Uptake of monoclonal antibodies and anti-viral therapies for COVID-19 in Scotland

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To The Editor:

SARS-CoV-2 has constantly been evolving since it was first detected in 2019. Virus mutations have impacted on transmissibility, virulence, and the effectiveness of vaccines and COVID-19 therapeutics. In Scotland, treatments recently made available for use in patients with COVID-19 are Sotrovimab, a neutralising monoclonal antibody (mAB) that specifically target SARS-CoV-2 spike proteins, and the SARS-CoV-2-specific antiviral drugs nirmatrelvir/ritonavir (Paxlovid) and molnupiravir, which inhibit viral replication by inhibiting viral protease and by increasing viral RNA mutagenesis. Current guidance is that these should be offered to vulnerable patients within five to seven days of presenting with mild-to-moderate COVID-19 to prevent disease progression.[1] Choice of treatment is mainly determined based on pre-existing conditions and/or concurrent drug treatment. Other more established therapeutics are also used in an in-patient setting to improve outcomes in hospitalised patients with severe COVID-19.[2]

We sought to assess uptake of these novel treatments and to assess whether these treatments are being used as recommended across Scotland.[3] To the best of our knowledge, this is one of the first national evaluations of this kind.

Data on COVID-19 therapeutics were extracted from the Hospital Electronic Prescribing and Medicines Administration system (HEPMA) from 6/14 Scottish Health Boards; we requested these data for the remaining 8 Health Boards that did not have HEPMA in place on a weekly basis. Data were obtained from December 21, 2021, (when treatment pathways for these novel therapeutics were first implemented in Scotland) up to September 26, 2022 (with different end dates per Health Board). These therapeutics records were then linked by pseudo-anonymised patient identifier to data on Scotland's national COVID-19 surveillance platform: Early Estimation of vaccine and Anti-Viral Effectiveness (EAVE II).[4] Non-hospitalised patients were identified by proxy of receiving treatment (administered or prescribed) outside of an inpatient admission. For those with multiple therapies prescribed, known as a 'treatment cocktail', the initiation date was considered the first treatment administration or prescription.

After excluding those with missing therapy (n=66), there were 14,464 treated patients identified. Of these, 11,465 were identified as having been treated in the outpatient setting (79.3%), of whom 3,056 (26.7%) were treated with Sotrovimab (monotherapy), 5,436 (47.4%) with Paxlovid, 2,793 (24.4%) with Molnupiravir, and 180 (1.6%) received multiple therapies. Figure 1 shows the distribution of therapeutics used each week.

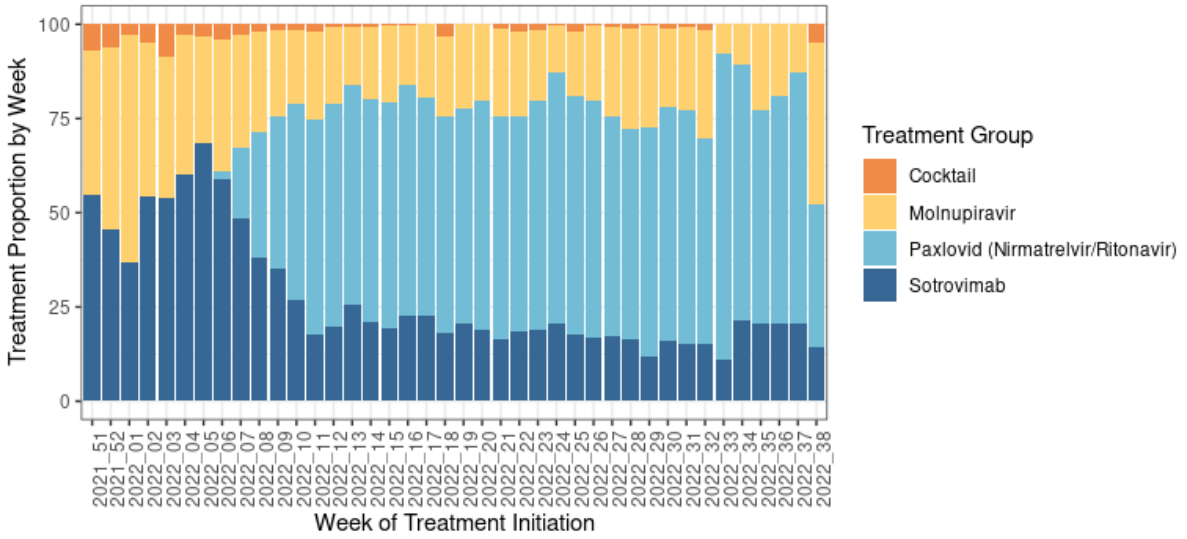

Figure 1: Distribution of COVID-19 therapeutics by week, by treatment setting

There were 28,660 people identified who were estimated to have met the eligibility criteria according to COVID-19 diagnosis and high-risk comorbidities, and were thus included in the denominator for the treated proportion analyses. Symptom severity was not routinely recorded, for example at the point of contact with Covid Medicines Delivery Units (CMDUs), and thus those ineligible for treatment due to mild symptoms could not be excluded from the denominator. Additionally, we are unable to ascertain those who did not contact a CMDU at all, and declined to be treated. Overall, 40.0% of those eligible for mABs or anti-virals were treated in the outpatient setting. Treatment was lowest in under 18s (20.3% of eligible 12-18 year-olds compared to 29.6-47.3% of 30-89 year-olds) and over 90s (23.0%), the deprived (30.1% in highest versus 47.7% in the lowest deprivation quintiles), and those sub-optimally protected through vaccination (11.3-33.5% in those receiving less than four vaccine doses compared with 97.7% and 77.1% in quintuple-plus- and quadruple-vaccinated individuals, respectively; see Supplementary materials).

Focusing on individual at risk groups, very low proportions of eligible individuals identified with HIV/AIDS (21.9%) and rheumatoid arthritis or systemic lupus erythematosus (22.5%) were treated, while 71.7% of stem cell transplant recipients were treated. Other comorbidities had treatment proportions between 26.8-61.2% (see Supplementary materials).

Overall, 98.5% of all outpatient-treated patients were treated within five days of diagnosis in the outpatient setting, the lowest target in the treatment guidelines.[3] Treatment was initiated a median one-day post-diagnosis for Paxlovid (Interquartile Range (IQR)=1-2, 99th percentile 5 days,

maximum 20), two days for Molnupiravir (IQR=2-3, p_{99}=8 days, maximum 21), Sotrovimab (IQR=2-3, p_{99}=5 days, maximum 17), and treatment cocktails (IQR=1-2, maximum 5 days). Not all treated patients had identifiable diagnosis dates, likely due to failure to record positive lateral flow tests (LFTs): 76.3% for Paxlovid, 61.5% for Molnupiravir, 47.5% for Sotrovimab, and 46.1% for treatment cocktails. The criteria met to ascertain a patient as treatment-eligible could not be identified for 28.2% of those who received outpatient care.

There were limitations to the estimation of comorbidities, primarily cancer, as there was limited availability of cancer therapy and diagnostic data. Additionally, only general/acute inpatient records (including RAPID) were available (see Supplementary materials), while other inpatient departments, such as maternity and mental health, were not available.

Despite these limitations, the creation of such a thorough data collection process enables continued monitoring of Scottish COVID-19 therapeutic use in community settings, which will be important as PANORAMIC and other trials begin to report. Identifying those who may be falling through the cracks can help to boost early treatment, reduce the need for acute, inpatient care and help improve access to care.

In summary, we show that only a minority of those who should have received mABs or anti-virals received these in Scotland, but the overwhelming majority of those who received treatment did so within the recommended time limit. There is a clear need to increase uptake of these treatment options in high-risk individuals, particularly in the young, socioeconomically disadvantaged, those with HIV and certain rheumatologically conditions and in those sub-optimally protected through vaccination.

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Data sharing: The data are stored in the Public Health Scotland TRE. To access these individual-level, confidential healthcare data, researchers will need to apply to HSC-PBPP (https://www.informationgovernance.scot.nhs.uk/pbpphsc/).

Conflict of interests: AS has served on COVID-19 Advisory Groups for the UK and Scottish Governments and AstraZeneca, all of which have been unremunerated. He holds a research grant on the effectiveness and safety of mABs from GSK.

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