Rituximab for Eosinophilic Granulomatosis with Polyangiitis: a Systematic Review of Observational Studies

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Abstract

Eosinophilic Granulomatosis with Polyangiitis (EGPA) is a rare systemic necrotizing and eosinophil-rich vasculitis affecting small- to medium-sized vessels and characterized by asthma, sinusitis, pulmonary infiltrates and neuropathy. Data on Rituximab (RTX) use, restricted to uncontrolled cohort studies and case reports, support its effectiveness and safety. However, most of the evidence comes from small sized studies, describing mixed population (i.e. ANCA Associated Vasculitis-AAV). Based on this background, we conducted a systematic review about the use of RTX in EGPA patients in order to analyze the available evidence and to provide useful findings to inform the design of future, reliable clinical trials. Although 53% out of the evaluable EGPA patients treated with RTX appears to achieve complete remission, with a higher rate of response in pANCA positive subgroup, we strongly believe that a number of sources of heterogeneity impairs a clear interpretation of the results and limits their transferability in clinical practice.

Introduction

Eosinophilic granulomatosis with polyangiitis (EGPA, formerly known as the Churg–Strauss syndrome) is a rare systemic necrotizing and eosinophil-rich vasculitis affecting small- to medium-sized vessels, characterized by asthma, sinusitis, pulmonary infiltrates and neuropathy (B1,B2,Z1).

American College of Rheumatology (ACR) established six classification criteria (B4) and additional criteria were added by Chapel Hill Consensus Conference (CHCC) (B5). EGPA is currently classified among antineutrophil cytoplasm autoantibody (ANCA)–associated vasculitis (AAV), sharing features with granulomatosis with polyangiitis (GPA, formerly Wegener's granulomatosis) and microscopic polyangiitis (MPA) (N2).

Due to the rarity of AAV and the inherent diagnostic difficulties in these complex diseases, clinical research is scarce, particularly for EGPA, whose prevalence (10–24/million) is 10 times lower than those of GPA and MPA (A2,H1). Studies considering EGPA an individual entity are few, small-sized, and underpowered (F1). Previous systematic reviews (SRs) (H5,H6,H7) analyzed the evidence on the therapeutic use of biological agents for all AAV and not specifically for EGPA. Rituximab (RTX) is approved for GPA and MPA, and it has been proposed for EGPA (H3). However, data on effectiveness and safety of RTX use for EGPA come from uncontrolled studies and anectodal reports (L2,G1). Moreover, heterogeneity among studies, such as disease's definition and staging, activity and outcome assessment, treatment schedule, adverse

events' definitions and reporting, impairs results extrapolations to practice (L3).

Based on this background, we performed a SR about the use of RTX in EGPA patients: 1. to evaluate the weakness of available research, providing useful findings to uniform the design of future clinical trials; 2. to critically summarize actual evidence about RTX efficacy and safety in EGPA.

Methods

Protocol and registration

This study has been registered on PROSPERO (registration number 137629). Search strategy, clinical study selection as well as data extraction and analysis were performed and reported according to PRISMA guidelines (Table S1). Institutional review board approval was not required.

Eligibility criteria

We included clinical studies (clinical trials, cohort observational studies, case series and case reports) reporting: 1. Adult patients affected by EGPA; 2. Treatment with RTX; 3. Any clinical outcomes defined as clinical remission, relapse, mortality. Research questions were formulated according to the PICO format: Population, Intervention, Comparator, Outcomes. Observational studies reported in subsequent publications through years, but describing the same cohort of patients, have been detected and the most recent article has been selected and included in the systematic review, in order to avoid duplicates.

Information sources

A systematic search was conducted in PubMed/MEDLINE, Scopus, Web of Science and the Cochrane library databases up to the end of January 2019, through a comprehensive

search strategy without language restriction, combining MeSH terms and free terms (Table S2). Reference lists of all pertinent retrieved clinical studies were also analyzed through a manual search, in order to identify additional relevant papers. Moreover, conference abstracts were searched in Scopus database and screened for pertinence.

Study selection and data extraction

Four blinded investigators (VGM, DO, GR and AA) independently screened titles and abstracts to identify potentially relevant articles. Duplicate publications were actively searched and excluded. Full-texts of potentially pertinent articles were obtained and analyzed by four independent investigators and data were extracted in a pre-designed structured form including patients' characteristics, study design, outcomes and results. Any disagreement about papers inclusion or data extraction was resolved by discussion with a fifth independent reviewer (GP).

In details, data from each study were extracted as follows: first author name and year of publication, study design, patients' characteristics (age, sex), sample size, diagnostic criteria used, baseline vasculitis activity score, ANCA status, disease extension (organ involvement) and refractoriness, Rituximab schedule of administration, concomitant treatments, median follow-up (months), complete and partial remission definitions and other evaluated outcomes, number of patients that achieved remission and steroid reduction (PDN≤7.5 mg/day), number of relapses, serious adverse events, infections, neoplasms and deaths reported.

Missing information or data were required to corresponding authors, contacting them by email. 113 emails were sent, aiming to obtain more details about patients' characteristics, diagnostic criteria used, outcome definitions and results, but only 13 corresponding authors answered.

Statistical Analysis

In order to identify factors influencing the response to rituximab therapy, five different logistic regression models have been performed, using complete remission, partial remission, steroid reduction, death and relapse as binary dependent variables, respectively. The following variables have been evaluated: patients' age, sex, concomitant treatments, and RTX schedule of administration, ANCA status and peripheral nervous system involvement. Missing data have been replaced using multiple imputation procedure. Odds ratios (together with their 95% confidence intervals) were directly estimated from regression coefficients. A significance level of 0.05 was used for all the statistical tests. Multiple imputation has been executed by a dedicated spreadsheet and all statistical analyses have been performed through SPSS Statistics, version 23.0.

Results

The extensive search of the literature followed by a careful manual screening of retrieved articles led to find 45 papers pertinent to our question (Table S1 and S3). Search algorithm is detailed in Figure 1. According to our aims, all retrieved studies have been admitted to data extraction regardless of their methodological quality.

In details, we found 16 retrospective cohort studies (T1-T16), describing 296 EGPA patients, 8 case series (T17-T24) (48 patients), 3 prospective cohort studies (T25-T27) which enrolled 6 cases, and 18 single case reports (T28-45), for a total of 368 EGPA patients. Table S1 shows characteristics and results of all studies.

Published reports are largely lacking. In particular, more than one-third of the studies (including about 80% of patients), do not provide specific critical information about subjects affected by EGPA (Table 1).

More than 80% of evaluable patients achieved complete or partial remission (Table 2). However, a significant percentage of studies reported results obtained from EGPA patients together with other AAV, preventing from a separate analysis. Multivariate analysis, although strongly limited by high rate of missing data, shows a clear tendency towards a better response in pANCA positive patients (Table 3). Moreover, studies enrolling mixed AAV populations show higher remission rates. Response rate does not seem to be influenced by type of diagnostic criteria, concomitant therapies, RTX schedules, extension of organ involvement.

About one-third of treated patients are evaluable for AEs. AEs occurred in 13 of 115 evaluable cases (11%). In particular, 5 pneumological complications and 8 infusion reactions are to be highlighted. Among minor effects, we notice hypogammaglobulinemia (1%), transient visual disturbance (1%) and nausea (1%). In addition we found reports of respiratory infections in 45 cases (17%), one Herpes Zoster infection (0,4%), one septic shock (0,4%), one invasive fungus infection (0.4 %), two pyelonephritis (0,8%) and one cellulitis (0,4%). Finally, neoplasms were observed in 12 of 117 evaluable patients (10%): one astrocytoma and 11 urological tumors**.**

Discussion

According to the EGPA Consensus Task Force (E1), patients should initially be treated with glucocorticoids (GCs) alone in limited disease (E2) and with a combination of GCs and an immunosuppressant, mainly cyclophosphamide, in severe forms, defined as the presence of a 5 factor score (FFS) ≥ 1 (E2,D1,F3). Remission can be achieved in >85% of patients after these first-line treatments, but it is noteworthy that 85% of them cannot stop GC treatment because of asthma and/or ear nose and throat (ENT) manifestations (F4,F5) with a high rate of side effects (E4,E6). Moreover, relapses occur in more than one-third of cases during glucocorticoid tapering. Given these important limits, there is a need for additional, more effective and safer therapies. From the first description in 2001 (A1) about the use of biological agent in a patient with AAV, substantial progress has been made. From the last 10 years, Rituximab has been using in the treatment of AAV and many RCTs have been successfully conducted, mainly enrolling patients affected by GPA and MPA (M1,M2,M4,M5).

While hundreds of EGPA patients have also been treated, data on RTX efficacy in this population are scarce, of poor quality and coming only from case reports, small case series and retrospective cohort studies. Indeed, RTX use for EGPA patients was recently recommended by an expert consensus to treat patients with EGPA with renal involvement or refractory disease (E1), but with a low grade of recommendation according to the European Vasculitis Society (EUVAS) survey participants (E2,H4).

To our knowledge, this is the first SR of observational studies including only adults with EGPA. Ramos-Casals e coworkers (Y1) in 2008 published a SR about the use of biological agents in adult patients with systemic autoimmune diseases and they concluded that experience with RTX in EGPA was anecdotal (3 cases reported), and no recommendations could be made. Muñoz et al. (U1) performed a search about RTX in the treatment of EGPA in MEDLINE and LILACS until 2014 and included 27 patients reporting clinical remission in 16 and clinical response in 8. In another SR about the role of RTX in treatment of some vasculitis (H7), the authors suggested that, considering the reported general efficacy in AAV, RTX was likely effective in EGPA, but data was limited to 3 articles only. The recent SR by Ayan et al. (Y3) underlined many uncertainties on optimal use of RTX in AAV, but there was no specific comment about its use in EGPA patients.

Our SR pointed out several methodological issues. First of all, more than one-third of the studies (about 80% of patients), did not provide specific information about subjects affected by EGPA. Second, we noticed a wide heterogeneity in disease definition and stages, activity status, outcomes definitions and measures, schedules of administration, follow-up duration, adverse events definition and reporting and use of concomitant drugs.

Regarding to disease definition, we found that only in half of the retrieved studies (and in one quarter of the total patients) criteria used for EGPA's diagnosis were reported. The 1990 ACR classification criteria (B4) are the most popular for this disease,

even if a formal validation has never been performed (Q1). Other classifications, such Lanham criteria (Q2), Chapel Hill consensus conference (CHCC) system (B5) or EMA algorithm (Q3), presented even more limits and new classification criteria for EGPA using the Classification of Vasculitis Study (DCVAS) dataset (Q4) is waiting for final endorsement by EULAR and ACR. Neverthless, ACR diagnostic criteria for EGPA have been used only in one third of the evaluable patients identified by our SR.

In our analysis more than 80% of evaluable patients achieved complete or partial remission, but we strongly believe that the above mentioned limits hamper the reliability of these data. In fact, a significant percentage of studies reported results obtained from EGPA patients together with other AAV, preventing from a separate analysis. Moreover, studies enrolling mixed AAV populations reported higher remission rates, as shown by the multyvariate analysis in which there is a trend to an association between studies which enrolled patients from AAV cohort as covariate and complete remission with an OR of 3.55 (95% CI: 1.14-11.09). Differences among criteria used to define outcomes further obstacle results interpretation and comparison. In fact, similarly to the diagnostic criteria, only in one fifth of the studies the reported data about the complete or partial remission were according the ACR criteria.

As previous reports (K1,K2), our SR confirmed a higher rate of response in pANCA positive subgroup with an OR of 3.97 (95% CI: 0.98-16.01) for complete remission in the multivariate analysis. It is noteworthy that Lyons et al. (X16) performer a first genome-wide association study (GWAS) with 684 EGPA patients suggesting that

treatment strategies might be different between ANCA-positive and -negative EGPA patients.

A minority of studies in our SR reported AEs: only one-third of treated patients are evaluable for this important outcome with an overall 11% of AEs , but more studies are needed to come to better conclusions about this topic.

Main limitations of our SR are the heterogeneity of the included studies regarding the characteristics of patient populations, concomitant immunosuppressive therapies, RTX protocols, outcome measures, and remission definitions and the high prevalence of missing data, only marginally corrected by contacting corresponding Authors. In particular, multivariate analysis was strongly limited.

Moreover, the available studies are very small-sized. The low methodological quality prevents any attempt to verify the consistency of the results and to generate reliable summary measures of efficacy. Thus, the pooled response rate shown should be interpreted as the theoretical average response rate perceived by readers of literature about use of RTX in EGPA, rather than the true effect.

Maybe the two ongoing RCTs evaluating the efficacy of RTX for EGPA as remission induction therapy vs CTX (the REOVAS trial [NCT02807103]) and as remission maintenance therapy vs azathioprine (the MAINRITSEG trial [NCT03164473]) respectively will shed more light on this important topic.

Conclusion

In conclusion, our SR identified major flaws in available literature. Accordingly, our key recommendation for further research is to conduct prospective cohort studies, using validate criteria for disease and outcomes definition. Embedded trials, possibly RCTs, conducted with homogeneous therapeutic schedules, stratification for ANCA status, appropriate follow-up and a careful data reporting, could then definitely clarify the effectiveness of RTX in EGPA.

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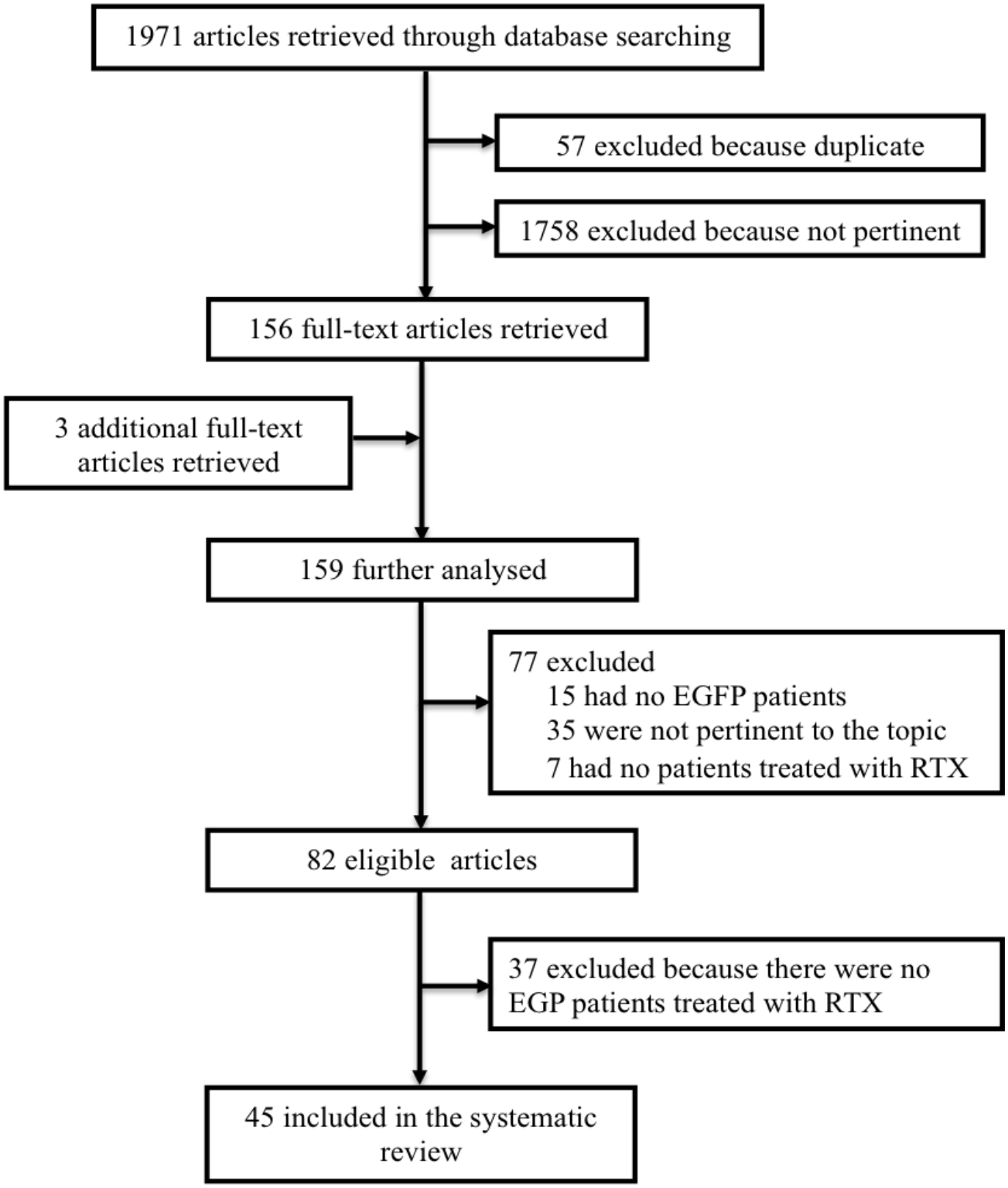

Figure 1: Flow diagram of the study selection process

	N of patients (% of evaluable patients)	Missing data	
		Studies (%)	Patients (%)
Age in years: **Median (IQR): 47 (24)** **Mean (range): 47 (16-72)**		16/45 (36)	319/368 (87)
EGPA diagnostic criteria:		23/45 (51)	271/368 (74)
- ACR	30 /97 (31)		
- Other or no specified	67/97 (69)		
ANCA Status		17/45(38)	320/368 (87)
- Negative	17/48 (35)		
- p-ANCA positive	25/48 (52)		
- c-ANCA positive	6/48 (12)		
Prevalent organ involvement:		16/45 (36)	319/368 (87)
≥ 2 organs involved and/or neuropathy	41/49 (84)		
RTX schedule		16/45 (33)	306/368 (83)
- 2 x 1000 mg	38/62 (61)		
- 4 x 375 mg	18/62 (29)		
- others	6/62 (10)		
Concomitant Therapy		13/45 (29)	292/368 (79)
- None	9/76 (12)		
- Immunosuppressive drugs	49/76 (64)		
- Prednisone ≤ 7,5 mg/dl	3/76 (4)		
- Others	15/76 (20)		

Table 1. Characteristics of patients enrolled in retrieved studies.

I denominatori in giallo tornano, ma io non capisco a cosa si riferiscano; ad esempio ANCA status negative sono 17/48, ma chi sono i 48? Scusate ma questa tabella non l'ho fatta io

Outcome	N of studies available	N of patients available	Results (%)	Missing Data N of studies (%)	Missing Data N of patients (%)
Complete remission:	33/45 (73)	236/368 (64)	126/236 (53)	12/45 (27)	132/368 (36)
CR not defined			52/126 (22)		
CR according to ACR criteria			55/126 (23)		
CR defined by authors			19/126 (8)		
Partial remission:	27/45 (60)	156/368 (42)	56/156 (36)	18/45 (40)	212/368 (58)
PR not defined			19/56 (12)		
PR according to ACR criteria			26/56 (17)		
PR defined by the authors			11/56 (7)		
Mortality	35/45 (78)	158/368 (43)	2/158 (1)	10/45 (22)	210/368 (57)
Steroid reduction ≤ 7,5 mg/die	26/45 (58)	129/368 (35)	73/129 (57)	19/45 (42)	239/368 (65)
Relapse	37/45 (82)	187/368 (51)	37/187 (20)	8/45 (18)	181/368 (49)

Table 2. Outcomes achieved by EGPA patients enrolled in retrieved studies.

Qui invece i denominatori sono evidenti

Covariates	Outcome	Multivariate analysis	Odd Ratio
Patients enrolled from AAV cohort	Complete Remission	p=0.092	3.55 (95% CI 1.14-11.09)
	Partial Remission	p>0.05	
	Steroid reduction	p>0.05	
	Death	p>0.05	
	Relapse	p>0.05	
Study Design:	Complete Remission	p>0.05	
	Partial Remission	p>0.05	
Case report	Reduction steroid	p>0.05	
Case series < 5 patients	Death	p>0.05	
Case series ≥ 5 patients	Relapse	p>0.05	
Age	Complete Remission	p>0.05	
	Partial Remission	p>0.05	
	Steroid reduction	p>0.05	
	Death	p>0.05	
	Relapse	p>0.05	
EGPA diagnostic criteria:	Complete Remission	p>0.05	
	Partial Remission	p>0.05	
ACR	Steroid reduction	p>0.05	
Others	Death	p>0.05	
	Relapse	p>0.05	
ANCA Type:	Complete Remission	ANCA+ p=0,093 pANCA+ p=0,53	3,97 (95% CI 0.98-16.01)
ANCA negative			
p- ANCA positive			
c- ANCA			
	Partial Remission	ANCA+ p=0.001 pANCA+ p<0.010	0.036 (95%CI 0,006-0,21)
	Steroid reduction	p>0.05	
	Death	p>0.05	
	Relapse	p>0.05	
Prevalent organ involvement:	Complete Remission	p>0.05	
	Partial Remission	p>0.05	
organs involved ≥2 and/or neuropathy	Steroid reduction	p>0.05	
	Death	p>0.05	

	Relapse	p>0.05
RTX schedule:	Complete Remission	p>0.05
	Partial Remission	p>0.05
1000 mg x2	Steroid reduction	p>0.05
375 mg x4	Death	p>0.05
Others	Relapse	p>0.05
Concomitant Therapy:	Complete Remission	p>0.05
	Partial Remission	p>0.05
None	Steroid reduction	p>0.05
Immunosuppressive drugs	Death	p>0.05
Prednisone <7,5 mg/die	Relapse	p>0.05
Others (plasmapheresis or Ig)		

Table 3. Multivariate analysis and Odd Ratio: measures of association between covariates and outcomes. Steroid reduction: Prednisone ≤ 7,5 mg/die.

	Article	Study design	Population	Intervention	Outcome	Results N (%)
1	Adami et al. (2018) [T28]	Case report	• **Enrolled from AAV cohort:** No • **EGPA diagnostic criteria:** ACR criteria • **N° of EGPA patients:** 1 • **Age median:** 17F • **BVAS at baseline:** 13 • **Refractory or relapsing:**0(0) • **Anca positive type:** negative • **Prevalent organ involvement:** lung, heart	• **RTX schedule:** 375 mg/m2/wk x 4 wks • **RTX cycles:**2 • **Concomitant therapy**: MP iv 1 grx3 • **Follow up (median months**):24	• **Complete remission according to ACR criteria**	1 (100)
					• **Partial remission**	0 (0)
					• **Steroid reduction PDN≤ 7,5 mg/die**	1 (100)
					• **Death**	0 (0)
					• **Relapse**	0 (0)
					• **Other outcomes:**	Reduction of EOS and RCP. Improvement of chest HRCT and cardiac MRI
					• **AES/Infections/Neoplasia**	0(0)/0(0)/0(0)
2	Aguirre-Valencia et al. (2017) [T29]	Case report	• **Enrolled from AAV cohort:** No • **EGPA diagnostic criteria:** ACR • **N° of EGPA patients: 1** • **Age median:** 16F • **BVAS at baseline: nd** • **Refractory or relapsing:** 1 (100) • **Anca positive type:** negative • **Prevalent organ involvement:** skin, rhinitis	• **RTX schedule:** 1gr x2 given 2 wks apart. • **RTX cycles:** 2 • **Concomitant therapy**: PS and AZA, MFM+OMA thereafter • **Follow up (median months**):24	• **Complete remission**	0 (0)
					• **Partial remission not defined**	1 (100)
					• **Steroid reduction PDN≤ 7,5 mg/die**	1 (100)
					• **Death**	0 (0)
					• **Relapse**	1 (100)
					• **Other outcomes:**	Control of asthma and rhinitis
					• **AES/Infections/Neoplasia:**	1 severe broncospasm (100)/0(0)/0(0)
3	Ananth et al. (2016) [T30]	Case report	• **Enrolled from AAV cohort:** No • **EGPA diagnostic criteria:** ACR criteria • **N° of EGPA patients: 1**	• **RTX schedule**: 50 mg/h iv (infusion stopped for AES after 15 minutes) • **RTX cycles:** 0	• **Complete remission**	nd
					• **Partial remission**	nd
					• **Steroid reduction PDN≤ 7,5 mg/die**	nd

			• **Age median:** 17M • **BVAS at baseline:** nd • **Refractory or relapsing:** 1 (100) • **Anca positive type:** negative • **Prevalent organ involvement:** asthma, sinusitis.	• **Concomitant therapy**: CYC 15 mg/kg, PS 50 mg/d, Ig: 12 gr/d for 5 ds • **Follow up (median months)**:nd		
					• **Death**	nd
					• **Relapse**	nd
					• **Other outcomes:**	0(0)
					• **AES/Infections/Neoplasia**	1 (100) severe dyspnea and wheezing/nd/nd
4	Baikunje et al. (2016) [T31]	Case report	• **Enrolled from AAV cohort:** No • **EGPA diagnostic criteria:** Lanham criteria • **N° of EGPA patients: 1** • **Age median:** 42 M • **BVAS at baseline:** nd • **Refractory or relapsing:** 1(100) • **Anca positive type:** p-ANCA+(100) • **Prevalent organ involvement:** lung, kidney, skin.	• **RTX schedule:** 375 mg/m2/wk x 4 wks • **RTX cycles:** 1 • **Concomitant therapy**: MS iv 3 gr pulses and then PS 1 mg/kg. • **Follow up (median months)**:12	• **Complete remission according to ACR criteria**	1 (100)
					• **Partial remission**	0 (0)
					• **Steroid reduction PDN≤ 7,5 mg/die**	0 (0)
					• **Death**	0 (0)
					• **Relapse**	0 (0)
					• **Other outcomes:**	0 (0)
					• **AES/Infections/Neoplasia**	0(0)/0(0)/0(0)
5	Bouldouyre et al. (2015) [T17]	Case series	• **Enrolled from AAV cohort:**No • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:** 2 F • **Age median:** 33 and 44 • **BVAS at baseline:** nd • **Refractory or relapsing:**2(100) • **Anca positive type:** 2 negative • **Prevalent organ involvement:** upper airway, lung, arthritis, mononeuritis	• **RTX schedule:** 375 mg/m2/wk x 4 wks • **Concomitant therapy**: PS unclear dose • **Follow up (median months)**: nd	• **Complete remission not defined**	nd
					• **Partial remission**	nd
					• **Steroid reduction PDN≤ 7,5 mg/die**	nd
					• **Death**	0 (0)
					• **Relapse**	nd
					• **AES/Infections/N**	2(100)bronchospasm/nd/nd

			multiplex		**eoplasia**	
6	Cartin Ceba et al. (2011) [T25]	Prospective cohort study	• **Enrolled from AAV cohort:** No • **EGPA diagnostic criteria:** Lanham's ACR 1990 or CHCC • **N° of EGPA patients:** 3 • **Age median:** 54 • **Sex (%):** 2F 1M • **BVAS at baseline:** 6 (6,6,8) • **Refractory or relapsing:** 1(33) • **Anca positive type:** 3 MPO+ • **Prevalent organ involvement:** kidney, lung, peripheral neuropathy, myophaty, lung	• **RTX schedule:** 375 mg/m2/wk x 4 wks • **Concomitant therapy**: PS <10 mg/d (n =1) • **Follow up (median months**): 12	• **Complete remission defined by the author**	3 (100)
					• **Partial remission**	nd
					• **Steroid reduction PDN≤ 7,5 mg/die**	2 (66)
					• **Death**	0 (0)
					• **Relapse**	1 (33)
					• **AES/Infections/Neoplasia**	0(0)/1 (33) bronchitis/0(0)
7	Charles et al. (2013) [T1]	Retrospective cohort study	• **Enrolled from AAV cohort:** Yes • **EGPA diagnostic criteria:** CHCC • **N° of EGPA patients:** 1 • **Age median:** 71 • **Sex (%):** 1M • **BVAS at baseline:** nd • **Refractory or relapsing:** 0(0) • **Anca positive type:** nd • **Prevalent organ involvement:** nd	• **RTX schedule:** 375 mg/m2/wk x 4 wks • **Concomitant therapy**: PS 15 mg/d • **Follow up (median months**):6	• **Complete remission according to ACR criteria:**	0 (0)
					• **Partial remission:**	0 (0)
					• **Steroid reduction:**	0 (0)
					• **Death:**	0 (0)
					• **Relapse:**	0 (0)
					• **AES/Infections/Neoplasia:**	0(0)/1(100) septic shock and pneumonitis/0(0)
8	Denis et al.(2017) [T2]	Retrospective cohort study	• **Enrolled from AAV cohort:** No • **EGPA diagnostic criteria:** ACR1990 or CHCC	• **RTX schedule:** nd • **Concomitant therapy**:nd	• **Complete remission defined by the author:**	5 (38)

			• **N° of EGPA patients:** 13 • **Age median:** nd • **Sex (%):** nd • **BVAS at baseline:** 4 (0-19) • **Refractory or relapsing:** 13(100) • **Anca positive type:** nd • **Prevalent organ involvement:** sinusitis, lung,heart and peripheral nervous system	• **Follow up (median months**):12	• **Partial remission defined by the author:**	3 (23)
					• **Steroid reduction:**	7(54)
					• **Death:**	0(0)
					• **Relapse:**	5(38)
					• **AES/Infections/Neoplasia:**	1(5) nausea/0(0)/0(0)
9	Diamanti et al (2014) [T32]	Case report	• **Enrolled from AAV cohort:** No • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:** 1 • **Age median:** 31 • **Sex (%):** F • **BVAS at baseline:** nd • **Refractory or relapsing:** 0(0) • **Anca positive type:** p-ANCA+ • **Prevalent organ involvement:** asthma, rhinitis, peripheral nervous system, eosinophilia	• **RTX schedule:** 500 mg/weakly for 4 week every 6 months(3 cycles) • **RTX cycles**: 3 • **Concomitant therapy**:PS (unclear dose) • **Follow up (median months**):12	• **Complete remission not defined:**	1(100)
					• **Partial remission not defined:**	0 (0)
					• **Steroid reduction PDN≤7,5 mg/dl:**	1 (100)
					• **Death:**	0 (0)
					• **Relapse:**	0 (0)
					• **AES/Infections/Neoplasia:**	0(0)/0(0)/0(0)
10	Donvik et al (2011) [T18]	Case series	• **Enrolled from AAV cohort:** no • **EGPA diagnostic criteria:** clinical manifestations and skin biopsy • **N° of EGPA patients:** 2 • **Age median:** 42,5(35 and 50)	• **RTX schedule:** 1000 mg given 2 weeks apart, followed by 1000 mg every 6 months. • **RTX cycles**: 5 and 2 • **Concomitant therapy**: PS 5 mg /d, MTX 7,5 mg/wk(n=1),AZA 50 mg x2/die (n=1) • **Follow up (median**	• **Complete remission not defined:**	1 (50)
					• **Partial remission not defined:**	1 (50)
					• **Steroid reduction PDN ≤7,5 mg/die :**	2 (100)

			• **Sex (%):** 1F e 1M • **BVAS at baseline:** nd • **Refractory or relapsing:** 0 (0) • **Anca positive type:** 2ANCA- • **Prevalent organ involvement:** asthma,nasal polyposis, sinusitis,skin, lung, ENT(hearing loss), eosinophilia	**months**): 19 and 6	• **Death:**	0 (0)
					• **Relapse:**	0 (0)
					• **Other outcomes**	Rise in FEV1:17% and 15% Rise in FEV1/FVC:1% and 18%
					• **AES/Infections/Neoplasia:**	0(0)/0(0)/0(0)
11	Dubrau et al(2012) [T3]	Retrospective cohort	• **Enrolled from AAV cohort:** No • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:** 11 • **Age median:** nd • **Sex (%):** nd • **BVAS at baseline:** 7(1-27) • **Refractory or relapsing:** nd • **Anca positive type:** 5ANCA+(45) • **Prevalent organ involvement:** sinusitis,skin, lung, peripheral neuropathy, GI tract, arthritis, eyes.	• **RTX schedule:** nd • **RTX cycles**: nd • **Concomitant therapy**: MTX, AZA,LE. • **Follow up (median months**): 8	• **Complete remission not defined:**	1 (9)
					• **Partial remission not defined:**	7 (64)
					• **Steroid reduction PDN ≤7,5 mg/die :**	Nd
					• **Death:**	Nd
					• **Relapse:**	Nd
					• **AES/Infections/Neoplasia:**	0(0)/3(27) 1 pneumonia and 2 bronchitis/nd
12	Edwards MH. Et al. (2015) [T33]	Case report	• **Enrolled from AAV cohort:** No • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:** 1 • **Age median:** 31 • **Sex (%):** F(post-partum)	• **RTX schedule:** nd • **RTX cycles**: nd • **Concomitant therapy**: IV and oral glucocorticoids,CF • **Follow up (median**	• **Complete remission:**	0(0)
					• **Partial remission:**	1(100)
					• **Steroid reduction PDN ≤7,5 mg/die**	Nd

			• **BVAS at baseline:** nd • **Refractory or relapsing:** 1(100) • **Anca positive type:** ANCA- • **Prevalent organ involvement:** dyspnoea, arthralgia, skin.	**months**): nd	**:**	
					• **Death:**	nd
					• **Relapse:**	nd
					• **Other outcomes:**	0(0)
					• **AES/Infections/Neoplasia:**	Nd
13	Emmi et al(2018) [T4]	Retrospective cohort	• **Enrolled from AAV cohort:** No • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:** 21 • **Age median:** nd • **Sex (%):** nd • **BVAS at baseline:** 11(2-24) • **Refractory or relapsing:** 21(100) • **Anca positive type:** 10ANCA+(48) • **Prevalent organ involvement:** renal,peripheral neuropathy,lung,GI tract,skin.	• **RTX schedule:** 1gr x 2 given 2 wks apart 9 schedule RTX maintenance(500 mg/6 months) • **RTX cycles**: nd • **Concomitant therapy**: PS, OMA or Ig. • **Follow up (median months**): 24	• **Complete remission according to ACR criteria**	6(29)
					• **Partial remission according to ACR criteria**	5(24)
					• **Steroid reduction PDN ≤7,5 mg/die**	6(29)
					• **Death:**	2(9)
					• **Relapse:**	5(24)
					• **Other outcomes:**	**Reduction of blood EOS**
					• **AES/Infections/Neoplasia:**	1(4) infusion reaction/3(14)1 pneumonia and 2 bronchitis/1(4) Astrocytoma
14	Emmi et al. (2015) [T34]	Case report	• **Enrolled from AAV cohort:** No • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:** 1 • **Age median:** 41 • **Sex (%):** F	• **RTX schedule:** 1gr x 2 given 2 wks • **RTX cycles**: nd • **Concomitant therapy**: PS tapered below 20 mg/d	• **Complete remission not defined:**	1(100)
					• **Partial remission not defined:**	0(100)
					• **Steroid reduction PDN ≤7,5 mg/die**	1(100)

			• **BVAS at baseline:** nd • **Refractory or relapsing:** 1(100) • **Anca positive type:** pANCA+(100) • **Prevalent organ involvement:** mononeuritis multiplex,asthma,nasal polyposis,sinusitisy, bloody diarrhoea,peripheral eosinophilia	• **Follow up (median months**): 6	• **Death:**	0(0)
					• **Relapse:**	0(0)
					• **Other outcomes:**	0(0)
					• **AES/Infections/Neoplasia:**	0(0)/0(0)/0(0)
15	Fanouriakis et al. (2015) [T35]	Case Report	• **Enrolled from AAV cohort:** No • **EGPA diagnostic criteria:** ACR • **N° of EGPA patients:** 1 • **Age median:** 51 • **Sex (%):** M • **BVAS at baseline:** 22 • **Refractory or relapsing:** 1(100) • **Anca positive type:** pANCA+(100) • **Prevalent organ involvement:** nasal polyposis, mononeuritis multiplex	• **RTX schedule:** 1gr x 2 given 2 wks, second course 6 months later • **RTX cycles**: 2 • **Concomitant therapy**: MP iv 1 grx2 pulses, MTX 25 mg/wk • **Follow up (median months**): 20	• **Complete remission according to ACR criteria:**	1(100)
					• **Partial remission not defined:**	0(0)
					• **Steroid reduction PDN ≤7,5 mg/die:**	1(100)
					• **Death:**	0(0)
					• **Relapse:**	0(0)
					• **Other outcomes:**	nd
					• **AES/infections/neoplasia n(%):**	0(0)/0(0)/0(0)
16	Gauckler et al. (2018) [T5]	Retrospective cohort	• **Enrolled from AAV cohort:** nd • **EGPA diagnostic criteria:** EMA algorithm • **N° of EGPA patients:** 30 • **Age median:** nd • **Sex (%):** nd • **BVAS at baseline:** nd	• **RTX schedule:** nd • **RTX cycles**: nd • **Concomitant therapy**: nd • **Follow up (median months**): 24	• **Complete remission:**	nd
					• **Partial remission:**	nd
					• **Steroid reduction PDN ≤7,5 mg/die:**	nd
					• **Death:**	nd

			• **Refractory or relapsing:** nd • **Anca positive type:** nd • **Prevalent organ involvement:** nd		• **Relapse:**	nd
					• **Other outcomes:**	nd
					• **AES/Infections/Neoplasia:**	nd/14(47) bronchopulmonary infections/nd
17	Grigoriou et al. (2014) [T36]	Case report	• **Enrolled from AAV cohort:** no • **EGPA diagnostic criteria:** hystological diagnosis • **N° of EGPA patients:** 1 • **Age median:** 22 • **Sex (%):** F • **BVAS at baseline:** nd • **Refractory or relapsing**: 0(0) • **Anca positive type:** ANCA+ • **Prevalent organ involvement:** lung,GI tract, skin	• **RTX schedule:** 1 gr given2 wks apart • **RTX cycles**: nd • **Concomitant therapy**: PS 10 mg/d • **Follow up (median months**): nd	**Complete remission not defined :**	1(100)
					Partial remission:	nd
					Steroid reduction PDN ≤7,5 mg/die:	0(0)
					Death:	0(0)
					Relapse:	0(0)
					Other outcomes:	0 (0)
					AES/Infections/Neoplasia:	nd/nd/nd
18	Hot et al. (2013) [T19]	Case series	• **Enrolled from AAV cohort:** NO • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:** 30 • **Age median:** nd • **Sex (%):** 14F(47) e 16M(53) • **BVAS at baseline:** nd • **Refractory or relapsing:** 30(100) • **Anca positive type:** nd • **Prevalent organ involvement:** nd	• **RTX schedule:** nd • **RTX cycles**: nd • **Concomitant therapy**: nd • **Follow up (median months**): 40	• **Complete remission not defined:**	26 (87)
					• **Partial remission not defined:**	2 (7)
					• **Steroid reduction PDN ≤7,5 mg/die:**	nd
					• **Death:**	0(0)
					• **Relapse:**	8 (26)
					• **Other outcomes:**	nd
					• **AES/Infections/Neoplasia:**	0/0/nd/nd
19	Kaushik et al. (2006) [T37]	Case report	• **Enrolled from AAV cohort:** NO • **EGPA diagnostic**	• **RTX schedule:** 375 mg/m2 x 3 ws. The third infusion was given as a	• **Complete remission:**	0(0)
					• **Partial remission:**	0 (0)

			criteria: ACR • **N° of EGPA patients:** 1 • **Age median:** 49 • **Sex (%):** M • **BVAS at baseline:** nd • **Refractory or relapsing:** 1(100) • **Anca positive type:** c-ANCA+ • **Prevalent organ involvement:** ENT, lung, skin, eyes, arthritis, Kidney.	bolus of 1 gr on the 4th wks. • **RTX cycles**: 1 • **Concomitant therapy**: 100 mg iv MP • **Follow up (median months)**: 3		
					• **Steroid reduction PDN ≤7,5 mg/die:**	0(0)
					• **Death:**	0(0)
					• **Relapse:**	0(0)
					• **Other outcomes:**	Normalisation of ESR,CRP, EOS count and skin vasculitis completed cleavered
					• **AES/Infections/Neoplasia:**	0/1(100) broncopneumonia and herpes zoster/0 (0)
20	Kawano-Dourado et al. (2017) [T6]	Retrospective cohort	• **Enrolled from AAV cohort:** si • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:** 2 • **Age median:** nd • **Sex (%):** nd • **BVAS at baseline:** nd • **Refractory or relapsing:** 2(100) • **Anca positive type:** nd • **Prevalent organ involvement:** lung,sinusitis, peripheral neurophaty, leg ulcer, otomastoiditis	• **RTX schedule:** nd • **RTX cycles**: nd • **Concomitant therapy**: PS20 mg/day • **Follow up (median months)**: 24	• **Complete remission:**	0 (0)
					• **Partial remission not defined:**	10 (100)
					• **Steroid reduction PDN ≤7,5 mg/die:**	0(0)
					• **Death:**	0(0)
					• **Relapse:**	0(0)
					• **Other outcomes:**	nd
					• **AES/Infections/Neoplasia:**	nd/nd/nd
21	Koukoulaki et al.(2006) [T20]	Case series	• **Enrolled from AAV cohort:** nd • **EGPA diagnostic criteria:** ACR • **N° of EGPA patients:** 2 • **Age median:** 35 and 37 • **Sex (%):** 2F • **BVAS at baseline:** 9(9-9)	• **RTX schedule:** 375 mg/m2 x4, 1grx2 weeks apart • **RTX cycles**: 3 and 1 • **Concomitant therapy**: PS • **Follow up (median months)**: 18 and 15	• **Complete remission according to ACR criteria:**	1(50)
					• **Partial remission according to ACR criteria:**	1(50)
					• **Steroid reduction PDN ≤7,5 mg/die:**	2(100)
					• **Death:**	0(0)

			• **Refractory or relapsing:** 2 (100) • **Anca positive type:** 1ANCA- 1nd • **Prevalent organ involvement:** nd		• **Relapse:**	1(50)
					• **Other outcomes:**	Reduction of blood EOS and rise CD19 cells
					• **AES/Infections/Neoplasia:**	0(0)/1 respiratory tract infections/nd
22	Lovric et al. (2009) [T21]	Case series	• **Enrolled from AAV cohort:** si • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:** 2 • **Age median:** 72 • **Sex (%):** F • **BVAS at baseline:** 9 • **Refractory or relapsing:** 1(100) • **Anca positive type:** ANCA- • **Prevalent organ involvement:** nd	• **RTX schedule:** 375mg/m2/wk x 4 wks • **RTX cycles**: 1 • **Concomitant therapy**: PS 40 mg/d • **Follow up (median months)**: 10	• **Complete remission according to ACR criteria:**	0 (0)
					• **Partial remission according to ACR criteria:**	1(100)
					• **Steroid reduction PDN ≤7,5 mg/die:**	nd
					• **Death:**	0(0)
					• **Relapse:**	1(100)
					• **Other outcomes:**	nd
					• **AES/Infections/Neoplasia:**	nd/nd/nd
23	Madsuda et al. (2017) [T38]	Case report	• **Enrolled from AAV cohort:** no • **EGPA diagnostic criteria:** ACR • **N° of EGPA patients:** 1 • **Age median:** 48 • **Sex (%):** F • **BVAS at baseline:** FFS 0 • **Refractory or relapsing:** 0(0) • **Anca positive type:** MPO+ • **Prevalent organ involvement:** subarachnoid haemorrhage, coronary vasculitis	• **RTX schedule:** 375mg/m2/wk x 4 wks • **RTX cycles**: 4 • **Concomitant therapy**: PS 55 mg/d, CYC 500 mg/m2/d x3 every 2 wks, Ig 0,4 g/kg/d x 5 days • **Follow up (median months)**: 2	• **Complete remission:**	nd
					• **Partial remission:**	nd
					• **Steroid reduction PDN ≤7,5 mg/die:**	1(100)
					• **Death:**	0(0)
					• **Relapse:**	0(0)
					• **Other outcomes:**	Disappearence of the sinusitis and SAH at the head CT scan and normal EKG
					• **AES/Infections/Neoplasia:**	0(0)/0(0)/0(0)
24	Martinez-Villaescusa et al. (2013) [T39]	Case report	• **Enrolled from AAV**	• **RTX schedule:**	• **Complete remission not defined:**	1(100)

			cohort: no • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:** 1 • **Age median:** 70 • **Sex (%):** M • **BVAS at baseline**: nd • **Refractory or relapsing:** 0(0) • **Anca positive type:** MPO+ • **Prevalent organ involvement:** kidney, lung.	375mg/m2/wk x 4 wks • **RTX cycles**: nd • **Concomitant therapy**: PS 5 mg/d • **Follow up (median months)**: 60	• **Partial remission:**	nd
					• **Steroid reduction PDN ≤7,5 mg/die:**	1(100)
					• **Death:**	0(0)
					• **Relapse:**	0(0)
					• **Other outcomes:**	0 (0)
					• **AES/Infections/Neoplasia:**	0(0)/0(0)/0(0)
25	Mohammad et al. (2016) [T7]	Retrospective cohort	• **Enrolled from AAV cohort:** no • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:41** • **Age median:** 54(IQR 38,5-61) • **Sex (%):** 21F e 20M • **BVAS at baseline**: 11(IQR6-17,5) • **Refractory or relapsing:** 21(51) • **Anca positive type:** 9p-ANCA+ 4c-ANCA+ 5 unspecified ANCA+ (44) • **Prevalent organ involvement:** lung,ENT, arthritis, skin, peripheral neuropathy, kidney, GI tract, heart, eyes, CNS	• **RTX schedule:** 375 mg/m2/Wks(=10) or 1 grx2 doses given 2 wks apart(=30). 800 mg 2 doses at 2 wk interval (n=1) • **RTX cycles**: nd • **Concomitant therapy**: MFM, AZA, CYC, MTX and Ig. • **Follow up (median months)**: 12	• **Complete remission according to ACR criteria:**	20(49)
					• **Partial remission according to ACR criteria:**	16 (39)
					• **Steroid reduction PDN ≤7,5 mg/die:**	17(41)
					• **Death:**	0(0)
					• **Relapse:**	4(11)
					• **Other outcomes:**	nd
					• **AES/Infections/Neoplasia:**	7 (17) infusion reactions: /5 severe infections : 2 upper respiratory infection, 3 chest infections, 1 pyelonephritis /nd
26	Moura et al. (2018) [T8]	Retrospective cohort	• **Enrolled from AAV cohort:** no • **EGPA diagnostic criteria:** nd	• **RTX schedule:** nd • **RTX cycles**: nd	• **Complete remission not defined:**	15(88)
					• **Partial remission:**	nd

			• **N° of EGPA patients:17** • **Age median:** nd • **Sex (%):** 8F e 9M • **BVAS at baseline**: nd • **Refractory or relapsing:** 6(35) • **Anca positive type: 13** MPO+(76) • **Prevalent organ involvement:** lung, peripheral neuropathy,ENT.	• **Concomitant therapy**: PS 25 mg/d • **Follow up (median months)**: 12	• **Steroid reduction PDN ≤7,5 mg/die:**	nd
					• **Death:**	0(0)
					• **Relapse:**	3(18)
					• **Other outcomes:**	0 (0)
					• **AES/Infections/Neoplasia:**	nd/nd/nd
27	Nagafuchi et al. (2015) [T40]	Case report	• **Enrolled from AAV cohort:** si • **EGPA diagnostic criteria:** CHCC • **N° of EGPA patients:1** • **Age median:** 70 • **Sex (%):** M • **BVAS at baseline**: 4 • **Refractory or relapsing:** 1(100) • **Anca positive type: Panca+**(100) • **Prevalent organ involvement:** Kidney, sinusitis, peripheral neuropathy.	• **RTX schedule:** 375 mg/m2/wk x 4 wks • **RTX cycles**: nd • **Concomitant therapy**: PS • **Follow up (median months)**: 72	• **Complete remission according to ACR criteria:**	1(100)
					• **Partial remission:**	0(0)
					• **Steroid reduction PDN ≤7,5 mg/die:**	1(100)
					• **Death:**	0(0)
					• **Relapse:**	0(0)
					• **Other outcomes:**	0(0)
					• **AES/Infections/Neoplasia:**	1(100) transient visual disturbance /0(0)/1 prostate cancer
28	Najem et al. (2014) [T41]	Case report	• **Enrolled from AAV cohort:** no • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:1** • **Age median:** 56 • **Sex (%):** F • **BVAS at baseline**: 32 • **Refractory or relapsing:** 1(100) • **Anca positive type: 1pANCA+**(100)	• **RTX schedule:** 375 mg/m2/wk x 4 wks • **RTX cycles**: nd • **Concomitant therapy**: PS 150 mg/d, CYC 100 mg/d • **Follow up (median months)**: nd	• **Complete remission not defined:**	1(100)
					• **Partial remission:**	0(0)
					• **Steroid reduction PDN ≤7,5 mg/die:**	Nd
					• **Death:**	0(0)
					• **Relapse:**	0(0)
					• **Other outcomes:**	0(0)

			• **Prevalent organ involvement:** asthma,lung, myositis, kidney,eyes, heart,CNS, retinal artery occlusion.		• **AES/Infections/Neoplasia:**	0(0)/0(0)/0(0)
29	Ng et al. (2014) [T42]	Case report	• **Enrolled from AAV cohort:** no • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:1** • **Age median:** 59 • **Sex (%):** F • **BVAS at baseline**: nd • **Refractory or relapsing:** 1(100) • **Anca positive type: 1cANCA+**(100) • **Prevalent organ involvement:** asthma, peripheral neuropathy ,eyes, skin.	• **RTX schedule:** 1 gr given 2 wks apart • **RTX cycles**: nd • **Concomitant therapy**: CYC iv 500 mg, PSL 1 mg/kg, then AZA • **Follow up (median months)**: nd	• **Complete remission:**	nd
					• **Partial remission:**	nd
					• **Steroid reduction PDN ≤7,5 mg/die:**	1(100)
					• **Death:**	0(0)
					• **Relapse:**	0(0)
					• **Other outcomes:**	1(100).Little improvement of visual acuity
					• **AES/Infections/Neoplasia:**	nd/nd/nd
30	Novikov et al. (2016) [T22]	Case series	• **Enrolled from AAV cohort:** no • **EGPA diagnostic criteria:** ACR and CHCC revisited • **N° of EGPA patients:6** • **Age median:** 49(26-67) • **Sex (%):** 4F e 2M • **BVAS at baseline**: 10(8-14) • **Refractory or relapsing:** 6(100) • **Anca positive type: 3pANCA+ e 1cANCA+**(66) • **Prevalent organ involvement:** asthma, peripheral neuropathy, sinusitis, heart.	• **RTX schedule:** 4 weekly infusions of 0,5 g(n=3), 2 infusion of 1 gr/2 weeks(n=1), 2 infusions of 0,5 g/2weeks(n=2) • **RTX cycles**: nd • **Concomitant therapy**: AZA. • **Follow up (median months)**: 10	• **Complete remission not defined:**	4(67)
					• **Partial remission not defined:**	2(33)
					• **Steroid reduction PDN ≤7,5 mg/die:**	4(67)
					• **Death:**	0(0)
					• **Relapse:**	2(33)
					• **Other outcomes:**	nd
					• **AES/Infections/Neoplasia:**	1(16)severe broncospasm/2(33) bronchitis/0(0)

31	Palamara et al. (2017) [T43]	Case report	• **Enrolled from AAV cohort:** no • **EGPA diagnostic criteria:** ACR 1990 • **N° of EGPA patients:1** • **Age median:** 64 • **Sex (%):** M • **BVAS at baseline**: nd • **Refractory or relapsing:** 0(0) • **Anca positive type: 1MPO+** (100) • **Prevalent organ involvement:** lung, sinusitis, sensory polyneuropathy.	• **RTX schedule:** nd • **RTX cycles**: nd • **Concomitant therapy**: MS iv 500 mgx3 and CYC thereafter. • **Follow up (median months)**: 11	• **Complete remission:**	0(0)
					• **Partial remission:**	0(0)
					• **Steroid reduction PDN ≤7,5 mg/die:**	0(0)
					• **Death:**	0(0)
					• **Relapse:**	1(100)
					• **Other outcomes:**	Improvement of symptons
					• **AES/Infections/Neoplasia:**	nd/nd/nd
32	Pepper et al. (2008) [T23]	Case series	• **Enrolled from AAV cohort: no** • **EGPA diagnostic criteria:** ACR1990 or CHCC • **N° of EGPA patients:2** • **Age median:** 40 and 66 • **Sex (%):** 2M • **BVAS at baseline**: nd • **Refractory or relapsing:** 0(0) • **Anca positive type: 1PR3+/ 1 MPO+** (100) • **Prevalent organ involvement:**lung, kidney,peripheral neurophaty,skin, arthritis, eyes.	• **RTX schedule:** 1 gr given 2 wks apart and 375 mg/m2/wks x4 wks. • **RTX cycles**: 1 • **Concomitant therapy**: steroid CYC and AZA. • **Follow up (median months)**: 9	• **Complete remission defined by the author:**	2(100)
					• **Partial remission:**	nd
					• **Steroid reduction PDN ≤7,5 mg/die:**	nd
					• **Death:**	0(0)
					• **Relapse:**	0(0)
					• **Other outcomes:**	0 (0)
					• **AES/Infections/Neoplasia:**	nd/nd/nd
33	Rees et al. (2011) [T9]	Retrospective cohort	• **Enrolled from AAV cohort:** si • **EGPA diagnostic criteria:** ACR1990 or CHCC • **N° of EGPA patients:1**	• **RTX schedule:** 1 gr given 2 wks apart, • **RTX cycles**: nd • **Concomitant therapy**: CYC	• **Complete remission according to ACR criteria:**	1(100)
					• **Partial remission:**	nd
					• **Steroid reduction PDN ≤7,5 mg/die:**	1(100)

			• **Age median:** 59 • **Sex (%):** M • **BVAS at baseline**: 11 • **Refractory or relapsing:** 0(0) • **Anca positive type: 1PR3+** (100) • **Prevalent organ involvement:**, kidney, peripheral neuropathy.	• **Follow up (median months**): 16		
					• **Death:**	0(0)
					• **Relapse:**	0(0)
					• **Other outcomes:**	0(0)
					• **AES/Infections/Neoplasia:**	0(0)/nd/0(0)
34	Roccatello et al. (2017) [T26]	Prospective observational study	• **Enrolled from AAV cohort:** yes • **EGPA diagnostic criteria:** CHCC • **N° of EGPA patients:2** • **Age median:** nd • **Sex (%):** nd • **BVAS at baseline**: nd • **Refractory or relapsing:** 1(50) • **Anca positive type: 2MPO**(100) • **Prevalent organ involvement:**, kidney, polyneuropathy, skin.	• **RTX schedule:** 375 mg/m2/wk x 4 WKS + 2 doses at 1 and 2 month • **RTX cycles**: nd • **Concomitant therapy**: PS tapered to 5 mg/d • **Follow up (median months**): 119	• **Complete remission defined by the author:**	1(50)
					• **Partial remission defined by the author:**	1(50)
					• **Steroid reduction PDN ≤7,5 mg/die:**	2(100)
					• **Death:**	1(50)
					• **Relapse:**	0(0)
					• **Other outcomes:**	Reduction of RCP and Blood EOS.
					• **AES/Infections/Neoplasia:**	0(0)/0(0)/0(0)
35	Saech et al. (2010) [T44]	Case report	• **Enrolled from AAV cohort:** no • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:1** • **Age median:** 46 • **Sex (%):** M • **BVAS at baseline**: nd • **Refractory or relapsing:** 0(0) • **Anca positive type: 1MPO+** (100) • **Prevalent organ involvement:**, CNS, peripheral neuropathy, asthma,	• **RTX schedule:** 1 gr given 2 wks apart, • **RTX cycles**: nd • **Concomitant therapy**: MFM • **Follow up (median months**): 4	• **Complete remission according to ACR criteria:**	nd
					• **Partial remission:**	nd
					• **Steroid reduction PDN ≤7,5 mg/die:**	nd
					• **Death:**	0(0)
					• **Relapse:**	0(0)
					• **Other outcomes:**	Improvement of CNS symptoms and RMI findings.
					• **AES/Infections/N**	nd/nd/nd

			paranasal sinusitis.		**eoplasia:**	
36	Smith et al. (2006) [T27]	Prospective study	• **Enrolled from AAV cohort:** si • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:1** • **Age median:** 36 • **Sex (%):** F • **BVAS at baseline**: nd • **Refractory or relapsing:** 1(100) • **Anca positive type: ANCA-**(0) • **Prevalent organ involvement:**lung heart, ENT, peripheral neurophaty,skin.	• **RTX schedule:**3x 375 mg 1 dose, 2X 1 gr at relapses. • **RTX cycles**: 3 • **Concomitant therapy**: CYC 500 MG iv along first ifusion of RTX • **Follow up (median months**): 12	• **Complete remission according to ACR criteria :**	nd (remission achieved but not specified if complete or partial)
					• **Partial remission according to ACR criteria:**	nd
					• **Steroid reduction PDN ≤7,5 mg/die:**	nd
					• **Death:**	0(0)
					• **Relapse:**	1(100)
					• **Other outcomes:**	nd
					• **AES/Infections/Neoplasia:**	nd/nd/nd
37	Solans-Laque et al. (2014) [T24]	Case series	• **Enrolled from AAV cohort:** si • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:2** • **Age median:** nd • **Sex (%):** nd • **BVAS at baseline**: nd • **Refractory or relapsing:** 2(100) • **Anca positive type: nd** • **Prevalent organ involvement:** kidney,nasal polyposis,sinusitis,lung,skin,heart, Arthralgia, neurological symptoms	• **RTX schedule:** nd • **RTX cycles**: nd • **Concomitant therapy**:PS 1 mg/kg • **Follow up (median months**): 82	• **Complete remission not defined:**	2(100)
					• **Partial remission:**	Nd
					• **Steroid reduction PDN ≤7,5 mg/die:**	Nd
					• **Death:**	nd
					• **Relapse:**	nd
					• **Other outcomes:**	0(0)
					• **AES/Infections/Neoplasia:**	nd/nd/nd
38	Teixeira et al. (2018) [T10]	Retrospective cohort	• **Enrolled from AAV cohort:** no	• **RTX schedule:** nd • **RTX cycles**: nd	• **Complete remission according to ACR criteria:**	23(43)

			• **EGPA diagnostic criteria:** nd • **N° of EGPA patients:69** • **Age median:** 51(IQR 39,5-58) • **Sex (%):** 44F e 25M • **BVAS at baseline**: 6(3-8,5) • **Refractory or relapsing:** 37(54) • **Anca positive type: 16MPO+, 9PR3+.** • **Prevalent organ involvement:** lung, ENT, arthritis ,skin, kidney, peripheral neuropathy, GI tract, heart, eyes, CNS.	• **Concomitant therapy**:PS • **Follow up (median months)**: 24	• **Partial remission:**	nd
					• **Steroid reduction PDN ≤7,5 mg/die:**	nd
					• **Death:**	nd
					• **Relapse:**	nd
					• **Other outcomes:**	no
					• **AES/Infections/Neoplasia:**	0(0)/9 bronchitis,1 pyelonephritis and 1 cellulitis/nd
39	Thiel et al. (2013) [T11]	Retrospective cohort	• **Enrolled from AAV cohort:** no • **EGPA diagnostic criteria:** Lanham,ACR 1990, CHCC. • **N° of EGPA patients:9** • **Age median:** 45±5 • **Sex (%):** 3F (33) and 6M (66) • **BVAS at baseline**: 18 (IQR 3-21) • **Refractory or relapsing:** 0(0) • **Anca positive type: 4P-MPO/1c-MPO/1p-ANCA.(56)** • **Prevalent organ involvement:**, kidney, peripheral neuropathy, CNS ,skin,heart.	• **RTX schedule:** 1 gr given 2 wks apart(2 doses) • **RTX cycles**: 2 • **Concomitant therapy**:CYC monthly x 3 months,AZA 125 mg/die, MTX 15 mg/wk, MMF • **Follow up (median months)**: 9	• **Complete remission according to ACR criteria:**	1(11)
					• **Partial remission according to ACR criteria:**	8(89)
					• **Steroid reduction PDN ≤7,5 mg/die:**	9(100)
					• **Death:**	0(0)
					• **Relapse:**	0(0)
					• **Other outcomes:**	0(0)
					• **AES/Infections/Neoplasia:**	0(0)/5(56) bronchopulmonary infections/1 seminoma(11)
40	Thiel et al. (2017) [T12]	Retrospective cohort	• **Enrolled from AAV cohort:** no	• **RTX schedule:** 1 gr given 2 wks apart;2x10g every 6	• **Complete remission defined by the author :**	5(36)

			• **EGPA diagnostic criteria:** ACR 1990. • **N° of EGPA patients:14** • **Age median:** 54 (IQR 31-58) • **Sex (%):** 5F (36) and 9M (64) • **BVAS at baseline**: 15 (IQR 10.0-19.0) • **Refractory or relapsing:** 12(86) • **Anca positive type: 5MPO(36)** • **Prevalent organ involvement:**, lung, sinusitis, peripheral neuropathy, CNS,heart, ENT, Kidney,skin,GI tract.	months x18-30 • **RTX cycles**: 2 • **Concomitant therapy**:PS:22,5 mg/d, AZA, MTX, LE or CSP, MFM • **Follow up (median months)**: 48	• **Partial remission defined by the author:**	9(64)
					• **Steroid reduction PDN ≤7,5 mg/die:**	14(100)
					• **Death:**	0(0)
					• **Relapse:**	4(28)
					• **Other outcomes:**	Riduction of EOS, CRP and IgE.
					• **AES/Infections/Neoplasia:**	2(14) hypogammaglobulinemia treated with Ig /0(0) /2 (14): seminoma and prostate carcinoma.
41	Umezawa et al. (2014) [T45]	Case report	• **Enrolled from AAV cohort:** no • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:1** • **Age median:** 44 • **Sex (%):** F • **BVAS at baseline**: nd • **Refractory or relapsing:** 0(0) • **Anca positive type: 1MPO+** • **Prevalent organ involvement: lung**, paralysis of cranial nerves, peripheral neuropathy.	• **RTX schedule:** 375 mg/m2 once wk x4 wks. • **RTX cycles**: nd • **Concomitant therapy**:PDN:10 mg/d • **Follow up (median months)**: 6	• **Complete remission :**	nd
					• **Partial remission:**	nd
					• **Steroid reduction PDN ≤7,5 mg/die:**	nd
					• **Death:**	0(0)
					• **Relapse:**	0(0)
					• **Other outcomes:**	Improvement of neurological symptoms
					• **AES/Infections/Neoplasia:**	0(0)/0(0)/0(0)
42	Ungrasertet al. (2017) [T13]	Retrospective cohort	• **Enrolled from AAV cohort:** si • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:2** • **Age median:** nd	• **RTX schedule:nd** • **RTX cycles**: nd • **Concomitant therapy**:nd • **Follow up (median months)**: 72	• **Complete remission defined by the author :**	2(100)
					• **Partial remission defined by the author:**	0(0)
					• **Steroid reduction PDN ≤7,5 mg/die:**	nd

			• **Sex (%):** nd • **BVAS at baseline:**nd • **Refractory or relapsing:** 0(0) • **Anca positive type: nd** • **Prevalent organ involvement:**, eyes, paralysis of cranial nerves.		• **Death:**	0(0)
					• **Relapse:**	0(0)
					• **Other outcomes:**	nd
					• **AES/Infections/Neoplasia:**	Nd/nd/nd
43	Van Daalen et al. (2017) [T14]	Retrospective cohort	• **Enrolled from AAV cohort:** si • **EGPA diagnostic criteria:** EMA algotithm • **N° of EGPA patients:54** • **Age median:** nd • **Sex (%):** nd • **BVAS at baseline**: nd • **Refractory or relapsing:** nd • **Anca positive type: nd** • **Prevalent organ involvement:** systemic(not specified which organs were involved)	• **RTX schedule:** nd • **RTX cycles**: nd • **Concomitant therapy**: nd • **Follow up (median months)**: 108	• **Complete remission :**	nd
					• **Partial remission:**	nd
					• **Steroid reduction PDN ≤7,5 mg/die:**	nd
					• **Death:**	0(0)
					• **Relapse:**	0(0)
					• **Other outcomes:**	nd
					• **AES/Infections/Neoplasia:**	0(0)/0(0)/7 Urological tumors (18)
44	Vehonoff et al. (2016) [T15]	Retrospective cohort	• **Enrolled from AAV cohort:** no • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:11** • **Age median:** nd • **Sex (%):** nd • **BVAS at baseline**: 14(nd) • **Refractory or relapsing:** 11(100) • **Anca positive type:** 8ANCA+(73) • **Prevalent organ involvement:**nd.	• **RTX schedule:** nd • **RTX cycles**: nd • **Concomitant therapy**:PS 17,5 mg/die • **Follow up (median months)**: 27	• **Complete remission :**	nd *All patients were in complete or partial remission at 3 months.*
					• **Partial remission:**	nd
					• **Steroid reduction PDN ≤7,5 mg/die:**	nd
					• **Death:**	nd
					• **Relapse:**	3(27)
					• **Other outcomes:**	peripherical B cell counts, serum concentrations of IgG, IgA, and IgM

					• **AES/Infections/Neoplasia:**	nd/nd/nd
45	Wendt et al. (2012) [T16]	Retrospective cohort study	• **Enrolled from AAV cohort:** no • **EGPA diagnostic criteria:** nd • **N° of EGPA patients:1** • **Age median:** 71 • **Sex (%):** M • **BVAS at baseline**: 27 • **Refractory or relapsing:** 0(0) • **Anca positive type:** 1MPO+(100) • **Prevalent organ involvement:** lung, kidney.	• **RTX schedule:** 0,5 g given 2 wks apart • **RTX cycles**: nd • **Concomitant therapy**: MFM, PDN, plasma exchange. • **Follow up (median months)**: 6	• **Complete remission according to ACR criteria :**	1(100)
					• **Partial remission according to ACR criteria:**	nd
					• **Steroid reduction PDN ≤7,5 mg/die:**	nd
					• **Death:**	0(0)
					• **Relapse:**	0(0)
					• **Other outcomes:**	nd
					• **AES/infections/Neoplasia**	1 Anaemia(100)/1 Invasive fungus infaction(100)/0(0)

Table S1. Table of evidence of the retrivied studies: characteristics of the population and outcomes..

AES: adverse events, AZA: azatioprina, BVAS: Birmingham Vasculitis Activity Score, CYC: cyclophosfamide, CNS: central nervous system,CR: complete remission, CSP: cyclosporine, CRP:C reactive protein, EGPA: eosinophilic granulomatosis with polyangiitis, ENT: ear, nose and throat, ESR: erythrocyte sedimentation rate, EOS: eosinophil, GI tract: Gastro intestinal tract, Ig: Immunoglobulin, LE: lenalidomide, MFM: micofenolato mofetile, MP: methylprednisolone, MTX: Methotrexate, nd: not defined, OMA: omalizumab, PR: partial remission, PDN: prednisolone, PS: prednisone, RTX: Rituximab.

Table S2. Search strategy.

1."Churg-Strauss Syndrome"[Mesh]

2."Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis"[Mesh]

3."Granulomatosis with Polyangiitis"[Mesh]

4."Microscopic Polyangiitis"[Mesh]

5."anti neutrophil cytoplasmic antibody associated vasculitis"[Title/Abstract]

6.anca associated vasculit*[Title/Abstract]

7.pauci immune vasculit*[Title/Abstract]

8."churg strauss"

9.Allergic Granulomat*[Title/Abstract]

10.Eosinophilic Granulomat*[Title/Abstract]

11.Allergic Angiit*[Title/Abstract]

12.Eosinoph*[Title/Abstract] AND granulomatous[Title/Abstract]))

13.Rituximab OR rituxan OR Mabthera OR cd20 antibod* OR "idec c2b8" OR "gp2013" OR "Rituximab"[Mesh]

14.12 and 13 6231

Filters: Humans; Adult: 19+ years; Adult: 19-44 years; Aged: 65+ years

Table S3. List of studies included in the analysis.

List of studies included in the analysis		
1	Adami G et al. (2018)	Eosinophilic Granulomatosis With Polyangiitis and Cardiac Involvement: A Case Report. Journal of investigational allergology & clinical immunology. 2018;28(4):285-6.
2	Aguirre-Valencia D et al. (2017)	Sequential rituximab and omalizumab for the treatment of eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome). Clin Rheumatol. 2017;36(9):2159-62.
3	Ananth S et al. (2016)	Aggressive eosinophilic granulomatosis with polyangiitis and transverse sinus thrombosis. BMJ Case Reports. 2016;2016.
4	Baikunje S et al. (2016)	Eosinophilic granulomatosis with polyangiitis with severe pulmonary hemorrhage treated with rituximab. Indian Journal of Nephrology. 2016;26(2):142-4.
5	Bouldouyre MA et al. (2015)	Severe bronchospasm associated with rituximab for refractory Churg-Strauss syndrome. Ann Rheum Dis. 2009;68(4):606
6	Cartin-Ceba R et al. (2011)	Rituximab for the treatment of Churg-Strauss syndrome with renal involvement. Nephrology Dialysis
7	Charles P et al. (2014)	Rituximab for induction and maintenance treatment of ANCA-associated vasculitides: a multicentre retrospective study on 80 patients. Rheumatology (Oxford). 2014;53(3):532-9.
8	Denis L et al. (2017)	Off-Label Use of Biological Therapies in Relapsing and/or Refractory Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss). Arthritis & Rheumatology. 2017;69.
9	Diamanti. L et al. (2014)	Spinal hemorrhage in eosinophilic granulomatosis with polyangiitis (Churg-Strauss). J Neurol. 2014;261(2):438-40.
10	Dønvik KK. et al. (2011)	Churg-Strauss syndrome successfully treated with rituximab. Rheumatology International. 2011;31(1):89-91.
11	Dubrau C et al. (2012)	Successful Treatment of Churg-Strauss Syndrome with Rituximab. Arthritis and Rheumatism. 2012;64(10):S1002-S3.
12	Edwards MH et al. (2015)	Postpartum onset and subsequent relapse of eosinophilic granulomatosis with polyangiitis. BMJ Case Reports.
13	Emmi G. et al. (2018)	Scheduled rituximab maintenance reduces relapse rate in eosinophilic granulomatosis with polyangiitis. Ann Rheum Dis. 2018;77(6):952-4.
14	Emmi G et al. (2015)	First report of FIP1L1-PDGFRalpha-positive eosinophilic granulomatosis with polyangiitis. Rheumatology (Oxford). 2015;54(9):1751-3.
15	Fanouriakis A et al. (2015)	Rituximab for eosinophilic granulomatosis with polyangiitis with severe vasculitic neuropathy: Case report and review of current clinical evidence. Seminars in Arthritis and Rheumatism. 2015;45(1):60-6.
16	Gauckler P. et al. (2018)	Trimethoprim-sulfamethoxazole prophylaxis reduces the rate of severe infection complications in patients with ANCA-associated vasculitis and rituximab therapy. Wien Klin Wochen. 2018;130:272-3.
17	Grigoriou A. et al. (2014)	B cell depletion therapy and eosinophilic granulomatosis with polyangiitis with hepatic involvement. Rheumatology (Oxford, England). 2014;53(10):1741.

18	Hot A. et al. (2013)	A multicenter survey of rituximab for eosinophilic granulomatosis with polyangiitis (Churg-Strauss). Presse Medicale. 2013;42(4):698.
19	Kaushik VV. et al. (2006)	Successful use of rituximab in a patient with recalcitrant Churg-Strauss syndrome. Ann Rheum Dis. 2006;65(8):1116-7.
20	Kawano-Dourado L. et al. (2017)	Rituximab For Refractory Granulomatosis With Polyangiitis And For Eosinophilic Granulomatosis With Polyangiitis. American Journal of Respiratory and Critical Care Medicine. 2017;195.
21	Koukoulaki M. et al. (2006)	Rituximab in Churg-Strauss syndrome. Ann Rheum Dis. 2006;65(4):557-9.
22	Lovric S. et al. (2009)	Rituximab as rescue therapy in anti-neutrophil cytoplasmic antibody-associated vasculitis: A single-centre experience with 15 patients. Nephrology Dialysis Transplantation. 2009;24(1):179-85.
23	Matsuda S. et al. (2018)	Eosinophilic granulomatosis with polyangiitis complicated by subarachnoid hemorrhage and coronary vasculitis: a case report and review of the literature. Rheumatol Int. 2018;38(4):689-96.
24	Martinez-Villaescusa M. et al. (2013)	Treatment-resistant Churg-Strauss syndrome: progression after five years using rituximab. Nefrologia. 2013;33(5):737-9.
25	Mohammad AJ. et al. (2016)	Rituximab for the treatment of eosinophilic granulomatosis with polyangiitis (Churg-Strauss). Annals of the Rheumatic Diseases. 2016;75(2):396-401.
26	Moura MC. et al. (2018)	Asthma in Eosinophilic Granulomatosis with Polyangiitis Treated with Rituximab. Arthritis & Rheumatology. 2018;70:1.
27	Nagafuchi H. et al. (2015)	Long-term safety and effi cacy of rituximab in 7 japanese patients with anca-associated vasculitis. Modern Rheumatology. 2015;25(4):603-8.
28	Najem CE. et al. (2015)	Successful use of Rituximab in a patient with recalcitrant multisystemic eosinophilic granulomatosis with polyangiitis. BMJ Case Reports. 2015;2015.
29	Ng CT et al. (2014)	Rituximab is not useful in bilateral ocular involvement caused by eosinophilic granulomatosis with polyangiitis. Acta Reumatologica Portuguesa. 2014;39(3):281-2.
30	Novikov P. et al. (2016)	Rituximab as induction therapy in relapsing eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome): A report of 6 cases. Revue du Rhumatisme (Edition Francaise). 2016;83(1):62-5.
31	Palamara K. et al. (2017)	Case 32-2017: A 64-year-old man with dyspnea, wheezing, headache, cough, and night sweats. New England Journal of Medicine. 2017;377(16):1569-78.
32	Pepper RJ et al. (2008)	Rituximab is effective in the treatment of refractory Churg-Strauss syndrome and is associated with diminished T-cell interleukin-5 production. Rheumatology (Oxford). 2008;47(7):1104-5..
33	Rees F. et al(2011)	Long-term follow-up of different refractory systemic vasculitides treated with rituximab. Clinical Rheumatology. 2011;30(9):1241-5.
34	Roccatello D. et al. (2017)	The "4 plus 2" rituximab protocol makes maintenance treatment unneeded in patients with refractory ANCA-associated vasculitis: A 10 years observation study. Oncotarget. 2017;8(32):52072-7.
35	Saech J. et al. (2010)	Successful use of rituximab in a patient with Churg-Strauss syndrome and refractory central nervous system involvement. Ann Rheum Dis. 2010;69(6):1254-5.

36	Smith KGC. et al. (2006)	Long-term comparison of rituximab treatment for refractory systemic lupus erythematosus and vasculitis: Remission, relapse, and re-treatment. Arthritis and Rheumatism. 2006;54(9):2970-82.
37	Solans-Laque R. et al. (2014)	Eosinophilic granulomatosis with poliangeitis (EGPA): clinical features and outcome in a large serie of spanish patients. Annals of the Rheumatic Diseases. 2014;73:697-8.
38	Teixeira V. et al. (2018)	A 24 Month Analysis of Rituximab Safety and Efficacy in Eosinophilic Granulomatosis with Polyangiitis. Arthritis & Rheumatology. 2018;70:2.
39	Thiel J.et al. (2013)	Rituximab in the treatment of refractory or relapsing eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome). Arthritis Research and Therapy. 2013;15(5).
40	Thiel J. et al. (2017)	Rituximab as Induction Therapy in Eosinophilic Granulomatosis with Polyangiitis Refractory to Conventional Immunosuppressive Treatment: A 36-Month Follow-Up Analysis. Journal of Allergy and Clinical Immunology: In Practice. 2017;5(6):1556-63.
41	Umezawa N.et al. (2014)	Successful treatment of eosinophilic granulomatosis with polyangiitis (EGPA; Formerly ChurgStrauss syndrome) with rituximab in a case refractory to glucocorticoids, cyclophosphamide, and IVIG. Modern Rheumatology. 2014;24(4):685-7.
42	Ungprasert P. et al. (2017)	Clinical characteristics of inflammatory ocular disease in anti-neutrophil cytoplasmic antibody associated vasculitis: A retrospective cohort study. Rheumatology (United Kingdom). 2017;56(10):1763-70.
43	Van Daalen EE et al. (2017)	Effect of rituximab on malignancy risk in patients with ANCA-Associated vasculitis. Annals of the Rheumatic Diseases. 2017;76(6):1064-9.
44	Venhoff N. et al. (2016)	Comparison of rituximab with cyclophosphamide as induction therapy in eosinophilic granulomatosis with polyangiitis (churg-strauss syndrome): a 24 months follow-up analysis. Annals of the Rheumatic Diseases. 2016;75:563.
45	Wendt M. et al. (2012)	Rituximab in relapsing or refractory ANCA-associated vasculitis: a case series of 16 patients. Scand J Rheumatol. 2012;41(2):116-9.