UK Coronavirus Cancer Project

NHS

The COVID-19 Safe Prescribing of Oncological Treatments initiative (COV-SPOT)

A protocol for evaluating optimal oncological treatment of cancer patients testing positive for COVID-19

Version (date)	Notes	Approved by
1.0 (14th June 2022)	First version of protocol	UKCCP clinical leads

[1]Acknowledgements. This initiative protocol was developed by the UK COVID/Cancer Operational Delivery clinical leads group consisting of Dr Lennard Lee, Dr Grisma Patel, Dr Isabella Watts, Dr Rosie Hattersley, Mr Nathan Appanna, Dr Alex Burnett, Dr Jamie D'Costa, Dr Sam Khan, Dr Arvind Tripathy, Dr Martin Little, Dr Matthew Fittall, Dr Justin Liu, Dr James Platt, Dr Hayley Mckenzie, Dr Vijay Patel, Dr Michael Tilby, Dr James Clark.

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1. Background

The UK coronavirus cancer project (UKCCP) is a national programme set up to pioneer the use of a real-world datasets and registries to safeguard and monitor cancer patients during the COVID-19 pandemic. The clinician-led project was set up in March 2020 and launched within a week, linking 69 cancer centres across the UK. It was the first to demonstrate that chemotherapy could be safely delivered during the pandemic in UK Cancer centres.

Increasing numbers of cancer patients who are about to commence or are already receiving systemic anti-cancer therapy (SACT) or radiotherapy, are testing positive for COVID-19. Many of these patients have mild symptoms or are asymptomatic, especially in the vaccinated cohort. Awaiting negative polymerase chain reaction (PCR) tests can lead to treatment delays, which could prove detrimental to cancer patients – particularly in those receiving curative or neoadjuvant/adjuvant therapies, and those with aggressive cancers (e.g., small cell/germ cell tumours). Furthermore, many cancer treatments may pose negligible risk, such as targeted therapies, immunotherapy, or radiotherapy. There is currently no evidence to support treatment decisions surrounding giving, delaying, or dose-adjusting cancer treatments in patients with an active COVID-19 infection. This lack of evidence could lead to variations in care and inequalities between different regions of the UK.

The **COVID-19 Safe Prescribing of Oncological Treatment Initiative** (COV-SPOT) is a nationally prioritised evaluation to deliver definitive evidence to guide treatment decisions in cancer patients who have recently tested positive for COVID-19. This project will cover factors including safe timing to restart treatments, a risk-benefit

treatment pathway in positive cases and a review of the risk of COVID-19 re-activation if therapy is delivered.

2. Project Aims

2.1 Primary Objectives

The specific aims for this initiative are:

1. To describe safe timings to restart cancer treatments following a COVID-19 infection.
2. To determine how many cancer patients test positive for COVID-19 before oncological treatment and subsequently have their treatment delayed.
3. To identify how many patients continue to receive oncological treatment despite testing positive for COVID-19.
4. To describe risk of severe COVID-19 outcomes in COVID-19-positive patients who are proceeding on a risk-benefit treatment pathway.
5. To determine whether certain types of oncological therapy are safer to continue than others.

2.2 Secondary Objectives

6. To determine whether cancer subtype or demographics correlate with COVID-19-related outcomes
7. To highlight the need for up-to-date national guidance to help clinicians with treatment decisions for these patients.

3. Project Design

An outline of the steps in the project design:

1. All centres that care for patients with cancer will be invited to participate in the UKCCP COV-SPOT programme. Steps are summarised in Appendix A.
2. A network will be established to deliver this initiative, through the UK COVID/Cancer Operational Delivery clinical leads group. All cancer centres will be invited to participate in this group. If a centre wishes to participate, they are required to complete an expression of interest (EOI) form and confirm participation to Dr Grisma Patel.
3. Each trust/hospital will identify a lead clinician (consultant or registrar) who will be termed the COV-SPOT Trust Lead.
4. The COV-SPOT Trust Lead will form a local group known as the trust COVID-SPOT team, that can have as many individuals as felt to be necessary to sustain the project throughout the pandemic and may include nurses, chemotherapy co-ordinators, data managers and clinicians.
5. The COVID-SPOT team, with oversight from the COV-SPOT Trust Lead will be responsible for completing the case reporting form (CRF).
6. The COV-SPOT Trust Lead at each centre should liaise with the trust's clinical lead to gain approval for this process (an invite letter is provided). If committee approval is needed this should be requested from the relevant individual.
7. Once approval is asserted as complete, the COV-SPOT Trust Lead will receive login details for the REDCap portal.

4. Eligibility

4.1 Inclusion Criteria

The COV-SPOT initiative will evaluate patients who fulfil all the following criteria:

- Aged 18 years or over.
- Diagnosed with an active malignancy, including solid and haematological cancers.
- About to receive or already receiving oncological therapy i.e., SACT or radiotherapy. SACT includes chemotherapy, immunotherapy, targeted treatment, and hormonal treatments.
- Tested positive for COVID-19, confirmed by lateral flow or PCR test, in any setting. This includes self/at-home testing and routine pre-treatment screening. Vaccinated and unvaccinated individuals are included.

4.2 Exclusion Criteria

Patients excluded from the cohort include:

- Any COVID-19 positive patient with active malignancy who will not receive oncological treatment/ are under active surveillance/ ‘watch and wait’ treatment plans.
- Any COVID-19 positive patient with active malignancy deemed unfit to proceed with oncological therapy for reasons unrelated to COVID-19. This includes progressive disease and co-morbidities leading to lower performance status.

5. Data Acquisition

5.1 Case Reporting Forms

The CRF can be viewed in Appendix B.

Initial Submission

The initial case-reporting process will be a retrospective capture of all cancer patients who tested positive for COVID-19 before oncological treatment and subsequently had their treatment affected. The timeframe for this will be 6 months retrospectively, i.e., from 1 December 2021 onwards.

This will allow a rapid understanding of the rate of treatment withdrawal, safe restart timings and those on a risk-benefit treatment pathway. It will report on UK-wide activity up to the point of commencement for recording activity in the COV-SPOT cohort.

Subsequent Submission

Following completion of the initial CRF, subsequent reporting will be completed prospectively on a weekly basis.

5.2 Case Identification

Identifying cancer patients testing positive for COVID-19 may rely on several sources, which will differ between centres. The exact mechanism of case

identification will depend on local knowledge and may consist of one or more of the following:

1. Pharmacy team
2. Chemotherapy lead/co-ordinator
3. Radiotherapy lead/co-ordinator
4. COVID-19 medicine delivery unit (CMDU) / neutralising monoclonal antibody (nMAb) referral list
5. Acute oncology service

6. Data Logging

An overview of how data will be logged:

1. The CRF can be found at the following webpage: https://redcap.medsci.ox.ac.uk/surveys/?s=JF9YFT7NWK
2. COV-SPOT Trust Leads or COVID-Spot team members with approval can login using the username and password provided.
3. A CRF should be created for each patient.
4. The CRF can be reopened and edited multiple times and remains active until the site completes data collection.

7. Data Platform

All data is collected on a central REDCap data platform hosted by The Medical Sciences Division, University of Oxford. Each centre will have a communal password to complete CRFs. For transparency, inputting sites can see each other's CRFs.

8. Statistical Analyses

This project is supported by clinical analytical support from the Universities of Oxford and Birmingham. Data will be concatenated on a weekly basis and fed back to key oncology stakeholders. An intermittent summary will be distributed to UK COVID/Cancer Operational Delivery clinical leads.

9. Ethics and Approvals

The project falls under the remit of Public Health Surveillance and is a service evaluation. It therefore does not require further ethical review or approval by the HRA. All data is de-identified at source with location level data blinded to the level of City/Town. Individuals wishing to participate should gain local approvals if required, as this process differs between Trusts. If this initiative identifies findings that have novel generalisable or transferable findings, these will be processed as outlined in registered project IRAS ID 285946, REC: 20/WA/0181.

10. Authorship Statement

Where formal paper publications are developed, they will be authored by the UK COVID/Cancer Operational Delivery clinical leads and COV-SPOT Trust Leads. Additional individuals from the Trust COVID-SPOT team may also be listed as authors with the support of the UK COVID/Cancer Operational Delivery clinical leads. Individuals making a significant contribution to the project will be invited to be UK COVID/Cancer Operational Delivery clinical leads.

11. Project Team

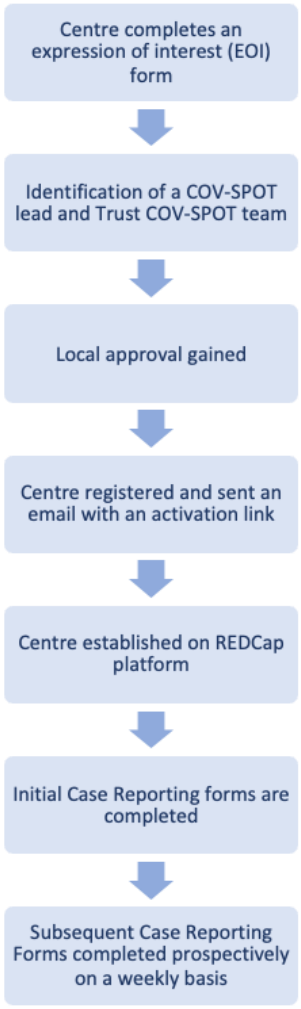
This initiative is co-delivered by Dr Lennard Lee, Dr Grisma Patel, Dr Isabella Watts, Dr Rosie Hattersley, Mr Nathan Appanna, Dr Alex Burnett, Dr Sam Khan, Dr Arvind Tripathy, Dr Martin Little, Dr Matthew Fittall, Dr Justin Liu, Dr James Platt, Dr Hayley Mckenzie, Dr Vijay Patel, Dr Michael Tilby, Dr James Clark.

Senior leadership advice is delivered by Dr Catherine Harper-Wynne and Dr Lennard Lee.

12. Appendices

Appendix A. Process for centre participation and data submission

Expression of interest (EOI) forms can be found at the following website: https://docs.google.com/forms/d/e/1FAIpQLSdMRI434F8RH59hM5btLfjEioICmdEAgAdjZsZHfTZ2Oi6ZyQ/viewform



Appendix B: Case Reporting Form

This Case Reporting Form can also be found at the following website:
https://redcap.medsci.ox.ac.uk/surveys/?s=JF9YFT7NWK

Question	Title	Field type	Options	Notes
1	**Local Hospital ID**	Free text	-	Local Hospital number (not NHS ID)
2	**Gender**	Drop down (single answer)	Male Female Other Undisclosed	
3	**Date of Birth**	Calendar input	-	
4	**Ethnicity**	Drop down (single answer)	White British Asian British Black British Other Asian Black Other Unknown	*Multiple selections if mixed ethnicity*
5	**COVID-19 vaccination doses**		1-5 doses or Unknown	
6	**Cancer type** (ICD-10 code)	Checkboxes (multiple answers)	Site with ICD C0-C97, Other	*More questions appear depending on selection for sub-specification of cancer type*
7	**Cancer status**	Drop down (single answer)	Treated/Never treated Treatment not indicated, Stable Disease, Progressive/Relapsed, Response Level, Complete Remission	

8	**Established** or **new to** cancer treatment(s)?	Radio button (single answer)	Established New to cancer treatment	
9	**Type** of cancer treatment(s)	Checkboxes (multiple answers)	Chemotherapy Radiotherapy Immunotherapy Targeted Hormonal B-cell depleting Stem cell transplantation (SCT)	
10	**Aim** of cancer treatment(s)	Drop down (single answer)	Neoadjuvant Primary Adjuvant Palliative Unknown N/A	
11	**Date** of positive COVID-19 test(s)	Calendar input	-	
12	Test **type**(s)	Checkboxes (multiple answers)	LFD PCR Other	*If Other selected, another question appears with free text for specification*
13	**Indication** for test(s)	Drop down (single answer)	Symptomatic Asymptomatic - routine screening pre-treatment Asymptomatic - routine other Asymptomatic - post-exposure Other/unknown	
14	Symptom **severity**	Drop down (single answer)	Mild Moderate Hospitalisation (with or without oxygen requirement) Intensive care admission Unknown	*Appears only if Symptomatic selected for **Q13***

15	**Early antiviral / monoclonal treatments given?**		Yes No Unknown	*If Yes selected, another question appears with drop down for type (Remdesivir, Sotrovimab, Paxlovid, Other, Unknown)*
16	**Any cancer treatment delayed following positive test?**	Yes/No	-	***Q17-Q21** only appear if Yes selected*
17	**Which** treatment(s) **delayed**?	Checkboxes (multiple answers)	As for Question 9	
18	**Duration** of delay (weeks)	Free text	-	
19	**Reason** for delay	Drop down (single answer)	NICE guidelines Clinical concern Capacity issue Patient choice	*Capacity issues may be e.g., patient clinically asymptomatic but no COVID+ isolated area available to deliver treatment*
20	**COVID status** when treatment restarted	Drop down (single answer)	Negative Positive (symptomatic or asymptomatic) Unknown	
21	**Which** treatment(s) **restarted**?	Checkboxes (multiple answers)	As for Question 9	
22	**COVID-19 outcomes 4 weeks** after restarting cancer treatment?	Drop down (single answer)	None Worsening symptoms Hospitalisation Hospitalisation with oxygen requirement Intensive care admission COVID-19 death Other death Other N/A	
23	**COVID-19 outcomes 8 weeks** after restarting	Drop down (single answer)	As for Q22	

	cancer treatment?			
24	Clinical impact of positive COVID-19 test on **cancer outcome?**	Drop down (single answer)	None Unknown Progressive disease due to delay Surgery delays due to coronavirus infection Decision to change regime in view of coronavirus infection Other	