ISARIC (International Severe Acute Respiratory and Emerging Infections Consortium)

A global federation of clinical research networks, providing a proficient, coordinated, and agile research response to outbreak-prone infectious disease

Analysis Plan for ISARIC International COVID-19 Patients

Title of proposed research
Characteristics, presentation, risk factors, treatments and outcomes in patients with cancer and COVID-19 (ARC: ISARC International Cancer)
Version: (Date: Day/Month/Year)
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Working Group Chair (name, ORCID ID, email, institution, country)
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[1]Working group co-chair (name, ORCID ID, email, institution, country)
Co-chair TBD - we seek a collaborator with cancer expertise/interest, ideally based in a low or middle income country, to help direct this analysis – please email laura.merson@ndm.ox.ac.uk if you are interested Jose A. Calvache (jacalvache@unicauca.edu.co, Universidad del Cauca, Colombia, ORCID: 0000-0001-9421-3717), with

[1] Either chair and/or co-chair are based in an institution in an LMIC. If you would like to be connected with an eligible co-chair please let us know at ncov@isaric.org.

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Final draft SAPs will be circulated to all ISARIC partners for their input with an invitation to participate. ISARIC can help to set up collaborator meetings; form a working group; support communications; and accessing data. Please note that the details of all approved applications will be made publicly available on the ISARIC website. Please complete all sections of this form fully and return to ncov@isaric.org

Introduction

Patients with cancer are at a higher risk of severe COVID-19 and death if infected with SARS-CoV-2. Among hospitalized patients with COVID-19, cancer has been shown to be associated with a higher risk of death, with relative risks up to ~5 compared to patients without cancer, which vary by age, comorbidities and other characteristics. Most evidence has been from high-income countries and global studies on patients from diverse settings are lacking. We aim to assess the associations of cancer with clinical presentation, risk factors, treatments, and outcomes among hospitalized patients with COVID-19.

This document details the initial analysis plan for publication on a subset of COVID-19 patients in the global cohort in the ISARIC database, as of 20 Aug 2021. There are currently 47 countries (as of 20 AUG 2021) contributing data and these have so far contributed data on 439922 patients. These data will represent the global experience of the first 16 months of this pandemic.

Participatory Approach

All contributors to the ISARIC database are invited to participate in this analysis through review and input on the statistical analysis plan and resulting publication. The outputs of this work will be disseminated as widely as possible to inform patient care and public health policy, this will include submission for publication in an international, peer-reviewed journal. ISARIC aims to include the names of all those who contribute data as cited collaborators of this publication, subject to the submission of contact details and confirmation of acceptance of the final manuscript within the required timelines, per ICMJE policies and the ISARIC publication policy.

Research Plan

Summary of Research Objectives
To describe the characteristics, presentation, risk factors, and treatments of patients with cancer and Covid-19, and to assess the associations of cancer with outcomes.

Proposed Target Population

All patients with a known cancer status (some analyses will be only among patients with cancer).

Clinical Questions/Descriptive Analyses

- Describe the demographic and clinical characteristics of patients with cancer in ISARIC including age, sex, comorbidities, smoking, and BMI
- To describe the clinical features and severity of COVID-19 in the overall cancer population within ISARIC and by the different tumour types (where data available)
- Investigate the reasons for admission – cancer-related vs COVID-19, where data available
- To compare the symptoms at presentation between patients with cancer and all others, and if many of the patients with cancer were admitted for cancer-related reasons do it separately for those and for those admitted for COVID-19
- To describe the clinical and laboratory variables that are associated with COVID-19 severity and mortality in different tumour types (where data available)
- Treatments in patients with cancer vs others
- To describe the use of healthcare resources (including intensive care and IMV) in the treatment of COVID-19 in the overall cancer population and by different tumour types (taking into account intensive care availability), and assess its relationship with GDP and healthcare capacity
- To determine the COVID-19 fatality rate overall in the cancer population as well as by different tumour types
- To determine the influence of disease stage, treatment intent and treatment history on severity and outcome of COVID-19 (where available)
- To undertake a matched cohort study using the cancer and non-cancer patients with COVID-19

Planned Statistical Analyses, Methodology and Representation

1. Overall frequencies of key demographic variables.
2. Frequencies of reasons for admission (or onset of COVID-19 symptoms before/after hospitalisation).
3. Frequencies of symptoms at presentation of patients with and without cancer.
4. Frequencies of comorbidities and risk factors among patients with and without cancer.
5. Medians and IQRs of serology measurements among patients with and without cancer.
6. Frequencies of treatments administered to patients with and without cancer.
7. Cox proportional hazards models will be fitted to estimate hazard ratios of death, ICU admission, and use of IMV comparing patients with and without cancer. Potential confounders will be identified and adjusted for. The

proportional hazards assumption will be assessed using Schoenfeld residuals.

8. Outcome of cancer patients compared with non-cancer patients by age, sex and over time

Analyses will be done overall, by cancer site (where data are available), for haematological and solid tumours, metastatic and non-metastatic, admitted for cancer-related reasons or because of COVID-19.

Subgroup analyses will be done by age, sex, region, time period, any proxy of performance status.

Handling of Missing Data
Analysis will be performed to ascertain a detailed overview of the extent of missingness in the data. This should enable the identification of variables which lack sufficient data to allow for any useful analysis to performed on them. The type of missingness will be considered including whether data are not missing at random and follow-up with sites will be conducted if appropriate. If appropriate, imputation will be performed using Multiple Imputation by Chained Equations (MICE).

Other Information

Findings will be submitted for publication.

References

C. Palmieri, L. Turtle, TM. Drake, A. Docherty, EM. Harrison, B. Greenhalf, P.Openshaw, JK. Baillie, MG Semple. Prospective data of >20,000 hospitalised patients with Cancer and COVID-19 derived from the COVID-19 Clinical Information Network and international Severe Acute Respiratory and Emerging Infections Consortium WHO Coronavirus Clinical Characterisation Consortium. ESMO Congress 2021.

C. Palmieri, D. Palmer , P. J. M. Openshaw , J. K. Baillie , M. G. Semple , L. Turtle. Cancer datasets and the SARS-CoV-2 pandemic: establishing principles for collaboration. ESMO Open 2020 May;5(3):e000825. doi: 10.1136/esmoopen-2020-000825.