ISBN <u>978-1-960740-75-5</u>

COVID-19 PANDEMIC — UNDERSTANDING THE CHALLENGES AND SOLUTIONS

Review Based Book Chapter

COVID-19 AND ONCOLOGIC IMMUNOMODULATION: PRECISION INSIGHTS INTO TUMOR-VIRUS INTERACTIONS AND VACCINE IMPACTS ON TIME

August 13, 2025

doi: 10.5281/zenodo.14830078



REVIEW BASED BOOK CHAPTER

COVID-19 AND ONCOLOGIC IMMUNOMODULATION: PRECISION INSIGHTS INTO TUMOR-VIRUS INTERACTIONS AND VACCINE IMPACTS ON TIME

Diego Tomassone¹

¹Holos Medica Clinical and Research, 38068 Rovereto, Italy

*For Correspondence

<u>diego.tomassone81@gmail.com</u>

Abstract

The COVID-19 pandemic has profoundly reshaped oncologic practice, introducing a range of clinical, biological, and ethical challenges. In particular, the interaction between SARS-CoV-2 and tumor biology has revealed complex mechanisms involving gene regulation, systemic inflammation, immune dynamics, and therapeutic vulnerability. Simultaneously, COVID-19 vaccination has introduced immunological and molecular variables that warrant thorough investigation, especially in cancer patients undergoing immunotherapy.

This chapter presents an interdisciplinary analysis of the biological interplay between cancer and COVID-19, with a specific focus on the implications of vaccination within the framework of precision oncology. It explores shared molecular pathways, alterations in the tumor immune microenvironment (TiME), therapeutic implications, and translational prospects. By integrating molecular oncology, immunology, virology, bioethics, and computational science, the chapter offers a comprehensive and up-to-date perspective.

Through a critical review of the literature and the exploration of predictive models, this work aims to contribute to the development of personalized, resilient, and evidence-based therapeutic strategies essential for navigating the evolving landscape of oncologic care in pandemic and post-pandemic settings.

Keywords

Cancer and COVID-19, Precision Oncology, COVID-19 Vaccination, Tumor Immune Microenvironment (TiME), Immunotherapy, Virus-tumor Interactions, Immune Response, Molecular Vulnerability, Multidisciplinary Approach, Translational Research

Introduction

The COVID-19 pandemic has exerted a deep and lasting impact on oncology, altering not only clinical and therapeutic pathways but also the priorities of translational research. Cancer patients already vulnerable due to disease-related



immunosuppression and the effects of anticancer treatments have faced heightened risks of infectious complications, treatment delays, and impaired immune responsiveness. In this context, a multidisciplinary approach integrating oncology, virology, immunology, bioinformatics, and precision medicine has become essential.

The biological interaction between SARS-CoV-2 and neoplastic processes has revealed complex and still-evolving mechanisms. Several studies have shown that the virus modulates the expression of cellular receptors such as ACE2 and TMPRSS2, which are implicated in various solid tumors. Moreover, SARS-CoV-2 infection influences molecular pathways linked to proliferation, inflammation, and immune signaling [1]. The viral insult may also disrupt the tumor immune microenvironment (TiME), promoting macrophage immunosuppressive polarization, T cell exhaustion, and dendritic cell dysfunction factors that may affect tumor progression and compromise immunotherapy efficacy.

In parallel, COVID-19 vaccination has introduced new immunological variables into the clinical management of cancer patients. Although mRNA and vector-based vaccines have proven safe and generally well tolerated, immune responses in oncologic populations have been heterogeneous modulated by tumor type, immune status, and ongoing therapy [2]. Vaccination has raised specific clinical questions: What is the optimal timing relative to chemotherapy or immunotherapy? Which biomarkers can predict effective response? How should long-term immune protection be monitored?

Precision oncology, based on molecular profiling and therapeutic customization, is now challenged to integrate these emerging complexities. The incorporation of viral, tumor, and immune data demands advanced analytical tools and real-time decision-support models. In this landscape, Al-enhanced Raman spectroscopy, multi-omic profiling, and liquid biopsy technologies are emerging as strategic resources for adaptive and resilient cancer care [3].

In Italy and across Europe, research initiatives such as INNOVA, COMETA, and RAMAN4CURE have embraced an interdisciplinary vision for post-pandemic oncology facilitating collaboration among clinicians, researchers, and engineers. These programs have shown that only through the convergence of diverse expertise can the challenges posed by the pandemic be transformed into opportunities for therapeutic innovation [4].



This chapter aims to examine, from a systemic and multidisciplinary standpoint:

- Biological interactions between SARS-CoV-2 and tumor physiology
- The immunological impact of COVID-19 vaccination in precision oncology
- Clinical and molecular implications for therapeutic stratification
- The role of interdisciplinary collaboration in translational research and clinical practice

By critically reviewing the literature and analyzing integrated models, the chapter seeks to offer an updated and actionable perspective for cancer management in the post-pandemic era—advancing personalized care, patient safety, and healthcare system resilience.

1. Biological Interactions Between SARS-CoV-2 and Cancer

The interplay between SARS-CoV-2 and tumor biology has opened a new frontier in translational research, where virology, molecular oncology, and immunology converge to investigate how viral infection impacts the neoplastic microenvironment. Cancer patients already immunocompromised due to disease and treatment display increased vulnerability not only to the clinical complications of COVID-19, but also to biological alterations that may influence tumor progression and therapeutic outcomes.

1.1 <u>Viral Receptors and Tumor Tropism</u>

SARS-CoV-2 enters host cells by binding to cellular receptors such as ACE2, TMPRSS2, and NRP1. Expression of these receptors has been observed across several tumor tissues, including lung, colon, prostate, and kidney suggesting a potential viral tropism for neoplastic cells [5]. TMPRSS2, notably implicated in prostate cancer, has been associated with increased tumor immunogenicity and modulation of response to immune checkpoint inhibitors.

In vitro studies have shown that tumor cells expressing high levels of TMPRSS2 exhibit:

- Activation of interferon signaling pathways
- Upregulation of HLA-I and PD-L1 molecules
- Reduced natural killer (NK) cell-mediated cytotoxicity

These findings underscore a possible intersection between viral entry mechanisms and immunotherapeutic sensitivity.



1.2 Modulation of the Tumor Immune Microenvironment (TiME)

SARS-CoV-2 infection may reshape the tumor immune microenvironment through various mechanisms:

- <u>Systemic inflammation</u>: Cytokine storm activation, with elevated IL-6, TNF-a, and IL-1β levels, promotes polarization of tumor-associated macrophages (TAMs) toward an immunosuppressive M2 phenotype.
- **Lymphocyte exhaustion**: Reduced CD8+T cell counts and dysfunctional dendritic cell activity impair antitumor immune surveillance.
- <u>Immune checkpoint expression</u>: Viral infection induces upregulation of PD-L1 and CTLA-4, potentially diminishing the efficacy of immune checkpoint blockade.

These effects are particularly relevant in solid tumors with high immune infiltration, such as melanoma, non-small cell lung cancer, and renal cell carcinoma.

1.3 Molecular and Transcriptomic Implications

Transcriptomic analyses of cancer patients with active SARS-CoV-2 infection have revealed significant alterations in gene expression related to immune response, cellular metabolism, and tumor proliferation [6]. Key observations include:

- Upregulation of pro-inflammatory and immunoregulatory genes
- Activation of oxidative stress and autophagy pathways
- Modulation of growth factors and angiogenic signaling

These molecular changes may influence tumor evolution and treatment sensitivity, necessitating enhanced biomolecular monitoring in oncology patients with COVID-19 history.

1.4 <u>Seroconversion and Immune Response in Cancer Patients</u>

The ability of cancer patients to mount an effective immune response against SARS-CoV-2 has been a subject of extensive investigation. While seroconversion defined by the production of SARS-CoV-2 specific IgG antibodies is generally robust in patients with solid tumors, it is significantly impaired in individuals with hematologic malignancies, particularly those undergoing anti-CD20 therapy or hematopoietic stem cell transplantation [7].



Furthermore, hematologic cancer patients tend to clear the virus more slowly, with an average of 61 days of viral positivity, compared to 33 days in solid tumor patients.

These findings suggest that SARS-CoV-2 infection elicits differential immune responses depending on tumor type and treatment history highlighting the need for tailored clinical management and vaccine planning in oncologic populations.

2. Immunological and Inflammatory Impact

SARS-CoV-2 infection has demonstrated a profound effect on both innate and adaptive immunity. In cancer patients who are often immunocompromised due to disease and treatment these effects can be amplified, triggering systemic inflammatory responses that may interfere with tumor progression, therapeutic efficacy, and vaccine safety.

2.1 Activation of the Innate Immune System

The entry of SARS-CoV-2 into alveolar epithelial cells activates the innate immune system via pattern recognition receptors (PRRs), including Toll-like receptors (TLR7/8) and RIG-I/MDA-5 signaling. This activation induces the production of type I interferons (IFN-a, IFN- β) and pro-inflammatory cytokines such as IL-6, TNF-a, and IL-1 β [8]. In oncology patients, this response may be either dysregulated or exacerbated, affecting the dynamics of the tumor immune microenvironment.

The inflammatory cascade triggered by the virus also involves the NLRP3 inflammasome, which drives the secretion of IL-1 β and IL-18 and induces inflammatory cell death (pyroptosis). If uncontrolled, this mechanism may lead to the so-called "cytokine storm" a hyperinflammatory syndrome associated with organ damage and poor clinical outcomes.

2.2 Lymphopenia and Immune Exhaustion

One of the most consistent immunological findings in severe COVID-19 cases is lymphopenia a reduction in circulating CD4+ and CD8+ T cells. This phenomenon has also been documented in infected cancer patients, directly impacting antitumor immune surveillance. Remaining T cells often exhibit an exhausted phenotype, characterized by overexpression of PD-1, TIM-3, and NKG2A, which impairs cytotoxic activity [9].



In addition, SARS-CoV-2 infection may damage lymphoid organs such as the spleen and lymph nodes, and disrupt cellular metabolism, limiting lymphocyte proliferation. This virally induced immunosuppression overlaps with tumor-driven and treatment-related immunosuppressive effects, creating a complex and dynamic vulnerability in cancer patients.

2.3 Central Role of IL-6 and Inflammatory Cytokines

Among the cytokines involved in SARS-CoV-2 inflammatory responses, interleukin-6 (IL-6) plays a central role. It contributes to the synthesis of acute-phase proteins such as CRP and fibrinogen and regulates adaptive immunity. In cancer patients, elevated IL-6 levels have been associated with tumor progression, resistance to immunotherapy, and worse prognosis [10].

Persistent and dysregulated IL-6 production may lead to chronic inflammation, cellular senescence, and systemic immunosuppression. Recent studies suggest that SARS-CoV-2 can induce DNA damage and inhibit repair mechanisms, promoting inflammatory cytokine production and premature cellular aging [11].

2.4 <u>Implications for Oncologic Therapy</u>

The immunological and inflammatory effects of viral infection have direct implications for cancer therapy. Specifically:

- They may reduce the efficacy of immunotherapy by impairing effector T cell function
- They may increase the risk of immune-related adverse events in patients receiving checkpoint inhibitors
- They may alter the pharmacokinetics of anticancer agents due to hepatic and systemic modifications

For these reasons, close monitoring of immunologic parameters in cancer patients with a history of COVID-19 is essential. Clinicians should consider adjusting therapeutic protocols and implementing immune modulation strategies to optimize safety and efficacy.



3. COVID-19 Vaccination in Oncology Patients

Vaccination against SARS-CoV-2 has marked a turning point in protecting vulnerable populations including patients with cancer. However, the immune response elicited by these vaccines in oncologic settings has been notably variable, influenced by tumor type, immune status, and ongoing treatments. Precision oncology has faced a new wave of clinical questions: How should vaccination be optimized for immunocompromised patients? Which biomarkers can predict vaccine efficacy? What is the ideal timing in relation to therapy?

3.1 Safety and Tolerability

mRNA-based vaccines (BNT162b2 and mRNA-1273) and vector-based vaccines (ChAdOx1) have proven to be safe and well tolerated among most cancer patients. Adverse events have been comparable to those observed in the general population, with a predominance of localized reactions and mild systemic symptoms [12]. The incidence of serious adverse events has been low and not directly linked to vaccination even in patients actively receiving chemotherapy, immunotherapy, or molecular targeted therapies.

3.2 <u>Humoral Immune Response</u>

The antibody response to COVID-19 vaccines has been studied extensively in oncology populations. Among patients with solid tumors, seroconversion after two vaccine doses exceeded 90%, matching results seen in healthy individuals [13]. However, patients with hematologic malignancies especially those treated with anti-CD20 agents or who underwent stem cell transplantation—showed markedly reduced responses, often falling below 50% seroconversion [7].

A higher booster dose improved immunogenicity, particularly in patients with solid tumors, while hematologic patients showed limited benefit highlighting the need for personalized vaccine strategies [14].

3.3 Cellular Immunity and Competence

In addition to humoral responses, T cell mediated immunity has been investigated. Studies conducted at the National Cancer Institute of Milan found that, despite systemic immunosuppression, many cancer patients retain a functional cellular immune



response to mRNA vaccines demonstrating IFN-γ production and activation of CD4⁺ and CD8⁺ T cells [15].

Nevertheless, the longevity of post-vaccination immunity remains uncertain. Ongoing longitudinal studies are assessing the kinetics of antibody decline and the durability of immunologic memory.

3.4 Timing and Interaction with Cancer Therapy

Vaccination timing in relation to cancer treatments is critical. Current recommendations suggest administering vaccines at least two weeks before initiating chemotherapy or radiotherapy where feasible to optimize immunogenicity [16]. In patients already undergoing treatment, vaccination can proceed safely, but immune monitoring and potential booster dosing should be considered.

For therapies involving B cell-targeting antibodies such as rituximab, a minimum interval of six months post-treatment is advised before vaccination to ensure responsiveness. Patients who have undergone stem cell transplantation require complete reimmunization according to post-transplant immunization protocols.

3.5 Clinical and Strategic Implications

Vaccination has demonstrated clear reductions in COVID-19 morbidity and mortality among cancer patients. Multicenter studies reveal that vaccinated individuals have lower rates of hospitalization, pneumonia, oxygen dependence, and death compared to unvaccinated controls [17]. Moreover, time to viral clearance was shorter in vaccinated patients, offering clinical and organizational advantages.

These findings support prioritization of cancer patients in vaccination campaigns and reinforce the importance of tailored booster strategies. Precision oncology can play a key role in defining individual immunologic profiles informing decisions on vaccine type, dosage schedule, and optimal timing.

4. Precision Medicine and Therapeutic Stratification

Precision oncology is grounded in the ability to tailor treatment to each patient's molecular, immunological, and clinical profile. In the COVID-19 era, this framework has become even more critical, as viral infection and vaccination introduce novel biological variables that influence therapeutic outcomes. Stratifying cancer patients



based on their immune status, viral history, and molecular vulnerability is now both a clinical and scientific imperative.

4.1 Post-COVID Molecular Profiling

SARS-CoV-2 infection can alter gene expression, immune function, and cellular metabolism producing a dynamic molecular signature that must be considered in treatment planning. Research conducted at the Regina Elena Institute and Sapienza University of Rome demonstrated that combining liquid biopsy, photonic spectroscopy, and genomic sequencing enables real-time monitoring of tumor status and post-infection immune response [2].

This profiling approach helps identify patients at higher risk of progression, toxicity, or therapeutic failure, allowing for personalized treatment adjustments.

4.2 <u>Predictive Biomarkers and Immunocompetence</u>

Therapeutic stratification relies on the identification of predictive biomarkers, such as:

- Expression of PD-L1 and CTLA-4 within the tumor immune microenvironment (TiME)
- Tumor mutational burden (TMB)
- Presence of viral and tumor-derived neoantigens
- Humoral and cellular response to COVID-19 vaccination

These variables can be incorporated into Al-driven predictive models to determine the most effective treatment strategy for each patient. According to Marchetti and Pruneri [18], the pandemic has accelerated the adoption of data-driven decision algorithms ushering in a more adaptive and responsive model of precision medicine.

4.3 Interaction Between Cancer Therapy and Vaccine Response

The immunogenicity of COVID-19 vaccines may be affected by the type of oncologic therapy administered. Patients receiving immunotherapy tend to maintain robust cellular responses, while those undergoing chemotherapy or B cell-depleting regimens (e.g., anti-CD20 antibodies) often exhibit diminished antibody production [7].

This underscores the need to stratify patients not only by tumor type, but also by treatment modality and vaccination timing. Precision medicine can inform optimal



vaccine selection, dosing schedules, and administration intervals to maximize protection while minimizing risks.

4.4 Computational Models and Clinical Decision-Making

Integrating clinical, molecular, and immunological data demands advanced computational tools. Machine learning and neural network-based models have been developed to:

- Predict individual vaccine response
- Estimate post-COVID tumor progression risk
- Optimize therapeutic sequencing and timing

According to Magrelli [19], artificial intelligence in precision oncology has the potential to improve therapeutic adherence, minimize adverse events, and reduce healthcare costs particularly for multi-treated patients.

4.5 Toward Adaptive and Sustainable Oncology

Therapeutic stratification is not only a biological concern it also encompasses organizational and ethical dimensions. Ensuring equitable and evidence-based access to precision medicine requires balancing innovation with patient privacy, model transparency, and healthcare provider education. Italy's National Bioethics Committee has emphasized the need to integrate ethical safeguards as precision oncology evolves [20].

In summary, precision cancer care in the post-COVID era must advance toward an adaptive, multidisciplinary, and patient-centered model one that integrates biological, clinical, and social data to guide personalized therapeutic decisions.

5. Multidisciplinary Approach to Clinical Management

Managing cancer patients during the COVID-19 pandemic required a substantial reorganization of care pathways, with the adoption of multidisciplinary models designed to ensure continuity of therapy, safety, and personalized care. The multidisciplinary approach already a cornerstone of precision oncology proved essential for addressing the clinical, logistical, and immunological challenges introduced by the public health crisis.



5.1 Clinical Networks and Tumor Boards

The pandemic accelerated the development of integrated clinical networks and multidisciplinary tumor boards, where oncologists, radiation oncologists, immunologists, virologists, pharmacologists, and bioinformaticians collaborate to define optimal therapeutic strategies. According to Cancer Core Europe [21], collegial case discussions enabled protocol adaptation, reduced hospital visits, and helped maintain immunological protection for patients [22].

In Italy, the Breast Unit model already recognized within Essential Levels of Care (LEA) has demonstrated the effectiveness of a multiprofessional approach in managing breast cancer, serving as a blueprint for other oncologic domains [23].

5.2 Coordination Across Disciplines and Decision-Making Flows

Collaborative networks enabled coordinated responses to key challenges during the pandemic, including managing chemoradiotherapy toxicity, vaccination planning, patient selection for immunotherapy, and adapting treatment schedules based on infectious risk. The Italian Association of Medical Oncology (AIOM) issued operational guidelines during phase two of the emergency, promoting clinical triage systems, telemedicine platforms, safety protocols, and COVID-free pathways for oncology patients [24].

These measures required active engagement from all professional figures, resulting in the establishment of crisis teams, shared digital platforms, and remote monitoring tools.

5.3 Telemedicine and Community-Based Oncology

Telemedicine played a pivotal role in managing patients in follow-up, oral therapy, or cancer rehabilitation. Virtual consultations, digital sharing of test results, and home delivery of medications reduced viral exposure risk and improved patient quality of life. However, as highlighted by the FAVO Observatory, it is essential to ensure equitable access to technology, provider training, and platform standardization [25].

Community-based oncology, working in synergy with hospital centers, can effectively handle chronic disease management, screening programs, and post-treatment surveillance contributing to system-wide sustainability.



5.4 Training and Interdisciplinary Culture

A true multidisciplinary approach requires dedicated training and a collaborative mindset. Healthcare professionals must cultivate cross-functional skills, communication abilities, and ethical sensitivity. As Fulop [26] noted, the quality of care depends not only on available resources, but also on the ability to work together in a coordinated and integrated manner.

The pandemic highlighted that medicine centered on isolated expertise is no longer sufficient. Instead, communities of practice must be built spaces where skills converge toward shared goals and informed decisions.

5.5 Toward Integrated Clinical Governance

The experience gained during the pandemic offers a blueprint for a permanent model of integrated clinical governance. This includes:

- Formalizing tumor boards across all oncology centers
- Implementing flexible clinical pathways (PDTA) adaptable to emergencies
- Integrating hospital and community-based care
- Systematically applying telemedicine and molecular diagnostics
- Continuously evaluating patient outcomes and quality of care

As emphasized by Cancer Core Europe, the crisis generated empirical knowledge that can reshape oncology care delivery making it more resilient, personalized, and patient-centered [21, 22].

6. Ethical and Translational Considerations

The integration of precision oncology, pandemic management, and technological innovation raises a series of ethical and translational challenges that must not be overlooked. The COVID-19 pandemic exposed the fragility of cancer patients, the need to rapidly adapt treatment protocols, and the urgency of ensuring equity, transparency, and accountability in clinical decision-making. In this context, the multidisciplinary approach is not merely an organizational strategy it is an ethical imperative.



6.1 Equity in Access to Care and Vaccination

Oncology patients represent a vulnerable population with complex and often urgent medical needs. During the pandemic, access to care was limited by containment measures, resource shortages, and hospital restructuring. COVID-19 vaccination introduced additional disparities, as immune responses varied widely and protocols were not always tailored to oncologic subgroups [27]. Therapeutic innovation must be accompanied by equity policies that account for both biological and social fragility.

6.2 Algorithmic Transparency and Clinical Accountability

The use of Al-based predictive models for therapeutic stratification and post-COVID management demands clear standards for transparency and accountability. Models must be validated, interpretable, and clinically supervised. As noted by Magrelli [19], computational tools should ethically inform not replace medical judgment. Clinical responsibility remains a shared process involving the physician, the patient, and the healthcare system.

6.3 Informed Consent and Communication

The pandemic has altered how physicians and patients communicate, introducing telemedicine and reducing in-person interactions. This shift has complicated the process of informed consent, particularly in complex scenarios such as cancer treatment planning in patients with a history of COVID-19. It is essential that patients fully understand not only treatment options but also the immunological and virological implications of those choices [28]. Communication must be clear, empathetic, and evidence-based.

6.4 Continuity of Care and Translational Adaptation

The pandemic forced rapid translation of scientific knowledge into clinical practice. European oncology centers affiliated with Cancer Core Europe developed shared guidelines to ensure treatment continuity, revising protocols and reorganizing care flows [21, 22]. This process generated valuable empirical insights that can inform the design of more adaptive, resilient care models. Translation extends beyond science it includes organizational frameworks, training, and clinical governance.



6.5 Psychological Well-Being and Social Support

Cancer patients experienced increased anxiety, stress, and isolation during the pandemic. Coping strategies such as meditation, music therapy, and digital tools for maintaining social connection have demonstrated benefits for quality of life [29]. Nonetheless, psychological support services must be strengthened, and emotional well-being must be fully integrated into the therapeutic journey. Precision medicine must also be personal medicine.

7. Future Perspectives

The COVID-19 pandemic has served as a catalyst for innovation in oncology accelerating the adoption of digital technologies, predictive models, and multidisciplinary approaches. At the same time, it has highlighted structural weaknesses in healthcare systems, disparities in access to care, and the need for more adaptive and resilient clinical governance. Looking ahead, precision oncology must evolve toward an integrated model that addresses not only the biological complexities of cancer, but also the realities of global health crises.

7.1 Toward Post-Pandemic Medicine

The end of the global health emergency, declared by the WHO in 2023, does not signal the end of COVID-19's clinical and organizational impact. Oncology patients with a history of infection or vaccination represent a newly defined clinical population characterized by specific immunological and molecular profiles that warrant tailored care protocols [30]. Post-pandemic medicine must incorporate these data into therapeutic stratification, clinical surveillance, and translational research.

7.2 <u>Technological Innovation and Predictive Modeling</u>

Recent experience has demonstrated the value of artificial intelligence, Raman spectroscopy, multi-omics, and telemedicine in oncology care. When ethically and rigorously integrated, these technologies can enhance therapeutic personalization, anticipate complications, and optimize resource utilization. According to Boniface and Tapia-Rico [31], future oncology will increasingly rely on adaptive predictive models capable of responding in real time to shifting clinical and environmental conditions.



7.3 Collaborative Research and European Networks

The Cancer Core Europe network has shown that collaboration among centers of excellence is essential during public health crises. Shared guidelines, reorganized clinical workflows, and the generation of empirical evidence enabled high-quality care delivery even under critical conditions [21, 22]. This experience must evolve into a permanent model of collaborative research one capable of producing actionable translational evidence and informing health policy.

7.4 Patient-Centered Care and Humanistic Medicine

Precision oncology must remain centered on the patient. The pandemic underscored the importance of psychological resilience, empathic communication, and social support. Technology should serve not replace the therapeutic relationship. As von Känel [29] emphasized, patient resilience is a clinical variable to consider, and the medicine of the future must also be a medicine of the person.

Conclusion

The COVID-19 pandemic has profoundly reshaped the landscape of oncologic medicine accelerating the adoption of predictive models, digital technologies, and multidisciplinary approaches. This chapter has provided a systemic analysis of the biological interplay between SARS-CoV-2 and tumor physiology, the impact of vaccination in cancer patients, immunological and therapeutic implications, and the role of artificial intelligence in clinical stratification. What emerged is the clear need for precision oncology to evolve toward an integrated, adaptive, and human-centered paradigm capable of responding to the complex and dynamic challenges posed by global health crises.

Experiences gained throughout the pandemic have demonstrated that computational models and innovative tools such as Raman spectroscopy, multi-omic profiling, and telemedicine can personalize care, enhance clinical resilience, and optimize resource allocation. Post-COVID oncologic governance now requires an ethical and translational vision that integrates equity, transparency, and psychological support into therapeutic pathway design.

Looking ahead, it will be essential to consolidate collaborative research networks, formalize multidisciplinary models, and promote a truly humanistic medicine that



recognizes the patient not only as a biological subject, but as a person with lived experience, vulnerabilities, and resilience. Though the pandemic brought unprecedented challenges, it also generated valuable knowledge that if properly harnessed can guide oncology toward a more sustainable, innovative, and inclusive future.

Conflicts of interest

The author does not have conflict of interest.

<u>References</u>

- [1] Jereczek-Fossa, B.A., Pepa, M., Zaffaroni, M., Marvaso, G., Bruni, A., Buglione di Monale E Bastia, M., Catalano, G., Filippi, A.R., Franco, P., Gambacorta, M.A., Genovesi, D., Iatì, G., Magli, A., Marafioti, L., Meattini, I., Merlotti, A., Mignogna, M., Musio, D., Pacelli, R., Pergolizzi, S., Tombolini, V., Trovo, M., Leonardi, M.C., Ricardi, U., Magrini, S.M., Corvò, R., Donato, V. 2021. COVID-19 safe and fully operational radiotherapy: An AIRO survey depicting the Italian landscape at the dawn of phase 2. Radiotherapy and Oncology, 155, 120-122.
- [2] Horgan, D., Ciliberto, G., Conte, P., Curigliano, G., Seijo, L., Montuenga, L.M., ... & Capoluongo, E.D. 2021. Bringing onco-innovation to Europe's healthcare systems: The potential of biomarker testing, real world evidence, tumour agnostic therapies to empower personalised medicine. Cancers, 13(3), 583.
- [3] Joseph, M.M.,P,S., Arya, J.S., & Nair, J.B. 2025. Bridging pandemic and oncology challenges: Surface-enhanced Raman spectroscopy in the fight against COVID-19 and cancer. Science Progress, 108(2), 00368504251342977.
- [4] Thakkar, A., Gonzalez-Lugo, J.D., Goradia, N., Gali, R., Shapiro, L.C., Pradhan, K., ... & Halmos, B. 2021. Seroconversion rates following COVID-19 vaccination among patients with cancer. Cancer Cell, 39(8), 1081-1090.
- [5] Subbarayan, K., Bieber, H., Massa, C., Rodríguez, F.A.E., Hossain, S.A.A., Neuder, L., ... & Seliger, B. 2025. Link of TMPRSS2 expression with tumor immunogenicity and response to immune checkpoint inhibitors in cancers. Journal of Translational Medicine, 23(1), 294.
- [6] Chadokiya, J., Chang, K., Sharma, S., Hu, J., Lill, J.R., Dionne, J., & Kirane, A. 2025. Advancing precision cancer immunotherapy drug development, administration, and response prediction with Al-enabled Raman spectroscopy. Frontiers in Immunology, 15, 1520860.
- [7] Siqueira, J.D., Goes, L.R., Alves, B.M., Carvalho, P.S.D., Cicala, C., Arthos, J., ... & Soares, M.A. 2021. SARS-CoV-2 genomic analyses in cancer patients reveal elevated intrahost genetic diversity. Virus Evolution, 7(1), veab013.
- [8] Islamuddin, M., Mustfa, S.A., Ullah, S.N.M.N., Omer, U., Kato, K., & Parveen, S. 2022. Innate immune response and inflammasome activation during SARS-CoV-2 infection. Inflammation, 45(5), 1849-1863.
- [9] Valsecchi, E., Coppola, E., Pires, R., Parmegiani, A., Casiraghi, M., Galli, P., & Bruno, A. 2022. A species-specific qPCR assay provides novel insight into range expansion of the Mediterranean monk seal (Monachus monachus) by means of eDNA analysis. Biodiversity and Conservation, 31(4), 1175-1196.
- [10] Istituto Medicina Biologica. 2020. Rapporto clinico interno sull'impatto dell'IL-6 nei pazienti oncologici durante la pandemia COVID-19. Milano: IMBIO.
- [11] Gioia, M., Payero, L., Salim, S., Fajish V,G., Farnaz, A.F., Pannafino, G., ... & Alani, E. 2023. Exo 1 protects DNA nicks from ligation to promote crossover formation during meiosis. PLoS Biology, 21(4), e3002085.

Publisher

COVID-19 PANDEMIC — UNDERSTANDING THE CHALLENGES AND SOLUTIONS

- [12] Cognetti, F., Biganzoli, L., De Placido, S., Del Mastro, L., Masetti, R., Naso, G., ... & Barni, S. 2021. Multigene tests for breast cancer: The physician's perspective. Oncotarget, 12(9), 936.
- [13] Patelli, G., Pani, A., Amatu, A., Scaglione, F., & Sartore-Bianchi, A. 2022. Seroconversion after SARS-CoV-2 mRNA booster vaccine in cancer patients. European Journal of Cancer, 167, 175.
- [14] Napuri, N.I., Curcio, D., Swerdlow, D.L., & Srivastava, A. 2022. Immune response to COVID-19 and mRNA vaccination in immunocompromised individuals: a narrative review. Infectious Diseases and Therapy, 11(4), 1391-1414.
- [15] Negahdaripour, M., Shafiekhani, M., Moezzi, S.M.I., Amiri, S., Rasekh, S., Bagheri, A., ... & Vazin, A. 2021. Administration of COVID-19 vaccines in immunocompromised patients. International Immunopharmacology, 99, 108021.
- [16] Gomez-Randulfe, I., Lavender, H., Symeonides, S., & Blackhall, F. 2025. Impact of systemic anticancer therapy timing on cancer vaccine immunogenicity: a review. Therapeutic Advances in Medical Oncology, 17, 17588359251316988.
- [17] Dimitrov, G., Kalinov, K., & Valkov, T. 2024. COVID-19 vaccination outcomes in patients with a solid malignancy: Insights from extensive real-world data and propensity score matched analyses. American Journal of Infection Control, 52(6), 678-682.
- [18] Marchetti, A., & Pruneri, L. 2020. Data-driven decision-making in precision oncology during the COVID-19 pandemic. In: Proceedings of the Italian Society of Pathology and Oncology.
- [19] Magrelli, V. 2024. Artificial intelligence and therapeutic adherence in precision oncology. Caracalla Festival Lecture Series, Roma.
- [20] CNB Comitato Nazionale per la Bioetica. 2023. Etica e medicina di precisione: Raccomandazioni per l'oncologia post-pandemica. Roma: Presidenza del Consiglio dei Ministri.
- [21] Eggermont, A.M., Apolone, G., Baumann, M., Caldas, C., Celis, J.E., de Lorenzo, F., ... & Calvo, F. 2019. Cancer Core Europe: a translational research infrastructure for a European mission on cancer. Molecular Oncology, 13(3), 521-527.
- [22] Apolone, G. 2020. Il cancro nella bufera della pandemia. Scienza in rete. https://www.scienzainrete.it/articolo/giovanni-apolone-cancro-nella-bufera-della-pandemia/luca-carra/2020-05-1
- [23] Cicchetti, A. 2018. Breast Unit e modelli multidisciplinari in oncologia. In: Atti del Congresso Nazionale AllC.
- [24] AIOM Associazione Italiana di Oncologia Medica. 2020. Linee guida operative per la gestione oncologica durante la pandemia COVID-19. https://www.aiom.it/linee-guida-aiom/
- [25] Cicchetti, A. 2020. Telemedicina e oncologia territoriale: sfide e prospettive. In: Osservatorio FAVO, Rapporto annuale.
- [26] Fulop, N.J., & Ramsay, A.I. 2019. How organisations contribute to improving the quality of healthcare. British Medical Journal, 365.
- [27] Lambertini, M., Peccatori, F.A., Demeestere, I., Amant, F., Wyns, C., Stukenborg, J.B., ... & ESMO Guidelines Committee. 2020. Fertility preservation and post-treatment pregnancies in post-pubertal cancer patients: ESMO Clinical Practice Guidelines. Annals of Oncology, 31(12), 1664-1678.
- [28] AIRC Fondazione Italiana per la Ricerca sul Cancro. 2020. Bilancio sociale e attività durante la pandemia. https://www.airc.it/fondazione/chi-siamo/bilancio/bilancio-2020
- [29] Zuccarella-Hackl, C., Jimenez-Gonzalo, L., von Känel, R., Princip, M., Jellestad, L., Langraf-Meister, R.E., ... & Ledermann, K. 2023. Positive psychosocial factors and the development of symptoms of depression and posttraumatic stress symptoms following acute myocardial infarction. Frontiers in Psychology, 14, 1302699.
- [30] Springer Nature. 2023. Post-pandemic oncology and tailored care protocols. Annual Progress Report. https://annualreport.springernature.com/2023/
- [31] Boniface, D., & Tapia-Rico, G. 2022. Oncology during the COVID-19 pandemic: A lockdown perspective. Current Oncology Reports, 24(10), 1219-1235.





<u>Disclaimer/Publisher's Note:</u> The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of Scientific Knowledge Publisher (SciKnowPub) and/or the editor(s). SciKnowPub and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

© 2025 by the authors. Published by Scientific Knowledge Publisher (SciKnowPub). This book chapter is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license.

(https://creativecommons.org/licenses/by/4.0/)