SARS CoV-2 infection among patients using immunomodulatory therapies

The risk of coronavirus disease 2019 (COVID-19) and disease progression among patients using immunomodulatory therapy is unclear. Accordingly, we implemented an active surveillance project with USA/Canada Infectious Disease specialists via the Emerging Infections Network (EIN) to identify COVID-19 cases occurring in patients who use immunomodulatory therapy and to describe their clinical outcomes.

EIN listserv members include 2396 infectious disease physicians in the USA/Canada linked via a moderated listserv. On 8 April via listserv, we requested reports of COVID-19 cases among patients receiving immunomodulatory therapy. Two weekly reminders were later sent and case reports were collected until 22 May. We collected information regarding patient demographics, COVID-19 test results, symptoms, hospitalisation details, complications, treatment, pre-existing conditions, concomitant therapies, and patient outcomes. We conducted descriptive analyses of these patient factors and compared differences between survivors and non-survivors. We grouped immunosuppressive therapies by class (table 1).

Thirty-eight physicians screened over 2500 COVID-19 cases from which 77 (3%) were identified using immunomodulatory drugs. Of these, 52% were female, median age of 60 years (range, 16–84) and 83.1% had autoimmune disease (rheumatoid arthritis (19, 24.7%), ulcerative colitis (5, 6.5%) and sarcoidosis (5, 6.5%) were most common). Comorbidities included hypertension (26, 33.8%), diabetes (19, 24.7%), underlying chronic kidney disease (11, 14.3%) and others. All patients had PCR-confirmed COVID-19. Symptoms included dyspnoea (70.1%), fever (68.8%) and cough (64.9%). At time of COVID-19 diagnosis, 31 (40%) were using biologic therapies including anti tumor necrosis factor (anti-TNF) therapies (n=16), rituximab (n=6), abatacept (n=2), tocilizumab (n=2) and other (n=5). Among those using non-biologics at baseline (46, 60%), the following therapies were in use: janus kinase (JAK) inhibitors (3, 6.5%), non-biologic disease-modifying antirheumatic drugs (DMARDs) (11, 24%), prednisone alone (5, 11%) or other (27, 59%). Among those who received anti-COVID-19 treatment (n=41), the most common treatment regimens included hydroxychloroquine (n=27), azithromycin (n=10) and/or tocilizumab (n=10). Overall, 63 (81.8%) patients were hospitalised, 27 (35.1%) required mechanical ventilation, 37 (48.1%) required ICU care and 9 (11.7%) died. Patients who died were slightly older (median 68 years vs 58

Table 1 COVID-19 outcomes among autoimmune patients receiving immunomodulatory therapy

	Autoimmune cohort							
	Anti-TNF* biologic with/ without DMARDs† and/ or corticosteroids (n=16)	Biologic‡ (non-TNF) with/ without DMARDs and/or corticosteroids (n=15)	Non-biologic DMARDs alone (n=11)	Non-biologic DMARDs and corticosteroids (n=3)	Corticosteroids§ alone (n=9)	JAK inhibitor¶ (n=3)	Other**immune-modulatory therapy with/ without DMARDs and/or corticosteroids (n=11)	Post solid organ transplant (n=13)
Female (%)	56.3	66.7	81.8	66.7	33.3	66.7	72.7	15.4
Median age, years	59 (27–81)	54 (26–79)	70 (38–84)	62 (52–68)	54 (34–62)	63 (49–63)	62 (16–71)	58 (46–74)
Comorbidities (%)								
Hypertension	37.5	20.0	36.4	66.7	11.1	0.0	36.4	61.5
Diabetes	12.5	6.7	36.4	0.0	11.1	0.0	27.3	69.2
Indication for immunosuppressive (%)								
Rheumatoid arthritis	56.3	20.0	54.6	33.3	0.0	33.3	9.1	N/A
IBD††	31.3	0.0	36.4	33.3	22.2	66.7	9.1	N/A
Sarcoidosis	6.3	0.0	0.0	33.3	33.3	0.0	9.1	N/A
COVID-19 Treatment‡‡ (%)								
Azithromycin	0.0	6.7	9.1	0.0	0.0	33.3	27.3	30.8
Hydroxychloroquine	6.3	46.7	18.2§§	66.7	22.2	33.3	45.5	61.5
Tocilizumab	0.0	20.0	9.1	0.0	44.4	0.0	9.1	15.4
Baseline immunomodulatory treatment (%)								
Unchanged	18.8	60.0	45.5	33.3	100.0	66.7	45.5	53.9
Modified	75.0	40.0	54.6¶¶	33.3	0.0	33.3	45.5	46.2
Unknown	6.3	0.0	0.0	33.3	0.0	0.0	9.1	0.0
Outcome (%)								
Hospitalised	50.0	73.3	90.9	100.0	100.0	66.7	81.8	100.0
Intensive care unit	6.3	53.3	27.3	66.7	77.8	33.3	63.6	61.5
Ventilator support	0.0	40.0	9.1	66.7	66.7	33.3	45.5	46.2
Deceased***	0.0	13.3	18.2	33.3	11.1	0.0	18.2	7.7

*Anti tumour necrosis factor (TNF) therapy includes (n): adalimumab (5), certolizumab (1), etanercept (7), golimumab (1), infliximab (2). Adalimumab, etanercept and infliximab biosimilars included.
†Non-biologic disease-modifying antirheumatic drugs (DMARDs) with/without immunomodulatory therapy (n): balsalazide (2), hydroxychloroquine (5), leflunomide (1), mesalamine (1), methotrexate (12) or sulfasalazine (2).
‡Non-TNF biologic therapy includes (n): abatacept (2), anakinra (1), dupilumab (1), ocrelizumab (1), omalizumab (1), rituximab (6), secukinumab (1) or tocilizumab (2).
§Corticosteroids include (n): prednisone (5) or inhaled steroids (4); n=26 for total prednisone use with/without immunomodulatory therapy, median daily dose 15 mg (2–60 mg).
¶Janus kinase (JAK) inhibitors include (n): tofacitinib (2) and upadacitinib (1); both tofacitinib patients continued dosing as prescribed.
**Other immunomodulatory therapy includes (n): azathioprine (2), cyclosporine (1), cyclophosphamide (1), fingolimod (2), interferon beta-1b (1), mycophenolate (3) and tacrolimus (2) includes Crohn's disease and ulcerative colitis.
††Inflammatory bowel disease (IBD) includes Crohn's disease and ulcerative colitis.
‡‡Treatment groups are not mutually exclusive
§§Mutually exclusive from patients with baseline hydroxychloroquine use
¶¶Among those on methotrexate alone (n=5), 80% modified treatment
***Deceased by drug (n): azathioprine (1), balsalazide (1), cyclosporine and prednisone (1), rituximab and prednisone (2), methotrexate alone (1), prednisone alone (1), methotrexate and prednisone (1), and mycophenolate, tacrolimus and prednisone (1).

years) and similar with regard to comorbidities as those who survived. No patients taking anti-TNF therapy at baseline died (table 1).

Like other early reports, our surveillance effort yielded few biologic or JAK inhibitor using patients severely ill with COVID-19. Certainly, a lower risk of exposure could help explain this (ie, those patients perceiving high risk are social distancing), but it is also possible these therapies are protective against severe outcomes. A rheumatology registry of over 600 COVID-19 patients with autoimmune disease observed that those using biologics, in particular anti-TNF therapy, were less likely to be hospitalised.[1]

While the overall proportion of patients who died in this case series is higher than reported in the US general population,[2] this would be expected given the likelihood that most COVID-19 cases being consulted on by ID physicians would be within the inpatient setting. While we identified only a small number of anti-TNF users, none of them died. TNF blockers could hypothetically inhibit innate antiviral responses with COVID-19 or predispose to secondary bacterial infection, although in animal models of viral pneumonia they can be protective, and among inflammatory bowel disease (IBD) COVID-19 patients, the clinical outcomes of those using TNF blockers have been observed to be comparable or better to those using non-biologic DMARDs.[3 4] While JAK inhibitors decrease innate viral immunity and might potentially increase the risk of viral progression, we found only two tofacitinib and one upadicitinib patients and all three had complete recovery. This and other studies involve small numbers of patients, making further population-based studies necessary to understand the risk of DMARDs with COVID-19.

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