Tixagevimab/cilgavimab in ANCA-associated vasculitis: a prospective observational study

Sir,

The available data on the impact of COVID-19 on patients with ANCA-associated vasculitis (AAV) who receive immunosuppressive therapy are limited. Overall, the current evidence suggests that patients with AAV on rituximab therapy have a reduced humoral response to vaccines against SARS-CoV-2 and are at increased risk of death from infection (1). Tixagevimab/cilgavimab (Evusheld), combination of fully human long-acting SARS-CoV-2 neutralising monoclonal antibodies, can be used for pre-exposure prophylaxis of COVID-19 in immunosuppressed patients (2-4). In January 2023, the US Food and Drug Administration (FDA) announced that Evusheld is not currently authorised for emergency use in the US due to the predominance of the unsusceptible SARS-CoV-2 variants (5). However, marketing authorisation granted for Evusheld remained effective in the European Union and other countries.

We report our prospective single-centre study of tixagevimab/cilgavimab in patients with AAV. The study was approved by the Ethics Committee of the Sechenov University, Moscow, Russia (protocol #22-21, 09 December 2021). We enrolled 18 consecutive patients (mean age 49.9±15.5 years) with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) who received tixagevimab/cilgavimab 150 mg/150 mg (an approved dose at the time of administration) between May 2022 and August 2022 and were followed monthly via scheduled visits or phone-calls for a median of 299 (253-345) days (Table I). Sixteen patients had comorbidities; the most frequent of them were arterial hypertension, obesity and chronic kidney disease. The mean duration of AAV at the time of tixagevimab/cilgavimab administration was 11.9±5.7 years. All patients were treated with immunosuppressive agents and/or glucocorticoids for maintenance (in 16) or induction (in 2) of AAV remission. Noteworthy, 12 (67%) patients were on rituximab therapy.

Mild adverse events after tixagevimab/cilgavimab administration occurred in two patients. One patient developed fever, chills, arthralgia and myalgia that resolved within one day after administration, whereas another patient reported medium intensity pain at the injection site lasting for two days.

Two (11%) of 18 patients developed COVID-19 within 85 and 96 days, respectively, after passive immunisation. Both patients had GPA and were treated with rituximab (cumulative dose 8.5 and 5 g in the first and the second patient, respectively) and glucocorticoids for 117 and 128 months, respectively. Rituximab was administered 2 days after tixagevimab/cilgavimab injection in the first patient, and 89 days prior to tixagevimab/cilgavimab in the second patient. The daily dosage of prednisolone at the time of immunisation was 2.5 and 5 mg, respectively. Both patients presented with mild COVID-19. They did not require hospitalisation and fully recovered without specific treatment within 7 and 16 days, respectively.

Table I. Characteristics of 18 patients with AAV.

Parameters	Value
Females, n (%)	12 (66.7)
Mean age, years	49.9 ± 15.5
AAV type, n (%)	
GPA	13 (72.2)
MPA	5 (27.8)
Immunosuppressive treatment, n (%)	
Glucocorticoids	14 (77.8)
Average daily dose, mg	2.5 - 20
Median duration of therapy, months	85 (44-149)
Azathioprine	4 (22.2)
Mycophenolate mofetil	2 (11.1)
Cyclophosphamide	1 (5.6)
Rituximab	12 (66.7)
Cumulative dose, g	6 (1.5-9)
Serum IgG (g/l) (n=17)	7.7 ± 2.6
Comorbidities, n (%)	
Any	16 (88.9)
Arterial hypertension	9 (50.0)
Chronic kidney disease	6 (33.3)
Obesity	8 (44.4)
Chronic lung disease	4 (22.2)
Chronic heart failure	2 (11.1)
Paroxysmal atrial fibrillation	1 (5.6)
Type 2 diabetes	1 (5.6)
Vaccinated against COVID-19 in the previous 12 months	14 (77.8)

To our knowledge, this is the first prospective study that followed the patients with AAV after tixagevimab/cilgavimab administration. Our data confirm a good safety profile and potential efficacy of tixagevimab/cilgavimab in immunosuppressed AAV patients and are consistent with previously published studies (6-8). The limitations of our study include a small sample size, absence of a control group and administration of tixagevimab/cilgavimab at a lower dose than currently recommended.

Overall, the development of tixagevimab/cilgavimab represents an important advancement in our ability to treat and prevent COVID-19, particularly in those individuals who may be at a higher risk of developing severe or prolonged disease or have inadequate immune response to vaccination. Prolonged infection can be associated with relapse of autoimmune disease due to discontinuation of immunosuppressive therapy and increases the risk of spreading the virus and foster new variants (9). Our findings suggest that passive immunisation is a valuable approach to prevention of COVID-19 in AAV patients and may allow to continue treatment with immunosuppressive agents including rituximab that is an important advantage over vaccines requiring temporary withdrawal of immunosuppressive medications (10). Evusheld currently remains authorised in other countries where it is approved for COVID-19 pre-exposure prophylaxis and treatment, including the EU and Japan. Currently, a Phase I/III trial has been initiated to investigate the safety and efficacy of new generation long-acting antibodies (LAAB) in the pre-exposure prophylaxis of COVID-19 among the immunocompromised population (11).

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Competing interests: none declared.

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