COVID-19 Scientific Advisory Group Rapid Response Report

Key Research Question:

What is the optimal strategy for assessing patients who were infected with COVID-19 for suitability for starting or resuming cancer treatment?

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?**
b. **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 appear to be at increased risk for serious complications from COVID-19.
- Cancer patients may have extra considerations for both recovery from infection and risk of transmission of infection due to immunocompromise from their underlying condition and its therapies.
- To reduce the chances 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) [1]. Decisions for clearing cancer patients who test positive for COVID-19 to 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 limited literature related to COVID-19 and cancer, existing 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 a previous version of this document (dated April 2020). Initially, both a test-based and a symptom-based strategy to clear patients with COVID-19 were considered, and a decision was made to adopt a test-based strategy as presented in the previous document. These revised recommendations reflect the adoption of a symptom-based strategy. This shift was made in consideration of new evidence and clinical experience showing that RT-PCR may remain positive for several weeks despite resolution of symptoms of infection, and that infectiousness cannot be inferred from a positive COVID-19 RT-PCR.

This review is not generalizable to other types of immunosuppressed or immunocompromised patients.

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 at increased risk for serious complications related to a COVID-19 infection.

- Cancer patients with COVID-19 who have undergone or are undergoing cancer treatment (specifically within a month of infection) might be at increased risk of worse outcomes 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 no evidence available to guide assessing recovery from COVID-19 for cancer patients. The recommendations presented in this review are made primarily based on the increased risk of poor outcomes in patients with cancer who have been infected with COVID-19.
- 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 deferring at least until the patient is recovered and meets the AHS guidelines for isolation precautions is reasonable, with guidance for acceptable durations based on the likelihood of progression of the underlying disease. Based on additional experience gained showing prolonged shedding of dead virus, and new evidence, the committee was in favor of using a symptom-based strategy to clear patients with COVID-19. It was acknowledged that further evidence around the correlation of positive RT-PCR with infectious and replicating virus in COVID-19 may alter these recommendations.

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 generally recommended that provincial public health disease management guidelines and isolation recommendations for immunocompromised patients should be respected when patients receive cancer treatment.
2. We recommend that the initiation (or re-initiation) of cancer treatment, and any visits to the cancer center, are deferred until symptoms of COVID-19 have 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). An exception should be made in highly immunosuppressed patients (e.g., bone marrow transplant patients). In these cases, the oncologist should consult Infection Prevention & Control for further direction about clearing individual patients of COVID-19-positive status, and in this circumstance, as there is less data in this patient population a repeat swab may be considered (for example, in patients who are >14 days from a COVID-19 diagnosis and have had symptomatic improvement without resolution).
3. 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, and 1-3 months for cancers with intermediate risk of progression. There are no deferrals for cancer therapeutics recommended in patients with high risk of progression.

4. 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 [2].

Additional Considerations:

In addition, the following pragmatic considerations apply:

- 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.
- Cancer patients who do not yet meet above criteria for “clearance” of COVID-19 precautions and who are in need of urgent cancer treatment should be managed as an outpatient as much as possible,

with admission only if previously established criteria for admission with COVID-19 are met. Admission to an area specializing in the clinical care of patients with COVID-19 area might be preferred over a cancer ward depending on the clinical context. After complying with provincial public health disease management guidelines and isolation recommendations, patients requiring non-urgent cancer treatment could potentially benefit from further treatment delays during a pandemic when healthcare resources may be limited to both deliver therapy and support patients who develop complications from therapy

Summary of Evidence

Credible information sources were identified through a rapid online search performed by Knowledge Resources Services, within Alberta Health Services, and writers of this review. Seventeen references are original research (including eleven articles related to SARS-coV-2 or COVID-19 [3-13], and three related to other viruses or viral respiratory outbreaks [14-16]), five are article reviews [17-21], and 11 are commentaries [22-26], opinion papers [27], editorials [28], or research letters [29-32]. Five of these references have not been peer-reviewed (pre-reprints) [3-5,9,21]. In addition, 15 references are publications produced by expert panels [33-36] or by local, national and international health organizations and/or authorities in response to managing the COVID-19 or similar pandemics [1,2,37-45] which use a range of research sources and likely expertise consensus within these organizations. Six of these references are Alberta internal policy documents [1,2,41,42,44,45]. Key limitations of this review are:

- Rapid turnaround time resulted in a limited time to conduct a thorough search of the research and grey literatures.
- Given the rapidly changing information and literature related to COVID-19, the literature available is limited primarily to guideline documents, published letters, and descriptive papers.

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 [34], patients should be assessed for holding cancer treatment until symptoms of COVID-19 have resolved and there is some certainty that the virus is no longer present.

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 [29]. There is no evidence to speak to the question of whether or not cancer patients who have been infected with COVID-19 develop immunity and are protected after recovery. In addition, there is no evidence available in cancer patients on what constitutes recovery (i.e. clinical recovery, serologic or PCR negativity).

The following provides an overview of recommendations from leading expert groups and health authorities to be considered when deciding whether a confirmed COVID-19 case can be safely (i.e. without being infectious) discharged from hospital or released from home isolation. Considering the literature and recommendations from national bodies in countries that have experienced COVID-19 local transmissions, the European Centre for Disease Prevention and Control [38] established the following criteria:

- At least 2 upper respiratory tract samples negative for COVID-19, collected at ≥24-hour intervals are recommended to document COVID-19 clearance.
- For symptomatic patients after the resolution of symptoms, samples should be collected at least 7 days after the onset or after >3 days without fever.
- For asymptomatic COVID-19-infected people, tests to document virus clearance should be taken at a minimum of 14 days after the initial positive test.

The Centers for Disease Control and Prevention [37] established two alternative strategies: a test-based and a symptoms-based strategy, for both symptomatic and asymptomatic patients. For symptomatic patients:

- Test-based strategy:
  - Resolution of fever without the use of fever-reducing medications, and
  - Improvement in respiratory symptoms (e.g., cough, shortness of breath), and
  - Negative results of an COVID-19 molecular assay for detection of COVID-19 RNA from at least 2 consecutive nasopharyngeal swab specimens collected ≥24 hours apart (total of 2 negative specimens)
- Symptom-based strategy:
  - At least 72 hours have passed since recovery defined as resolution of fever without the use of fever-reducing medications and improvement in respiratory symptoms (e.g., cough, shortness of breath), and
  - At least 10 days have passed since symptoms first appeared (note: recently updated to 10 days based on evidence suggesting a longer duration of viral shredding)

For patients with a lab-confirmed COVID-19 diagnosis who have not had symptoms, Centers for Disease Control and Prevention [37] recommends:

- Test-based strategy:
  - Negative results of an COVID-19 molecular assay for detection of COVID-19 RNA from at least 2 consecutive nasopharyngeal swab specimens collected ≥24 hours apart (total of 2 negative specimens)
- Symptom-based strategy
  - 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.

Based on available hospital data of infected patients in China, the World Health Organization reported that the median time from onset of COVID-19 to clinical recovery for mild cases is approximately 2 weeks and for patients with severe or critical symptom manifestation it is 3-6 weeks [40].

In April 2020, Alberta Health Services established that hospitalized patients with a confirmed COVID-19 diagnosis who are immunosuppressed were to be isolated for 14 days from the onset of symptoms and until symptoms had resolved for at least 48 hours. In addition, they had to have at least 2 consecutive negative nasopharyngeal swabs collected at least 7 days apart [41]. Updated guidelines (May, 2020) by Alberta Health do not include follow-up testing as a requirement, and establish that immunocompromised patients should be isolated for 14 days from the onset of symptoms or until symptoms have been resolved for at least 48 hours, whichever is longer [44,45]. In alignment with this, and based on the lack of evidence about the effectiveness of lab testing to define the duration of the infectious period of respiratory viruses, the World Health Organization [43] discourages its routine use to guide infection prevention and control precautions, and suggests that decisions on whether or not a patient has recovered and does not represent an infection threat to others are made on the basis of the patient's clinical condition.

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, Weinberg [27] 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 Insitute of Clinical Excellence [39] recommended a delay of at least 3 months for haematopoietic 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.

Guckenberger, Belka [36] 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, Curioni-Fontecedro [17] propose a tool to support oncologists and physicians in treatment decision for patients with lung cancer.

The FRANCOGYN group recommended that surgical management of patients with gynecologic cancers should be postponed for at least 15 days [33]. Penel, Bonvalot [35] 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. Other tumour groups may have their own tumor-specific recommendations.

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?*

In a case report it has been suggested that recurrence in patients with positive COVID-19 testing may occur, and that patients may remain persistently positive despite symptoms being resolved [7]. A small cluster study by Wolfel, Corman [13] was the first study to report prolonged shedding of non-viable virus. A recent article by Bullard, Dust [8] reports that prolonged positivity represents non-viable virus in all types of patients. Although results are 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 suggest that cycle thresholds >24 in conjunction with duration of symptoms >8 days may be used to determine duration of infectivity in patients. No data specific to cancer or immunosuppressed patients has been identified in this review.

There is no specific evidence for COVID-19, immunocompromised patients. But in the literature it has been discussed that they may shed SARS-CoV-2 virus for prolonged periods similar to other respiratory viruses due to a constrained immune response [15,16], and that they may remain infectious for a longer period of time and therefore may need a longer duration of contact and droplet precautions than others with COVID-19 [46]. Further research on this new virus is required to confirm this.

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 [18,19,47]. There is also extensive literature indicating that cancer patients are at increased risk for serious complications such as pneumonia and hospitalization [6,18,24]. 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 [14]. 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%) [32], and in China (1-2%) [5,12,24], Italy (5.0%), France (6.0%), South Korea (4.0%) [9].

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 [31]. 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, Guan [24] 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%) [24]. 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, Ouyang [31] 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, Zhang, Zhu [12] arrived at similar conclusions that 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 1.086-15.322, p=0.037) [12]. Another interesting finding of this study is that almost 30% of infection among cancer patients was suspected to have occurred in the hospital [12], which may account for some of the excess prevalence of infection in this cohort. Based on these findings the authors of the three studies 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 [12,24,31]. It is important to note that the three studies had a small sample of cancer patients, and implied that hospital admissions was an independent risk factor to acquiring a COVID-19 infection. In addition, cancer patients in the first and third studies [12,24] 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 [28].

In late May 2020 two other relevant studies have been published bringing new insights. Both present early investigations of multicenter, prospective observational studies. Kuderer, Choueiri [10]'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 [10]. Lee, Cazier [11] followed-up 800 patients with COVID-19 and cancer in the UK and reported a mortality rate of 28%. Similar to Kuderer, Choueiri [10], 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 [11]. 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 [20,21]. Data from both studies suggest the need for proactive strategies to protect cancer patients from a potential COVID-19 infection. Importantly, they also suggest 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. This evidence points at the importance of offering standard cancer treatment and overall oncological care should if feasible during the pandemic [25].

A third relevant study also published at the end of May 2020 reached conclusions that conflict with those by Kuderer, Choueiri [10] and Lee, Cazier [11]. Tang and Hu [26] 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 in the past 2-4 weeks and death in hospital. This analysis is limited by the small cohort size and wide confidence intervals around the odds ratio in the individual studies.

Further research is needed. Current evidence suggests that 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 [26].

Evolving Evidence and Future Research Needs

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 impact this rapid review. Further research is required to clarify the role of serologic testing in clearing patients from COVID-19 infection, especially those who continue to have positive swab tests, and those who are to receive immune suppressive therapies such as many types of cancer therapy.

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(If applicable) Date of re-assessment: June 23, 2020

Authorship & Committee Members

This review was written by Anna Pujadas-Botey and scientifically reviewed by Douglas Stewart, Charles Butts, Uma Chandran and Nelson Lee. The full Scientific Advisory Group was involved in discussion and revision of the document: Braden Manns (co-chair), Lynora Saxinger (co-chair), John Conly, Alexander Doroshenko, Shelley Duggan, Nelson Lee, Elizabeth Mackay, Andrew McRae, Jeremy Slobodan, James Talbot, Brandie Walker, and Nathan Zelyas.

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Appendix

Literature Search Details

The literature search was conducted by Rachael Zhao from Knowledge Resources Services, Alberta Health Services.

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to April 07, 2020

1 exp Coronavirus/ or exp Coronavirus Infections/ or coronaviru*.mp. or "corona virus*".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 cov 2".mp. or "2019 ncov".mp. or "2019ncov".mp. (38229)
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7 or/2-6 (1905266)
8 1 and 7 (1149)
9 limit 8 to (English language and yr="2003 -Current") (822)
10 limit 9 to yr="2020 -Current" (199)
11 limit 9 to (guideline or meta analysis or practice guideline or "review" or "systematic review" or systematic reviews as topic) (258)
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("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] OR nephroblastom*[tiab] OR chemoradiation[tiab] OR immunoradiotherap*[tiab])

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