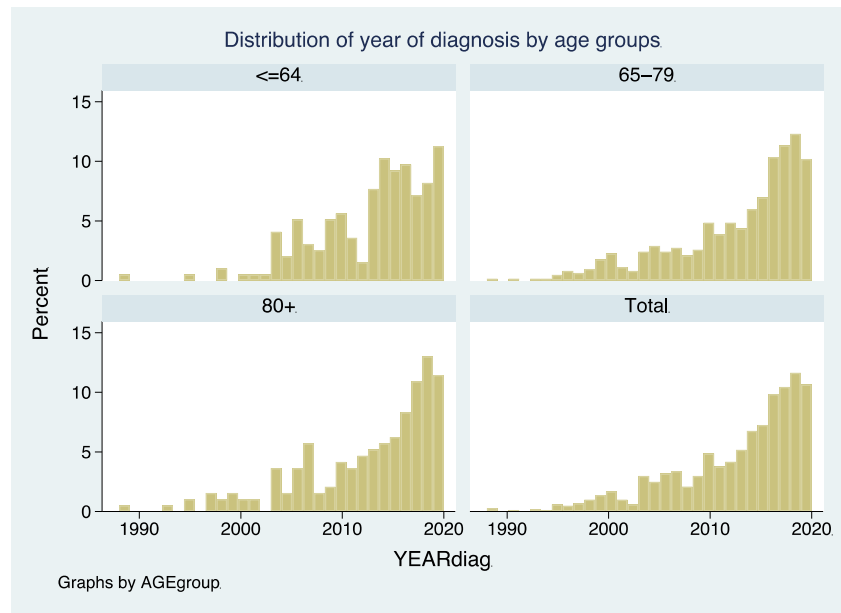


Supplementary material

Distribution of year of diagnosis

The percentage of patients diagnosed before 2000 (potentially influencing availability of immunosuppressive drugs and treatment strategies) is very small (66 patients, 6.57% of the cohort, compared to 93.43% of patients diagnosed in more recent years).

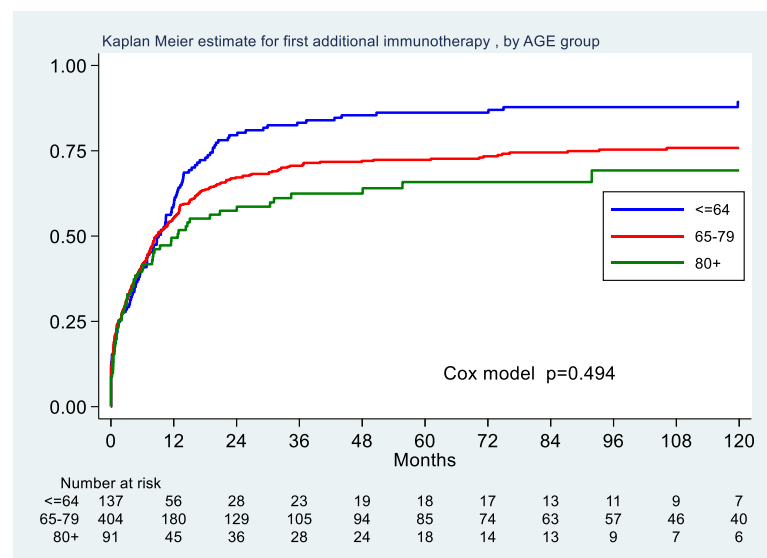


List of collected variables and definitions

The following variables were collected for all patients: demographics (including age at onset of GCA), disease subtype (cranial, defined as patients presenting with typical cranial or ocular/neurological ischaemic symptoms of GCA, and LV-GCA, defined as evidence of extra-cranial vasculitic involvement at imaging [ultrasound of extra-cranial arteries, ^{18}F -fluorodeoxyglucose positron emission tomography-computed tomography (^{18}F -FDG

PET-CT), CT angiography, or magnetic resonance angiography], onset manifestations [new onset headache, jaw claudication, tongue claudication, scalp tenderness, transient visual loss (amaurosis fugax), diplopia, PVL, stroke, transient ischaemic attack (TIA), arthralgia/myalgia, peripheral arthritis, polymyalgia rheumatica, fatigue, fever, anorexia, weight loss, night sweats, dry cough, upper or lower limbs ischaemic manifestations]. Onset symptoms were grouped in the following categories: (i) systemic: fatigue, fever, anorexia, weight loss, night sweats; (ii) ischaemic: PVL, stroke, transient ischaemic attack (TIA), limbs ischaemia; (iii) cranial symptoms: headache, scalp tenderness, jaw claudication, tongue claudication, visual loss, diplopia, amaurosis fugax, stroke, TIA. At disease onset, the following laboratory parameters were collected: erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), haemoglobin (Hb), renal function. ESR and CRP were defined as very elevated if above the median for the population (ESR > 77 mm/h; CRP > 64 mg/L). Initial and follow-up treatment strategies were recorded with GC doses and type and dose of adjunctive immunosuppressive drugs when prescribed. The time to reach a low GC dose ≤ 5 mg/day was recorded.

Serious infections were defined as infections requiring hospitalisation.



Supplementary Figure 1. Kaplan Meier curves for the estimate for the first additional immunosuppressive drug according to age group

Supplementary Table 1. Multivariable analysis for the predictors of the disease- and treatment-related outcomes at 12 months follow-up

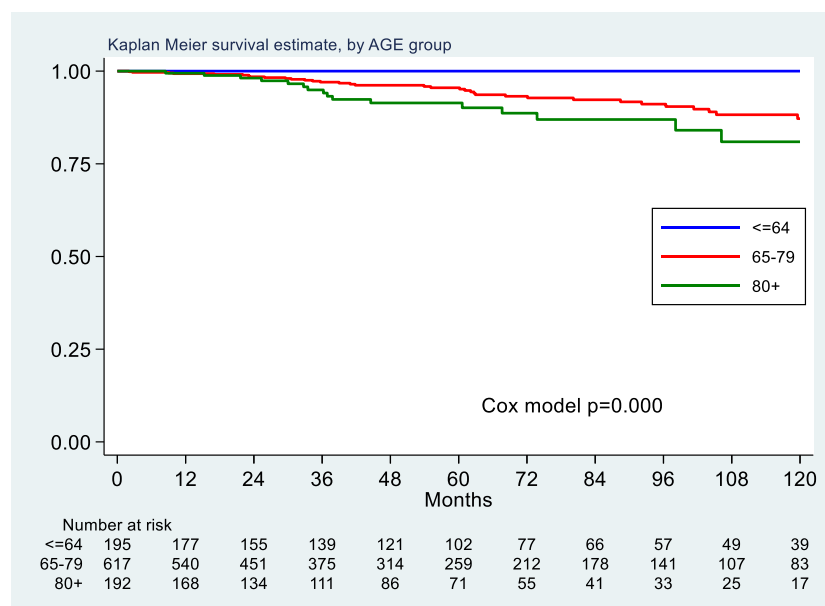
	Aortic aneurysm			Serious infections			Hypertension/diabetes/fractures		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
<i>Age group</i>			0.005			0.044			0.156
≤ 64	1.00			1.00			1.00		
65-79	0.66	0.39; 1.12	0.126	11.90	1.69; 83.63	0.013	1.69	0.99; 2.90	0.055
≥ 80	2.03	1.10; 3.75	0.023	13.71	1.59; 117.91	0.017	1.55	0.80; 2.99	0.191
<i>Sex</i>									
Female	1.00			1.00			1.00		
Male	8.20	5.30; 12.68	<0.0001	1.19	0.53; 2.67	0.680	0.73	0.40; 1.31	0.293
<i>Onset phenotype</i>									
LV-GCA	1.00			1.00			1.00		
Cranial	0.21	0.12; 0.36	<0.0001	0.94	0.68; 1.31	0.718	0.97	0.71; 1.33	0.862
<i>Onset Ischaemic</i>									
No	1.00			1.00			1.00		
Yes	0.84	0.45; 1.57	0.579	0.98	0.54; 1.75	0.933	1.38	0.95; 2.02	0.094
<i>Onset Cranial</i>									
No	1.00			1.00			1.00		
Yes	0.47	0.25; 0.87	0.016	0.82	0.37; 1.83	0.630	1.50	0.94; 2.39	0.091
<i>Onset Systemic</i>									
No	1.00			1.00			1.00		
Yes	1.11	0.76; 1.62	0.584	1.70	1.04; 2.78	0.035	2.10	1.23; 3.59	0.007
<i>Onset very elevated APR</i>									
No	1.00			1.00			1.00		
Yes	0.84	0.45; 1.55	0.569	1.24	0.62; 2.46	0.548	1.02	0.58; 1.80	0.934
<i>Initial GC dose</i>									
≤ 50 mg/day	1.00			1.00			1.00		
>50 mg/day	0.47	0.16; 1.42	0.181	2.24	1.11; 4.54	0.025	1.18	0.86; 1.64	0.306
<i>Onset Hb</i>	0.91	0.82; 1.26	0.071	1.00	0.76; 0.13	0.976	0.94	0.83; 1.06	0.300

Supplementary Table 2. Multivariable analysis for the predictors of the disease- and treatment-related outcomes at 60 months follow-up

	Aortic aneurysm			Serious infections			Hypertension/diabetes/fractures		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
<i>Age group</i>			0.002			0.003			0.196
≤ 64	1.00			1.00			1.00		
65-79	0.63	0.20; 2.02	0.438	3.95	1.72; 9.09	0.001	2.02	0.90; 4.56	0.089
≥ 80	2.27	0.76; 6.75	0.142	6.41	1.90; 21.61	0.003	1.12	0.29; 4.28	0.867
<i>Sex</i>									
Female	1.00			1.00			1.00		
Male	18.79	4.41; 80.17	<0.0001	1.90	0.69; 5.25	0.215	0.92	0.43; 1.95	0.824
<i>Onset phenotype</i>									
LV-GCA	1.00			1.00			1.00		
Cranial	0.53	0.30; 0.92	0.023	0.66	0.39; 1.55	0.471	0.84	0.58; 1.21	0.344
<i>Onset Ischaemic</i>									
No	1.00			1.00			1.00		
Yes	0.69	0.25; 1.94	0.486	0.85	0.35; 1.27	0.212	1.82	0.88; 3.79	0.108
<i>Onset Cranial</i>									
No	1.00			1.00			1.00		
Yes	0.26	0.16; 0.44	<0.0001	1.39	0.21; 3.40	0.814	1.27	0.71; 2.26	0.425
<i>Onset Systemic</i>									
No	1.00			1.00			1.00		
Yes	3.35	0.65; 17.22	0.148	0.98	0.25; 7.81	0.711	1.95	1.18; 3.21	0.009
<i>Onset very elevated APR</i>									
No	1.00			1.00			1.00		
Yes	1.98	0.76; 5.13	0.161	1.23	0.57; 1.67	0.929	0.99	0.60; 1.62	0.969
<i>Initial GC dose</i>									
≤ 50 mg/day	1.00			1.00			1.00		
>50 mg/day	1.14	0.26; 5.05	0.865	2.23	0.69; 7.16	0.180	0.77	0.82; 1.07	0.643
<i>Onset Hb</i>	0.82	0.54; 1.23	0.338	1.05	0.81; 1.37	0.701	0.94	0.04; 1.15	0.315

Supplementary Table 3. Multivariable analysis of the risk factors for mortality

	Survival		
	HR	95% CI	P value
<i>Age group</i>			
≤ 64	1.00		
65-79	8.40	2.52; 28.07	0.001
≥ 80	14.91	4.61; 48.28	<0.0001
<i>Sex</i>			
Female	1.00		
Male	1.01	0.57; 1.77	0.975
<i>Onset phenotype</i>			
LV-GCA	1.00		
Cranial	6.56	1.14; 37.82	0.035
<i>Onset Ischaemic</i>			
No	1.00		
Yes	1.06	0.61; 1.83	0.839
<i>Onset Cranial</i>			
No	1.00		
Yes	0.29	0.17; 0.50	<0.0001
<i>Onset Systemic</i>			
No	1.00		
Yes	2.18	1.08; 4.40	0.029
<i>Onset very elevated APR</i>			
No	1.00		
Yes	0.98	0.48; 1.99	0.955
<i>Initial GC dose</i>			
≤ 50 mg/day	1.00		
>50 mg/day	1.58	0.77; 3.26	0.211
<i>Onset Hb</i>	0.98	0.83; 1.17	0.857



Supplementary Figure 2. Kaplan Meier curves for survival estimates according to age groups

Sensitivity analyses

- **Sensitivity analysis on the frequency of permanent visual loss by excluding patients with a clinical diagnosis only.**

PVL was significantly more frequent in the oldest age group with 52 (49.52%) presenting with blindness, compared to 76 (23.38%) in the age group 65-79, and 8 (7.21%) in the ≥ 64 years old group; $p < 0.0001$.

- **Multivariate analysis for the sensitivity analysis for the primary endpoint by adding the variable “immunosuppressive drug started from diagnosis”**

	Number of relapses		
	IRR	95% CI	P value
<i>Age group</i>			0.454
≤ 64	1.00	0.90; 1.30	
65-79	1.08	0.90; 1.61	0.384
≥ 80	1.20		0.220
<i>Sex</i>			0.885
Female	1.00		
Male	1.03	0.69; 1.54	
<i>Onset phenotype</i>			0.414
Cranial	1.00		
LV-GCA	0.85	0.57; 1.26	
<i>Onset Ischaemic</i>			0.003
No	1.00		
Yes	0.78	0.67; 0.92	
<i>Onset Cranial</i>			0.003
No	1.00		
Yes	1.28	1.09; 1.51	
<i>Onset Systemic</i>			0.700
No	1.00		
Yes	0.97	0.82; 1.15	
<i>Onset very elevated APR</i>			0.099
No	1.00		
Yes	0.86	0.71; 1.03	
<i>Initial GC dose</i>			
≤ 50 mg/day	1.00		

>50 mg/day	1.05	0.86; 1.27	0.650
<i>Onset Hb</i>	1.05	0.96; 1.14	0.318
<i>Immunosuppressive drug from diagnosis</i>			
No	1.00		
Yes	0.76	0.65;0.90	0.002

- **Multivariate analysis for the sensitivity analysis for the primary endpoint by excluding patients with a clinical diagnosis only**

	Number of relapses		
	IRR	95% CI	P value
<i>Age group</i>			0.772
≤ 64	1.00		
65-79	1.07	0.89; 1.29	0.719
≥ 80	1.09	0.82; 1.45	0.556
<i>Sex</i>			
Female	1.00		
Male	1.04	0.76; 1.41	0.770
<i>Onset phenotype</i>			
Cranial	1.00		
LV-GCA	0.77	0.57; 1.05	0.099
<i>Onset Ischaemic</i>			
No	1.00		
Yes	0.77	0.62; 0.95	0.016
<i>Onset Cranial</i>			
No	1.00		
Yes	1.29	1.09; 1.53	0.003
<i>Onset Systemic</i>			
No	1.00		
Yes	0.82	0.76; 0.99	<0.0001
<i>Onset very elevated APR</i>			
No	1.00		
Yes	0.87	0.76; 0.99	0.036
<i>Initial GC dose</i>			
≤ 50 mg/day	1.00		
>50 mg/day	1.21	0.98; 1.48	0.077
<i>Onset Hb</i>	1.01	0.94; 1.10	0.724

- **Multivariate analysis for the sensitivity analysis for the impact of the variable “immunosuppressive drug started from diagnosis” on the time to reach a glucocorticoid dose ≤ 5 mg/day**

	Time to GC ≤ 5 mg/day		
	HR	95% CI	P value
<i>Age group</i>			
≤ 64	1.00		
65-79	1.18	0.98; 1.42	0.077
≥ 80	1.10	0.79; 1.53	0.558
<i>Sex</i>			
Female	1.00		
Male	0.96	0.75; 1.23	0.765
<i>Onset phenotype</i>			
Cranial	1.00		
LV-GCA	0.86	0.62; 1.19	0.365
<i>Onset Ischaemic</i>			
No	1.00		
Yes	0.93	0.72; 1.20	0.577
<i>Onset Cranial</i>			
No	1.00		
Yes	1.11	0.86; 1.43	0.444
<i>Onset Systemic</i>			
No	1.00		
Yes	0.72	0.51; 1.01	0.060
<i>Onset very elevated APR</i>			
No	1.00		
Yes	1.04	0.84; 1.28	0.898
<i>Initial GC dose</i>			
≤ 50 mg/day	1.00		
>50 mg/day	0.92	0.64; 1.33	0.675
<i>Onset Hb</i>	1.07	1.11; 1.44	<0.0001
<i>Immunosuppressive drug from diagnosis</i>			
No	1.00		
Yes	1.26	1.11;1.44	<0.0001