

Wytyczne i rekomendacje / Guidelines and recommendations

Zdrowie publiczne / Public health

Infectious disease prophylaxis and treatment in cancer patients, with particular emphasis on COVID-19. Interdisciplinary position statement of Polish experts

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Infectious diseases constitute a significant burden for cancer patients. This became particularly evident during the COVID-19 pandemic. Due to cancer itself and its treatment, the course of infectious diseases in oncology patients is often unpredictable and may negatively affect them. Preventing infectious diseases through a wide range of vaccinations may help maintain the continuity of treatment and constitute an element of holistic patient care. Testing patients with symptoms or suspected infectious allows proper treatment and may avoid unfavorable consequences. More education on preventing and treating infectious diseases is necessary to improve the standard of cancer care.

Key words: infectious diseases, cancer, vaccines, COVID-19

Introduction

Cancer patients present an increased risk of severe infections. However, their awareness of the need for preventive measures is low. In the United States of America, the number of cancer-related deaths among cancer patients increased slightly between 2018 and 2021 [1]. In parallel, a significant increase in other death causes was observed, mainly due to the COVID-19 pandemic. The number of deaths in cancer patients caused by non-cancer causes was highest in the winter months of 2021 and 2022, corresponding to subsequent waves of COVID-19 [1]. In Poland, a significant increase in the mortality of cancer patients was also observed during the COVID-19 pandemic, although some deaths may be attributed to delayed diagnosis and poorer access to health care. The highest 30-day mortality was noted in patients with lung cancer. Mortality rates due to vaccine-preventable infections (including influenza, COVID-19 and pneumococcal diseases) in cancer patients are higher than 10%, reaching up to 50% in cases of invasive pneumococcal disease [2–4].

Jak cytować / How to cite:

Rutkowski P, Cybulska-Stopa B, Jassem J, Plużański A, Tomasiewicz K, Wyrwicz L, Wysocki P, Wysocki J, Flisiak R. *Infectious disease prophylaxis and treatment in cancer patients, with particular emphasis on COVID-19. Interdisciplinary position statement of Polish experts.* NOWOTWORY J Oncol 2024; 74: 203–212.

Taking into account Polish cancer patients' insufficient awareness of the burden of infectious diseases, their prevention, testing and treatment, we present herewith the interdisciplinary expert position statement on these aspects from the perspective of infectious diseases, vaccinology and oncology. Considering the significant impact of the COVID-19 pandemic on cancer patients, this article focuses mainly on this infectious disease. We aim to facilitate actions to implement the prevention of infectious diseases in cancer patients, focusing on COVID-19 [1].

Infectious diseases burden in cancer patients, focusing on COVID-19

Infectious diseases have a significant impact on cancer patients. Vaccinations can effectively protect against the consequences of infectious diseases, allow the continuity of anticancer therapy, and a decrease in mortality [1, 5]. This impact is apparent for COVID-19, where subsequent infection waves were accompanied by peaks of excess deaths [1]. Indeed, people with a history or current cancer are at high risk of severe disease and death from this infection [6-8]. In the case of seasonal influenza, hospitalized cancer patients were shown to have higher mortality, longer hospital stays and a greater risk of health-related complications, including pneumonia, neutropenia and sepsis [9]. Importantly, viral infections pave the way for bacterial infections. Therefore, Streptococcus pneumoniae infections are secondary infections or co-infections, which in immunosuppressed cancer patients may be particularly harmful [10-12].

Typically, hematologic malignancies carry an increased risk of severe infections compared to solid tumors, as shown for COVID-19 [13, 14]. At the same time, however, solid malignancies are more common than hematologic malignancies [15]. Importantly, cancer patients are not a homogeneous group. The main risk factors for severe COVID-19 in cancer patients are:

- multiple comorbidities [6, 16–18],
- type of cancer (including acute leukemia, lung cancer, genital cancer, thyroid cancer) [6, 17, 19, 20],
- cytotoxic treatment (including time elapsed since therapy) [18],
- bone marrow transplants,
- advanced age [6, 16–18],
- male gender [6, 16, 17, 19],
- ethnicity [6, 16, 17, 19],
- multi-neoplastic syndromes [17],
- smoking [16],
- average or poor Eastern Cooperative Oncology Group
 performance status [16],
- history of active cancer versus cancer in remission [16].

Due to impaired immune system and treatment-related immunosuppression, cancer patients are more susceptible to unpredictable courses of infections and post-infectious complications [21]. Numerous factors related to cancer influence the course of infectious diseases:

- corticosteroids and other immunosuppressive drugs reduce the immune response,
- cytotoxic drugs may cause bone marrow suppression, which may lead to thrombocytopenia and neutropenia, thus prompting bacterial infections [22],
- radiotherapy-related lymphopenia increases the risk of severe viral infections [22],
- inhibiting the activity of immune checkpoints may result in excessive cytokine production and may contribute to the development of a cytokine storm.

Multiple factors increase the risk of severe COVID-19 infections in cancer patients. These include impaired immune system function, synergistic inflammatory reaction, chronic inflammation, increased expression of the ACE2 receptor (in some cancer types) and TMPRSS2 (prostate cancer), and increased procoagulant activity. The SARS-CoV-2 virus is evolving, which changes the burden of COVID-19. During the dominance of the BA.1 and BA.2 subvariants (early Omicron phase), the mortality among hospitalized patients was 12-14%. During the dominance of BA.5, BA.2.75, BQ.1 and XBB.1.5 subvariants (late Omicron phase), the overall burden of COVID-19 was lower in the general population but persisted in hospitalized patients at the alarming level of 9% [23]. The number of deaths among cancer patients was the highest during the COVID-19 wave in early 2022 and was disproportionately higher than that in the general population [24]. Unvaccinated individuals are much more susceptible to COVID-19 sequelae; therefore, vaccination appears to be the most effective prevention of severe COVID-19 infection [25].

Complications of infectious diseases in cancer patients

Recently, much attention has been paid to complications following infection with the SARS-CoV-2 virus called long-COVID syndrome [26, 27]. It is estimated that this syndrome may affect as many as $\frac{1}{3}$ of patients [27]. It manifests as persistent impaired functioning of the respiratory and cardiovascular systems, fatigue and cognitive disorder [28], which may last several weeks or months after the infection [29]. An analysis of the OnCovid registry showed that complications persisted after COVID-19 for 6 and 12 months in 9.8% and 8.0% of patients, respectively. Factors associated with a higher complication risk included male gender, age \geq 65 years, \geq 2 comorbidities, history of smoking and a severe course of COVID-19 [29].

The time of virus elimination (identified as a positive PCR test) is longer in cancer patients than in patients with an effective immune system [30–33]. Such situations may affect the continuity of anticancer treatment. Indeed, the data from the OnCovid registry showed that anticancer treatment was modified or discontinued in 14.6% and 22.9% of patients, respectively, and treatment termination due to COVID-19 complications was associated with a significantly reduced survival compared to that among patients who continued treatment

(hazard ratio [HR]: 6.75; 95% confidence interval [CI]: 2.37–19.9) [34]. Current recommendations advise treatment continuation in the case of asymptomatic chronic viremia.

The vaccination benefits for cancer patients include preventing severe disease, hospitalization and death. Still, vaccinations may also shorten possible infection duration, limit potential therapeutic breaks, or avoid deferring the antitumor treatment. Interruption of the ongoing treatment due to any infection is a significant problem that intensifies during seasonal infection peaks, mainly considering COVID-19 and influenza. The general public underestimates infections as a medical problem, and this also applies to cancer patients. Often, patients who require anticancer treatment, including surgery, show up with an active infection and rarely use vaccination. The COVID-19 pandemic caused a significant increase in the number of excess cancer deaths resulting from delayed cancer diagnosis [35]. The spread of the SARS-CoV-2 virus affected cancer screening, health problems reporting, diagnosis, access to treatment and clinical research. Consequently, preventive vaccinations are gaining new importance as a basis for maintaining the continuity of the diagnostics and therapy of cancer patients [36].

Vaccinations in cancer patients

Cancer itself and immunosuppressive anticancer treatment hinder the protective effects of some vaccinations by reducing seroconversion and accelerating the waning of immunity over time [37, 38]. For these reasons, cancer patient vaccination schedules may differ from those used in the general population (e.g., the number of doses and revaccination frequency), therefore the vaccination history should be in particular documented (e.g. centralized electronic vaccination system) [39]. Unfortunately, knowledge of this topic is scarce. Of note, the example of vaccination against COVID-19 shows that despite a significantly weakened humoral response, the cellular response often remains satisfactory [37].

A comprehensive approach to vaccinations for cancer patients is often presented in a graphic form as the so-called vaccination calendar. Developing such calendars for the general cancer population is difficult due to limited knowledge. However, vaccination schedules exist for some risk groups, including patients with hematologic malignancies or asplenia [40] and rheumatic diseases [41]. Table I shows the recommended seasonal and year-round vaccinations for cancer patients [21].

In Poland, detailed data on vaccination rates in particular risk groups are lacking; thus, assessing cancer patients' vaccination willingness is difficult. Available data indicate that overall influenza vaccination coverage in Poland is low (around 5% each year in the general population and around 20% among people aged ≥65 years) [42]. The primary COVID-19 vaccination rate is about 60%, and the first and second booster doses were taken by 30% and 7.7% of Poles, respectively. According to the American Society of Clinical Oncology (ASCO) data, the COVID-19 vaccination rate is about 20% lower than in the general population, which may also apply to other vaccinations [43, 44].

Table I. Recommended seasonal and year-round vaccinations for cancer patients [21]

Vaccination type	Infectious disease	Optimal vaccination time	Practical remarks
seasonal	COVID-19	vaccination against COVID-19 should be performed in line with the latest national or international recommendations for a given season once the adapted vaccine becomes available. However, the vaccination should not be delayed, awaiting the availability of the adapted vaccine [70]. Revaccination should take place every 6–12 months in consultation with a health care provider, and at least 3 months after COVID-19 recovery [71]	for detailed vaccination schedules, refer to current vaccination calendars recommended by the Polish Vaccinology Society [72] for brand names of specific vaccines, see table II. The non-seasonal infections may overlap with seasonal infections during the autumnal-winter period,
	influenza	in Poland, the influenza epidemic season lasts from October to May and peaks from January to March [76]. Considering it takes about 2 weeks to develop protective antibodies, the best time to get vaccinated is in September. However, if this optimal vaccination period is missed, vaccination is indicated till the circulation of given viral strains [77]	presenting more severe clinical outcomes, such as influenza and pneumococcal disease [73]. Vaccination against seasonal and non-seasonal infections may be administered during a single visit or at separate visits, provided they contain non-live antigens [74].
	RSV	RSV vaccine is currently a single-dose vaccine with no need for revaccination. This vaccination should be provided before RSV infections peak, which typically starts in October, meaning in late summer or early fall [78–80]	Considering seasonal infections, it is important to protect patients before the fall-winter period. It is also worth getting vaccinated
non-seasonal	pneumococcal disease, meningococcal disease, HBV, HiB, HPV, VZV, Tdap	no specific vaccination time throughout the year is indicated. Therefore, a year-round vaccination is possible; however, the faster vaccination is administered the better for patient protection	during the season. For best protection time see the "Optimal vaccination time" column [75]

COVID-19 – coronavirus disease; HBV – hepatitis B virus; HiB – Haemophilus influenzae type B; HPV – human papillomavirus; RSV – respiratory syncytial virus; VZV – varicella zoster virus; Tdap – tetanus, diphtheria, pertussis vaccine

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1 dose during the infectious seaso	1 dose during the infectious seaso			PCV13 + PPV23** after min. 8 week ugate or PVC20; people who previously received PPV23 should receive PCV13 or PC after ≥1 year	st 1 dose t 1 dose	ogroup B 2 doses at an interval of not less th ainst 1 month 2 doses 6 months apart	3 doses administered at 0, 2 and 6 months	2 doses 2–6 months apart in immunocompromised individua who would benefit from achieving optimal immunization in a shorter
		Comirnaty – mRNA vaccine Nivraxovid – mortein varcrine	Nuvaxovia – protein vaccine Spikevax – mRNA vaccine	Prevenar 20 Prevenar 13 (PCV13) – 13-valent conju vaccine Pneumovax 23 (PPV23) – 23-valent polysaccharide vaccine	NeisVac-C – conjugate vaccine against serogroup C Niment's – conjugate vaccine against the ACNV servorion	Bexsero – protein vaccine against sero, Trumenba – recombinant vaccine aga serogroup B	Cervarix – bivalent vaccine Gardasil 9 – 9-valent vaccine	Shingrix
season with an inactivated vaccine	season with an inactivated vaccine	all cancer patients or those previously treated for cancer should be varcinated against	ior cancer snouid be vaccinated against COVID-19	Pneumococcal conjugate vaccine should be administered to adult cancer patients who have not been vaccinated against pneumococci	patients at increased risk of meningococcal infection: with functional or anatomical asplenia, complement deficiencies, taking a C5 complement inhibitro (en entizunab	ACUT Structure in the second structure of the second structure against meningococci of serogroup ACWY and a monovalent vaccine against meningococci of serogroup B	the recombinant 3-dose HPV vaccine should be administered to men and women ≤ 26 years and may be considered for patients ≤ 45 years	administration of recombinant herpes zoster vaccine (VZV) is recommended for adult patients \geq 50 years and for persons \geq 18 years at risk for herpes zoster
		COVID-19		pneumococcal diseases	meningococcal diseases		human papillomavirus (HPV)	shingles (VZV)

Vaccination	Indication	Trade name*	Dosage schedule	Reimbursement charge
respiratory syncytial virus (RSV)	passive protection against lower respiratory tract diseases caused by respiratory syncytial virus (RSV) in infants from birth to 6 months of age after maternal vaccination during pregnancy	Abrysvo – bivalent vaccine	1 dose	fully paid
	active immunization of people ≥60 years against lower respiratory tract diseases caused by RSV. The effectiveness of the vaccine in cancer patients is unknown	Arexvy – monovalent vaccine	1 dose	fully paid
diphtheria/tetanus/whooping cough (Tdap)	administered every 10 years	Adacel Boostrix	1 dose	The National Immunization Program for 2024 provides free of-charge Tdap vaccinations for all people who are before or after transplantation of hematopoietic cells, internal organs, splenectomy, with asplenia, or splenic dysfunction
				-

Table II cont. Indications, vaccines, dosage regimens and patient payment levels of vaccines available in Poland (46, 80–87)

Tetra is reimbursed for the entire group aged 18–64, and Vaxigrip Tetra for people aged 18–64 with additional risk factors; *– vaccines available in Poland as of January 3, 2024; ** – additional doses may be administered to people with severe immune disorders by national recommendations. As of January 3, 2024, no published recommendations exist for this patient population ¹ Influvac

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The implementation of vaccination depends on the patient's attitude and individual understanding of the importance of the recommendation. Therefore, there is an apparent need for educational activities to address both patients and their immediate environment [36]. One such element is the vaccination advice based on current recommendations given by an oncologist. Issuing a vaccine prescription against, e.g., pneumococci, RSV, or shingles may motivate the patient. The patient should be informed that several preventive vaccinations, except those using live microorganisms, can be administered during one visit. Within the scope of permissions, primary care physicians and pharmacists may implement oncologists' recommendations. Additionally, an important issue is the implementation of the cocoon strategy, which includes, among others, vaccination of household members, close relatives and healthcare workers [36, 45].

Vaccination recommendations for adult patients with hematological malignancies are available in Polish, implemented into clinical practice and updated [40]. However, there are no similar national recommendations for patients with solid tumors. In 2018, joint recommendations for preventing infectious diseases were developed by ASCO and the Infectious Diseases Society of America (IDSA) [46]. That said, they do not respond to all current medical needs. In turn, the latest National Comprehensive Cancer Network (NCCN) guidelines cover the prevention and treatment of infectious diseases in a more up-to-date and comprehensive way, taking into account influenza, COVID-19, pneumococcal and meningococcal infections, HPV, RSV, VZV, Tdap and other infections (47). Table II summarizes these recommendations, pointing out the vaccines available in Poland, their standard dosages and reimbursement status.

Diagnosis of cancer is a rough emotional experience and may distract patients from the implementation of prophylactic measures, including vaccinations [48, 49]. Additionally, the COVID-19 pandemic hampered cancer treatment and appropriate prevention implementation [50]. The patient should be clearly informed that infection may affect anticancer treatment. The vaccination should ideally be performed at cancer diagnosis and before anticancer treatment, as this may lower vaccine effectiveness. Inactivated vaccines should be administered at least two weeks (vaccines containing live microorganisms at least four weeks) before starting treatment. Due to the risk of infection induction, vaccinations containing live microorganisms are contraindicated during chemotherapy and in immunocompromised patients [51]. In turn, vaccinations without live microorganisms can be safely used in these populations [21]. If vaccination is substantiated after anticancer therapy, the optimal time is from three to 12 months after its completion, depending on the vaccine and oncological treatment [51].

The vaccinations indicated in table II are safe for cancer patients. The contraindications to vaccination are limited and include, among others:

- active infection,
- active cancer during intensive chemotherapy and/or radiotherapy (however, there are no clear contraindications to the administration of influenza and COVID-19 vaccines),
- intensive immunosuppression, i.e., corticosteroid therapy (calculated for prednisone >0.5 mg/kg/day for over 14 days), rituximab, or other anti-CD20 monoclonal antibodies,
- allergic reactions to a given vaccine [51].

Notably, influenza vaccinations were shown to prolong overall survival (OS) in cancer patients administered immune checkpoint inhibitors (ICI) [52]. Given influenza's relatively low mortality, vaccination against more deadly infections (e.g., COVID-19) may carry even greater OS benefit [53].

Vaccination access for cancer patients in Poland

Cancer patients should be among the vaccination priority groups due to their high risk of severe infections and complications [21, 36, 47]. Access to vaccinations in Poland has been recently significantly improved (tab. II), due the extension of reimbursement of pneumococcal and influenza vaccines and local vaccination prevention programs [54, 55].

An essential step in improving the protection of cancer patients by vaccination should be the development of national practice guidelines addressed to medical oncologists, surgeons and radiation oncologists. Currently, the reimbursement system for medicinal products is dispersed between pharmacies and primary care facilities, and in the case of vaccinations, it does not cover specialist treatment. Hence, although oncologists know the importance of vaccinations, they are not implemented in clinical practice. To facilitate this process, vaccination points should be located in cancer centers. A good example is the Świętokrzyskie Oncology Center, where vaccinations against pneumococci are carried out in patients with most common solid and hematological malignancies [56]. It is postulated that all vaccines necessary for comprehensive primary prevention should be available in hospitals and administered within the facility. All of the above ventures should increase vaccination rates in a population that is particularly sensitive to the severe course of infections, and these actions may also include other groups of patients.

The National Oncology Strategy provides an opportunity to popularize vaccination prevention [57]. So far, the popularization of vaccinations in Poland has been limited, illustrated by low HPV vaccination rates [58]. Therefore, broad educational activities in the field of vaccinations in Poland are still needed.

Testing and treatment of COVID-19 in cancer patients

Despite preventive measures, infectious diseases in cancer patients remain a significant challenge. The American Covid Data Tracker data for 2018–2021 clearly shows increased mortality due to cancer as an underlying cause and a significant increase in the number of deaths due to infectious diseases, particularly COVID-19 [1].

Despite the accessibility of combo antigen tests (including COVID-19, RSV, influenza A and B) as part of primary health care services in Poland, they are not performed sufficiently frequently. This situation hinders causal treatment implementation, e.g., influenza (oseltamivir) and COVID-19 [59, 60]. Subsequently, the number of these infections and the overall data for the Polish population are blurred. Considering these facts, the WHO focuses on testing all symptomatic and high--risk asymptomatic patients [61]. According to the current IDSA diagnostic algorithm, testing for COVID-19 should only be performed in symptomatic patients [62]. It is recommended to use antigen tests with a diagnostic sensitivity and specificity of at least 90% and 97%, respectively. If symptoms suggestive of COVID-19 persist and the first test is negative, it should be repeated after 3-4 days, when the highest concentration of antigens is recorded [63].

According to the recently updated WHO COVID-19 treatment guidelines, depending on the clinical condition of cancer patients, the risk of severe COVID-19 may be classified as high or moderate, corresponding to a hospitalization risk of 6% and 3%, respectively [64]. The current guidelines are similar to those in the general population [64]. These recommendations are in line with those of the Polish Society of Epidemiologists and Infectious Disease Physicians from 2022 because inhaled budesonide and the use of monoclonal antibodies against the S protein of the SARS-CoV-2 virus are principally no longer relevant for clinical practice [64, 65].

According to Polish guidelines, antiviral treatment can be used in the first and second COVID-19 stages, i.e., in the mild and full-symptomatic phases, before the development of respiratory failure [65]. According to the latest WHO recommendations, the only strongly recommended therapy in the early phase of COVID-19 in patients at high risk of hospitalization is a short-term oral course of nirmatrelvir/ritonavir (NIR/RIT). The use of NIR/RIT may be considered in patients with a moderate risk of hospitalization [61]. In contrast, the indications for molnupiravir and remdesivir in patients at high risk of hospitalization are weak or conditional.

According to NCCN guidelines for cancer-related infections, NIR/RIT or remdesivir may be used in patients with acute illness, recent onset of symptoms and high risk of COVID-19 progression (prolonged neutropenia, lymphopenia, or T-cell dysfunction accompanying hematologic malignancies and lung cancer). During hospitalization, treatment with remdesivir is recommended. NIR/RIT and/or remdesivir may be used in patients with persistent SARS-CoV-2 infection, typically in patients with B-cell hematologic malignancies [47].

The authorization of molnupiravir in the European Union was withdrawn in June 2023 [66]. So far, remdesivir and NIR/RIT are not reimbursed in Poland, although the reimbursement process for NIR/RIT is ongoing [67]. Given the burden of COVID-19 and the high mortality of cancer patients, access to effective treatment of this infection in Poland remains an unmet medical need [61].

NIR/RIT may interact with anticancer drugs; it is therefore recommended that potential interactions be checked using a simple online tool on the University of Liverpool website [68]. Since NIR/RIT therapy is short-term (up to 5 days from COVID-19 symptoms' onset), in most cases, drug interactions can be prevented by modifying treatment doses or changing some active substances [64]. Of great importance is that drugdrug interactions for NIR/RIT are based on data obtained from ritonavir studies in HIV, where these compounds were used at a higher dose and in a chronic manner [61, 64]. Ritonavir, being an inhibitor of some cytochrome P450 isoenzymes (mainly CYP3A4, CYP2D6) and having a high affinity for P-glycoprotein (P-gp), may affect the concentration of other concomitantly administered drugs [64]. Hence, when implementing the NIR/RIT, a risk-benefit ratio should always be considered.

Many patients are not aware of the risk of severe COVID-19 and neglect antigen testing after viral exposure or symptoms emergence. Likewise, few at-risk people know that appropriate treatment may reduce their risk of hospitalization and death due to COVID-19. Further, patients must realize that delayed intervention may substantially reduce treatment efficacy. Patients must be educated about the risk of progression to severe COVID-19 and know what to do once they develop symptoms and test positive for COVID-19. The post-vaccination immunity weakens over time, whereas the willingness to receive subsequent booster doses decreases, allowing for SARS-CoV-2 immune escape. It is expected, therefore, that the number of hospitalizations among vaccinated people, especially among high-risk groups, will increase [61]. A cross-sectional study in the US showed that hospitalizations due to breakthrough infection were reported in up to 25% of vaccinated patients during the dominance of the Omicron variant. Therefore, owing to the low rate of booster vaccinations, the proportion of patients hospitalized with COVID-19 is expected to increase [69]. For this reason, providing effective COVID-19 treatment for cancer patients and other high-risk patients remains an important issue.

Conclusions

Infections pose a significant threat to cancer patients. The COVID-19 pandemic caused a significant disruption in cancer management, worsened treatment outcomes and significantly increased cancer mortality – directly and indirectly. Vaccinations remain the cornerstone of preventing the consequences of infections. However, the COVID-19 booster and influenza vaccination rates remain low in Poland.

A vital issue hindering the implementation of recommended vaccinations in cancer patients is a concern of primary care physicians and patients about vaccination safety after cancer diagnosis. Therefore, the development of Polish vaccination recommendations for patients with solid malignancies is an urgent medical need. Cancer patients themselves are often unaware of the risk of severe infections, especially COVID-19, which reduces their willingness to vaccination, testing and implementing casual treatment. A limited number of cancer patients are aware of outpatient COVID-19 treatment options. Therefore, education on this matter is essential. The health care system should shorten the patient clinical path and enable the co-administration of necessary vaccinations during a single visit. The organization and financing of the health care system should also support rapid diagnosis and treatment of infections in cancer patients. Organizational, logistic and reimbursement changes are warranted to improve patients'safety in all cancer care institutions.

Article information and declarations Author contributions

Piotr Rutkowski - conceptualization, supervision, writing original draft preparation, writing - review and editing. Bożena Cybulska-Stopa – conceptualization, writing – original draft preparation, writing - review and editing. Jacek Jassem - conceptualization, writing - original draft preparation, writing – review and editing. Adam Płużański – conceptualization, writing – original draft preparation, writing - review and editing. Krzysztof Tomasiewicz – conceptualization, writing – original draft preparation, writing - review and editing. Lucjan Wyrwicz - conceptualization, writing - original draft preparation, writing - review and editing. Piotr Wysocki - conceptualization, writing - original draft preparation, writing - review and editing. Jacek Wysocki - conceptualization, writing - original draft preparation, writing - review and editing. Robert Flisiak - conceptualization, writing - original draft preparation, writing - review and editing.

Acknowledgments

We acknowledge Karolina Wieruszewska-Kowalczyk and Michał Abendrot for critical manuscript review and editing support. We thank Urszula Sot for her contribution in literature search that helped develop this paper.

Financial support

Pfizer Polska has organized the meeting of the Expert Committee on infectious diseases in cancer patients with particular attention to COVID-19. Medical writing support was provided by Marcin Balcerzak (Medink) and was funded by Pfizer.

Conflicts of Interest

Piotr Rutkowski – consulting fees (Bristol-Myers Squibb, MSD, Novartis, Pierre Fabre, Philogen, Pfizer), honoraria (Bristol Myers Squibb, MSD, Novartis, Pfizer, Pierre Fabre, Sanofi, Merck, Astra Zeneca), Speakers' Bureau (Pfizer, Novartis, Pierre Fabre, MSD, BMS), support for attending meetings and/or travel (Orphan Europe, Pierre Fabre). Bożena Cybulska-Stopa – honoraria for lectures, grants, consultancies and fees (MSD, BMS, Novartis, Pierre Fabre, Sanofi, Merck, GlaxoSmithKline, Roche, Pfizer). Jacek Jassem – consulting or advisory roles (from BMS, Roche, and MSD), travel, accommodation, and expenses (Takeda), speakers bureau support (from Roche – not compensated, Pfizer, Novartis, and MSD). Adam Płużański – advisory board, travel grant (Pfizer). Krzysztof Tomasiewicz - consultancy, advisory board, speaker (AbbVie, Alfasigma, AstraZeneca, Bausch Healthcare, Gilead, GSK, Novo Nordisk, Pfizer, Promed), grant or research (AbbVie, Gilead, GSK). Lucian Wyrwicz – no conflict to declare in connection with this publication. Piotr Wysocki - consulting fees (Bristol-Myers Squibb, MSD, Novartis, Pierre Fabre, Immunicom, Merck, Astellas, Janssen, Ipsen), honoraria (Bristol-Myers Squibb, MSD, Novartis, Pierre Fabre, Immunicom, Pfizer, Merck, Astellas, Janssen, Ipsen), support for attending meetings and/or travel (BMS, Astra Zeneca, Pierre Fabre), participation in Data Safety Monitoring or Advisory Boards (Bristol-Myers Squibb, MSD, Novartis, Pierre Fabre, Immunicom, Pfizer, Merck, Astellas, Janssen, Ipsen). Robert Flisiak – grants (AbbVie, Gilead, MSD, Pfizer, Roche), Consultations (AbbVie, Baush, Gilead, MSD, Moderna, Novo Nordisk, Pfizer), honoraria (AbbVie, Baush, Gilead, MSD, Pfizer).

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Received: 11 Apr 2024 Accepted: 19 Apr 2024

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