

World Journal of *Gastrointestinal Pathophysiology*

World J Gastrointest Pathophysiol 2022 September 22; 13(5): 128-177



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INDEXING/ABSTRACTING

The WJGP is now abstracted and indexed in PubMed, PubMed Central, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Yi-Xuan Cai; Production Department Director: Xu Guo; Editorial Office Director: Jia-Ping Yan.

NAME OF JOURNAL

World Journal of Gastrointestinal Pathophysiology

ISSN

ISSN 2150-5330 (online)

LAUNCH DATE

April 15, 2010

FREQUENCY

Bimonthly

EDITORS-IN-CHIEF

Kusum K Kharbanda, Tsutomu Nishida, Somchai Amornvotin

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2150-5330/editorialboard.htm>

PUBLICATION DATE

September 22, 2022

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INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

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<https://www.wjgnet.com/bpg/gerinfo/287>

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<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/gerinfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/gerinfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



COVID-19 in patients with gastrointestinal stromal tumors: Recommendations for management and vaccination

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Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Afzal MS, Pakistan; Chen D, China

Received: March 26, 2022

Peer-review started: March 26, 2022

First decision: May 11, 2022

Revised: June 20, 2022

Accepted: August 16, 2022

Article in press: August 16, 2022

Published online: September 22, 2022



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Abstract

The coronavirus disease 2019 (COVID-19) pandemic profoundly affected the management and treatment of patients with malignancies. Based on the progress reported in the literature, we reviewed the recommendations for treatment and vaccination in patients with gastrointestinal stromal tumor (GIST) during COVID-19. We focus on whether there is a risk and what could be the possible effects of vaccinating patients with GIST/cancer. Since the situation is quickly changing, and the health services have been severely disrupted, the diagnosis, treatment and recommendations for vaccination of these patients against COVID-19 are still not updated. The approval of vaccines in the pandemic gave hope that we would soon be able to return to a more normal life. However, the oncology community needs to adapt and provide the most effective treatment and care models for patients with rare cancer, such as GIST. Collecting data on the impact of

vaccination in patients with GIST/cancer also will be beneficial in expanding knowledge about the future planning of treatment strategies and optimizing care in the event of a subsequent pandemic.

Key Words: Gastrointestinal stromal tumor; GIST; Cancer; COVID-19 vaccination; efficacy; Treatment strategy; Side effects

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Core Tip: Even under normal operating conditions, appropriate monitoring and treating patients with gastrointestinal stromal tumors (GISTs) require complex decision-making. Given the growing number of deaths worldwide and the failure of many countries to control the pandemic, vaccination against COVID-19 in these patients must be accelerated. The data show no significant difference in the efficacy of vaccines for the GIST population compared to that of other cancers. Vaccination between cycles of therapy and after waiting periods for patients with stem cell transplantation and immunoglobulin therapy can be used to reduce the risks while protecting patients from risk groups.

Citation: Snegarova V, Miteva D, Gulina M, Peshevska-Sekulovska M, Batselova H, Velikova T. COVID-19 in patients with gastrointestinal stromal tumors: Recommendations for management and vaccination. *World J Gastrointest Pathophysiol* 2022; 13(5): 170-177

URL: <https://www.wjgnet.com/2150-5330/full/v13/i5/170.htm>

DOI: <https://dx.doi.org/10.4291/wjgp.v13.i5.170>

INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic in China at the end of 2019 and coronavirus disease 2019 (COVID-19) are considered risk factors for severe outcomes in cancer patients[1]. Statistics indicate that by March 13, 2022, there have been > 6 million deaths caused by COVID-19 worldwide, and the number of confirmed cases recorded is > 455 million[2].

In line with this, according to a number of reports, diseases such as diabetes, hypertension, cardiovascular diseases, respiratory diseases, and cancer are associated with an increased risk of fatality in patients diagnosed with COVID-19[3]. In addition, an international study involving 1035 patients with COVID-19 who have concomitant cancer showed that these patients had a higher risk of hospitalization and need for intensive care and mechanical ventilation, regardless of the type of malignancy and antitumor therapy[4].

Patients with malignant diseases represent a heterogeneous group. Therefore, it remains to be determined which factors related to tumor type and treatment increase the risk of infection with COVID-19 and adverse outcomes[5]. According to a study that aimed to identify the risk factors of severe COVID-19 infection in patients with malignancy, the administration of antitumor treatment (chemotherapy, radiotherapy, targeted therapy or immunotherapy) within 14 d of diagnosis significantly increases the risk[6].

To assist health care facilities and minimize the negative effects of the pandemic associated with COVID-19 in patients with malignancies, the European Society for Medical Oncology (ESMO), the American Society of Clinical Oncology, the National Comprehensive Cancer Network (NCCN) and other organizations have developed recommendations for patient categorization based on the Ontario Health Cancer Care criteria[7].

Gastrointestinal tumors are a relatively new tumor group that has emerged in recent decades from other mesenchymal tumors in this field, mainly neurinomas and leiomyomas, thanks to the achievements of modern medicine in molecular biology and pharmacotherapy. Therefore, the justification for a separate tumor form merits an in-depth multidisciplinary study. Furthermore, it represents a model for successfully applying targeted therapy in treating solid tumors[8].

Gastrointestinal stromal tumors (GISTs) are rare neoplasms of the gastrointestinal tract associated with high rates of malignant transformation. They represent 1%–2% of all gastrointestinal neoplasms [9]. The mean age at diagnosis is 58 years, with most patients being between the ages of 40 and 80 years [10].

Although the risk of SARS-CoV-2 infection is not increased in GIST patients, they may experience other consequences during the COVID-19 pandemic, such as delay in treatment, delayed surgery or long waiting period for elective surgery, a heavy burden on medical resources, and the need for emergency surgery[11]. Additionally, neoadjuvant imatinib is routinely used to shrink locally advanced GISTs and if there is a danger of positive margins, unresectable, or borderline resectable tumors[12]. Imatinib may be a beneficial alternative to minimize the possibility of tumors developing in

intermediate or high-risk cancers bearing imatinib-sensitive mutations that would otherwise be excised during a time of limited access to surgical therapy[12]. Even if imatinib is generally well tolerated, patients may develop adverse effects such as myelosuppression (grade 3 in up to one-fifth of all patients), which might be concerning if the patient becomes infected with SARS-CoV-2[13]. Finally, initial watchful waiting would not rule out the possibility of starting imatinib if the tumor progressed.

The term GIST was introduced by Mazur and Clark in 1983 for a group of nonepithelial mesenchymal tumors of the gastrointestinal tract (most often leiomyomas, leiomyosarcomas and neurinomas), which differ from the eponymous tumors in other areas of the body in their immunohistochemical characteristics[14]. It is now commonly accepted that GISTs derive from so-called pacemaker cells in the intestinal tract – the interstitial cells of Cajal or similar stem cells[15]. Cajal cells are intermediates of gastrointestinal autonomic nervous system cells and smooth muscle cells and regulate the motility and autonomic nerve conduction and function activity. They are positive for Kit and Kit-ligand (stem cell marker), localized around the myenteric plexus and in the stratum muscularis propria along the entire gastrointestinal tract. Cajal cells can either be or include a subclass of multipotent, stem-like cells that can differentiate into smooth muscle cells if the Kit signaling pathway is disrupted[16]. In most cases, GISTs are specifically Kit (CD117) positive or caused by mutations in *Kit* or *PDGFRA* genes, and are the primary mesenchymal tumors of the gastrointestinal tract with characteristic histological features[17].

In the 1990s, GIST were found to express CD34 antigen, which has been identified as a distinguishing feature of neurinomas and leiomyomas. However, in a new study phase, GISTs were found to have standard immunohistochemical and ultrastructural features with Cajal interstitial cells or related stem cells, as stated above. For this reason, studying Kit (CD117) expression in tumor cells is the best immunostaining method for identifying GIST[14,18-20].

GISTs have malignant and insufficiently predictable biology and behavior, even with benign histological features. Morphologically, GISTs vary from spindle cell tumors to epithelioid and pleomorphic tumors. GISTs have approximately the same distribution in both sexes. Most are localized in the stomach (50%–60%) and the small intestine (30%). Esophageal, colorectal and rectal GISTs are rare (3%)[21].

The diagnosis of GIST is based on pathomorphological evidence by histological examination of biopsy material, and when taking a biopsy, the recommendations of NCCN. The NCCN organized a multidisciplinary panel composed of experts in surgery, pathology, medical oncology and molecular diagnostics to discuss the optimal approach for the care of patients with GIST at all stages of the disease [22,23].

SEARCH STRATEGY

We performed a modified form of a narrative review where a search through scientific databases combined solid evidence from studies on vaccine effectiveness and safety in patients with gastrointestinal tumors and GISTs. The first literature search was carried out in Medline (PubMed) and Scopus bibliographic databases. Both MeSH and relevant free-text terms were used, as follows: (COVID-19 OR SARS-CoV-2) AND (GIST OR gastrointestinal stromal tumor) AND (vaccine* OR mRNA). Our search was confined to articles published up to April 2022. Finally, references of retrieved publications were further hand-searched for supplements.

Official recommendations for COVID-19 vaccination in patients with GIST

Up to date, no specific and official recommendations are included in the ESMO–EURACAN–GENTURIS Clinical Practice Guidelines for diagnosis, treatment and follow-up for GIST (2022)[24]. However, ESMO statements on vaccination against COVID-19 in people with cancer conclude that all the approved COVID-19 vaccines could be administered to patients with cancer taking into account their effectiveness and safety, according to the official international recommendations[25]. Furthermore, ESMO has confirmed that the mass vaccination program is a crucial strategy for protecting against severe infection. This also stands for vulnerable patients, such as cancer patients, who take advantage of the most preferable benefit–risk ratio[25]. Since some patients with cancer, especially those with active malignancies, may experience a greater risk of severe SARS-CoV-2 infection, ESMO recommends COVID-19 vaccination. Despite reduced effectiveness for specific subgroups of cancer patients, the protection is still meaningful, and vaccination is strongly advised. Patients with hematological malignancies, particularly those undergoing cytotoxic chemotherapy, anti-CD20, CAR-T cell, or stem-cell-transplant-based treatments, are also among these populations.

Effectiveness and safety of COVID-19 vaccines in patients with GIST

Prior to the COVID-19 pandemic, there was little evidence of the humoral and cellular immune responses to antiviral vaccination in cancer patients. Additionally, this primarily addressed the influenza vaccination[26,27]. Despite a general exclusion of cancer patients from the major clinical studies of COVID-19 and COVID-19 vaccination, subsequent results repeatedly proved the effectiveness

and safety of SARS-CoV-2 immunization in these patients. Overall, after complete COVID-19 immunization, persons with cancer have clinically significant seroconversion rates[28-32]. Although the efficiency of mRNA and adenoviral vector vaccines appears almost identical[30], there is a lack of comparative effectiveness data, particularly in cancer patients. Notably, when only one dose of an mRNA vaccine is delivered, the incidence of seroconversion is much reduced, emphasizing the necessity of vaccination completion and, eventually, booster for cancer patients[33,34].

However, there are not enough data from studies for COVID-19 vaccination in patients with GIST. There have been a few studies[30,35-39] that mainly recruited patients with gastrointestinal tumors, some with GIST, as summarized in Table 1. Thakkar *et al*[30] and Suenaga *et al*[35] demonstrated that even on chemotherapy, patients with gastrointestinal tumors tolerated COVID-19 vaccines well. Additionally, the effectiveness was assessed as adequate for SARS-CoV-2 infection protection. This observation was also valid for immunocompromised patients due to cancer treatment[36-38]. Given the scientific and logistical challenges in identifying cancer patients with weak or decreasing immunity, the global strategy of a booster dosage vaccination should be investigated for cancer patients. However, until better quality information on booster dosage benefits becomes available, international recommendations considering the risk of poor COVID-19 outcomes in cancer patients, vaccine availability/access, immunization progress, and the pandemic burden should be followed.

Are there any risks for vaccination of patients with GIST/cancer

The most significant driver for public health protection is the availability and equal access to COVID-19 immunization, with conformity to international criteria to be encouraged and supported. Therefore, vaccination plans have been established worldwide to prioritize vaccine delivery in various groups, including cancer patients. On the other hand, cancer patients do not constitute a homogenous group. And GISTs are among the rare cancer types.

In general, cancer patients can be divided into three groups: patients with active disease undergoing treatment, patients with chronic illness following specific therapy, and patients in the survival phase. Vaccination is essential to protect all of these patient groups[25]. If we translate this knowledge to the patients with GIST, we can assume that COVID-19 vaccination is strongly advised for them.

However, despite increasing compliance rates and existing evidence/data, 10%–20% of patients remain skeptical about the COVID-19 vaccine. These patients are at a higher risk of developing severe COVID-19 illness. In addition, they are a more likely source of SARS-CoV-2 transmission to other, more sensitive cancer patients[25]. It is critical to reinforce trust, education, and easy, transparent communication with those patients and their relatives based on the accumulated knowledge and better understanding of their concerns and hesitancy. In addition, communication of available data on vaccine safety and efficacy to people with cancer should also include assuring them that COVID-19 vaccines will not interfere with their cancer treatment[40]. Furthermore, there is no indication that COVID-19 immunizations substantially influence anticancer medication's efficacy or safety profile, such as cytotoxic chemotherapy, immune checkpoint inhibitors, or targeted therapies. Thus, COVID-19 vaccination is strongly advised[25]. More data on the preference for a specific type of vaccine and potential unusual interactions of SARS-CoV-2 vaccines with antineoplastic therapy should be collected by in-trial, post-trial, and registry monitoring.

Suppose an anticancer medication is urgently required for disease control. It is advised that suitable medication be implemented first, followed by COVID-19 immunization, as soon as the patient is clinically stable and significant symptoms are under control. To minimize misattribution of any short-term reactions/side effects, providers may consider administering anticancer medication and COVID-19 vaccinations on different days[41].

Therefore, since we do not have studies on the effectiveness and safety of COVID-19 vaccination for patients with GISTs, we have to rely on the official recommendations for patients with cancer generally. The data for rare diseases usually accumulate slowly. To protect patients from a “double jeopardy”, informed consent and collaborative decision-making should be the rule when discussing the advantages and risks of COVID-19 immunization and SARS-CoV-2 infection.

CONCLUSION

Before the COVID-19 pandemic, most vaccination research with cancer patients was conducted for vaccines against hepatitis B, influenza and other infections. However, as the immune response is reduced in those patients, the risk of severe COVID-19 should be noted. Therefore, patients have to receive complete vaccination and booster doses to acquire higher levels of protection. This is also valid for patients with GIST. COVID-19 vaccination could be administered to patients who are even on therapy if some vaccine components are not contraindicated. The data show no significant difference in the efficacy of vaccines for the GIST/cancer population compared to other cancers. Oncologists have extensive experience in vaccinating cancer patients who are being treated, so they can effectively help save their patients' lives.

Table 1 Studies of COVID-19 vaccination in patients with gastrointestinal tumors

Ref.	Type of study	Type of COVID-19 vaccine	Participants	Efficacy/effectiveness	Adverse effects
Suenega <i>et al</i> [35], 2022	Retrospective observational study	mPNA (BNT162b2 or mRNA-1273)	Gastrointestinal cancer patients, <i>n</i> = 52	BNT162b2 (approximately 95%), mRNA-1273 (approximately 94%)	82.2% had adverse events: Injection site pain (approximately 67%), fatigue (approximately 12%), fever (approximately 6%), headache (approximately 4%), gastrointestinal problems (approximately 4%), redness (approximately 2%), insomnia (approximately 2%); no vaccine-related deaths
Fendler <i>et al</i> [36], 2022	Retrospective observational study	BNT162b2; mRNA-1273	115	mRNA vaccines (against omicron approximately 75%) (against delta approximately 79%); against omicron increased from 47.8% to 88.9% following a third vaccine dose	Injection site pain (approximately 63%), local swelling (9%), muscle pain (34%), fatigue (34%), headache (16%), fever (10%), chills (10%) and gastrointestinal events (10%); no vaccine-related deaths
Thakkar <i>et al</i> [30], 2021	Retrospective study	BNT162b2, mRNA-1273, Ad26.COV2.S	27 (14%) from 200 are with GIST	BNT162b2 (95%), mRNA-1273 (94%), Ad26.COV2.S (85%)	Sore arm (20%–37%), fatigue (5%–16%), muscle ache (5%–17%), fatigue (1%–5%), rash (1%–3%), redness (approximately 2%), other (1%–5%); no vaccine-related deaths
Embi <i>et al</i> [37], 2021	Observational study	BNT162b2; mRNA-1273	20 101 immunocompromised patients	BNT162b2 (71%), mRNA-1273 (81%)	Sore arm (20%–47%), fever (10%), fatigue (1%–5%), other (1%–5%); no vaccine-related deaths
Karacin <i>et al</i> [38], 2021	Prospective observational study	CoronaVac vaccine	47	Sero-response rate 63.8%	Pain at the injection site (4.2%), fever (2.1%), fatigue (4.2%–10.5%), headache (2.1%), and myalgia (2.1%), There were no serious side effects or toxic deaths
Ariamanesh <i>et al</i> [39], 2022	Prospective study	BBIBP-CorV	364 (32 patients with gastrointestinal tumors)	Sero-response rate 86.9%	Injection site pain, fever, fatigue, headache

FOOTNOTES

Author contributions: Snegarova V, Miteva D and Velikova T conceptualized the idea; Snegarova V and Miteva D reviewed the literature and wrote the draft; Gulinac M, Batselova H, Peshevska-Sekulovska M, and Velikova T contributed to reviewing the literature and manuscript drafting; Velikova T and all authors were responsible for critically revising the manuscript for relevant intellectual content; All of the authors approved the final version of the paper before submission.

Conflict-of-interest statement: All the authors declare no conflict of interest.

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S-Editor: Liu JH

L-Editor: Kerr C

P-Editor: Liu JH

REFERENCES

- Johannessen TB, Smeland S, Aaserud S, Buanes EA, Skog A, Ursin G, Helland Å. COVID-19 in Cancer Patients, Risk Factors for Disease and Adverse Outcome, a Population-Based Study From Norway. *Front Oncol* 2021; **11**: 652535 [PMID: 33842366 DOI: 10.3389/fonc.2021.652535]

- 2 World Health Organization HEP. Coronavirus disease (COVID-19) Weekly Epidemiological Update and Weekly Operational Update. Geneva: WHO; (2021). Available from: <https://www.who.int/publications/m/item/weekly-operational-update-on-covid-19---1-march-2021>
- 3 Deng G, Yin M, Chen X, Zeng F. Clinical determinants for fatality of 44,672 patients with COVID-19. *Crit Care* 2020; **24**: 179 [PMID: 32345311 DOI: 10.1186/s13054-020-02902-w]
- 4 Kuderer NM, Choueiri TK, Shah DP, Shyr Y, Rubinstein SM, Rivera DR, Shete S, Hsu CY, Desai A, de Lima Lopes G Jr, Grivas P, Painter CA, Peters S, Thompson MA, Bakouny Z, Batist G, Bekaii-Saab T, Bilen MA, Bouganim N, Larroya MB, Castellano D, Del Prete SA, Doroshow DB, Egan PC, Elkrief A, Farmakiotis D, Flora D, Galsky MD, Glover MJ, Griffiths EA, Gulati AP, Gupta S, Hafez N, Halfdanarson TR, Hawley JE, Hsu E, Kasi A, Khaki AR, Lemmon CA, Lewis C, Logan B, Masters T, McKay RR, Mesa RA, Morgans AK, Mulcahy MF, Panagiotou OA, Peddi P, Pennell NA, Reynolds K, Rosen LR, Rosovsky R, Salazar M, Schmidt A, Shah SA, Shaya JA, Steinharter J, Stockerl-Goldstein KE, Subbiah S, Vinh DC, Wehbe FH, Weissmann LB, Wu JT, Wulff-Burchfield E, Xie Z, Yeh A, Yu PP, Zhou AY, Zubiri L, Mishra S, Lyman GH, Rini BI, Warner JL; COVID-19 and Cancer Consortium. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet* 2020; **395**: 1907-1918 [PMID: 32473681 DOI: 10.1016/S0140-6736(20)31187-9]
- 5 Brunetti O, Derakhshani A, Baradaran B, Galvano A, Russo A, Silvestris N. COVID-19 Infection in Cancer Patients: How Can Oncologists Deal With These Patients? *Front Oncol* 2020; **10**: 734 [PMID: 32391283 DOI: 10.3389/fonc.2020.00734]
- 6 Fox TA, Troy-Barnes E, Kirkwood AA, Chan WY, Day JW, Chavda SJ, Kumar EA, David K, Tomkins O, Sanchez E, Scully M, Khwaja A, Lambert J, Singer M, Roddie C, Morris EC, Yong KL, Thomson KJ, Ardeshtna KM. Clinical outcomes and risk factors for severe COVID-19 in patients with haematological disorders receiving chemo- or immunotherapy. *Br J Haematol* 2020; **191**: 194-206 [PMID: 32678948 DOI: 10.1111/bjh.17027]
- 7 Ontario Health Cancer Care Ontario. Pandemic planning clinical guideline for patients with cancer. [cited 2020 Apr 9]; Available from: https://www.accc-cancer.org/docs/documents/cancer-program-fundamentals/oh-cco-pandemic-planning-clinical-guideline_final_2020-03-10.pdf?sfvrsn=d2f04347_2
- 8 Mazur MT, Clark HB. Gastric stromal tumors. Reappraisal of histogenesis. *Am J Surg Pathol* 1983; **7**: 507-519 [PMID: 6625048 DOI: 10.1097/00000478-198309000-00001]
- 9 Beltran MA, Cruces KS. Primary tumors of jejunum and ileum as a cause of intestinal obstruction: a case control study. *Int J Surg* 2007; **5**: 183-191 [PMID: 17509501 DOI: 10.1016/j.ijsu.2006.05.006]
- 10 Tryggvason G, Gislason HG, Magnússon MK, Jónasson JG. Gastrointestinal stromal tumors in Iceland, 1990-2003: the icelandic GIST study, a population-based incidence and pathologic risk stratification study. *Int J Cancer* 2005; **117**: 289-293 [PMID: 15900576 DOI: 10.1002/ijc.21167]
- 11 Wang XR, Hu XH, Li Z, Li BK, Niu WB, Zhou CX, Yu B, Zhang ZY, Zhang XN, Gao Y, Wang GY. [Treatment strategy of gastrointestinal stromal tumors in the background of COVID-19]. *Zhonghua Wei Chang Wai Ke Za Zhi* 2021; **24**: 825-829 [PMID: 34530566 DOI: 10.3760/cma.j.cn.441530-20210213-00064]
- 12 Callegaro D, Raut CP, Keung EZ, Kim T, Le Pechoux C, Martin-Broto J, Gronchi A, Swallow C, Gladly R. Strategies for care of patients with gastrointestinal stromal tumor or soft tissue sarcoma during COVID-19 pandemic: A guide for surgical oncologists. *J Surg Oncol* 2021; **123**: 12-23 [PMID: 33022754 DOI: 10.1002/jso.26246]
- 13 Blanke CD, Demetri GD, von Mehren M, Heinrich MC, Eisenberg B, Fletcher JA, Corless CL, Fletcher CD, Roberts PJ, Heinz D, Wehre E, Nikolova Z, Joensuu H. Long-term results from a randomized phase II trial of standard- versus higher-dose imatinib mesylate for patients with unresectable or metastatic gastrointestinal stromal tumors expressing KIT. *J Clin Oncol* 2008; **26**: 620-625 [PMID: 18235121 DOI: 10.1200/JCO.2007.13.4403]
- 14 Fülöp E, Marcu S, Milutin D, Borda A. Gastrointestinal stromal tumors: review on morphology, diagnosis and management. *Rom J Morphol Embryol* 2009; **50**: 319-326 [PMID: 19690756]
- 15 Kindblom LG, Remotti HE, Aldenborg F, Meis-Kindblom JM. Gastrointestinal pacemaker cell tumor (GIPACT): gastrointestinal stromal tumors show phenotypic characteristics of the interstitial cells of Cajal. *Am J Pathol* 1998; **152**: 1259-1269 [PMID: 9588894]
- 16 Miettinen M, Sarlomo-Rikala M, Lasota J. Gastrointestinal stromal tumors: recent advances in understanding of their biology. *Hum Pathol* 1999; **30**: 1213-1220 [PMID: 10534170 DOI: 10.1016/s0046-8177(99)90040-0]
- 17 DeMatteo RP, Lewis JJ, Leung D, Mudan SS, Woodruff JM, Brennan MF. Two hundred gastrointestinal stromal tumors: recurrence patterns and prognostic factors for survival. *Ann Surg* 2000; **231**: 51-58 [PMID: 10636102 DOI: 10.1097/00000658-200001000-00008]
- 18 Parab TM, DeRogatis MJ, Boaz AM, Grasso SA, Issack PS, Duarte DA, Urayeneza O, Vahdat S, Qiao JH, Hinika GS. Gastrointestinal stromal tumors: a comprehensive review. *J Gastrointest Oncol* 2019; **10**: 144-154 [PMID: 30788170 DOI: 10.21037/jgo.2018.08.20]
- 19 Miettinen M, Majidi M, Lasota J. Pathology and diagnostic criteria of gastrointestinal stromal tumors (GISTs): a review. *Eur J Cancer* 2002; **38** Suppl 5: S39-S51 [PMID: 12528772 DOI: 10.1016/s0959-8049(02)80602-5]
- 20 Sornmayura P. Gastrointestinal stromal tumors (GISTs): a pathology view point. *J Med Assoc Thai* 2009; **92**: 124-135 [PMID: 19260254]
- 21 Miettinen M, Lasota J. Gastrointestinal stromal tumors (GISTs): definition, occurrence, pathology, differential diagnosis and molecular genetics. *Pol J Pathol* 2003; **54**: 3-24 [PMID: 12817876]
- 22 Demetri GD, Benjamin RS, Blanke CD, Blay JY, Casali P, Choi H, Corless CL, Debiec-Rychter M, DeMatteo RP, Ettinger DS, Fisher GA, Fletcher CD, Gronchi A, Hohenberger P, Hughes M, Joensuu H, Judson I, Le Cesne A, Maki RG, Morse M, Pappo AS, Pisters PW, Raut CP, Reichardt P, Tyler DS, Van den Abbeele AD, von Mehren M, Wayne JD, Zalberg J; NCCN Task Force. NCCN Task Force report: management of patients with gastrointestinal stromal tumor (GIST)--update of the NCCN clinical practice guidelines. *J Natl Compr Canc Netw* 2007; **5** Suppl 2: S1-29; quiz S30 [PMID: 17624289]
- 23 Demetri GD, von Mehren M, Antonescu CR, DeMatteo RP, Ganjoo KN, Maki RG, Pisters PW, Raut CP, Riedel RF, Schuetz S, Sundar HM, Trent JC, Wayne JD. NCCN Task Force report: update on the management of patients with gastrointestinal stromal tumors. *J Natl Compr Canc Netw* 2010; **8** Suppl 2: S1-41; quiz S42 [PMID: 20457867 DOI: 10.1097/00000658-201002000-00008]

- 10.6004/jncn.2010.0116]
- 24 **Casali PG**, Blay JY, Abecassis N, Bajpai J, Bauer S, Biagini R, Bielack S, Bonvalot S, Boukovinas I, Bovee JVMG, Boye K, Brodowicz T, Buonadonna A, De Álava E, Dei Tos AP, Del Muro XG, Dufresne A, Eriksson M, Fedenko A, Ferraresi V, Ferrari A, Frezza AM, Gasperoni S, Gelderblom H, Gouin F, Grignani G, Haas R, Hassan AB, Hindi N, Hohenberger P, Joensuu H, Jones RL, Jungels C, Jutte P, Kasper B, Kawai A, Kopeckova K, Krákorová DA, Le Cesne A, Le Grange F, Legius E, Leithner A, Lopez-Pousa A, Martin-Broto J, Merimsky O, Messiou C, Miah AB, Mir O, Montemurro M, Morosi C, Palmerini E, Pantaleo MA, Piana R, Piperno-Neumann S, Reichardt P, Rutkowski P, Safwat AA, Sangalli C, Sbaraglia M, Scheipl S, Schöffski P, Sleijfer S, Strauss D, Strauss SJ, Hall KS, Trama A, Unk M, van de Sande MAJ, van der Graaf WTA, van Houdt WJ, Frebourg T, Gronchi A, Stacchiotti S; ESMO Guidelines Committee, EURACAN and GENTURIS. Electronic address: clinicalguidelines@esmo.org. Gastrointestinal stromal tumours: ESMO-EURACAN-GENTURIS Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2022; **33**: 20-33 [PMID: [34560242](#) DOI: [10.1016/j.annonc.2021.09.005](#)]
- 25 ESMO statements on vaccination against COVID-19 in people with cancer. Last access on 20 March 2022. Available from: <https://www.esmo.org/covid-19-and-cancer/covid-19-vaccination>
- 26 **Ward EM**, Flowers CR, Gansler T, Omer SB, Bednarczyk RA. The importance of immunization in cancer prevention, treatment, and survivorship. *CA Cancer J Clin* 2017; **67**: 398-410 [PMID: [28753241](#) DOI: [10.3322/caac.21407](#)]
- 27 **Rubin LG**, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, Bousvaros A, Dhanireddy S, Sung L, Keyserling H, Kang I; Infectious Diseases Society of America. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clin Infect Dis* 2014; **58**: e44-100 [PMID: [24311479](#) DOI: [10.1093/cid/cit684](#)]
- 28 **Oosting SF**, van der Veldt AAM, GeurtsvanKessel CH, Fehrmann RSN, van Binnendijk RS, Dingemans AC, Smit EF, Hiltermann TJN, den Hartog G, Jalving M, Westphal TT, Bhattacharya A, van der Heiden M, Rimmelzwaan GF, Kvistborg P, Blank CU, Koopmans MPG, Huckriede ALW, van Els CACM, Rots NY, van Baarle D, Haanen JBAG, de Vries EGE. mRNA-1273 COVID-19 vaccination in patients receiving chemotherapy, immunotherapy, or chemoimmunotherapy for solid tumours: a prospective, multicentre, non-inferiority trial. *Lancet Oncol* 2021; **22**: 1681-1691 [PMID: [34767759](#) DOI: [10.1016/S1470-2045\(21\)00574-X](#)]
- 29 **Shepherd STC**, Fendler A, Au L, Byrne F, Wilkinson K, Wu M, Schmitt AM, Joharatnam-Hogan N, Shum B, Del Rosario L, Edmonds K, Carlyle E, Nicholson E, Howell M, Swanton C, Walker S, Kassiotis G, Wilkinson R, Larkin J, Turajlic S. 1557O Adaptive immunity to SARS-CoV-2 infection and vaccination in cancer patients: The CAPTURE study. *Ann Oncol* 2021; **32**: S1129. [DOI: [10.1016/j.annonc.2021.08.1550](#)]
- 30 **Thakkar A**, Gonzalez-Lugo JD, Goradia N, Gali R, Shapiro LC, Pradhan K, Rahman S, Kim SY, Ko B, Sica RA, Kornblum N, Bachier-Rodriguez L, McCort M, Goel S, Perez-Soler R, Packer S, Sparano J, Gartrell B, Makower D, Goldstein YD, Wolgast L, Verma A, Halmos B. Seroconversion rates following COVID-19 vaccination among patients with cancer. *Cancer Cell* 2021; **39**: 1081-1090.e2 [PMID: [34133951](#) DOI: [10.1016/j.ccell.2021.06.002](#)]
- 31 **Thomas SJ**, Perez JL, Lockhart SP, Hariharan S, Kitchin N, Bailey R, Liao K, Lagkadinou E, Türeci Ö, Şahin U, Xu X, Koury K, Dychter SS, Lu C, Gentile TC, Gruber WC. Efficacy and safety of the BNT162b2 mRNA COVID-19 vaccine in participants with a history of cancer: subgroup analysis of a global phase 3 randomized clinical trial. *Vaccine* 2022; **40**: 1483-1492 [PMID: [35131133](#) DOI: [10.1016/j.vaccine.2021.12.046](#)]
- 32 **Subbiah IM**, Williams LA, Peek A, Shete S, Granwehr BP, D'Achiardi D, Turin A, Garcia EA, Finder J, Chemaly R, Beltran K, Shaw KR, Whisenant M, Woodman SE, Ravi V, Tawbi HAH, Subbiah V, Chung C, Futreal PA, Jaffray DA, and on behalf of the MD Anderson Cancer Center D3CODE Team. Real-world patient-reported and clinical outcomes of BNT162b2 mRNA COVID-19 vaccine in patients with cancer. *J Clin Oncol* 2021; **39**: 6510-6510 [DOI: [10.1200/JCO.2021.39.15_suppl.6510](#)]
- 33 **Mair MJ**, Berger JM, Berghoff AS, Starzer AM, Ortmayr G, Puhr HC, Steindl A, Perkmann T, Haslacher H, Strassl R, Tobudic S, Lamm WW, Raderer M, Mitterer M, Fuehrer T, Fong D, Preusser M. Humoral Immune Response in Hemato-oncological Patients and Health Care Workers Who Received SARS-CoV-2 Vaccinations. *JAMA Oncol* 2022; **8**: 106-113 [PMID: [34591965](#) DOI: [10.1001/jamaoncol.2021.5437](#)]
- 34 **Monin L**, Laing AG, Muñoz-Ruiz M, McKenzie DR, Del Molino Del Barrio I, Alaguthurai T, Domingo-Vila C, Hayday TS, Graham C, Seow J, Abdul-Jawad S, Kamdar S, Harvey-Jones E, Graham R, Cooper J, Khan M, Vidler J, Kakkassery H, Sinha S, Davis R, Dupont L, Francos Quijorna I, O'Brien-Gore C, Lee PL, Eum J, Conde Poole M, Joseph M, Davies D, Wu Y, Swampillai A, North BV, Montes A, Harries M, Rigg A, Spicer J, Malim MH, Fields P, Patten P, Di Rosa F, Papa S, Tree T, Doores KJ, Hayday AC, Irshad S. Safety and immunogenicity of one versus two doses of the COVID-19 vaccine BNT162b2 for patients with cancer: interim analysis of a prospective observational study. *Lancet Oncol* 2021; **22**: 765-778 [PMID: [33930323](#) DOI: [10.1016/S1470-2045\(21\)00213-8](#)]
- 35 **Suenaga M**, Yamauchi S, Masuda T, Hanaoka M, Iwata N, Sato Y, Tomii C, Tokunaga M, Kinugasa Y. COVID-19 vaccination in gastrointestinal cancer patients receiving chemotherapy: A single institute experience. *J Clin Oncol* 2022; **30**: 30 [DOI: [10.1200/JCO.2022.40.4_suppl.030](#)]
- 36 **Fendler A**, de Vries EGE, GeurtsvanKessel CH, Haanen JB, Wörmann B, Turajlic S, von Lilienfeld-Toal M. COVID-19 vaccines in patients with cancer: immunogenicity, efficacy and safety. *Nat Rev Clin Oncol* 2022; **19**: 385-401 [PMID: [35277694](#) DOI: [10.1038/s41571-022-00610-8](#)]
- 37 **Embi PJ**, Levy ME, Naleway AL, Patel P, Gaglani M, Natarajan K, Dascomb K, Ong TC, Klein NP, Liao IC, Grannis SJ, Han J, Stenehjem E, Dunne MM, Lewis N, Irving SA, Rao S, McEvoy C, Bozio CH, Murthy K, Dixon BE, Grisel N, Yang DH, Goddard K, Kharbanda AB, Reynolds S, Raiyani C, Fadel WF, Arndorfer J, Rowley EA, Fireman B, Ferdinands J, Valvi NR, Ball SW, Zerbo O, Griggs EP, Mitchell PK, Porter RM, Kiduko SA, Blanton L, Zhuang Y, Steffens A, Reese SE, Olson N, Williams J, Dickerson M, McMorrow M, Schrag SJ, Verani JR, Fry AM, Azziz-Baumgartner E, Barron MA, Thompson MG, DeSilva MB. Effectiveness of 2-Dose Vaccination with mRNA COVID-19 Vaccines Against COVID-19-Associated Hospitalizations Among Immunocompromised Adults - Nine States, January-September 2021. *MMWR Morb Mortal Wkly Rep* 2021; **70**: 1553-1559 [PMID: [34735426](#) DOI: [10.15585/mmwr.mm7044e3](#)]
- 38 **Karacin C**, Eren T, Zeynelgil E, Imamoglu GI, Altinbas M, Karadag I, Basal FB, Bilgetekin I, Sutcuoglu O, Yazici O, Ozdemir N, Ozet A, Yildiz Y, Esen SA, Ucar G, Uncu D, Dinc B, Aykan MB, Erturk İ, Karadurmus N, Civelek B, Çelik İ,

- Ergun Y, Dogan M, Oksuzoglu OB. Immunogenicity and safety of the CoronaVac vaccine in patients with cancer receiving active systemic therapy. *Future Oncol* 2021; **17**: 4447-4456 [PMID: [34342517](#) DOI: [10.2217/fon-2021-0597](#)]
- 39 **Ariamanesh M**, Porouhan P, PeyroShabany B, Fazilat-Panah D, Dehghani M, Nabavifard M, Hatami F, Fereidouni M, Welsh JS, Javadinia SA. Immunogenicity and Safety of the Inactivated SARS-CoV-2 Vaccine (BBIBP-CorV) in Patients with Malignancy. *Cancer Invest* 2022; **40**: 26-34 [PMID: [34634986](#) DOI: [10.1080/07357907.2021.1992420](#)]
- 40 **Hwang JK**, Zhang T, Wang AZ, Li Z. COVID-19 vaccines for patients with cancer: benefits likely outweigh risks. *J Hematol Oncol* 2021; **14**: 38 [PMID: [33640005](#) DOI: [10.1186/s13045-021-01046-w](#)]
- 41 Guidance COVID-19: the green book, chapter 14a. Coronavirus (COVID-19) vaccination information for public health professionals. 2022, last accessed on 20 March 2022. Available from: <https://www.gov.uk/government/publications/covid-19-the-green-book-chapter-14a>



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