LETTER

Outcomes of COVID-19 in patients with ANCA-associated vasculitis receiving avacopan

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The complement C5a-C5a receptor (C5aR) signalling axis plays a crucial role in the pathogenesis of both antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) and COVID-19. Complement components such as the membrane attack complex, C5a, C3a and factor B are higher in patients with active AAV compared with healthy controls.1 Similarly, experimental studies have shown abundant expression of C5aR1 and increased levels of soluble C5a in severe COVID-19.2

Following the ADVOCATE trial, avacopan, a C5aR antagonist, has been approved by the US Food and Drug Administration (FDA) as an adjunct therapy for remission induction in AAV.3 Similarly, viloblimab, an anti-C5a monoclonal antibody, was granted Emergency Use Authorization by the FDA for severe COVID-19 based on the results of the PANAMO study.4

The risk of severe COVID-19 is increased in patients receiving rituximab and high-dose glucocorticoids.5

Here, we report the outcomes of eight patients with AAV treated with avacopan who developed COVID-19, which to our knowledge has not been reported to date. We retrospectively identified patients ≥18 years old with AAV at the Johns Hopkins Vasculitis Center in Baltimore, Maryland and the Vasculitis and Glomerulonephritis Center at the Massachusetts General Hospital in Boston, Massachusetts who contracted COVID-19 while on avacopan. Data on ANCA serotype, concomitant immunosuppressive drug use, COVID-19 severity, treatment and vaccination status were retrieved.

Patient characteristics are outlined in table 1. All patients were previously vaccinated against COVID-19. The timing of vaccination in relation to B cell depletion is outlined in table 1. Spike antibody levels prior to this episode of COVID-19 were positive (n=3), negative (n=1) or not tested (n=4). The median (IQR) time from the start of induction therapy to avacopan initiation was 15 (10–30) days. The median (IQR) time from the start of induction therapy to COVID-19 infection was 116 (75–161) days. The median (IQR) time from avacopan initiation to COVID-19 was 78 (59–149) days. In addition to avacopan, induction treatment included rituximab+cyclophosphamide+glucocorticoids (n=6) and rituximab+glucocorticoids (n=2). Concomitant immunosuppression at the time of COVID-19 infection included rituximab (n=8), prednisone (n=2) and oral cyclophosphamide (n=1). All patients remained on their treatment, but cyclophosphamide was held. Two patients did not receive COVID-19 treatment, while the remainder received nirmatrelvir/ritonavir (n=3), bebtelovimab (n=1), molnupiravir (n=1), and remdesivir and dexamethasone (n=1). The severity of COVID-19 was mild in all patients except for one who was hospitalised and died from acute on chronic respiratory failure secondary to severe COVID-19. In this patient, the diffusing capacity of the lungs for carbon monoxide was 31% predicted preceding COVID-19. Of the seven surviving patients, all recovered completely from acute COVID-19, and no patient experienced long COVID.

Despite significant immunosuppression, COVID-19 was mild in nearly all patients with AAV receiving avacopan. The one patient with severe COVID-19 had advanced fibrotic lung disease. Larger studies with a
comparator arm are needed to confirm the effects of C5aR blockade with avacopan in COVID-19.

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REFERENCES

Table 1 Patient characteristics and details of COVID-19

<table>
<thead>
<tr>
<th>ID</th>
<th>Age, sex</th>
<th>ANCA serotype</th>
<th>Concomitant immunosuppressant at the time of COVID-19</th>
<th>Vaccination status</th>
<th>Spike antibody level*</th>
<th>Prevailing COVID-19 variant</th>
<th>Days from induction treatment to COVID-19</th>
<th>COVID-19 treatment</th>
<th>COVID-19 severity</th>
<th>Outcome</th>
<th>Long COVID</th>
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<tbody>
<tr>
<td>1</td>
<td>83F</td>
<td>MPO</td>
<td>RTX</td>
<td>3 mRNA doses during BCD</td>
<td>Positive</td>
<td>Omicron</td>
<td>165</td>
<td>Nirmatrelvir/ritonavir</td>
<td>Mild</td>
<td>Resolved</td>
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<td>54F</td>
<td>PR3</td>
<td>RTX</td>
<td>3 mRNA doses preceding BCD</td>
<td>NT</td>
<td>Omicron</td>
<td>77</td>
<td>Nirmatrelvir/ritonavir</td>
<td>Mild</td>
<td>Resolved</td>
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<tr>
<td>3</td>
<td>71M</td>
<td>PR3</td>
<td>RTX</td>
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<td>Omicron</td>
<td>160</td>
<td>Molnupiravir</td>
<td>Mild</td>
<td>Resolved</td>
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<tr>
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<td>81M</td>
<td>PR3</td>
<td>RTX, CYC prednisone 15 mg</td>
<td>3 mRNA doses preceding BCD</td>
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<td>Omicron</td>
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<td>Remdesivir, dexamethasone</td>
<td>Severe</td>
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<td>MPO</td>
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<tr>
<td>6</td>
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<td>Positive</td>
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<td>Bebtelovimab</td>
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<td>Resolved</td>
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<td>67</td>
<td>Nirmatrelvir/ritonavir</td>
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</table>

*Positive spike antibody levels preceding this episode of COVID-19 resulted from either vaccination or prior infection during peripheral B cell presence, or through prior receipt of tixagevimab/cilgavimab.

ANCA, antineutrophil cytoplasmic antibody; BCD, B cell depletion; CYC, cyclophosphamide; F, female; M, male; MPO, myeloperoxidase; mRNA, messenger RNA; NT, not tested; PR3, proteinase-3; RTX, rituximab.