



The Impact of New Coronavirus on Cancer Patients

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ABSTRACT

At the end of 2019, a new coronavirus (severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)) emerged in China and then spread worldwide. Presently, Coronavirus Disease 2019 (COVID-19) is a main public health issue. As of August 2021, more than 200 million confirmed cases from coronavirus and more than 4 million deaths have been reported by WHO in 222 countries. The data sources are Google Scholar, PubMed, and Science Direct articles. Publications were searched without regard to time in order to obtain a holistic and comprehensive perspective of the research done on this issue thus far. The SARS-CoV-2 can be transmitted from the human-to-human by respiratory droplets and shows great potential for a pandemic. Therefore, on March 11, 2020, COVID-19 was introduced as a global pandemic by WHO. Cancer patients are at high risk for exposure to the coronavirus. In the present article, we discuss the impact of the COVID-19 pandemic on the quality of life of cancer patients and their treatment process. One of these challenges is not visiting the patients in medical centers and hospitals for afraid of contracting the virus. Therefore, the diagnosis and treatment of cancer patients may be delayed, which is a serious threat to the lives of cancer patients. In this article, in addition to the impact of coronavirus on the lives of cancer patients, the severity of the disease in these patients, their required medical care, and the vaccination process are discussed.

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Introduction

A novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused an outbreak of coronavirus disease 2019 (COVID-19) in Wuhan, China, in December 2019. SARS-CoV-2 was first assumed to have spread by a zoonotic transmission linked to the seafood market in Wuhan (1). It was later discovered that human-to-human transmission had a significant part in the ensuing pandemic (2). The SARS-CoV-2 is transmitted via respiratory droplets and can be asymptomatic between 2 and 14 days. This period

makes it prominently hard to reach a primary diagnosis and initiate treatment timely (3). On December 31, 2020, the World Health Organization (WHO) officially announced the first verified case of the new coronavirus, which first manifested as “pneumonia with unclear etiology.” COVID-19 was designated a worldwide pandemic by WHO on March 11, 2020, when the infectious illness spread around 114 nations, resulting in 118,000 confirmed cases and 4291 fatalities. There were 213,345,924 reported cases throughout the world as of August 24, 2021, with 4,454,131 fatalities, 17,981,168 active

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cases, and 190,910,625 recovered cases. Among the 222 countries, the United States currently has the most confirmed cases (38,814,596) and deaths (646,667), followed by India (32,474,773 confirmed cases and 435,050 deaths), Brazil (20,583,994 confirmed cases and 574,944 deaths), Russia (6,766,541 confirmed cases and 176,820 deaths), France (6,624,777 confirmed cases and 113,419 deaths), and the United Kingdom (6,524,581 confirmed cases and 131,680 deaths). The global pandemic triggered by the COVID-19 is still a serious health concern in 2021. Those who catch the virus are also at risk of having problems with the respiratory, neurological, and renal systems. It is remarkable which patients mostly present with a notable decrease in CD8+ and CD4+ T-cells in the primary stages of the disease (4). According to this reduction, patients suffer from acute respiratory distress syndrome (ARDS) for almost 7-10 days after the beginning of the disease due to rapid viral replication, the release of a storm of proinflammatory cytokines, initiating chemokine responses, and infiltration of inflammatory cells (5). COVID-19 prevention efforts may have a larger influence on health issues that aren't directly connected to the virus. Depression and anxiety are likely to be exacerbated by changes in a person's level of functioning. Pain, tiredness and a diminished capacity to contribute to family resources or community obligations may all contribute to a worse on health-related quality of life (HRQoL) (6). Many nations have reallocated health care and other related social services, including community medicine, to best handle the COVID-19 epidemic. As a result, many therapeutic operations, including oncology, have been pushed to the back burner. The lockdown measures and the general population's loss of cancer knowledge might have a substantial impact on cancer outcomes (7). Cancer patients have twice the case fatality rates as the general population, a study has found. COVID-19 was found to be present in about 2.0 percent of cancer patients in a systematic study (8, 9). The most unfortunate are newly diagnosed early-stage cancer patients, for whom a single cancer treatment option may prove to be incurable. The signs of disease development in the chest (e.g., dyspnea, tachypnea) may be misdiagnosed as COVID-19 infection and treated incorrectly (10). Oncologic patients are thought to be more vulnerable to infections than people without cancer. Immunosuppression can also expose cancer patients to significant infection-related problems. These individuals have a worse prognosis in the event of infectious complications and may be more susceptible to viral infections like COVID-19 (11, 12). AntieSARS-CoV-2 humoral and T-cell immune responses in cancer patients are less effective, raising concerns regarding vaccination efficacy. Cancer patients may not acquire as much humoral immunity as healthy individuals, and they may be infectious and transmit SARS for up to two months (13). Clinical features and outcomes of cancer patients with COVID-19 were reported in reports from China and the United States, as well as risk factors for mortality in this group; they revealed a higher probability of death owing to COVID-19 and poor outcomes in cancer patients (14). Approximately

over 40% of patients may need breathing support, with about 6% needing ventilators, according to the World Health Organization's (WHO) latest estimates (15). The fatality rate is anticipated to range from 1% to 4% (16). According to early Chinese studies, cancer patients died at a higher rate than non-cancer patients. In an 18-patient retrospective study in China, patients with cancer and COVID-19 seemed to have a higher probability of COVID-19 issues, but the limited sample size precluded investigation of particular cancer-associated risk factors for worse outcomes (17). Lung cancer, metastatic disease, and hematologic malignancy may be associated to higher rates of COVID-19-related mortality and intensive care unit (ICU) admission, according to a 105-patient study (18). These findings are supported by more recent data from Europe and the United States (19).

Methods

This is a review research, and the data sources are Google Scholar, PubMed, and Science Direct articles. Publications were searched without regard to time in order to obtain a holistic and comprehensive perspective of the research done on this issue thus far, using the following terms: (Cancer, SARS-CoV-2, Cancer patient routine, New Coronaviruses, Vaccination, New Coronaviruses mortality rate, COVID-19 prevention methods, Medical services difficulties, COVID-19 pandemic psychological effects, COVID-19 infection severity and Drug treatment before and during COVID-19 infection in Cancer patient).

Results and Discussion

From 2008 through 2021, we included all review, original, and clinical trial research on all aspects of Coronaviruses and their relevance to cancer patient therapy. We didn't include letters, theses, seminar abstracts, book chapters, or articles written in non-English. In addition, we discovered a total of 125 researches, from which 89 publications were chosen for this study.

Quality of life in cancer patients during the COVID-19 pandemic

COVID-19, a rapidly spreading coronavirus, has caused significant job losses, isolation, and death (20). As a result of the high number of individuals who have been urged to stay at home to prevent the virus from spreading, the health-care system is underfunded and understaffed. Because people are encouraged to avoid going to the hospital, cancer patients may not receive treatment in a timely manner. The economic situation deepens as the cost of caring for those who have been affected by the virus grows. Physicians and patients alike value the influence on the quality of life (QoL), which is directly linked to cancer development. Most patients were also concerned about their financial situation, which might be influenced by the COVID-19 epidemic and, as a result, their treatment alternatives. Furthermore, the COVID-19 pandemic's long-term increase in the demand for health services will impose

strain on healthcare professionals and, at some time, impair the clinical management of cancer patients. When examining the effects of the pandemic on cancer patients' familial and social lives, it was discovered that they are substantially worse than a similar group under more favorable epidemiological conditions, particularly for patients living alone. The limitation of mobility, the prohibition of social meetings, and the banning of the use of public green areas have all had a major impact on patients' social functioning and sleep (21-23).

Psychological effects of COVID-19 on cancer patients

Most cancer patients experience tiredness while on COVID-19 lockdown, probably as a result of worry and anxiety about their cancer therapy and the possibility of COVID-19 infection. A study by Magdalena Ciążynska et al., analyzed "Quality of life of cancer patients during coronavirus disease" (24). The study showed that during this historic period, the oncology community faces enormous challenges in improving the mental health and quality of life of those living with cancer. According to a recent research by Julio Torales et al., half of the patients believed their COVID-19 risk was greater than the general population, which is consistent with the known risks of COVID-19 in cancer patients. Patients also reported that the pandemic had a broad variety of impacts on their mental health, finances, work, family, and social life, which is consistent with general population trends (25). A worldwide research of 149 doctors from five continents discovered that all treatments for patients with musculoskeletal tumors were decreased, including surgery, radiation, and chemotherapy. Palliative chemotherapy and radiation were both discontinued or postponed in 20% and 17% of cancer patients, respectively (26). In a Dutch study, almost 4000 cancer patients were compared to a matched control group without cancer (27). The quality of life ratings were similar; however, cancer sufferers were more worried about COVID-19 infection, and norm-participants were significantly more likely than cancer patients to feel sorrow and loneliness (27). Another study found that almost half of breast cancer patients reported anxiety, despair, or sleeplessness, with 83 percent showing signs of discomfort (28). Frey et al., investigated the effect of COVID-19 on ovarian cancer patients. The majority of individuals were worried about cancer, with half experiencing moderate or unusual anxiety and a fourth experiencing moderate or serious unhappiness (29). Romito et al., evaluated emotional trauma in lymphoma patients during the pandemic and found anxiety and depression symptoms in approximately one-third of cases (30). Individuals with strong cancer-related worries showed significantly worse emotional functioning during the coronavirus epidemic. Psychological therapy may be beneficial for patients who have a high degree of anxiety and a low level of resilience (31). The impact of current cancer treatments, such as cytotoxic chemotherapy, on the course of COVID-19 remains unknown.

Cancer patients and Chemotherapy during the COVID-19 pandemic

Cancer patients taking chemotherapy (CTx) require special monitoring due to an elevated risk of death associated with their prevalent immunocompromised state. CTx should be regarded a personalized choice based on clinical results (32). Two major observational studies showed no indication of an increased risk of death after receiving recent cytotoxic treatment (33). In contrast, a 205-patient study showed that COVID-19 patients who had active chemotherapy had a greater risk of death, while a 107-patient Chinese investigation discovered that rates of severe respiratory COVID-19 were related to recent chemotherapy. The end points and statistical methodologies used in these researches differ, making comparisons difficult (34). In another research, Jee et al., found that the hazard ratio (HR) for the composite end goal, ICU admission, or death was not increased in patients who received cytotoxic treatment 90 to 14 days before testing positive for SARS-CoV-2. This is consistent with larger trials from Spain, Canada, and the United Kingdom, which found that therapy had no impact on COVID-19-related cancer mortality (35). Overall, COVID-19-related mortality in cancer patients appears to be mostly impacted by age, gender, and comorbidities, according to another study by Lee et al., They discovered no indication that cancer patients who get cytotoxic chemotherapy or other anticancer therapies had a greater risk of dying from COVID-19 infection than those who do not (33).

COVID-19 infection severity in cancer patients (mild, moderate, or severe)

COVID-19 can manifest itself in a variety of ways, ranging from mild flu-like symptoms to asymptomatic periods to life-threatening ARDS. During the categorization of COVID-19 severity levels, several respiratory variables such as oxygen saturation rate, lesion development in pulmonary rate, and respiratory rate were taken into account. In SARS-CoV-2-infected patients, anticancer treatment such as chemotherapy or surgery may worsen the infection and increase the chance of mortality (36). Laboratory variations in numerous serological parameters, including renal and liver function tests, coagulation parameters, inflammatory, biochemical, and hemocytometric parameters, were found in the majority of verified COVID-19 patients. In severe patients, neutrophils to lymphocyte ratio (NLR) was raised as compared to those with mild or moderate disease (37). There are little data on immunocompromised hosts, however early published studies from China on the outcomes of COVID-19-infected cancer patients showed a 3.5-fold increase in the requirement for mechanical ventilation, ICU hospitalization, or death compared to those without cancer (20). It is still debatable if malignancy affects the state of sickness or leads to a poor prognosis. A novel study by Li et al., used meta-analysis to investigate the severity of COVID-19 by Clinical determinants (38). Though their analysis revealed a possible link between malignancy and severe condition, some studies produced contradictory results, and some even suggested that some cancer patients may have better clinical

outcomes because the emergence of cytokine storm was slowed due to their compromised immune systems (38).

Required medical care for cancer patients during the COVID-19 pandemic

The COVID-19 pandemic had a wide range of effects on health-care services, including disrupting regular patient flow. Cancer patients need more frequent visits to medical centers than patients with other illnesses owing to the symptoms of the illness and its treatment. Oncologists have struggled to strike a balance between delivering superior, continuing medical services and minimizing the danger of exposing to patients during treatment (39). It is critical to properly manage medical workers during the emergency in order to treat all patients and safeguard them from harm such as infection, mental illness, and exhaustion (40). Personal protective equipment (PPE) shortages are a major source of concern because they put patients and healthcare workers at risk of infection or treatment interruption, impede care delivery, and create stress and discontent among staff. To solve this issue, all stakeholders, including the government, must use a multifaceted approach (41-44). Drug shortages are handled by major regulatory bodies such as the US Food and Drug Administration and the European Medicines Agency during a pandemic. Telehealth and digital health may be an excellent technique for real-time video consultations for primary care triage in cancer. It may also help with health education, physical activity, nutritional monitoring, risk assessment, medication adherence, and cognitive fitness (45). Adjuvant treatment should most likely be continued to cure solid tumors. Treatment delays in individuals with metastatic illness may result in decreased performance status and the loss of the opportunity to treat. Delaying cancer surgery is not an option; surgical intervention must be prioritized as well. It's still a work in progress to see how much we can prioritize the therapies supplied to specific patients in order to lessen the load on our system. Cancer centers should make it their duty to do everything necessary to keep their doors open and offer care until the situation becomes untenable in terms of staff and patient safety. The critical focus for inpatient oncology units has been to prepare for future bed and resource constraints as a result of the expected spike of COVID-19 patients requiring acute care and ICU beds. During pandemics, large epidemics may need the reallocation of units, hospital wards, or even whole systems to care for patients. Due to a decrease in community blood drives, blood product shortages at both the clinic and the hospital demand greater adherence to and consideration of lower transfusion thresholds (46-48). A large percentage of hospitalized patients with COVID-19 will require respiratory assistance. The optimal amount of symptom treatment for cancer patients is likely to be influenced by the patient's estimated survival time. Caregivers should urge their patients to discuss their treatment escalation priorities in advance(49).

Drug treatment for cancer patients with COVID-19

Unfortunately, there is no targeted particular treatment against COVID-19 presently. Several treatments have been proposed for use in COVID-19 pandemic with the understanding of SARS-CoV-2 structure. Each of these classes affects one or more well-known pathomechanisms of viral infection or infection-induced outcomes. Antimalarials (Chloroquine (50), Hydroxychloroquine (51)), Azithromycin (52), Antivirals (Remdesivir (53), Favipiravir/Oseltamivir/Umifenovir (54), Ribavirin (55), Lopinavir/Ritonavir (56), Sofosbuvir (57), Nitazoxanide (58)), and Classic Immunomodulators (Colchicine (59), Interferons (56), Corticosteroids (60), Intravenous immunoglobulin (61)) are some of the most significant medication types for novel coronavirus. Some of these medicines target the virus itself, while others influence viral-associated cytokine storm, immunological dysregulation, and organ failures, and some (e.g., Azithromycin) may have a beneficial effect on concurrent problems such as bacterial infection (62).

The usage of antiviral medicines in patients with COVID-19

Antiviral medications may be designed to block any step of the virus's life cycle. Camostat mesylate, for example, may significantly decrease SARS-CoV-2 penetration by reducing the activity of host transmembrane protease serine subfamily member 2 (TMPRSS2), which is a factor enabling SARS-CoV-2 penetration (63). By targeting the S protein, EK1, a pan-coronavirus fusion inhibitor, can prevent SARS-CoV-2 from fusing to the host cell's membrane (64). As indicated by the molecular docking studies, Sofosbuvir, Galidesivir, and Tenofovir may likewise function as the substrate of viral RNA-dependent RNA polymerase (RdRp) to suppress SARS-CoV-2 genome replication, similar to Remdesivir (65). Because the 3CLpro enzyme is important for cleaving polymeric protein precursors to create numerous non-structural proteins necessary for SARS-CoV-2 replication, 3CLpro inhibitors such as Celecoxib and Alprazolam might be utilized to combat COVID-19 (66). By using the computational techniques, a prior study found many possible anti-COVID-19 medicines based on targeting the recombinant soluble angiotensin-converting enzyme 2 (ACE2) receptor, including Xanthones and Hesperidin (67). Although certain contemporary therapeutic drugs have shown promise in alleviating symptoms and lowering mortality in patients, an increasing number of COVID-19-related side events have been reported in the course of medical treatment (68). Some of these medications, such as Hydroxychloroquine, can cause a variety of complications, including acute widespread exanthemata's pustulosis (AGEP) (69, 70).

Chloroquine might be beneficial for covid-19 infected people

Chloroquine, a malaria drug, has been tested in several clinical trials to see if it may stop coronavirus 2 from causing COVID-19 infection. Unfortunately, a recent study has shown that Hydroxychloroquine or Chloroquine have little effect on COVID-19 in-hospital outcomes. Instead, there has

been a decline in hospital survival as well as an increase in ventricular arrhythmias (71). M. Plaze et al., observed that because numerous psychiatric medications have established antiviral effects, they might function as a prophylactic against SARS-CoV-2 and protect patients against the symptomatic and severe forms of the virus. Chlorpromazine (CPZ), a phenothiazine derivative with antiviral properties, is identified to inhibit clathrin-mediated endocytosis. CPZ has anti-MERS-CoV and anti-SARS-CoV-1 action. The medication has a multitude of adverse effects, including anticholinergic effects and a prolonged QT interval. It's also simple to use and may be recommended by a doctor without the need for a prescription or over-the-counter drugs. CPZ is utilized in clinical practice for the treatment of headaches in a variety of neurological conditions, including pregnant women with drug-resistant nausea and vomiting and patients with advanced malignancy (72, 73). Indeed, the absence of particular medicines to treat SARS-CoV-2 was primarily owing to a lack of understanding of the virus's infection process in host cells (74). In COVID-19 infection, artificial intelligence predicts that Janus kinase (JAK) inhibitors like Baricitinib will prevent viral entrance into pneumocytes (75, 76). Inhibition of JAK can also have an impact on inflammation (77). Furthermore, COVID-19 patients had greater TNF levels, which are linked to illness severity. COVID-19 anti-TNF therapy has been suggested as a potential option, and a randomized, controlled study with Adalimumab has started. Some of the cutaneous side effects of anti-TNFs include infusion and injection site reactions, psoriasis and psoriasiform lesions, lupus-like syndromes, cutaneous vasculitis, cutaneous infections, eczematous reactions, lichenoid eruptions, granulomatous reactions, cutaneous lymphoma, epithelial skin cancers, or melanoma (78-80). When used with Chloroquine, the five medicines Methotrexate, Prednisolone, Folate, Omeprazole, and Lisinopril had the highest incidence of adverse drug reactions (ADR). Methotrexate, which is commonly prescribed to cancer patients, has a lot of adverse effects that are also related to cancer. When Chloroquine and Methotrexate medicines are taken together, these results might be regarded as a reduction in Methotrexate's impact. Adenopathy, for example, affects the lymph nodes or 'lung neoplasms' in the lungs, and is frequently seen in cancer patients (81, 82).

COVID-19 Vaccination

On January 11, 2020, the genetic sequence of SARS-CoV-2, was revealed, igniting a global race to find a vaccine against the sickness. The scale of the COVID-19 pandemic's humanitarian and economic impact is driving evaluation of next-generation vaccine technology platforms through novel paradigms to speed development, and on March 16, 2020, the first COVID-19 vaccine candidate entered human clinical testing with unprecedented speed. As of August 24, 2021, there are 296 vaccine candidates worldwide, 184 candidates have been entered into pre-clinical development, and 112 vaccines into clinical development. Candidate vaccines are classified according to their components and vary from classic whole-

pathogen vaccinations to new-generation vaccines. Live attenuated and inactivated vaccines are two types of traditional whole-pathogen vaccinations. mRNA vaccines and plasmid DNA vaccines are among the new generation vaccinations. Vaccinations, vaccines based on viral vectors, and vaccines based on nonpathogenic bacterial vectors (83-86). COVID-19 vaccinations are a crucial instrument in the current worldwide pandemic's containment. The Food and Drug Administration (FDA) has granted three COVID-19 vaccines Emergency Use Authorizations for use in the United States (87). Vaccine hesitancy (VH) is defined as a "delay in accepting or refusing vaccines despite the availability of vaccine services," and it is a growing public health issue fueled by misinformation about vaccine efficacy and safety (88).

Vaccination in cancer patients

During this pandemic, it is critical to rethink how cancer patients are treated and protected, as these patients are more vulnerable to COVID-19 infection and have a higher fatality rate (89). Depending on the jurisdiction, several SARS-CoV-2 vaccines have been developed, and many have been approved or are under development (Table 1). Cancer patients may be included in certain phase III studies using these vaccines; however, no outcomes in this group of patients have yet been published (Table 1). The Russian Sputnik V vaccination had 91.6 percent effectiveness in a phase III study. Although no particular data on cancer patients exists at this time, it is worth noting that these non-replicating viral vectors are not contraindicated in immunocompromised patients. Vaccines based on the inactivated complete virus or a portion of the virus are now being developed (Sinopharm, China). They may be useful in cancer patients, although they do not seem to be very immunogenic. Immune checkpoint inhibitors such as anti-cytotoxic T lymphocyte-associated antigen 4 and programmed cell death protein 1/programmed death-ligand 1 do not increase the risk of viral infection, but they may induce autoimmune adverse effects that need immunosuppressive therapy. Despite the lack of evidence on mRNA vaccines in patients treated with immune checkpoint inhibitors, SARS-CoV-2 immunization is not expected to have an effect on autoimmune adverse effects. In individuals using immune checkpoint inhibitors, the influenza vaccine is both safe and effective (no increased risk of immune-induced adverse effects). All SARS-CoV-2 vaccinations are viable in cancer patients using immune checkpoint medications (Table 2). Vaccination should, however, be postponed in individuals who are experiencing a severe autoimmune adverse effect (13, 36). However, the SARS-CoV-2 vaccine is being tested on individuals with solid cancer who are undergoing therapy or who have finished treatment within the last three years. The goal is to see if SARS vaccinations are safe and effective in this group. Vaccine dosages are limited, and 'ultrapriority' cancer patients are those undergoing chemotherapy and/or other curative treatments. It is critical to establish specialized clinical trials or cohorts for these individuals.

Table 1. Main vaccines available or in the ongoing phase II/III.

| Vaccines | Type | Trial | Population | Usable in immunocompromised patients |
|--------------------------------------|-------------|-------------|--|--------------------------------------|
| Comirnaty® | mRNA | Phase III | Exclusion of patients with cancer with ongoing | Yes |
| BNT162b2 | | Approved by | chemotherapy (no subgroup result available) | |
| Pfizer/BioNtech | | the EMA and | | |
| | | FDA | | |
| mRNA-1273 | mRNA | Phase III | Exclusion of patients with cancer with ongoing | Yes |
| Moderna/NIH | | Approved by | chemotherapy or immunotherapy more than 14 days during | |
| | | the EMA and | the past 6 months (no subgroup result available) | |
| | | FDA | | |
| CVnCoV | mRNA | Phase III | Exclusion of patients with cancer with ongoing treatment | Yes |
| CUREVAC | | | (no subgroup result available) | |
| AstraZeneca/Oxford University | Adenovirus | Phase III | Exclusion of patients with cancer history except curative | Yes |
| AZD1222 | | Approved by | treatment and low risk of recurrence according to the | |
| | | the EMA | investigator | |
| Ad26.COV2.S/JNJ-78436735 | Adenovirus | Phase III | Exclusion of patients with cancer since less than one year | Yes |
| Beth Israel Deaconess | | Approval | | |
| Medical Center and | | request | | |
| Johnson & Johnson | | | | |
| (Janssen) Gam-Covid-Vac (Sputnik V®) | Adenovirus | Phase III | Exclusion of patients with a cancer history | Yes |
| Russia MH/Gamaleya | | | | |
| Research Institute | | | | |
| Ad5-nCoV/Convidecia | Adenovirus | Phase III | Exclusion of patients with cancer with ongoing treatment | Yes |
| CanSino Biologics | | | (no subgroup result available) | |
| GRAd-COV2 | Adenovirus | Phase II | Exclusion of patients with a cancer history | Yes |
| Italy | | | | |
| ReiThera | | | | |
| WIBPCoV | Inactivated | Phase III | Exclusion of patients with a cancer history | Yes |
| Wuhan Institute of | SARS-CoV-2 | | | |
| Biological Products/ | | | | |
| Sinopharm | | | | |
| BBIBPCoV | Inactivated | Phase III | Exclusion of patients with a cancer history | Yes |
| Beijing Institute of | SARS-CoV-2 | | | |
| Biological Products/ | | | | |
| Sinopharm | | | | |
| NVXCoV2373 | Recombinant | Phase III | Exclusion of patients with a cancer history and with | Yes |
| Novavax | protein | | treatment completed since less than 1 year | |
| CoVLP | Virus-like | Phase III | Exclusion of patients with a cancer history and with | Yes |
| Medicago/GSK | particles | | chemotherapy completed since less than 3 months | |

Conclusion

As shown in this review (Table 3), the outbreak of coronavirus has changed the lives of people with cancer. Generally, the mortality rate of cancer patients is twice as high as that of people without cancer, and the spread of COVID-19 disease and the infection of these patients increases the probability of mortality among these people. Cancer patients are more vulnerable to infection with the coronavirus because of the weak immune system generated through cancer or anti-cancer therapies, including surgery, radiation, and chemotherapy. In addition to the treatment problems for these patients, COVID-19 disease harms their quality of life. The lockdown of cities and the closure

of recreation facilities can lead to serious psychological distress in these patients. On the other hand, some cancer patients have lost their jobs as a result of the outbreak of COVID-19, and financial worries have been added to their problems, which may affect their treatment process. In addition to the problems mentioned above, pharmacological considerations should be considered for the treatment of these patients when they are infected with the coronavirus. According to the mentioned cases, it seems that the health systems of different communities are obliged to prioritize the process of vaccination of these patients and pay special attention to meeting the medical needs of this segment of society.

Table 2. Summary of recommendations (expert agreement).

| |
|---|
| <p>1) Indications of SARS-CoV-2 vaccination</p> <ul style="list-style-type: none"> ● Indication for patients with cancer under treatment or whose treatment ended less than 3 years ago. ● Priority for patients with cancer treated with chemotherapy. ● Ultrapriority for (1) patients with curative intent treatment (including surgery) excluding basal cell skin carcinoma, (2) patients on palliative first- or second-line chemotherapy and (3) patients receiving radiotherapy for a primary thoracic tumour with a large lung volume, radiotherapy on large lymph node areas and/or radiotherapy on a large volume of haematopoietic tissue. ● Patients treated only with hormone therapy and recent patients with COVID-19 are not 'ultrapriority'. ● Vaccination of the immediate entourage of patients with cancer (the person living in the same house and frequent contacts (home helps, nurses and so on)) (expert opinion). |
| <p>2) SARS-CoV-2 vaccination in patients with cancer treated with immune checkpoint inhibitors</p> <ul style="list-style-type: none"> ● SARS-CoV-2 vaccination is recommended for patients with cancer treated with immune checkpoint inhibitors. ● In case of severe immune-related adverse events due to immune checkpoint inhibitors, it seems reasonable to postpone SARS-CoV-2 vaccination. |
| <p>3) Strategy of SARS-CoV-2 vaccination</p> <ul style="list-style-type: none"> ● Vaccination could be carried out using mRNA vaccines (or using a non-replicating adenoviral vaccine in non-immunocompromised patients younger than 65 years). ● If possible, vaccination is recommended at least 10 days before the start of chemotherapy. ● For patients with cancer already on chemotherapy, vaccination can be carried out during chemotherapy, avoiding periods of bone marrow aplasia. ● There is no need to postpone the chemotherapy course for SARS-CoV-2 vaccination. ● If a chemotherapy holiday is planned soon, the SARS-CoV-2 vaccination can be postponed for a few days and carried out during this chemotherapy holiday. ● Serological monitoring after vaccination could be useful (if possible in a specific cohort) (expert opinion). Patients with cancer who are vaccinated must continue to follow SARS-CoV-2 protection. |
| <p>4) Contraindications of SARS-CoV-2 vaccination</p> <ul style="list-style-type: none"> ● No 'oncological' contraindication. ● Definitive contraindications to mRNA vaccines are history of allergy to one of the vaccine components (in particular PEG or poly-sorbate) or anaphylactic reaction during the first dose. ● Temporary contraindications requiring postponement of vaccination: <ul style="list-style-type: none"> - Pregnancy or breastfeeding - Ongoing infectious disease - Flare of inflammatory or autoimmune disease - Symptomatic COVID-19 less than 3 months previous - Influenza vaccination less than 3 weeks previous or with another vaccine less than 2 weeks previous - History of severe reaction to another vaccine or to an unidentified drug requires an allergist's opinion before vaccination and longer follow-up after SARS-CoV-2 vaccination (30 min) |
| <p>5) SARS-CoV-2 vaccination and cancer clinical trials</p> <ul style="list-style-type: none"> ● The vaccine strategy is identical for patients participating in clinical trials, but specific recommendations have been proposed for phase I (30): <ul style="list-style-type: none"> - Not started phase I trial: avoid starting trial investigational medicinal products until 2-4 weeks after the second dose of the SARS-CoV-2 vaccine and administered safely for the trial with risk of cytokine release syndrome. - Already in phase I trial: administer the SARS-CoV-2 vaccine during the phase I trial, but avoid vaccination on days of parenteral investigational medicinal product dosing and the dose-limiting toxicity period. <p>SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; mRNA: messenger RNA; PEG: polyethylene glycol; COVID-19: coronavirus disease 2019.</p> |

Table 3. Table represents the papers used for all sections

| Topic | Study characteristics | Population | Study design | Study outcome |
|---|--|--|--------------------------------|--|
| Quality of life in cancer patients during the COVID-19 pandemic | Liang, Guan et al. 2020(20) | 18 (1%; 95% CI 0.61–1.65) of 1590 COVID-19 cases had a history of cancer | A nationwide analysis in China | First, in endemic regions, deliberate postponement of adjuvant chemotherapy or elective surgery for stable disease should be explored. Second, greater personal protection safeguards for cancer patients and survivors should be created. Third, when cancer patients are infected with SARS-CoV-2, more extensive surveillance or therapy should be considered, especially in older patients or those with additional comorbidities. |
| | Balanzá-Martínez, Aienza-Carbonell et al. 2020(21) | 20 studies were summarized | Observation | During the coronavirus outbreak, infection control and safety measures must be maintained at home. Long-term home stays may lead to inactivity, which can lead to anxiety, despair, and a sedentary lifestyle. Regular physical exercise is an essential approach for maintaining a healthy lifestyle at this period. |
| | Chen, Mao et al. 2020(22) | 36 studies were summarized | Observation | The globe will recover from the COVID-19 epidemic and return to so-called normalcy, but the PI/SB pandemic will persist. We just cannot allow this to happen as a global civilization. After COVID-19, aggressive efforts must be made to get individuals physically active again. |
| | Hall, Laddu et al. 2021(23) | 19 studies were summarized | Observation | In the context of this pandemic, remote data gathering through social networks, georeferencing, and big data technologies is accessible, possible, and essential. |

Table 3. Continued

| Topic | Study characteristics | Population | Study design | Study outcome |
|--|--|--|--------------------------------|---|
| Psychological effects of COVID-19 on cancer patients | Ciążyńska, Pabianek et al. 2020(24) | 260 patients with stage III and IV of different types of cancer undergoing chemotherapy | Survey study | Public health crises, such as a pandemic, have a significant impact on cancer patients' quality of life, and they need immediate care, as well as the support of doctors, families, and society. |
| | Torales, O'Higgins et al. 2020(25) | Published articles concerning mental health related to the COVID-19 outbreak and other previous global infections have been considered and reviewed. | Observation | Patients' and the general population's mental health should be a focal point of a global response. Information from the media and social media should be carefully monitored, and community-based psychological treatments should be pushed worldwide. |
| | Thaler, Khosravi et al. 2020(26) | One hundred forty-nine physicians | Survey study | Although the coronavirus illness has significant medical consequences, serious collateral harm, such as mortality from delayed or untreated sarcomas, should be avoided. Delaying or discontinuing these therapies may result in serious morbidity, discomfort, and loss of function. |
| | Van de Poll-Franse, de Rooij et al. 2020(27) | 3,960 cancer patients | Observation | In the initial weeks of the COVID-19 crisis, up to one-fourth of cancer patients reported changes in cancer treatment, which were linked to vulnerability characteristics. The effect of follow-up on outcomes will be revealed. On the general population, the crisis seems to have a greater effect on QoL and mental health than in cancer patients. |
| | Juanjuan, Santa-Maria et al. 2020(28) | A total of 658 individuals were recruited from multiple BC centers in Hubei Province. | A Cross-sectional Survey Study | In conclusion, our findings suggest that the psychological well-being of BC patients should be prioritized during the COVID-19 epidemic. Patients with BC are more prone to have poor mental health. Effective efforts to reduce mental health problems and offer psychological assistance should be implemented. |
| | Frey, Ellis et al. 2020(29) | Six hundred and three women with a current or prior diagnosis of ovarian cancer, The median age was 58 years 84 (range 20-85). | Observation | Ovarian cancer patients' treatment is being impacted by the COVID-19 issue. Younger age, assumed immunocompromised status, and a delay in cancer treatment are all linked to greater levels of cancer anxiety, despair, and concern. To weigh the conflicting dangers of COVID-19 and cancer, providers must engage with patients. |
| | Romito, Dellino et al. 2020(30) | Consecutive outpatients diagnosed with a lymphoproliferative neoplasm were prospectively enrolled in the study, age ≥ 18 years | Observation | They emphasize the significance of paying close attention to onco-hematologic patients' psychological requirements during this trying time by arranging regular psychological screenings of their emotional and stress states. |
| | Younger, Smrke et al. 2020(31) | 350 COVID-19 patients completed the survey; median age 58 (16–92) years | Survey | COVID-19 anxiety was linked with cancer-related concern, poor resilient coping, and ambiguity regarding treatment aim. During the pandemic and beyond, these patients may benefit from extra psychological care. |

Table 3. Continued

| Topic | Study characteristics | Population | Study design | Study outcome |
|--|-----------------------------------|---|---|--|
| Cancer patients and Chemotherapy during the COVID-19 pandemic | Rakhsha, Azghandi et al. 2020(32) | The experience of the Clinical Oncology Department of Shohada-e Tajrish Hospital | A Review and a Practical Approach | During the COVID-19 epidemic, this paper may offer a realistic method for our colleagues to treat cancer patients who are candidates for CTx. |
| | Lee, Cazier et al. 2020(33) | 800 patients with a diagnosis of cancer and symptomatic COVID-19 | Prospective observational study | COVID-19-related mortality in cancer patients seems to be mostly influenced by age, gender, and comorbidities. We couldn't find any evidence that cancer patients receiving cytotoxic chemotherapy or other anticancer treatment had a higher chance of dying from COVID-19 illness than those who aren't. |
| | Zhang, Wang et al. 2020(34) | A total of 107 patients with cancer were diagnosed with COVID-19, with a median age of 66 years | Observation | The present research found that more than 50.0 percent of cancer patients infected with COVID-19 are vulnerable to severe COVID-19. This risk is exacerbated by concurrent anticancer therapy, implying a worse chance of survival despite COVID-19 medication. |
| | Jee, Foote et al. 2020, Lee(35) | patients with cancer and concurrent COVID-19 | Observation | Patients who had active hematologic or lung cancers, peri-COVID-19 lymphopenia, or baseline neutropenia had worse outcomes than those who did not have any of these conditions. Interactions between antineoplastic treatment and cancer type should be investigated further. |
| COVID-19 infection severity in cancer patients (mild, moderate, or severe) | Luo, Li et al. 2021(36) | 47 studies were summarized | REVIEW ARTICLE | There are no COVID-19 vaccination recommendations that specify whether or not cancer patients should be vaccinated, or if only particular subsets of cancer patients should be vaccinated. However, a study indicates that ICI therapy following COVI immunization improves viral protection as well as its effectiveness and safety. During ICI treatment, the toxicity associated with COVI immunization has minimal effect. |
| | Waris, Din et al. 2021(37) | A total of 101 COVID-19 positive patients were examined, The overall mean age observed in our study was 48.94 years, where the mean age for critical individuals was 62.12 ± 14.35 years. | An observational cross-sectional study | These blood measures may be useful as a biomarker for COVID-19 prognosis and severity. The use of new hemograms such as NLR, PLR, and LMR may help physicians detect potentially severe cases early on, start appropriate treatment, and perform early triage, all of which can help COVID-19 patients live longer. |
| | Liang, Guan et al. 2020(20) | 18 (1%; 95% CI 0-61-1-65) of 1590 COVID-19 cases had a history of cancer | A nationwide analysis in China | First, in endemic regions, deliberate postponement of adjuvant chemotherapy or elective surgery for stable disease should be explored. Second, greater personal protection safeguards for cancer patients and survivors should be created. Third, when cancer patients are infected with SARS-CoV-2, more extensive surveillance or therapy should be considered, especially in older patients or those with additional comorbidities. |
| | Li, Huang et al. 2021(38) | From 6007 articles, 212 studies from 11 countries/regions involving 281 461 individuals were analyzed. Overall, mean age was 46.7 years, 51.8% were male, 22.9% had severe disease, and mortality was 5.6%. Underlying immunosuppression, diabetes, and malignancy were most strongly associated with severe COVID19. | A systematic review and meta-analysis of clinical characteristics | We conclude that our results may aid in the identification of susceptible groups for whom extra precautions may be required to prevent the illness from spreading. |

Table 3. Continued

| Topic | Study characteristics | Population | Study design | Study outcome |
|--|--|--|--|--|
| Required medical care for cancer patients during the COVID-19 pandemic | Jazieh, Akbulut et al. 2020(39) | A total of 356 centers from 54 countries across six continents participated | A cross-sectional study | The COVID-19 pandemic has had a wide-ranging negative effect on cancer treatment, with varied degrees of severity in different locations across the globe. Additional study is needed to determine the effect on patients. |
| | Jazieh, Coutinho et al. 2021(40) | Of the 1,010 physicians who participated in the study, 54.75% were male and 64.95% were medical or clinical oncologists. | A cross-sectional study | The COVID-19 epidemic has had a negative impact on oncologists' personal and professional life. Interventions should be undertaken to reduce the negative effect and to better educate oncologists to deal with future emergencies. |
| | Bauchner, Fontanarosa et al. 2020(41) | COVID-19 infected patients | Observation | Health-care professionals will get ill if they do not have sufficient PPE, putting the whole health-care system at risk. That scenario's human and economic consequences should not be underestimated. |
| | Gondi, Beckman et al. 2020(42) | patients and health-care workers alike during the COVID-19 pandemic | Observation | Importantly, rather than being created or managed by a physician-run non-profit organization, this information resource should have been developed or maintained by the government. |
| | Livingston, Desai et al. 2020(43) | health care workers (HCWs) and patients relies on effective use of personal protective equipment (PPE) | Observation | Given the fast rise of sick COVID-19 patients, an increase in PPE supply in response to this increased demand would need a significant increase in PPE production, a procedure that will take time that many health care systems do not have. |
| | Ranney, Griffith et al. 2020(44) | A Call for Ideas | Observation | Conserving Supply of Personal Protective Equipment |
| | Qian, Ren et al. 2020(45) | 19 studies were summarized | Observation | We, as a community with a common destiny for humanity, must act collaboratively and promptly to combat the new coronavirus. All international community partners and country leaders are asked to adopt proactive strategic steps as soon as feasible to combat COVID-19. |
| | Ueda, Martins et al. 2020(46) | patients with respiratory symptoms and healthy staff | Observation | The COVID-19 healthcare situation is still evolving, and new circumstances may cause some of our previous suggestions to alter. |
| | Wang and Zhang 2020(47) | 18 COVID-19 patients with cancer histories among 1590 COVID-19 patients from 575 hospitals in 31 provincial regions. | Observation | In endemic regions outside of Wuhan, choices about whether or not to delay cancer treatment must be decided patient by patient, based on the patient's risk and the current circumstances. Patients with cancer need online medical counseling, as well as proper diagnosis and treatment of severe cases, during this pandemic. |
| | Xia, Jin et al. 2020(48) | 1590 cases with confirmed coronavirus disease 2019 (COVID-19), 18 patients had a history of cancer | Observation | Overall, there is insufficient data to explain a definitive link between cancer and COVID-19. |
| Wu and McGoogan 2020(49) | Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention | REVIEW ARTICLE | People's rights, as well as the rights of those who are not sick but are at danger of infection, must be addressed. For years, it will be argued whether these methods were successful (e.g., fewer illnesses and fatalities avoided) or if the costs (e.g., economic losses) exceeded the benefits. | |

Table 3. Continued

| Topic | Study characteristics | Population | Study design | Study outcome |
|--|---|--|---|--|
| Drug treatment for cancer patients with COVID-19 | Devaux, Rolain et al. 2020(50) | 101 studies were summarized. | Observation | Chloroquine has been shown to be capable of inhibiting the in vitro replication of several coronaviruses. |
| | Yao, Ye et al. 2020(51) | SARS-CoV-2–infected Vero cells | Experimental | Hydroxychloroquine was found to be more potent than chloroquine to inhibit SARS-CoV-2 in vitro. |
| | Gautret, Lagier et al. 2020(52) | Hospitalized patients with confirmed COVID-19, age >12 years | Experimental | People who have been infected with COVID-19 are being treated with hydroxychloroquine and azithromycin to cure their illness and prevent the virus from spreading to others. This may lead to a real-time approach to combat this new viral illness, even if previous tactics and studies, such as vaccine development, have failed. |
| | Wang, Cao et al. 2020(53) | Cell lines | Experimental | In vitro, remdesivir and chloroquine are very effective in controlling 2019-nCoV infection. We believe that these chemicals should be evaluated in human patients suffering from the new coronavirus illness since they have been used in human patients with a proven track record of safety and effectiveness against a variety of diseases. |
| | Huang, Yu et al. 2021(54) | A total of 12 studies with 1052 patients were included | A systemic review and meta-analysis | There is no evidence to support the use of umifenovir in patients with COVID-19 to improve patient-important outcomes. |
| | Hung, Lung et al. 2020(55) | A total of 115 patients with laboratory-confirmed COVID19 were retrospectively analysed | A retrospective cohort study | Ribavirin treatment is not linked with a faster negative conversion time for the SARS-CoV-2 test or a lower death rate in patients with severe COVID-19. |
| | Nourian and Khalili 2020(56) | 127 COVID-19 infected patients | This was a phase 2, multicentre, open-label, randomised trial | Early triple antiviral treatment was shown to be safe and effective in patients with mild to moderate COVID-19, outperforming lopinavir–ritonavir alone in terms of symptom relief, viral shedding duration, and hospital stay. |
| | Kelleni 2020(57) | Docking studies | Observation | Sofosbuvir is being considered as a possible treatment option for COVID-19 patients, particularly in the beginning of the illness and before the virus has infiltrated the lung parenchymal cells. Future clinical trials may look at the efficacy and safety of sofosbuvir in the treatment of COVID-19. |
| | Deftereos, Siasos et al. 2020(58) | The FDA-approved anti-diarrhea medication is recommended based on a combination pathophysiological and pharmacological approach. | Observation | More interferon studies against SARS CoV-2 are needed, according to the author, particularly in severe and serious COVID-19 patients. He also suggests evaluating their combination administration as soon as feasible throughout COVID-19's clinical course. |
| | Hung, Lung et al. 2020(59) | Patients with laboratory confirmed SARS-CoV-2 infection- A total of 180 patients | Prospective, randomized, open labeled, controlled study | Colchicine may favorably intervene in the clinical course of COVID-19, according to the GRECCO-19 study. |
| | Budhathoki, Shrestha et al. 2020(60) | Observational studies, case series, and randomized controlled trials (RCTs) that focused on mortality, clinical improvement, and adverse events among COVID-19 patients taking steroid. | A Systematic Review and Meta-Analysis | Corticosteroids have been successfully used in medicine for a long time, and in unusual times like these, any proof of effectiveness should be carefully scrutinized. The administration of corticosteroids resulted in no survival advantages, as well as a slower recovery and a longer stay in the hospital. |
| | Mohtadi, Ghaysouri et al. 2020(61) | Five severely ill COVID-19 patients, women between 50 and 66 years old, | Case series | In COVID-19 patients with severe symptoms who have failed to respond to conventional therapies, IVIG at a therapeutic dosage of 0.3–0.5 g/kg may improve clinical condition and O2 saturation while also preventing the development of pulmonary lesions. |
| | Najar Nobari, Seirafianpour et al. 2021(62) | Databases PubMed (http://pubmed.ncbi.nlm.nih.gov), Scopus (http://www.scopus.com), Embase (https://www.embase.com) and Google Scholar (https://scholar.google.com) and CEBD Covid-19 Resource for Dermatology (https://skin.cochrane.org/news/cebd-covid-19-resource-dermatology) have been searched for the evidence | A Systematic review | The frequency of use of antivirals may influence the rate of dermatologic side effects. Lopinavir/ritonavir is the most often used antiviral medication with the greatest skin side effects. Rarely, reactions that are potentially life-threatening may occur. |

Table 3. Continued

| Topic | Study characteristics | Population | Study design | Study outcome |
|--|--|---|---------------------------|--|
| The usage of antiviral medicines in patients with COVID-19 | Hoffmann, Kleine-Weber et al. 2020(63) | Cell Lines and viruses | Experimental | significant similarities between SARS-CoV-2 and SARS-CoV infection and suggest a possible target for antiviral treatments |
| | Xia, Liu et al. 2020 Elfiky 2020(64) | Cell Lines, viruses and peptides | Experimental | When mice were treated to the virus before or after being exposed to live human coronaviruses, intranasal administration protected them against infection. |
| | Gimeno, Mestres-Truyol et al. 2020(65) | The newly-emerged SARS-CoV-2 nucleotide gene (NC 045512.2) was obtained from the nucleotide database of the National Center for Biotechnology Information (NCBI). | A molecular docking study | Ribavirin, Remdesivir, Sofosbuvir, Galidesivir, and Tenofovir are some of the most promising antiviral therapies for the SARS-CoV-2 strain. Guanosine derivative (IDX-184) and Setrobuvir (YAK) may potentially be effective therapies, according to the findings. |
| | Wu, Liu et al. 2020(66) | library of 1930 drugs and active metabolites approved by the FDA and library of 4536 drugs labeled as "marketed" in the field "Highest clinical phase" from the Reaxys database | Computational methods | The method they devised may potentially be used to predict additional possible SARS-CoV-2 M-pro inhibitors from commercial databases of unapproved medicines. It has the potential to expand the number of drugs accessible for in vitro bioactivity tests against COVID-19. |
| | Wu, C., et al.2020(67) | The complete genome of SARS-CoV-2/WHU02 (MN988669.1) | Computational methods | In reaction to recent reports that the anti-AIDS medicines lopinavir and ritonavir tablets have a poor impact on the treatment of new coronavirus pneumonia and have hazardous side effects. |
| | Wu, Q., et al.2020 (68) | Different databases | REVIEW ARTICLE | We can create bridges between fundamental medical research and clinical results in this way, which may reduce the time it takes to prioritize medication side effects and alert to possible drug adverse effects throughout COVID-19's pharmacotherapy course. |
| | Sharma, Vora et al. 2008(69) | The review included 94 articles comprising 689 dermatologic adverse effects. | REVIEW ARTICLE | Despite the fact that hydroxychloroquine is usually well tolerated, dermatologic side effects affecting the skin, hair, or nails are a common and serious problem. The majority of these responses happened after autoimmune diseases were treated, and they often manifested on the skin after a broad range of cumulative doses. |
| | Sharma, Me sinkovska et al. 2020(70) | A hundred patients with acquired immune deficiency syndrome (AIDS) on antiretroviral treatment (ART) were studied. | Experimental | Clinicians must concentrate on avoiding side effects wherever feasible, and distinguishing those that are self-limited from those that are potentially severe, in order to maximize adherence and therefore ART efficacy. |

Table 3. Continued

| Topic | Study characteristics | Population | Study design | Study outcome |
|--|---|--|---|--|
| Chloroquine might be beneficial for covid-19 infected people | Mehra, Desai et al. 2020(71) | 96 032 patients (mean age 53.8 years, 46.3% women) with COVID-19 | Experimental | These results indicate that these medication regimens should not be utilized outside of clinical trials, and that randomised clinical studies are required as soon as possible. |
| | Plaze, Atali et al. 2020(72) | COVID-19 infected patients who require respiratory support without the need for ICU care | Recovery study | This repurposing of CPZ for anti-SARS-CoV-2 action might provide an alternate, quick way to reduce the severity of infection. It might save time by quickly establishing an anti-COVID-19 treatment with few and manageable adverse effects. |
| | Nobile, B., et al.2020(73) | COVID-19 infected patents | Observation | The results of the newly launched RCTs will give robust information on CPZ place in COVID-19 management |
| | Huang, Chen et al. 2020(74) | 85 studies have been summarized. | REVIEW ARTICLE | Antiviral medicines are those that are capable of inhibiting any stage of the virus's life cycle. |
| | Richardson, Griffin et al. 2020(75) | BenevolentAI's knowledge graph | Observation | Using outcomes like the MuLBSTA score, an early warning model for predicting death in viral pneumonia, it may be tested in a suitable patient group with 2019-nCoV acute respiratory illness to decrease both viral entry and inflammation in patients. |
| | Praveen, Puvvada et al. 2020(76) | COVID-19 infected patients with an absolute neutrophil and absolute lymphocyte | Observation | For the treatment of COVID-19, baricitinib may not be the best option. To avoid death in individuals with this illness, available treatment alternatives must be investigated. |
| | Peterson, Damsky et al. 2020(77) | Data from JAKi clinical trials | Observation | Because JAKis have such short half-lives, their biologic effects fade quickly when the medication is stopped. The potential function of JAKi therapy in patients with cytokine release syndrome caused by severe SARS-CoV-2 infection is more complicated and is still being researched. |
| | Türsen, Türsen et al. 2020(78) | 49 studies have been summarized. | REVIEW ARTICLE | After evaluating all of the therapies, which have the potential to be successful against COVID-19, we may begin them one at a time, using the safest and most effective suitable medication to limit the development of cutaneous drug eruptions and to facilitate diagnosis. |
| | Le Cleach, Dousset et al. 2020(79) | The majority of patients were female, with a median age of 25.7 years, and there were 481 instances of cutaneous symptoms, including 311 cases of acral manifestations. | Experimental | SARS-CoV-2 may be directly responsible for certain instances of chilblains, however during the COVID-19 lockdown period in France, researchers discovered no evidence of infection in the vast majority of patients with acral lesions. |
| | Freeman, McMahon et al.2021(80) | 619 instances of pernio in patients with suspected or confirmed COVID-19 skin symptoms, for a total of 1176 cases of COVID-19 skin manifestations.They had a median age of 22 years. | Research letter | This result raises the likelihood that previous to the COVID-19 pandemic, additional instances of recurrent perniois were caused by viral infection. |
| | Aygün, Kaya et al. 2020(81) | The medicines whose interactions with other pharmaceuticals would be computed were chosen using a mixture of three different sources in this research. | Observation | With the experimental results obtained, it is aimed to facilitate the selection of the drugs and increase the success of Covid 19 treatment according to the targeted patient |
| Aygün, Kaya et al. 2020(82) | The 'drug names' dataset included 645 medications from the Decagon project. | Observation | With the findings of the experiments, it is hoped to make medication selection easier and improve the effectiveness of Covid 19 therapy for the targeted patient. | |

Table 3. Continued

| Topic | Study characteristics | Population | Study design | Study outcome |
|-------------------------|-------------------------------------|---|------------------------------------|---|
| COVID-19 Vaccination | Wang, Peng et al. 2020(83) | 93 studies have been summarized. | REVIEW ARTICLE | The COVID-19 pandemic is putting a lot of pressure on scientists to come up with vaccinations. Needle-free mucosal immunization through intranasal or pulmonary routes provides protective benefits. Vaccines may be converted from liquid to a thermally stable solid powder using several technologies. |
| | Zheng, Diaz-Arévalo et al. 2018(84) | In preclinical and clinical research, they look at the development of noninvasive immunization using vaccines based on live attenuated virus, recombinant adenovirus, inactivated virus, viral components, virus-like particles, DNA, RNA, and antigen expression in rice. | Observation | In the foreseeable future, noninvasive vaccination administration will become increasingly common in clinics. |
| | Dai, Han et al. 2020(85) | This research examines problems and possible solutions that will require global cooperation among governments, businesses, and scientists from both the physical and social sciences. | Observation | Vaccinating the entire population will be critical in the present fight against COVID-19 until scientists find a perfect treatment for treating illnesses caused by the new coronavirus. |
| | Duta2020(86) | There are now around 164 candidate vaccines in development, including 24 vaccines in advanced phases of research. | REVIEW ARTICLE | Vaccination is one of the most cost-effective methods of disease prevention. By the end of 2020 or the beginning of 2021, a vaccine against the SARS-CoV2 virus may be available. Even if a vaccination is available, getting the necessary number of doses may be difficult. |
| | Zhang, H., et al. 2020(87) | Persons who are fully vaccinated | Observation | Many people with vaccine-related illnesses, particularly those who are asymptomatic or have a minor sickness, may not seek medical attention and sequencing data for SARS-CoV-2 is only accessible for a limited percentage of reported cases. |
| | Riad, Pokorná et al. 2021(88) | Czech healthcare workers A total of 922 participants filled in the questionnaire, then The final analyses comprised 877 individuals, 776 (88.5%) of whom were females, 100 (11.4%) of whom were men, and 1 (0.1%) of whom chose not to declare their gender. The median age was 43 years old, and the mean age was 42.56 10.5 years old. The age varied from 19 to 78 years old. | Cross-sectional survey-based study | Injection site discomfort, tiredness, headache, and muscular pain were the most frequent adverse effects of the Pfizer-BioNTech COVID-19 vaccination among Czech healthcare professionals. Headache, nausea, muscular discomfort, fever, and lymphadenopathy were all linked to the oral side effects. |

Table 3. Continued

| Topic | Study characteristics | Population | Study design | Study outcome |
|--------------------------------|------------------------------------|---|----------------------------|---|
| Vaccination in cancer patients | Tougeron, Hentzien et al. 2021(13) | SARS-CoV-2 vaccination of adult patients with solid tumors, excluding doctors and patients with hematologic malignancies, is the present emphasis. Available data is sparse in several ways, with a low degree of proof (expert agreement or expert opinion). | Observation | Patients with solid cancer who are undergoing therapy or who have finished treatment less than three years ago are candidates for SARS-CoV-2 immunization, according to current scientific evidence. Patients with cancer who are receiving chemotherapy and/or other curative purpose treatment are considered 'ultrapriority' due to vaccination dosage restrictions. |
| | Luo, Li et al. 2021(36) | 47 studies have been summarized. | REVIEW ARTICLE | There are no guidelines indicating whether all cancer patients or only specific subgroups should be vaccinated. According to the findings, ICI therapy following COVID-19 immunization has high effectiveness and safety, as well as improved viral protection. The toxicity associated with vaccines during ICI treatment has had little effect. |
| | Zhang, Zhu et al. 2020(89) | Cancer patients with laboratory-confirmed COVID-19. There were a total of 28 COVID-19-infected cancer patients in the study, with 17 (60.7%) of them being male. The median age (interquartile range) was 65.0 (56.0-70.0). | A retrospective case study | Cancer patients who are undergoing antitumor therapy should be thoroughly screened for COVID-19 infection. In the event of a coinfection, patients should avoid immunosuppressive therapies or have their dosages reduced. |

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