Scientific Advisory Group

COVID-19 Scientific Advisory Group Rapid Evidence Report

Cancer treatment after a COVID-19 infection

February 18, 2021 [Update to June 2020 review]

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Lay Summary

- Delivering cancer treatment during the COVID-19 pandemic is challenging given that cancer patients, particularly those receiving active chemotherapy, and those with recent bone marrow transplants, appears to be at increased risk for serious complications from COVID-19.
- Cancer patients may have extra considerations for both risk of transmission of infection and recovery from infection due to being immunocompromised from their underlying condition and its treatments.
- The information in this rapid review is meant to be used in addition to clinical judgment and knowledge of the patient.
- Recommendations:
    1. Patients diagnosed with cancer and COVID-19 positive status should defer their visit to the cancer centre until symptoms of COVID-19 have substantially resolved for at least 48 hours, and at least 14 days have passed from the onset of COVID-19 symptoms (or 14 days since specimen collection date if asymptomatic). Patients who experienced critical COVID-19 illness, or are highly immunosuppressed (e.g., bone marrow transplant patients, patients receiving active chemotherapy), should wait for at least 21 days before visiting a cancer centre. Decisions about the specific number of days will be made by the patient's oncologist in consultation with an infection prevention and control physician on a case-by-case basis.
    2. Cancer treatment for patients with a COVID-19 positive status should generally be deferred for at least 3 months for cancers with low risk progression, and 1-3 months for cancers with intermediate risk of progression. No delays are recommended for cancer with high risk of progression.
    3. Patients should fulfill standard eligibility criteria for the specific cancer treatment (e.g., adequate performance status and organ function), and provide informed consent considering relative risks and benefits of the specific treatment.
- These recommendations supersede the recommendations presented in the last version of this document (dated June 2020). Updates in the recommendations include an extension of the time period from at least 14 days to at least 21 days that patients who experienced critical COVID-19 illness or who are highly immunosuppressed have to wait until they can visit the cancer centre. This report also emphasizes the need for oncologists to consult with an infection prevention and control physician to determine the optimal timing for removal from isolation.

Authorship and Committee Members

Name	Contribution
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Topic: What is the optimal strategy for assessing patients who were infected with COVID-19 for suitability for starting or resuming cancer treatment? (Updated February 2021)

1. **What criteria can be used to assess both clinical suitability for proceeding with therapy in the setting of recent infection, as well as infection control criteria to reduce risk of transmission of COVID-19 in cancer care environments?**
2. **What criteria should be used to ensure that patients are well enough to have cancer treatment after COVID-19 infection?**

Context

- Delivering cancer treatment during the COVID-19 pandemic is challenging given that cancer patients, particularly those receiving active chemotherapy, and those with recent bone marrow transplants, appears to be at increased risk for serious complications from COVID-19.
- Cancer patients may have extra considerations for both risk of transmission of infection and recovery from infection due to being immunocompromised from their underlying condition and its treatments.
- To reduce the risk of COVID-19 infection among cancer patients and staff, all patients and visitors in Alberta are screened before their appointments at the cancer centre (questionnaire) (CancerControl Alberta, 2020b). Decisions for clearing cancer patients infected by COVID-19 so they can safely initiate or re-initiate cancer treatment are currently made by cancer teams, based on their expertise and opinion.
- This rapid review has been based upon existing literature related to COVID-19 and cancer, published guideline documents related to the COVID-19 pandemic, and clinical experience with the SARS and MERS coronaviruses, as well as experience in influenza epidemics.
- This review does not address the following aspects related to standard strategies for clearing patients for cancer treatment: 1) increased risk of suffering toxicities related to treatment, 2) consent from patients to proceed with treatment.
- The information in this rapid review is meant to be used in addition to clinical judgment and knowledge of the patient.
- The recommendations presented in this document supersede the recommendations presented in previous versions of this document (dated April 2020, and June 2020). Initial recommendations (document dated April 2020) considered a combination of a test-based and a symptom-based strategy to ensure that patients are no longer infectious. Updated recommendations (document dated June 2020, and present document) reflect the adoption of a symptom-based strategy. The shift to a symptom-based strategy was made in June 2020 in consideration of clinical experience and early evidence showing prolonged test positivity for up to 12 weeks despite resolution of symptoms of infection. Since June 2020, further research has consolidated existing evidence

supporting the adoption of a symptom-based strategy. In addition, the updated recommendations presented in this document differ from the last update in that patients who had critical COVID-19 symptoms and are highly immunosuppressed are not recommended to visit the cancer centre (and proceed with cancer treatment) until at least 21 days have passed from symptom onset. Decisions about the specific number of days should be made by the patient's oncologist in consultation with an infection prevention and control physician on a case-by-case basis.

- This review is not generalizable to other types of immunosuppressed or immunocompromised patients (i.e., non-cancer-related immunosuppression).

Key Messages from the Evidence Summary

- Cancer patients may be more susceptible to infections than individuals without cancer by virtue of their cancer therapy and sometimes their underlying disease, and may be at increased risk for serious complications related to a COVID-19 infection.
- Cancer patients with COVID-19 who are undergoing or have recently undergone cancer treatment might be at increased risk of severe complications from a COVID-19 infection. The reasons for worse outcomes in cancer patients are uncertain, and recent studies suggest they might be related to demographics (advanced age, male sex) and comorbidities of cancer patients.
- There is limited evidence to support a definitive answer to how long highly immunocompromised patients are contagious and at risk for forward transmitting SARS-CoV-2, but growing evidence suggests some may have a prolonged duration of detection potentially infectious virus.
- Assessment of clinical recovery can be somewhat subjective and challenging. Recommendations presented are based on avoidance of transmission risk in cancer care settings because of the serious consequences.
- For cancer patients with COVID-19 it is recommended that cancer treatment is deferred until symptoms of COVID-19 have resolved, unless the cancer is rapidly progressing and the risk-benefit assessment favours proceeding with cancer treatment.
- There are no accepted guidelines to ensure safe initiation or re-initiation of cancer treatment after a COVID-19 infection. Expert consensus suggests reasonable durations of delay are >3 months for cancers with low risk progression, 1-3 months for cancers with intermediate risk of progression, and no delay for cancer with high risk of progression depending on the patient context and prognosis.

Committee Discussion

The committee achieved consensus on the key messages and recommendations. The committee reviewed the recommendations and felt that the changes made since their last update of this document (dated June 2020) are reasonable and appropriate. In particular, they agreed about updating the recommendation made for highly immunosuppressed patients with COVID-19 positive status about not visiting the cancer centre (and proceeding with cancer treatment) for at least 21 days from symptom onset (compared with the 14 days previously recommended). They also deemed appropriate to frame these recommendations around the Infection Prevention & Control disease management guidelines and isolation precautions, and endorsing that decisions about allowing highly immunocompromised patients infected with COVID-19 to come off isolation and visit a cancer centre are to be done in consultation with an infection prevention and control physician on a case-by-case basis.

Recommendations

1. For cancer patients infected with COVID-19 (regardless of whether the individual patients are symptomatic or asymptomatic upon COVID-19 testing) it is recommended that provincial Infection Prevention & Control disease management guidelines and isolation recommendations for immunocompromised patients should be respected when patients receive cancer treatment, and in general, that any visits to the cancer centre (and proceeding with cancer treatment), are deferred until symptoms of COVID-19 have substantially resolved for at least 48 hours, and the patient is at least 14 days from the onset of COVID-19 symptoms (or 14 days since specimen collection date if asymptomatic).

   For patients who experienced critical COVID-19 illness, or are highly immunosuppressed (e.g., bone marrow transplant patients, patients receiving active chemotherapy), the deferral of visits to the cancer centre (and treatment) should be extended to 21 days or longer. In these cases, the oncologist should consult an infection prevention and control physician for further direction about clearing individual patients of COVID-19 positive status, and decisions will be made on a case-by-case basis. For patients who are highly immunocompromised, and when the oncologist feels a repeat swab result would help in the decision about allowing a patient visit the cancer center so they are able to start or restart treatment (e.g., patients who are >21 days from a COVID-19 diagnosis and have had partial symptomatic improvement), a lab-based PCR test, preferably using the same platform, may be considered in consultation with the infection prevention and control physician, to determine test negativity or to assess serial cycle threshold (Ct) values if the swab is not negative.

2. Reasonable ranges of deferral of cancer therapeutics to allow convalescence and optimal healthcare supports are suggested as follows: >3 months may be acceptable for cancers with low risk of progression, 1-3 months for cancers with

intermediate risk of progression, and no deferrals for effective cancer therapeutics in patients with high risk of progression.

3. Patients should fulfill standard eligibility criteria for the specific cancer treatment (e.g., adequate performance status and organ function), and provide informed consent considering relative risks and benefits of the specific treatment (CancerControl Alberta, 2020a).

Practical Considerations

In addition to these recommendations, the following practical considerations apply:

- Cancer patients who do not yet meet above criteria for clearance of COVID-19 (Recommendation 1) and who require urgent cancer treatment that is expected to be highly effective should be managed in the outpatient setting as much as possible and hospital admission should proceed only if patients meet established criteria for admission with COVID-19. Admission to a COVID-19 clinical care area might be preferred over a cancer ward depending on the clinical context and should be considered.
- After complying with provincial Infection Prevention & Control disease management guidelines and isolation recommendations (Recommendation 1), it may still be reasonable to defer cancer treatment for patients requiring non-urgent cancer treatment, both to avoid any potential complications arising from COVID-19, and given the availability of health care resources during this pandemic (e.g., limited ability to both deliver therapy and support patients who develop complications from therapy).
- Preventive and mitigation strategies should be in place and adhered to including patient symptom screening, use of masks, accessible hand hygiene, and appropriate physical distancing.

Research Gaps

Further data collection on cancer patients who subsequently receive cancer treatment should be undertaken to inform future decisions about when it is safe to remove individual patients with COVID-19 from isolation and allow them to visit a cancer centre, and the impact of delaying cancer treatment. Extending these observations to better understand mid- and long-term outcomes for these patients is encouraged.

Strength of Evidence and limitations of this review

Credible information sources were identified through a rapid online search performed by Knowledge Resources Services, within Alberta Health Services, and the writer of this review. Relevant sources synthesized in this review include 67 references.

Thirty two references are original research including 26 articles related to SARS-CoV-2 or COVID-19 (Arons et al., 2020; Baang et al., 2021; Bullard et al., 2020; Chen et al., 2020; Chin et al., 2020; Crolley et al., 2020; Dai et al., 2020; Ferrari et al., 2021; Gao et al., 2020; Joharatnam-Hogan et al., 2020; Kuderer et al., 2020; Kujawski et al., 2020; Lee et al., 2020; Li et al., 2020; Liu, Lu, Wang, Liu, & Zhu, 2020; Lu et al., 2020; Park,

Lee, Kim, de Melo, & Kasi, 2021; Saini et al., 2020; Song et al., 2021; van Kampen et al., 2021; Williams et al., 2020; Wolfel et al., 2020; Young et al., 2020; H.-Y. Zhang et al., 2020; H. Zhang et al., 2020; L. Zhang et al., 2020), and three related to other viruses or viral respiratory outbreaks (Dignani et al., 2014; Falcone et al., 2013; Lehners et al., 2013). Six references are review articles (Banna, Curioni-Fontecedro, Friedlaender, & Addeo, 2020; Derosa et al., 2020; Giannakoulis, Papoutsi, & Siempos, 2020; Kamboj & Sepkowitz, 2009; Russell et al., 2020; Venkatesulu et al., 2020). Fifteen references are commentaries (Aydillo et al., 2020; Melissa Bersanelli, 2020; M Bersanelli et al., 2020; Gelderblom, Veelken, & Stiggelbout, 2021; Liang et al., 2020; Poortmans, Guarneri, & Cardoso, 2020; Tang & Hu, 2020), opinion papers (Kutikov et al., 2020), editorials (Rassy et al., 2020), or research letters (Desai, Sachdeva, Parekh, & Desai, 2020; Li N, Wang X, & T., 2020; Oh, 2020; Xiao et al., 2020; Yu, Ouyang, Chua, & Xie, 2020; Zou et al., 2020). Five of these references have not been peer-reviewed (preprints) (Chin et al., 2020; Gao et al., 2020; Venkatesulu et al., 2020; Williams et al., 2020; H.-Y. Zhang et al., 2020).

In addition, 15 references are publications produced by expert panels (Akladios et al., 2020; American Society of Clinical Oncology, 2020; Guckenberger et al., 2020; Penel et al., 2020) or by local, national and international health organizations and/or authorities in response to managing the COVID-19 or similar pandemics (Alberta Health Services, 2020a, 2020b, 2020c, 2021; CancerControl Alberta, 2020a, 2020b; Centers for Disease Control and Prevention, 2020a; European Centre for Disease Prevention and Control, 2020a, 2020b; Ministry of Health, 2020; National Institute of Clinical Excellence, 2020), which use a range of research sources and likely expertise consensus within these organizations. Seven of these references are Alberta internal policy documents (Alberta Health Services, 2020a, 2020b, 2020c, 2021; CancerControl Alberta, 2020a, 2020b; Ministry of Health, 2020).

Key limitations of this review include:

- Rapid turnaround time resulted in a limited time to conduct a thorough search of the research and grey literatures.
- The evidence related to COVID-19 is rapidly evolving, thus some new developments in the literature might not have been captured in this review.
- Some of the most updated literature available has not yet been peer-reviewed, and available literature on particular aspects is often limited to grey expert panels and jurisdictional reports.

Summary of Evidence

Evidence from existing policies and guidelines

Governments across the globe have made it clear that cancer treatment should continue to be prioritized whenever possible during the COVID-19 pandemic. For cancer patients with a confirmed COVID-19 infection it is established that, unless the cancer is rapidly progressing and the risk-benefit assessment favours proceeding with cancer treatment (American Society of Clinical Oncology, 2020), patients should be

assessed for holding cancer treatment until symptoms of COVID-19 have resolved and there is some certainty they are no longer infectious.

a) *What criteria can be used to assess both clinical suitability for proceeding with therapy in the setting of recent infection, as well as infection control criteria to reduce risk of transmission of COVID-19 in cancer care environments?*

There is a paucity of research on follow-up of recovered COVID-19 patients. Evidence related to the recovery of cancer patients after a COVID-19 infection has been rapidly evolving since the beginning of the pandemic, and is still limited.

Earlier in the pandemic, recommendations from leading expert groups and health authorities to determine when patients with COVID-19 could be no longer be considered an infection threat to others were based on both test-based and symptom-based criteria. For example, the European Centre for Disease Prevention and Control (2020b) in April 2020 established that patients were to be considered clear when they have had at least 2 upper respiratory tract samples negative for COVID-19, collected at ≥24-hour intervals. For symptomatic patients, tests should be performed after the resolution of symptoms, at least 7 days after the onset of symptoms, or after >3 days without fever. For asymptomatic patients, tests should be performed at a minimum of 14 days after the initial positive test confirming the COVID-19 diagnosis. Based on accumulating evidence on the viral shedding and infectiousness, in October 2020 these recommendations were updated (European Centre for Disease Prevention and Control, 2020a) to indicate that symptomatic patients are considered clear after 14 days and up to 20 days from the onset of symptoms based on individual risk assessment. Asymptomatic patients who had a positive SARS-CoV-2 test should self-isolate for 10 days from the date the sample was taken. For the severely ill or immunocompromised cases, European Centre for Disease Prevention and Control (2020a) recommends two consecutive negative PCR tests in a 24-hour period for the discontinuation of isolation; the second test is needed as confirmatory, to exclude the possibility of a false negative result.

Similarly, earlier in the pandemic the Centers for Disease Control and Prevention (2020a, May 2020) established two alternative strategies to clear patients infected with COVID-19: a test-based and a symptoms-based strategy. In August 2020, the Centers for Disease Control and Prevention no longer recommended the test-based strategy in response to new evidence suggesting that in the majority cases the test-based strategy resulted in prolonged isolation of patients who continued to shed detectable SARS-CoV-2 RNA but were no longer infectious. Since August 2020, their revised recommendation is solely based on the symptom-based strategy, and consists of:

- For symptomatic patients:
    - at least 10 days have passed since symptoms first appeared, and
    - at least 24 hours have passed since recovery defined as resolution of fever without the use of fever-reducing medications, and
    - respiratory symptoms (e.g., cough, shortness of breath) have improved

- For asymptomatic patients:
    - 10 days have passed since the date of their first positive COVID-19 diagnostic test, assuming they have not subsequently developed symptoms since their positive test

In addition, the revised strategy (Centers for Disease Control and Prevention, 2020a) establishes that for patients with severe to critical illness or patients who are severely immunocompromised, transmission-based precautions may be discontinued when:

- For symptomatic patients:
    - at least 10 days and up to 20 days have passed since symptoms first appeared, and
    - at least 24 hours have passed since last fever without the use of fever-reducing medications, and
    - symptoms (e.g., cough, shortness of breath) have improved

- For asymptomatic patients:
    - at least 10 days and up to 20 days have passed since the date of their first positive viral diagnostic test

As new evidence in the topic has emerged, Alberta Health Services has also shifted from a test-based to a symptom-based strategy. In April 2020, Alberta Health Services established that hospitalized patients with a confirmed COVID-19 diagnosis who were immunosuppressed were to be isolated for 14 days from the onset of symptoms and until symptoms had resolved for at least 48 hours, and had to have at least 2 consecutive negative nasopharyngeal swabs collected at least 7 days apart (Alberta Health Services, 2020b). Guidelines by Alberta Health updated in May 2020, and revised in August 2020, do not include follow-up testing as a requirement, and establish that immunocompromised patients can end their isolation when 14 days from the onset of symptoms have passed, they have not had a fever within the last 24 hours (without taking fever-reducing medications), and their other symptoms have improved (Alberta Health Services, 2021; Ministry of Health, 2020).

For acute care settings, as it is the case of cancer centres, Infection Prevention & Control guidelines supersede the presented public health guidelines. For highly immunosuppressed patients, oncologists are to consult an infection prevention and control physician for direction about clearing these patients of COVID-19 positive status. Recommendations are to be made on a case-by-case basis, but in general immunocompromised patients will be cleared when:

For non-severely immunocompromised patients:
- 14 days have passed since symptoms first appeared (/positive test), and
- at least 48 hours have passed since symptoms improved to new or pre-existing baseline

For severely immunocompromised patients:

- at least 21 days have passed since symptoms first appeared, and
- at least 48 hours have passed since symptoms improved to new or pre-existing baseline, and
- there is at least one negative PCR test (on day 21 or later)

These Infection Prevention & Control guidelines are currently being drafted, and have not been published yet. When published, they will include specifics about the definition for severe immunocompromise, and details about different types of malignancies and their treatments.

b) What criteria should be used to ensure that patients are well enough to have cancer treatment after COVID-19 infection?

Currently, there is no evidence to support withholding or postponing cancer treatment, and there are no accepted guidelines as to when cancer treatment can be safely initiated or reinitiated after a COVID-19 infection. Given that reinfection rates are unknown, the potential effects of further suppressing or augmenting a patient's immune system quickly after a COVID-19 infection must be weighed heavily against the prognosis and risks of delaying treatment. Clinicians will need to decide locally and on a case-by-case basis based on expert judgement.

Kutikov et al. (2020) developed the following guidelines based on expert consensus:

- Based on **low risk** of progression in certain cancers, it may be safe to **delay for more than 3 months** certain treatments, regardless of age (including surgery and radiation for non-melanoma skin cancer, and treatments for chronic hematologic cancers).
- Based on **intermediate risk** of progression in other cancers, **a delay up to 3 months** may be acceptable the following settings, particularly for individuals aged 50 and older: 1) surgery for high-risk prostate cancer, colon cancer with low risk for imminent obstruction, low-risk melanoma, 2) radiation for post-resection endometrial cancer and high-risk resected prostate cancer, 3) chemotherapy for advanced breast, colorectal, and lung cancer.
- Given a **high risk** of progression in certain cancers, **no delay** is recommended in treatments for under age 70: 1) surgery for ≥2 cm lung mass; colon cancer with imminent obstruction; type 2 endometrial cancer; pancreatic, ovarian, or liver mass(es) suspicious for malignancy; high-risk non-muscle invasive or muscle invasive urothelial cancer; 2) radiation for lung cancer; locally advanced rectal cancer; head and neck cancer; 3) chemotherapy for acute leukemia, large cell lymphoma, Hodgkin lymphoma, symptomatic myeloma, and all other non-low-grade hematologic cancers; testicular cancer; small cell lung cancer; most head and neck cancers, except thyroid.

In addition to these guidelines:

- The National Institute of Clinical Excellence (2020) recommended a delay of at least 3 months for hematopoietic stem cell transplantation, except for patients

who have a high risk of disease progression, morbidity or mortality, in which case they suggest deferral until patients no longer show symptoms and have 3 repeated negative PCR tests, at least 1 week apart. This recommendation was still valid in the last revision of the guidance document, in July 2020.

- Guckenberger et al. (2020, April) made practical recommendations to treat patients with lung cancer including postponing the initiation of radiotherapy until the patient becomes asymptomatic and tests negative for COVID-19, and interrupting radiotherapy until the patient becomes asymptomatic and tests negative for COVID-19 in the three cases of non-curative intent radiotherapy. Banna et al. (2020) proposed a tool to support oncologists and physicians in treatment decision for patients with lung cancer.
- Penel et al. (2020, April) presented recommendations for sarcoma patients including postponing any treatment at least 15 days after the start of the symptoms and when the patient has recovered.
- The FRANCOGYN group recommended that surgical management of patients with gynecologic cancers should be postponed for at least 15 days (Akladios et al., 2020, June). An overview of published guidelines for gynecological cancer patients can be found in (Uwins et al., 2020)
- Katims et al. (2020, June) presented recommendations related to delays in surgery for urologic cancers. Surgical management of T3 renal masses, high-grade upper tract urothelial carcinoma, and penile cancer should not be delayed. Treatment of unfavorable intermediate or high-risk prostate cancer, can be delayed for 3 to 6 months without affecting oncologic outcomes.

Other tumour groups may have their own tumor-specific recommendations. Recommendations might be regularly updated as new evidence emerges.

Evidence from the primary literature

a) *What criteria can be used to assess both clinical suitability for proceeding with therapy in the setting of recent infection, as well as infection control criteria to reduce risk of transmission of COVID-19 in cancer care environments?*

Earlier in the pandemic, in a case report by Chen et al. (2020) it was suggested that recurrence in patients with positive COVID-19 testing may occur, and that patients may remain persistently positive despite symptoms being resolved. A small cluster study by Wolfel et al. (2020) was the first study to report prolonged shedding of non-viable virus. A subsequent article by Bullard et al. (2020) reported that prolonged positivity represents non-viable virus in all types of patients. Although results were not generalizable beyond the lab of this research team, we could extrapolate from this study that in general RT-PCR cycle >30 is likely non-viable virus. Based on their data, they suggested that cycle thresholds >24 in conjunction with duration of symptoms >8 days may be used to determine duration of infectivity in patients.

Studies published over the summer 2020 showed that patients recovered from COVID-19 could continue to have SARS-CoV-2 RNA detected in their upper respiratory specimens for up to 12 weeks after illness onset (Li N et al., 2020; Xiao et al., 2020).

Other studies have indicated that both concentrations of SARS-CoV-2 RNA measured in upper respiratory specimens and likelihood of recovering replication-competent virus decline after onset of symptoms (Kujawski et al., 2020; van Kampen et al., 2021; Young et al., 2020; Zou et al., 2020). A number of publications show that replication-competent virus was not recovered after 10 days following symptom onset for patients with mild to moderate COVID-19 (Arons et al., 2020; Lu et al., 2020; Wolfel et al., 2020). However, evidence regarding the period of active shedding and contagiousness is still limited. Li et al. (2020), for example, have reported that patients who recovered from acute disease may still shed infectious SARS-CoV-2 for over 3 months.

In relation to immunosuppressed patients, academic discussions occurring prior to the pandemic indicated that these patients may shed SARS-CoV-2 virus for prolonged periods, similar to other respiratory viruses due to a constrained immune response (Falcone et al., 2013; Lehners et al., 2013). During the pandemic, discussions have pointed out that immunocompromised patients diagnosed with COVID-19 may remain infectious for longer periods of time, and may therefore need a longer duration of contact and droplet precautions than non-immunocompromised patients with COVID-19 (Centers for Disease Control and Prevention, 2020b). A study by van Kampen et al. (2021) that included immunocompromised patients reported recovery of replication-competent virus between 10 and 20 days after symptom onset in some patients with severe COVID-19 symptoms, but estimated that 88% and 95% of the participating patients' specimens no longer yielded replication-competent virus after 10 and 15 days, respectively, following symptom onset. However, there still is limited data to support definitive answer to how long immunocompromised patients are contagious. A study by Aydillo et al. (2020) reported that patients with profound immunosuppression after undergoing hematopoietic stem-cell transplantation or receiving cellular therapies may shed viable SARS-CoV-2 for at least 2 months. A case report by Baang et al. (2021) of a patient with lymphoma and associated B-cell immunodeficiency demonstrated ongoing replication of infectious SARS-CoV-2 for at least 119 days.

b) *What criteria should be used to ensure that patients are well enough to have cancer treatment after COVID-19 infection?*

It is well established that cancer patients are more susceptible to infections than individuals without cancer because of their immunosuppressive state caused by the malignancy, cancer treatments and comorbidities (Kamboj & Sepkowitz, 2009; Longbottom et al., 2016; Russell et al., 2020). There is also extensive literature indicating that cancer patients are at increased risk for serious complications such as pneumonia and hospitalization (Dai et al., 2020; Derosa et al., 2020; Kamboj & Sepkowitz, 2009; Liang et al., 2020). For example, in a retrospective study during the 2009 influenza A (H1N1) virus pandemic, the cancer patient population was at higher incidence of pneumonia (66%) and 30-day mortality (18.5%) compared with the general population (Dignani et al., 2014). For the specific case of COVID-19, currently available evidence suggests a correlation between cancer and COVID-19 as cancer prevalence in patients with COVID-19 seems higher than in the general population, as reported

across countries (2%) (Desai et al., 2020), and in China (1-2%) (Liang et al., 2020; H.-Y. Zhang et al., 2020; L. Zhang et al., 2020), Italy (5.0%), France (6.0%), South Korea (4.0%) (Gao et al., 2020).

A number of studies have reported high mortality rates and severity of symptoms among patients with cancer and infected with COVID-19, particularly those who are receiving cancer treatment (Saini et al., 2020; Yu et al., 2020). But the effect of COVID-19 on cancer patients remains poorly understood, with many studies limited in sample size or geography. In an initial retrospective analysis of 1,590 patients with COVID-19 in China, Liang et al. (2020) observed that cancer patients (n=18) when compared to patients without cancer had a higher risk of severe events (ICU admission, invasive ventilation or death; 39% vs. 8%, p=0.003). Among cancer patients, this study showed that patients receiving treatment (chemotherapy or surgery) within the last month had higher risk of severe events than patients not receiving treatment (75% vs. 43%) (Liang et al., 2020). Two other cohorts were conducted during the same time fame in Wuhan, China. In a cross-sectorial analysis of 1,524 patients with cancer, Yu et al. (2020) estimated that the infection rate of COVID-19 among cancer patients was higher than the cumulative incidence reported over the same time period in that city (12 patients, 0.79% vs. 0.37%), and reported that 33% of patients with cancer and COVID-19 (4 patients) experienced adverse events (ICU admission or death). In a retrospective analysis, with 1,276 patients with COVID-19 including 28 patients with cancer, L. Zhang et al. (2020) arrived at conclusions similar to the ones in the first study mentioned. Results showed that severe events were more prevalent among cancer patients (ICU admission, mechanical ventilation or death; 53.6% vs. 4.7%), and that cancer patients who underwent treatment (chemotherapy, immunotherapy and radiation) within 14 days of COVID-19 infection were at increased risk of complications with a hazard ratio >4 (95% CI 1.09-15.32, p=0.037) (L. Zhang et al., 2020). Another interesting finding of this study is that almost 30% of infection among cancer patients was suspected to have occurred in the hospital (L. Zhang et al., 2020), which may account for some of the excess prevalence of infection in this cohort. Based on these findings the authors of the three studies (Liang et al., 2020; Yu et al., 2020; L. Zhang et al., 2020) discussed that hospital visits and admissions are a potential risk for COVID-19 infection, and recommended the use of strong personal protection, an intentional postponement of adjuvant chemotherapy and elective surgery for less aggressive cancers, and a decrease in dosage of treatments that cause immunosuppression. It is important to note that the three studies included a small sample of cancer patients, and implied that hospital admission was an independent risk factor to acquiring a COVID-19 infection. In addition, cancer patients in the first and third studies (Liang et al., 2020; L. Zhang et al., 2020) were older and had more co-morbidities than their control, suggesting that these factors might be more associated with worse COVID-19 outcomes than the cancer history itself. Despite these limitations, and the lack of conclusive evidence, the majority of position papers and guidelines developed since the start of the pandemic have been based on the data provided by these studies (Rassy et al., 2020).

There are other studies conducted later in the pandemic that arrived at similar conclusions about higher severity of COVID-19 symptoms and mortality rates among

patients with cancer and COVID-19, especially those who are currently undergoing or have recently underwent treatment. For example, Crolley et al. (2020) collected data from 2,871 patients in two cancer centres in the UK who were receiving chemotherapy (68 patients diagnosed with COVID-19), and concluded that patients with cancer receiving chemotherapy were more likely to die if they contracted COVID-19 than those who did not contract COVID-19 (odds ratio 9.84, 95% CI 5.73-16.90). Tang and Hu (2020) reported the results of a pooled analysis of four cohort studies from China including over 400 patients with COVID-19 and cancer. The authors found a significant association (odds ratio 3.99, 95% CI 2.08-7.64) between cancer treatment (chemotherapy, targeted therapy, immunotherapy or surgery) in the past 2-4 weeks and death in hospital. Song et al. (2021) conducted a similar study also in China, with 248 patients, and reported that the mortality rate of patients who recently received cancer treatment was significantly higher than the mortality rate of patients who had not recently received treatment (24.8% vs 10.2%; hazard ratio 2.010, 95% CI, 1.80-3.75, p=0.027). After controlling to confounders, the authors identified that recent chemotherapy (odds ratio 7.495, 95% CI 1.40-34.19; p=0.015), radiotherapy (odds ratio 15.213, 95% CI 2.10-110.70; p=0.007) and surgery (odds ratio 8.24, 95% CI 1.64-41.95; p=0.012) were independently associated with a higher risk of mortality. It is important to note that the three mentioned studies (Crolley et al., 2020; Song et al., 2021; Tang & Hu, 2020) are limited by the small cohort sizes, restricted geography, and in the case of Tang and Hu (2020) and Crolley et al. (2020) wide confidence intervals around the odds ratio. Park et al. (2021) conducted a systematic review and meta-analysis of 16 retrospective and prospective studies (3,558 patients) to summarize existing evidence for the effect of active cancer treatment on COVID-19 outcomes. They reported that active chemotherapy was associated with higher risk of death compared to no active chemotherapy (odds ratio 1.60, 95% CI, 1.14-2.23), and no significant association with risk of death for active targeted therapy, immunotherapy, chemoimmunotherapy, or recent surgery. Meta-analysis of multivariate adjusted OR of death for active chemotherapy was consistently associated with higher risk of death compared to no active chemotherapy (odds ratio 1.42, 95% CI, 1.01-2.01) (Park et al., 2021).

Starting in late May 2020, new studies conducted with bigger cohorts and diverse geographies brought fresh insights. Of particular relevance are the studies by Kuderer et al. (2020) and Lee et al. (2020), both presenting investigations of multicentre, prospective observational studies. Kuderer et al. (2020)'s study included 928 patients from the US, Canada and Spain with current and past history of cancer and a confirmed COVID-19 diagnosis. The authors reported that 13% of patients died and 26% experienced severe events (death, ICU admission, hospital or ICU admission, mechanical ventilation). They did not find mortality to be associated with cancer treatment (chemotherapy, targeted therapy, immunotherapy, radiotherapy) within 4 weeks of COVID-19 diagnostic, but with general risk factors and risk factors unique to cancer (Kuderer et al., 2020). Lee et al. (2020) followed-up 800 patients with COVID-19 and cancer in the UK and reported a mortality rate of 28%. Similar to Kuderer et al. (2020), they found no interaction between treatment (chemotherapy, immunotherapy, hormonal therapy, targeted therapy, and radiotherapy) received 4 weeks before a positive COVID-19 test and COVID-19 mortality or morbidity. Data showed that cancer

combined with COVID-19 mortality is mainly driven by advancing age, male sex, and other non-cancer comorbidities (Lee et al., 2020).

Other studies support these findings by suggesting that worse outcomes of cancer patients are likely related to more advanced age and a greater number of comorbidities of patients with cancer as compared to patients without cancer (Ferrari et al., 2021; Giannakoulis et al., 2020; Venkatesulu et al., 2020). Meta-analyses conducted in this topic area are of particular relevance. Chin et al. (2020) analyzed 13 studies including 5,678 patients with cancer and showed that age of 65 and above (relative risk 2.27, 95% CI 1.12-4.62, p=0.04), presence of co-morbidities (relative risk 1.70, 95% CI 1.09-2.65, p=0.03), and cardiovascular disease (relative risk 2.66, 95% CI 1.67-4.24, p=0.004) were statistically significant risk factors for death following COVID-19 infection. They found no evidence that patients who had received cancer treatment within 60 days of their COVID-19 diagnosis were at a higher risk of death. Liu et al. (2020) conducted a review of 17 relevant studies that explored the risk factors for mortality, including 3,268 patients with cancer and a COVID-19 diagnosis. They concluded that male sex (relative risk 1.16, 95% CI 0.70-1.95, p=0.006), age over 65 years (relative risk 1.27, 95% CI 1.08-1.49, p=0.004), and comorbidities (especially hypertension and chronic obstructive pulmonary disease; relative risk 1.12, 95% CI 1.04-1.20, p=0.002) were risk factors for death, and recent cancer treatment did not increase mortality (p<0.05). H. Zhang et al. (2020) conducted a review of 15 studies with 3,019 patients diagnosed with cancer and COVID-19, and identified age greater than 65 years (odds ratio 3.16, 95% CI 1.45-6.88) and male sex (odds ratio 2.29, 95% CI 1.07-4.87) were associated with increased risk of severe events (ICU admission, invasive ventilation or death). Although all meta-analyses have found substantial heterogeneity among the included studies, it is important to note that they have found no evidence of interaction between cancer treatment and serious complications or death, and suggest that advanced age and presence of comorbidities are the driver of such complications and death.

In summary, more research is needed to further understand the effects of COVID-19 on the clinical outcomes of patients with cancer, particularly those that are immunocompromised. However, current evidence suggests the need for proactive strategies to protect cancer patients from a potential COVID-19 infection. Importantly, evidence also suggests that withholding cancer treatment during the pandemic might represent a risk to increasing cancer morbidity, perhaps greater than the risks related to COVID-19 itself. The evidence points at the importance of offering standard cancer treatment and overall oncological care if feasible during the pandemic (Poortmans et al., 2020). Decisions about interrupting cancer treatment in patients with active COVID-19 should be based on a clinical assessment that considers the risk of interrupting cancer treatment versus the still poorly defined risk of adverse COVID-19 outcomes in these patients receiving active treatment (Gelderblom et al., 2021; Tang & Hu, 2020).

Evolving Evidence

We acknowledge that the evidence regarding the care and management of individuals that are suspect or confirmed COVID-19 is rapidly evolving. Therefore, significant changes in clinical guidelines may occur and affect this rapid review. Further research is

required to clarify the impacts of new variants of COVID-19 on patients in general and on patients with cancer (with emphasis on those immunocompromised), and the resulting implications for clearing patients from COVID-19 infection so they can proceed with cancer treatment.

Appendix

Literature search details

This literature search was conducted by Xurong (Rachel) Zhao from Knowledge Researches Services, Alberta Health Services, on January 27 and 28, 2021.

The search was done in OVID MEDLINE, LitCovid, PubMed, TRIP PRO, WHO Global research on coronavirus (database), ESMO COVID-19 and Cancer, National Comprehensive Cancer Network, Cambridge Coronavirus Free Access Collection, Cochrane, medRxiv & bioRxiv, Google and Google Scholar. Citation tracking was also conducted in Google Scholar.

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to January 26, 2021

#	Searches	Results
1	exp Coronavirus/ or Coronavirus Infections/ or coronaviru*.mp. or corona viru*.mp. or ncov*.mp. or n-cov*.mp. or novel cov*.mp. or COVID-19.mp. or COVID19.mp. or COVID-2019.mp. or COVID2019.mp. or SARS-CoV-2.mp. or SARSCoV-2.mp. or SARSCoV2.mp. or SARSCoV19.mp. or SARS-Cov-19.mp. or SARSCov-19.mp. or SARSCoV2019.mp. or SARS-Cov-2019.mp. or SARSCov-2019.mp. or severe acute respiratory syndrome coronaviru*.mp. or severe acute respiratory syndrome cov 2.mp. or 2019 ncov.mp. or 2019ncov.mp.	117330
2	exp Antineoplastic Agents/	1118544
3	exp antineoplastic protocols/ or exp chemoradiotherapy/ or consolidation chemotherapy/	156020
4	Chemotherapy, Cancer, Regional Perfusion/	3790
5	Induction Chemotherapy/	2911
6	(antineoplastic* or chemo* or cytotoxic or radiochemo* or myeloma* or neuroblastoma* or osteosarcoma* or glioma* or adenocarcinoma* or hematooncological* or hemato-oncological* or haematooncological* or haemato-oncological* or nephroblastom* or immunoradiotherap*).kf,tw.	1142474
7	or/2-6	1974474
8	1 and 7	2919
9	limit 8 to ed="20200601-20210128"	1327
10	limit 9 to english language	1302

TRIP Database PRO
(antineoplastic* or chemo* or cytotoxic or radiochemo* or myeloma* or neuroblastoma* or osteosarcoma* or glioma* or adenocarcinoma* or hematooncological* or hemato-oncological* or haematooncological* or haemato-oncological* or nephroblastom* or immunoradiotherap*) AND (coronaviru* OR "corona virus" OR ncov* OR n-cov* OR

COVID-19 OR COVID19 OR COVID-2019 OR COVID2019 OR SARS-COV-2 OR SARSCOV-2 OR SARSCOV2 OR SARSCOV19 OR SARS-COV-19 OR SARSCOV-19 OR SARSCOV2019 OR SARS-COV-2019 OR SARSCOV-2019 OR "severe acute respiratory syndrome cov 2" OR "severe acute respiratory syndrome coronavirus*" OR "2019 ncov" OR 2019ncov OR Hcov*) from:2020

PubMed

((("COVID-19"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR COVID-19[tiab] OR COVID19[tiab] OR COVID2019[tiab] OR COVID-2019[tiab] OR SARS-CoV-2[tiab] OR SARSCoV2[tiab] OR SARS coronavirus 2[tiab] OR 2019-nCoV[tiab] OR 2019nCoV[tiab] OR nCoV2019[tiab] OR nCoV-2019[tiab] OR ((Wuhan[tiab] OR Hubei[tiab]) AND coronavirus*[tiab]) OR ((2019[dp] OR 2020[dp]) AND (new[tiab] OR novel[tiab] OR pandemic*[tiab] OR epidemic*[tiab]) AND (coronavirus*[tiab] OR corona virus*[tiab]))) AND ("Antineoplastic Agents"[Mesh] OR "Antineoplastic Combined Chemotherapy Protocols"[Mesh] OR "Antineoplastic Protocols"[Mesh] OR "Chemotherapy, Cancer, Regional Perfusion"[Mesh] OR "Chemoradiotherapy"[Mesh] OR "Consolidation Chemotherapy"[Mesh] OR "Induction Chemotherapy"[Mesh] OR Antineoplastic*[tiab] OR Chemotherap*[tiab] OR chemoradiotherap*[tiab] OR cytotoxic[tiab] OR radiochemotherap*[tiab] OR myeloma*[tiab] OR neuroblastoma*[tiab] OR osteosarcoma*[tiab] OR glioma*[tiab] OR adenocarcinoma*[tiab] OR hematooncological*[tiab] OR hemato-oncological*[tiab])) AND (("2020/06/01"[Date - Entry] : "3000"[Date - Entry]))) AND ("english"[Language])

WHO Global research on coronavirus (database)

antineoplastic* or chemo* or cytotoxic or radiochemo* or myeloma* or neuroblastoma* or osteosarcoma* or glioma* or adenocarcinoma* or hematooncological* or hemato-oncological* or haematooncological* or haemato-oncological* or nephroblastom* or immunoradiotherap*

References

Akladios, C., Azais, H., Ballester, M., Bendifallah, S., Bolze, P.-A., Bourdel, N., Bricou, A., Canlorbe, G., Carcopino, X., Chauvet, P., Collinet, P., Coutant, C., Dabi, Y., Dion, L., Gauthier, T., Graesslin, O., Huchon, C., Koskas, M., Kridelka, F., Lavoue, V., Lecointre, L., Mezzadri, M., Mimoun, C., Ouldamer, L., Raimond, E., & Touboul, C. (2020). Recommendations for the surgical management of gynecological cancers during the COVID-19 pandemic - FRANCOGYN group for the CNGOF. *Journal of gynecology obstetrics and human reproduction*, 101729-101729. doi:10.1016/j.jogoh.2020.101729

Alberta Health Services. (2020a). *Discontinuation of contact and droplet precautions for suspected or confirmed COVID-19*. Retrieved from https://www.albertahealthservices.ca/frm-21624.pdf

Alberta Health Services. (2020b). *Discontinuation of contact+droplet precautions for hospitalized patients tested for COVID-19*. Retrieved from https://www.albertahealthservices.ca/assets/healthinfo/ipc/hi-ipc-emerging-issues-ncov.pdf

Alberta Health Services. (2020c). *Key research question: Can people with previous COVID-19 infection become re-infected by the virus?* Retrieved from https://www.albertahealthservices.ca/topics/Page17074.aspx

Alberta Health Services. (2021). Isolation and quarantine information -COVID-19. Retrieved from https://www.albertahealthservices.ca/topics/Page17239.aspx#when-my

American Society of Clinical Oncology. (2020, December 21, 2020). COVID-19 patient care information. Retrieved from https://www.asco.org/asco-coronavirus-information/care-individuals-cancer-during-covid-19

Arons, M. M., Hatfield, K. M., Reddy, S. C., Kimball, A., James, A., Jacobs, J. R., Taylor, J., Spicer, K., Bardossy, A. C., Oakley, L. P., Tanwar, S., Dyal, J. W., Harney, J., Chisty, Z., Bell, J., Methner, M., Paul, P., Carlson, C. M., McLaughlin, H. P., Thornburg, N., Tong, S., Tamin, A., Tao, Y., Uehara, A., Harcourt, J., Stone, N. D., Clark, T. A., Honein, M. A., Jernigan, J. A., Clark, S., Brostrom-Smith, C., Page, L. C., Kay, M., Lewis, J., Duchin, J. S., & Montgomery, P. (2020). Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. *New England Journal of Medicine, 382*(22), 2081-2090. doi:10.1056/NEJMoa2008457

Aydillo, T., Gonzalez-Reiche, A. S., Aslam, S., van de Guchte, A., Khan, Z., Obla, A., Dutta, J., van Bakel, H., Aberg, J., García-Sastre, A., Shah, G., Hohl, T., Papanicolaou, G., Perales, M.-A., Sepkowitz, K., Babady, N. E., & Kamboj, M. (2020). Shedding of Viable SARS-CoV-2 after Immunosuppressive Therapy for Cancer. *New England Journal of Medicine, 383*(26), 2586-2588. doi:10.1056/NEJMc2031670

Baang, J. H., Smith, C., Mirabelli, C., Valesano, A. L., Manthei, D. M., Bachman, M. A., Wobus, C. E., Adams, M., Washer, L., Martin, E. T., & Lauring, A. S. (2021). Prolonged Severe Acute Respiratory Syndrome Coronavirus 2 Replication in an Immunocompromised Patient. *Journal of Infectious Diseases, 223*(1), 23-27. doi:10.1093/infdis/jiaa666

Banna, G., Curioni-Fontecedro, A., Friedlaender, A., & Addeo, A. (2020). How we treat patients with lung cancer during the SARS-CoV-2 pandemic: Primum non nocere. *ESMO open, 4*, e000765. doi:10.1136/esmoopen-2020-000765

Bersanelli, M. (2020). Controversies about COVID-19 and anticancer treatment with immune checkpoint inhibitors. *Immunotherapy, 12*(5), 269-273. doi:10.2217/imt-2020-0067

Bersanelli, M., Scala, S., Affanni, P., Veronesi, L., Colucci, E., Banna, G., Cortellini, A., & Liotta, F. (2020). Immunological insights on influenza infection and vaccination during immune checkpoint blockade in cancer patients. *Immunotherapy, 12*(2), 105–110.

Bullard, J., Dust, K., Funk, D., Strong, J. E., Alexander, D., Garnett, L., Boodman, C., Bello, A., Hedley, A., Schiffman, Z., Doan, K., Bastien, N., Li, Y., Van Caeseele, P. G., & Poliquin, G. (2020). Predicting infectious SARS-CoV-2 from diagnostic samples. *Clinical Infectious Diseases*. doi:10.1093/cid/ciaa638

CancerControl Alberta. (2020a). *CancerControl Alberta's cancer treatment prioritization framework for systemic therapy, radiation therapy, and supportive care. For contingency service delivery planning during a pandemic*. Retrieved from https://www.albertahealthservices.ca/assets/info/ppih/if-ppih-covid-19-pandemic-prioritization-framework.pdf

CancerControl Alberta. (2020b). *COVID-19 and cancer treatment information for patients and families*. Retrieved from https://www.albertahealthservices.ca/assets/info/ppih/if-ppih-cancer-treatment-info-pf.pdf

Centers for Disease Control and Prevention. (2020a, August 10). Discontinuation of transmission-based precautions and disposition of patients with COVID-19 in healthcare settings (interim guidance). Retrieved from https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-hospitalized-patients.html

Centers for Disease Control and Prevention. (2020b, December 16). If you are immunocompromised, protect yourself from COVID-19. Retrieved from https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/immunocompromised.html

Chen, D., Xu, W., Lei, Z., Huang, Z., Liu, J., Gao, Z., & Peng, L. (2020). Recurrence of positive SARS-CoV-2 RNA in COVID-19: A case report. *International Journal of Infectious Diseases, 93*(297-299), 297-299. doi:10.1016/j.ijid.2020.03.003

Chin, I. S., Galavotti, S., Yip, K. P., Curley, H., Arnold, R., Sharma-Oates, A., Chegwidden, L., Lee, S. I., Lee, L. Y. W., & Pinato, D. J. (2020). Influence of clinical characteristics and anti-cancer therapy on outcomes from SARS-CoV-2 infection: a systematic review and meta-analysis of 5,678 cancer patients. *medRxiv*.

Crolley, V. E., Hanna, D., Joharatnam-Hogan, N., Chopra, N., Bamac, E., Desai, M., Lam, Y.-C., Dipro, S., Kanani, R., & Benson, J. (2020). COVID-19 in cancer patients on systemic anti-cancer therapies: outcomes from the CAPITOL (COVID-19 Cancer PatIenT Outcomes in North London) cohort study. *Therapeutic advances in medical oncology, 12*, 1-14. doi:10.1177/1758835920971147

Dai, M.-Y., Liu, D., Liu, M., Zhou, F.-X., Li, G.-L., Chen, Z., Zhang, Z.-A., You, H., Wu, M., Zhen, Q.-C., Xiong, Y., Xiong, H.-H., Wang, C., Chen, C.-C., Xiong, F., Zhang, Y., Peng, Y.-Q., Ge, S.-P., Zhen, B., Yu, T.-T., Wang, L., Wang, H., Liu, Y., Chen, Y.-S., Mei, J.-H., Gao, X.-J., Li, Z.-Y., Gan, L.-J., He, C., Li, Z., Shi, Y.-Y., Qi, Y.-W., Yang, J., Tenen, D. G., Chai, L., Mucci, L. A., Santillana, M., & Cai, H.-B. (2020). Patients with cancer appear more vulnerable to SARS-CoV-2: A multi-center study during the COVID-19 outbreak. *Cancer discovery, 10*(6), 783-791. doi:10.1158/2159-8290.CD-20-0422

Derosa, L., Melenotte, C., Griscelli, F., Gachot, B., Marabelle, A., Kroemer, G., & Zitvogel, L. (2020). The immuno-oncological challenge of COVID-19. *Nature Cancer, 1*(10), 946-964. doi:10.1038/s43018-020-00122-3

Desai, A., Sachdeva, S., Parekh, T., & Desai, R. (2020). COVID-19 and Cancer: Lessons From a Pooled Meta-Analysis. *JCO global oncology, 6*, 557-559. doi:10.1200/GO.20.00097

Dignani, M. C., Costantini, P., Salgueira, C., Jordán, R., Guerrini, G., Valledor, A., Andrea, N., Herrera, F., Mora, C., Roccia-Rossi, I., Stecher, D., Carbone, E., Laborde, A., Efron, E., Altclas, J., Calmaggi, A., & Cozzi, J. (2014). Pandemic 2009 Influenza A (H1N1) virus infection in cancer and hematopoietic stem cell transplant recipients; a multicenter observational study. *F1000Research, 12*(3), 221. doi:10.12688/f1000research.5251.1

European Centre for Disease Prevention and Control. (2020a). *Guidance for discharge and ending of isolation of people with COVID-19*. Retrieved from https://www.ecdc.europa.eu/sites/default/files/documents/Guidance-for-discharge-and-ending-of-isolation-of-people-with-COVID-19.pdf

European Centre for Disease Prevention and Control. (2020b). *Novel coronavirus (SARS-CoV-2) discharge criteria for confirmed COVID-19 cases – When is it safe to discharge COVID-19 cases from the hospital or end home isolation?* Retrieved from https://www.ecdc.europa.eu/sites/default/files/documents/COVID-19-Discharge-criteria.pdf

Falcone, V., Bierbaum, S., Kern, W., Kontny, U., Bertz, H., Huzly, D., & Panning, M. (2013). Influenza virus A(H1N1)pdm09 hemagglutinin polymorphism and associated disease in southern Germany during the 2010/11 influenza season. *Archives of virology, 158*(6), 1297-1303. doi:10.1007/s00705-013-1610-1

Ferrari, B. L., Ferreira, C. G., Menezes, M., De Marchi, P., Canedo, J., Melo, A. C. d., Jácome, A. A., Reinert, T., Paes, R. D., & Sodré, B. (2021). Determinants of COVID-19 Mortality in Patients With Cancer From a Community Oncology Practice in Brazil. *JCO global oncology, 7*, 46-55.

Gao, Y., Liu, M., Shi, S., Chen, Y., Sun, Y., Chen, J., & Tian, J. (2020). Cancer is associated with the severity and mortality of patients with COVID-19: a systematic review and meta-analysis. *medRxiv*. doi:10.1101/2020.05.01.20087031

Gelderblom, H., Veelken, H., & Stiggelbout, A. M. (2021). COVID-19 and systemic anticancer therapy: exploiting uncertainty. *The Lancet Oncology, 22*(1), 3-5.

Giannakoulis, V. G., Papoutsi, E., & Siempos, I. I. (2020). Effect of Cancer on Clinical Outcomes of Patients With COVID-19: A Meta-Analysis of Patient Data. *JCO global oncology, 6*, 799-808. doi:10.1200/GO.20.00225

Guckenberger, M., Belka, C., Bezjak, A., Bradley, J., Daly, M. E., DeRuysscher, D., Dziadziuszko, R., Faivre-Finn, C., Flentje, M., Gore, E., Higgins, K. A., Iyengar, P., Kavanagh, B. D., Kumar, S., Le Pechoux, C., Lievens, Y., Lindberg, K., McDonald, F., Ramella, S., Rengan, R., Ricardi, U., Rimner, A., Rodrigues, G. B., Schild, S. E., Senan, S., Simone Ii, C. B., Slotman, B. J., Stuschke, M., Videtic, G., Widder, J., Yom, S. S., & Palma, D. (2020). Practice recommendations for lung cancer radiotherapy during the COVID-19 pandemic: An ESTRO-ASTRO consensus statement. *Radiotherapy and Oncology, 146*, 223-229. doi:10.1016/j.radonc.2020.04.001

Joharatnam-Hogan, N., Hochhauser, D., Shiu, K.-K., Rush, H., Crolley, V., Butcher, E., Sharma, A., Muhammad, A., Vasdev, N., Anwar, M., Kantser, G., Saha, A., Raja, F., Bridgewater, J., & Khan, K. (2020). Outcomes of the 2019 Novel Coronavirus in patients with or without a history of cancer - a multi-centre North London experience. *Therapeutic Advances in Medical Onolcogy, 12*, 1-9. doi:10.1101/2020.04.16.20061127

Kamboj, M., & Sepkowitz, K. (2009). Nosocomial infections in patients with cancer. *The Lancet Oncology, 10*(6), 589-597. doi:10.1016/S1470-2045(09)70069-5

Katims, A. B., Razdan, S., Eilender, B. M., Wiklund, P., Tewari, A. K., Kyprianou, N., Badani, K. K., & Mehrazin, R. (2020). Urologic oncology practice during COVID-19 pandemic: A systematic review on what can be deferrable vs. nondeferrable. *Urologic oncology, 38*(10), 783-792. doi:10.1016/j.urolonc.2020.06.028

Kuderer, N. M., Choueiri, T. K., Shah, D. P., Shyr, Y., Rubinstein, S. M., Rivera, D. R., Shete, S., Hsu, C.-Y., Desai, A., de Lima Lopes Jr, G., & others. (2020). Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *The Lancet, 395*(10241), P1907-1918. doi:10.1016/S0140-6736

Kujawski, S. A., Wong, K. K., Collins, J. P., Epstein, L., Killerby, M. E., Midgley, C. M., & Abedi, G. R. (2020). Clinical and virologic characteristics of the first 12 patients with coronavirus disease 2019 (COVID-19) in the United States. *Nature Medicine*(6), 861-868. doi:10.1038/s41591-020-0877-5

Kutikov, A., Weinberg, D. S., Edelman, M. J., Horwitz, E. M., Uzzo, R. G., & Fisher, R. I. (2020). A war on two fronts: Cancer care in the time of COVID-19. *Annals of internal medicine, 172*(11), 756–758. doi:10.7326/M20-1133

Lee, L. Y. W., Cazier, J. B., Starkey, T., Turnbull, C. D., Kerr, R., & Middleton, G. (2020). COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. *The Lancet, 395*(10241), 1919-1926. doi:10.1016/S0140-6736(20)31173-9

Lehners, N., Schnitzler, P., Benner, A., Buchholz, U., Aichinger, E., Frank, U., Heeg, K., Ho, A. D., Egerer, G., Geis, S., Puthenparambil, J., Benz, M. A., Alber, B., Luft, T., Dreger, P., Eisenbach, C., & Kunz, C. (2013). Risk factors and containment of respiratory syncytial virus outbreak in a hematology and transplant unit. *Bone marrow transplantation, 48*(12), 1548-1553.

Li N, Wang X, & T., L. (2020). Prolonged SARS-CoV-2 RNA Shedding: Not a Rare Phenomenon. *Journal of medical virology, 92*, 2286-2287. doi:10.1002/jmv.25952

Li, Q., Zheng, X.-S., Shen, X.-R., Si, H.-R., Wang, X., Wang, Q., Li, B., Zhang, W., Zhu, Y., Jiang, R.-D., Zhao, K., Wang, H., Shi, Z.-L., Zhang, H.-L., Du, R.-H., & Zhou,

P. (2020). Prolonged shedding of severe acute respiratory syndrome coronavirus 2 in patients with COVID-19. *Emerging microbes & infections, 9*(1), 2571-2577. doi:10.1080/22221751.2020.1852058

Liang, W., Guan, W., Chen, R., Wang, W., Li, J., Xu, K., Li, C., Ai, Q., Lu, W., Liang, H., Li, S., & He, J. (2020). Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *The Lancet. Oncology, 21*(3), 335-337. doi:10.1016/S1470-2045(20)30096-6

Liu, Y., Lu, H., Wang, W., Liu, Q., & Zhu, C. (2020). Clinical risk factors for mortality in patients with cancer and COVID-19: a systematic review and meta-analysis of recent observational studies. *Expert review of anticancer therapy*, 1-13.

Longbottom, E., Torrance, H., Owen, H., Fragkou, P., Hinds, C., Pearse, R., & O'Dwyer, M. (2016). Features of postoperative immune suppression are reversible with interferon gamma and independent of interleukin-6 pathways. *Annals of Surgery*(264), 370-377. doi:10.1097/SLA.0000000000001484

Lu, J., Peng, J., Xiong, Q., Liu, Z., Lin, H., Tan, X., Kang, M., Yuan, R., Zeng, L., Zhou, P., Liang, C., Yi, L., du Plessis, L., Song, T., Ma, W., Sun, J., Pybus, O. G., & Ke, C. (2020). Clinical, immunological and virological characterization of COVID-19 patients that test re-positive for SARS-CoV-2 by RT-PCR. *EBioMedicine, 59*, 102960. doi:10.1016/j.ebiom.2020.102960

Ministry of Health. (2020). *Coronavirus, Novel Public Health Disease Management Guideline*. Retrieved from https://www.alberta.ca/notifiable-disease-guidelines.aspx

National Institute of Clinical Excellence. (2020). *COVID-19 rapid guideline: Haematopoietic stem cell transplantation*. Retrieved from https://www.nice.org.uk/guidance/ng164/resources/covid19-rapid-guideline-haematopoietic-stem-cell-transplantation-pdf-66141900749509

Oh, W. K. (2020). COVID-19 Infection in cancer patients: Early observations and unanswered questions. *Annals of Oncology, 31*(17), 838–839. doi:10.1016/j.annonc.2020.03.297

Park, R., Lee, S. A., Kim, S. Y., de Melo, A. C., & Kasi, A. (2021). Association of active oncologic treatment and risk of death in cancer patients with COVID-19: a systematic review and meta-analysis of patient data. *Acta oncologica (Stockholm, Sweden), 60*(1), 13-19. doi:https://dx.doi.org/10.1080/0284186X.2020.1837946

Penel, N., Bonvalot, S., Minard, V., Orbach, D., Gouin, F., Corradini, N., Brahmi, M., Marec-Berard, P., Briand, S., Gaspar, N., Llacer, C., Carrere, S., Dufresne, A., Le Cesne, A., & Blay, J.-Y. (2020). Options thérapeutiques de prise en charge des sarcomes durant la pandémie COVID-19: Propositions du groupe sarcome français. *Bulletin du cancer, 107*(4), 398–399. doi:10.1016/j.bulcan.2020.03.009

Poortmans, P. M., Guarneri, V., & Cardoso, M.-J. (2020). Cancer and COVID-19: What do we really know? *The Lancet, 395*(10241), 1884-1885. doi:10.1016/S0140-6736(20)31240-X

Rassy, E., Khoury-Abboud, R.-M., Ibrahim, N., Kattan, C., Assi, T., & Kattan, J. (2020). What the oncologist needs to know about COVID-19 infection in cancer patients. *Future Oncology, 16*, 1153-1156. doi:10.2217/fon-2020-0312

Russell, B., Moss, C., George, G., Santaolalla, A., Cope, A., Papa, S., & Van Hemelrijck, M. (2020). Associations between immune-suppressive and stimulating drugs and novel COVID-19-a systematic review of current evidence. *Ecancermedicalscience, 14*, 1022-1022. doi:10.3332/ecancer.2020.1022

Saini, K. S., Tagliamento, M., Lambertini, M., McNally, R., Romano, M., Leone, M., Curigliano, G., & de Azambuja, E. (2020). Mortality in patients with cancer and coronavirus disease 2019: A systematic review and pooled analysis of 52 studies. *European Journal of Cancer, 139*, 43-50.

Song, K., Gong, H., Xu, B., Dong, X., Li, L., Hu, W., Wang, Q., Xie, Z., Rao, Z., Luo, Z., Chu, Q., Li, F., & Wang, J. (2021). Association between recent oncologic treatment and mortality among patients with carcinoma who are hospitalized with COVID-19: A multicenter study. *Cancer, 127*(3), 437-448. doi:10.1002/cncr.33240

Tang, L. V., & Hu, Y. (2020). Poor clinical outcomes for patients with cancer during the COVID-19 pandemic. *The Lancet. Oncology, 21*(7), 862-864. doi:10.1016/S1470-2045(20)30311-9

Uwins, C., Bhandoria, G. P., Shylasree, T. S., Butler-Manuel, S., Ellis, P., Chatterjee, J., Tailor, A., Stewart, A., & Michael, A. (2020). COVID-19 and gynecological cancer: a review of the published guidelines. *International Journal of Gynecological Cancer, 30*(9), 1424-1433. doi:10.1136/ijgc-2020-001634

van Kampen, J., van de Vijver, D., Fraaij, P., Haagmans, B., Lamers, M., Okba, N., van den Akker, J., Endeman, H., Gommers, D., Cornelissen, J., Hoek, R., van der Eerden, M., Hesselink, D., Metselaar, H., Verbon, A., de Steenwinkel, J., Aron, G., van Gorp, E., van Boheemen, S., Voermans, J., Boucher, C., Molenkamp, R., Koopmans, M., Geurtsvankessel, C., & van der Eijk, A. (2021). Duration and key determinants of infectious virus shedding in hospitalized patients with coronavirus disease-2019 (COVID-19). *Nature communications, 12*(1), 1-6. doi:10.1038/s41467-020-20568-4

Venkatesulu, B. P., Thoguluva Chandrasekar, V., Giridhar, P., Advani, P., Sharma, A., Hsieh, C. E., Elumalai, T., Elghazawy, H. I., Verma, V., & Krishnan, S. (2020). A systematic review and meta-analysis of cancer patients affected by a novel coronavirus. *medRxiv*, 2020.2005.2027.20115303-20112020.20115305.20115327.20115303. doi:10.1101/2020.05.27.20115303

Williams, M., Le Calvez, K., Mi, E., Chen, J., Dadhania, S., & Pakzad-Shahabi, L. (2020). Estimating the risks from COVID-19 infection in adult chemotherapy patients. *medRxiv*. doi:10.1101/2020.03.18.20038067

Wolfel, R., Corman, V. M., Guggemos, W., Seilmaier, M., Zange, S., Muller, M. A., & Niemeyer, D. (2020). Virological assessment of hospitalized patients with COVID-2019.(Clinical report). *Nature, 581*(7809), 465. doi:10.1038/s41586-020-2196-x

Xiao, F., Sun, J., Xu, Y., Li, F., Huang, X., Li, H., Zhao, J., Huang, J., & Zhao, J. (2020). Infectious SARS-CoV-2 in Feces of Patient with Severe COVID-19. *Emerging Infectious Diseases*(8), 1920.

Young, B. E., Ong, S. W. X., Kalimuddin, S., Low, J. G., Tan, S. Y., Loh, J., Ng, O.-T., Marimuthu, K., Ang, L. W., Mak, T. M., Lau, S. K., Anderson, D. E., Chan, K. S., Tan, T. Y., Ng, T. Y., Cui, L., Said, Z., Kurupatham, L., Chen, M. I. C., & Chan,

M. (2020). Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore. *JAMA: Journal of the American Medical Association, 323*(15), 1488-1494. doi:10.1001/jama.2020.3204

Yu, J., Ouyang, W., Chua, M. L. K., & Xie, C. (2020). SARS-CoV-2 transmission in patients with cancer at a tertiary care hospital in Wuhan, China. *JAMA Oncology, 6*(7), 1108-1110. doi:10.1001/jamaoncol.2020.0980

Zhang, H.-Y., Wang, L.-W., Chen, Y.-Y., Shen, X.-K., Wang, Q., Yan, Y.-Q., Yu, Y., Wu, Q., Wang, X., Zhong, Y.-H., & others. (2020). A multicentre study of 2019 novel coronavirus disease outcomes of cancer patients in Wuhan, China. *medRxiv*. doi:10.1101/2020.03.21.20037127

Zhang, H., Han, H., He, T., Labbe, K. E., Hernandez, A. V., Chen, H., Velcheti, V., Stebbing, J., & Wong, K.-K. (2020). Clinical Characteristics and Outcomes of COVID-19–Infected Cancer Patients: A Systematic Review and Meta-Analysis. *JNCI: Journal of the National Cancer Institute, 00*(0), djaa16.

Zhang, L., Zhu, F., Xie, L., Wang, C., Wang, J., Chen, R., Jia, P., Guan, H. Q., Peng, L., Chen, Y., Peng, P., Zhang, P., Chu, Q., Shen, Q., Wang, Y., Xu, S. Y., Zhao, J. P., & Zhou, M. (2020). Clinical characteristics of COVID-19-infected cancer patients: A retrospective case study in three hospitals within Wuhan, China. *Annals of Oncology, 31*(7), 894-901. doi:10.1016/j.annonc.2020.03.296

Zou, L., Ruan, F., Mingxing, H., Liang, L., Huang, H., Hong, Z., Yu, J., Kang, M., Song, Y., Xia, J., Guo, Q., Song, T., He, J., Yen, H.-L., Peiris, M., & Wu, J. (2020). SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. *New England Journal of Medicine, 382*(12), 1177-1179. doi:10.1056/NEJMc2001737