RC GP LEARNING

Top tips on new treatments for COVID-19

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1) There are treatments available for community management of COVID-19

For most of the pandemic, the primary care management of those with COVID-19 was supportive – if the patients weren't unwell enough to be admitted then we managed them in the same way as patients with other viral respiratory tract infections. This changed in early 2022 with the arrival of new community treatments, which can be divided into two groups – antivirals and neutralising monoclonal antibodies (nMABs).

NICE[1] has approved two drugs for use in the community. The first is nirmatrelvir plus ritonavir (an antiviral, given orally) and it is approved for adults who do not need supplemental oxygen for COVID-19 and have an increased risk for progression to severe COVID-19. The second option is sotrovimab (an nMAB, given intravenously), which is approved for adults and children who are at least 12 and weigh at least 40kg, for whom nirmatrelvir plus ritonavir is contraindicated or unsuitable. They also have to have no need for supplemental oxygen and be in the group with an increased risk for progression to severe COVID-19.

2) Only the highest risk patients are eligible for these treatments

Patients who are a member of the 'highest risk group' should have all received a letter from NHSEI telling them about these new treatments. They were also initially sent a PCR test kit to keep at home so that they can test promptly if they have symptoms of COVID-19. Advice has now changed and they are advised to take a lateral flow test as soon as possible if they have any symptoms that could be COVID-19[2]. If positive, this should be uploaded online.

The group of patients defined as being in the 'highest risk group' is given in the table below – it is not identical to the group who were asked to shield during the pandemic, nor is it the same as the group who are usually invited for flu vaccinations.

The following patient cohorts were determined by an independent advisory group commissioned by the Department of Health and Social Care (DHSC)[3].

Cohort	Description
Down's syndrome	All individuals with Down's syndrome or other chromosomal disorders known to affect immune competence (decision to treat to be at the discretion of the treating clinician).
Patients with a solid cancer	• Metastatic or locally advanced inoperable cancer. • Lung cancer (at any stage). • People receiving any chemotherapy (including antibody-drug conjugates), PI3K inhibitors or radiotherapy within 12 months.

	• People who have had cancer resected within 3 months and who received no adjuvant chemotherapy or radiotherapy. • People who have had cancer resected within 3 to 12 months and receiving no adjuvant chemotherapy or radiotherapy are expected to be at less risk (and thus less priority) but still at increased risk compared with the non-cancer population.

Patients with a haematological diseases and recipients of haematological stem cell transplant (HSCT)	• Allogeneic HSCT recipients in the last 12 months or active graft versus host disease (GVHD) regardless of time from transplant (including HSCT for non-malignant diseases).
	• Autologous HSCT recipients in the last 12 months (including HSCT for non-malignant diseases).
	• Individuals with haematological malignancies who have received CAR-T cell therapy in the last 24 months, or radiotherapy in the last 12 months.
	• Individuals with haematological malignancies receiving systemic anti-cancer treatment (SACT) within the last 12 months.
	• All people who do not fit the criteria above, and are diagnosed with:
	  ○ myeloma (excluding monoclonal gammopathy of undetermined significance (MGUS))
	  ○ AL amyloidosis
	  ○ chronic B-cell lymphoproliferative disorders (chronic lymphocytic leukaemia, follicular lymphoma)
	  ○ myelodysplastic syndrome (MDS)
	  ○ chronic myelomonocytic leukaemia (CMML)
	  ○ myelofibrosis.
	• All people with sickle cell disease.
	• People with thalassaemia or rare inherited anaemia with any of the following (the decision to treat these patients will need to be at the individual patient level with input from the haematology consultant responsible for the management of the patient's haematological condition):
	  ○ severe cardiac iron overload (T2 * less than 10ms on magnetic resonance imaging)
	  ○ severe to moderate iron overload (T2 * greater than or equal to 10ms on magnetic resonance imaging) plus an additional co-morbidity of concern (for example, diabetes, chronic liver disease or severe hepatic iron load on MRI).
	• Individuals with non-malignant haematological disorders (for example, aplastic anaemia or paroxysmal nocturnal haemoglobinuria) receiving B-cell depleting systemic treatment (for example, anti-CD20, anti-thymocyte globulin (ATG) and alemtuzumab) within the last 12 months.

Patients with renal disease	• Renal transplant recipients (including those with failed transplants within the past 12 months), particularly those who have:
	  ○ received B cell depleting therapy within the past 12 months (including alemtuzumab, rituximab (anti-CD20), anti-thymocyte globulin)
	  ○ an additional substantial risk factor which would in isolation make them eligible for monoclonals or oral antivirals
	  ○ not been vaccinated prior to transplantation.

	• Non-transplant renal patients who have received a comparable level of immunosuppression. Please refer to the section on 'Immune-mediated inflammatory diseases' below for a list of qualifying immunosuppressive therapies. • Patients with chronic kidney disease (CKD) stage 4 or 5 (an eGFR less than 30ml per min per 1.73m^2) without immunosuppression.
Patients with liver disease	• People with cirrhosis Child-Pugh class A,B and C, whether receiving immune suppressive therapy or not. Those with decompensated liver disease (Child-Pugh B and C) are at greatest risk. • People with a liver transplant. • People with liver disease on immune suppressive therapy (including people with and without cirrhosis) – please refer to the section on 'Immune-mediated inflammatory diseases' below for a list of qualifying immunosuppressive therapies.
Solid organ transplant recipients	All recipients of solid organ transplants not otherwise specified above.
Patients with immune-mediated inflammatory disorders (IMID)	• People who have received a B-cell depleting therapy (anti-CD20 drug for example rituximab, ocrelizumab, ofatumab, obinutuzumab) in the last 12 months. • People who have been treated with cyclophosphamide (IV or oral) in the 6 months prior to positive PCR. • People who are on biologics or small molecule JAK-inhibitors (except anti-CD20 depleting monoclonal antibodies) or who have received these therapies within the last 6 months. • People who are on corticosteroids (equivalent to greater than 10mg per day of prednisolone) for at least the 28 days prior to positive PCR. • People who are on current treatment with mycophenolate mofetil, oral tacrolimus, azathioprine/mercaptopurine (for major organ involvement such as kidney, liver and/or interstitial lung disease), methotrexate (for interstitial lung disease) and/or ciclosporin. • People who exhibit at least one of: (a) uncontrolled or clinically active disease (that is required recent increase in dose or initiation of new immunosuppressive drug or IM steroid injection or course of oral steroids within the 3 months prior to positive PCR); and/or (b) major organ involvement such as significant kidney, liver or lung inflammation or significantly impaired renal, liver and/or lung function).
Primary immune deficiencies	• Common variable immunodeficiency (CVID). • Undefined primary antibody deficiency on immunoglobulin (or eligible for Ig). • Hyper-IgM syndromes. • Good's syndrome (thymoma plus B-cell deficiency). • Severe combined immunodeficiency (SCID). • Autoimmune polyglandular syndromes or autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome). • Primary immunodeficiency associated with impaired type 1 interferon signalling.

	• X-linked agammaglobulinaemia (and other primary agammaglobulinaemias). • Any person with secondary immunodeficiency receiving, or eligible for, immunoglobulin replacement therapy.
HIV/AIDS	• Patients with high levels of immune suppression, have uncontrolled or untreated HIV (high viral load) or present acutely with an AIDS defining diagnosis. • People on treatment for HIV with CD4 less than 350 cells per mm3 and stable on HIV treatment or CD4 greater than 350 cells per mm3 and additional risk factors (for example, age, diabetes, obesity, cardiovascular, liver or renal disease, homeless, alcoholic dependency).
Rare neurological and severe complex life-limiting neurodisability conditions	• Multiple sclerosis. • Motor neurone disease. • Myasthenia gravis. • Huntington's disease.

[7]For paediatric/adolescent patients (aged 12-17 years inclusive), paediatric multi-disciplinary team (MDT) assessment should be used to determine clinical capacity to benefit from the treatment

Table 1: Patient cohorts considered at highest risk from COVID-19 and to be prioritised for treatment with nMABs. NHS England and NHS Improvement coronavirus. Interim Clinical Commissioning Policy: Neutralising monoclonal antibodies or antivirals for non-hospitalised patients with COVID-19. Published on: 24 December 2021.

3) Commissioning of these treatments in England has changed.

When these treatments were first offered they were centrally commissioned - a high-risk patient in England who uploaded a positive COVID-19 test would be contacted directly by a COVID-19 medicine delivery unit (CMDU). Commissioning is now done locally[4] and patients need to make contact themselves. Depending on local arrangements, they may do this via the GP, via their hospital consultant, via 111 or by contacting the CMDU directly. As time passes, it may be that some areas choose to use a mechanism other than a CMDU to deliver care. It would be sensible to find out how care is offered in your area, before you need to signpost a patient to it. The provision of these medications is arranged differently in Scotland[5], Wales[6], and Northern Ireland[7].

4) Some patients may not realise that they are at high risk.

COVID-19 and the shielding programme revealed some of the limitations of coding and it is likely that there will be patients in the highest risk group who are unaware of their risk, particularly if they have only recently acquired the condition which makes them high risk. If you speak to such a patient then you can let them know that they are at high risk and should have some COVID-19 tests at home, and how to access treatment in your area.

5) Referring to a CMDU should be easy

If you have a patient who you think needs to be seen at a CMDU then you can refer directly, via e-RS. Your local CMDU should be found within the infectious diseases menu. At the moment, none of these drugs can be prescribed by a GP or by any doctor outside of a CMDU

and they are not stocked by community pharmacies. Some of them have significant drug interactions, so if referring from primary care it is important to provide a list of current medication.

6) Lower risk patients can access these drugs via the PANORAMIC trial

The **P**latform **A**daptive trial of **NO**vel antivi**R**als for e**A**rly treat**M**ent of Covid-19 **I**n the **C**ommunity trial[5] is also open to those with PCR proven COVID-19 whose symptoms have started in the last five days, but unlike CMDU provision those who want to join the trial can have a wider range of medical co-morbidities. The range of co-morbidities accepted for the trial, listed below, is closer to the flu vaccination group than the shielding group and those aged 50 or over can join the trial even in the absence of a pre-existing condition.

- Chronic Respiratory disease (including chronic obstructive pulmonary disease (COPD), cystic fibrosis and asthma requiring at least daily use of preventative and/or reliever medication)
- Chronic heart or vascular disease
- Chronic kidney disease
- Chronic liver disease
- Chronic neurological disease (including dementia, stroke, epilepsy)
- Severe and profound learning disability
- Down's syndrome
- Diabetes mellitus (Type I or Type II)
- Immunosuppression: primary (e.g., Inherited immune disorders resulting from genetic mutations, usually present at birth and diagnosed in childhood) or Secondary due to disease or treatment (e.g., sickle cell, HIV, cancer, chemotherapy)
- Solid organ, bone marrow and stem cell transplant recipients
- Morbid obesity (BMI >35)
- Severe mental illness
- Care home resident
- Judged by recruiting clinician or research nurse (registered medical practitioner or trained study nurse) to be clinically vulnerable

Table 2: Who can join the PANORAMIC Study. The **P**latform **A**daptive trial of **NO**vel antivi**R**als for e**A**rly treat**M**ent of Covid-19 **I**n the **C**ommunity trial. University of Oxford. Reproduced with permission.

7) The trial involves a treatment group and a control group

Those who join the PANORAMIC trial will be assigned to usual NHS care, or usual NHS care plus a COVID-19 therapeutic – there is no group which will be given a placebo. Women who are pregnant or breastfeeding are excluded from the trial.

8) Patients can sign up to the PANORAMIC trial without their GP's involvement…

There is no GP involvement necessary for a patient to sign up to the PANORAMIC trial – the patient can self-refer via the trial website.[8]

9) … but those who are eligible for CMDU treatment should not join the trial

Participants in the PANORAMIC trial have only a 50% chance of being in the treatment arm. Those who are in the highest risk group and are eligible for CMDU treatment should therefore go down that route rather than joining the trial.

10) The PANORAMIC trial may help with our understanding of long COVID and any future treatments

Those who take part in the PANORAMIC trial will have to answer questions online for 28 days (a phone call will be offered for those who do not have internet access) and will be contacted at three and six months to be asked about longer-term COVID-19 symptoms. It has been designed as a multi-platform trial so if any future treatments become available, they will be added to the same trial.

References

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