF- $\alpha$ : anti-tumor necrosis factor-alpha; BVAS: Birmingham Vasculitis Activity Score; CRP: serum C-reactive protein; ENT: ear, nose and throat; GCs: glucocorticoids; IFX: Infliximab; MPO: myeloperoxidase; IV: intravenous; PR3: proteinase 3

**Table 2. Patients' characteristics at the initiation of biologics.**

	All (n=26)	Anti-TNF- $\alpha$		ABA (n=6)
		IFX (n=18)	ADA (n=2)	
<b>Characteristics of the disease requiring biologics</b>				
Delay between diagnosis and initiation, median (IQR, months)	63 (21-144)	45 (16-70)	104 (64-144)	145 (72-178)
Number of lines before biologics, median (IQR)	4 (3-6)	4 (3-5)	3.5 (3-4)	5.5 (4-7)
Relapsing and/or refractory disease	23 (88%)	16 (89%)	1 (50%)	6 (100%)
High dose GCs-dependency	8 (31%)	4 (22%)	1 (50%)	3 (50%)
<b>Clinical characteristics at the initiation of biologics</b>				
ENT involvement, n (%)	15 (58%)	9 (50%)	2 (100%)	4 (67%)
Lung involvement, n (%)	15 (58%)	12 (67%)	0	3 (50%)
Constitutive symptoms, n (%)	5 (19%)	4 (22%)	0	1 (17%)
Tracheobronchial stenosis, n (%)	6 (23%)	3 (17%)	0	3 (50%)
Arthralgia/arthritis, n (%)	4 (15%)	3 (17%)	1 (50%)	0
Glomerulonephritis, n (%)	4 (15%)	4 (22%)	0	0
Ocular manifestations, n (%)	3 (12%)	2 (11%)	1 (50%)	0
Central nervous system, n (%)	2 (8%)	1 (6%)	0	1 (17%)
Peripheral neuropathy, n (%)	1 (4%)	0	0	1 (17%)
BVAS, median (IQR)	6 (2-7)	6 (3-7)	8.5 (7-10)	2 (1-6)
<b>Laboratory findings at initiation of biologics</b>				
Positive ANCA, n (%)	11 (42%)	8 (44%)	1 (50%)	2 (33%)
PR3-ANCA, n	11/11	8/8	1/1	2/2
CRP, median (IQR), mg/l	14 (2-43)	16 (5-77)	12*	2 (2-23)
Serum creatinine, median (IQR), $\mu$ mol/L	75 (61-83)	78 (62-84)	55*	73 (60-85)
<b>Ongoing treatments at the time of biologic use</b>				
Oral glucocorticoids, n (%)	20 (77%)	13 (72%)	2 (100%)	5 (83%)
<i>Prednisone dose, median (range)</i>	20 (14-30)	20 (13-30)	30 (20-40)	20 (15-25)
Methotrexate, n (%)	7 (27%)	6 (33%)	0	1 (17%)
Cotrimoxazole, n (%)	5 (19%)	1 (6%)	1 (50%)	3 (50%)
Azathioprine, n (%)	6 (23%)	3 (17%)	0	3 (50%)
Others drugs, n (%)	4 (15%)	4 (22%)**	0	0
Oral cyclophosphamide, n (%)	3 (12%)	3 (17%)	0	0
Pulse methylprednisolone, n (%)	1 (4%)	1 (6%)	0	0

\* Data from only one patient

\*\* Others concomitant treatments: IV cyclophosphamide (n=1), IV immunoglobulins (n=1), mycophenolate mofetil (n=2)

Abbreviations: ABA: Abatacept; ADA: Adalimumab; ANCA: Antineutrophil cytoplasmic antibodies; Anti-TNF- $\alpha$ : anti-tumor necrosis factor-alpha; BVAS: Birmingham Vasculitis Activity Score; CRP: serum C-reactive protein; ENT: ear, nose and throat; GCs: glucocorticoids; IFX: Infliximab; IV: intravenous; PR3: proteinase 3

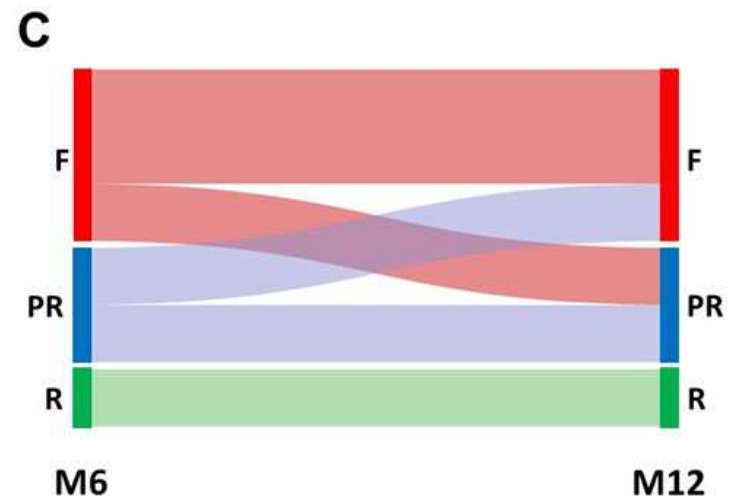
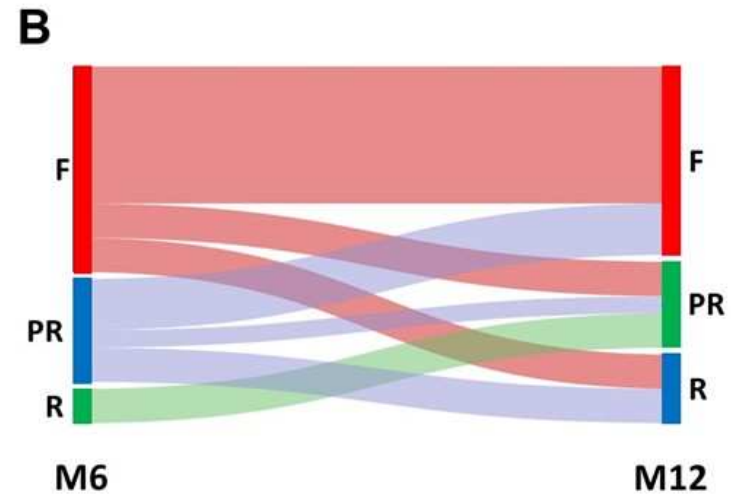
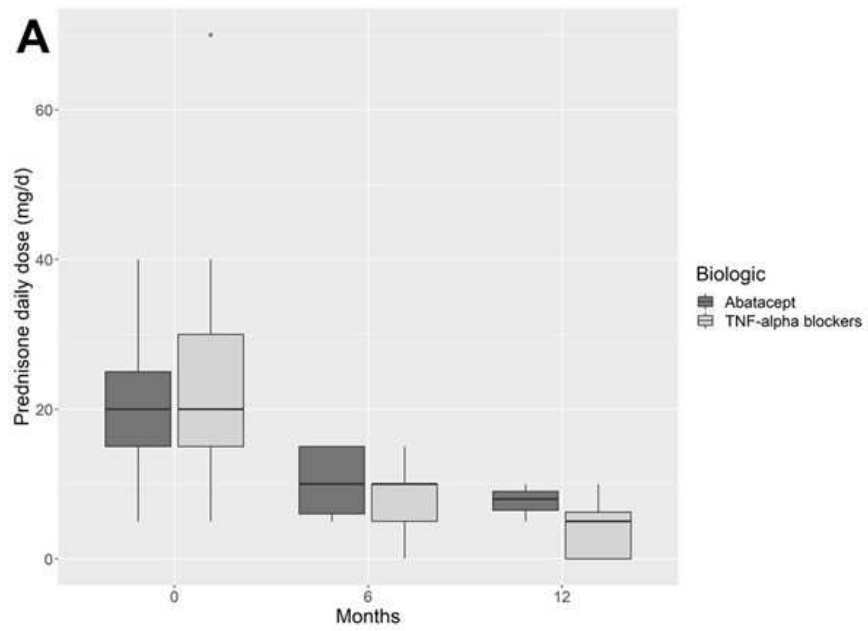


Figure 1. Patients' outcome with off-label use of biologics.

Biologic	Delay (years)	Follow-up	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	Associated IS drugs
ADA	12							F						F													0
ADA	5							R						R													0
IFX	1							F						R													MTX
IFX	12							R						R													MTX-AZA
IFX	6							F						F													0
IFX	4							F						R													AZA
IFX	5							PR						F													0
IFX	1							F						F													0
IFX	4							PR						PR													0
IFX	0							PR						F													0
IFX	5							F						F													oralCYC
IFX	1							F						PR													MTX
IFX	5							PR						F													0
IFX	13							F						PR													0
IFX	16							F						F													0
IFX	1							F						F													0
IFX	13							F						F													0
IFX	2							PR						PR													oralCYC
IFX	1							F						F													0
IFX	3							PR						R													MTX
ABA	15							F						F													0
ABA	2							F						PR													MTX
ABA	15							PR						F													AZA
ABA	6							PR						PR													AZA
ABA	11							F						F													AZA
ABA	13							R						R													0

Figure 2. Patients' follow up with off-label use of biologics.

## Off-label use of biologics for the treatment of refractory and/or relapsing granulomatosis with polyangiitis

**OBJECTIVE :** Efficacy and safety of biologics in refractory and/or relapsing GPA

### METHODS



**FRENCH  
NATIONWIDE STUDY**



**RETROSPECTIVE  
2001-2020**



**PATIENTS WITH  
REFRACTORY  
RELAPSING GPA**  
n=26  
Median age 44.5 yrs  
ANCA+ : 81%

### BIOLOGICS

#### 4<sup>TH</sup>-LINE THERAPY

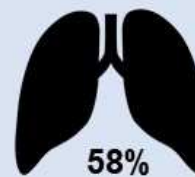
TNF- $\alpha$  blockers n=20  
*Infliximab* n=18  
*Adalimumab* n= 2  
Abatacept n=6



#### INDICATIONS

Relapsing and/or refractory disease (88%)  
Glucocorticoid-dependency (31%)

#### CLINICAL MANIFESTATIONS requiring biologics

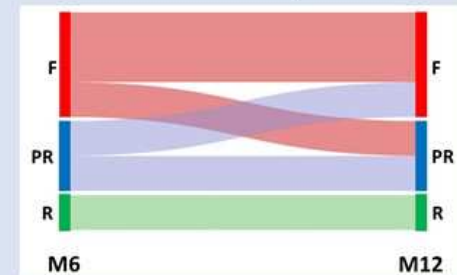


### OUTCOME

#### TNF $\alpha$ -blockers



#### Abatacept



**CONCLUSION** This retrospective study suggests that off-label use of TNF-alpha blockers and abatacept, after failure of conventional immunosuppressive regimens, shows efficacy in less than 50% of refractory and/or relapsing GPA

Abbreviations: F: Failure, M6: 6 months after biologic initiation, M12: 12 months after biologic initiation, PR: Partial response, R: Remission, SAE: severe adverse event.

Graphical abstract