MANAGEMENT OF CHICKENPOX IN CANCER PATIENTS

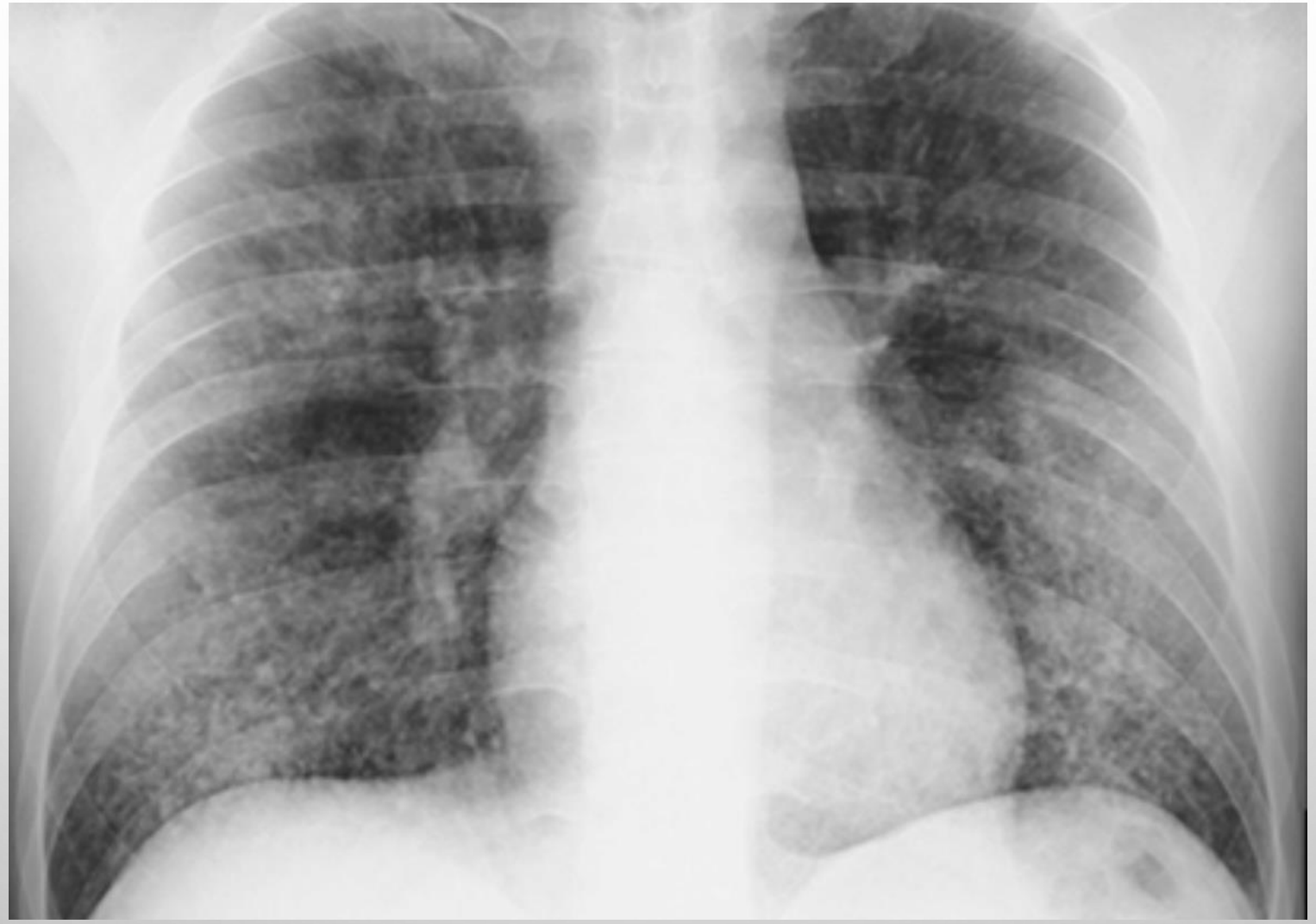
case presentation

A 29-year-old male patient followed for B-cell non-Hodgkin lymphoma (NHL) subtypes diffuse large B-cell lymphoma **(DLBCL)** treated by the **R-CHOP** (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone). protocol presented to our department for cough, fever, dyspnea, generalized necrotic vesicular rash, and malaise evolving 5 days before.

Vital signs demonstrated tachycardia (109bpm), temperature 39°, and SpO2 of 82% on room air.

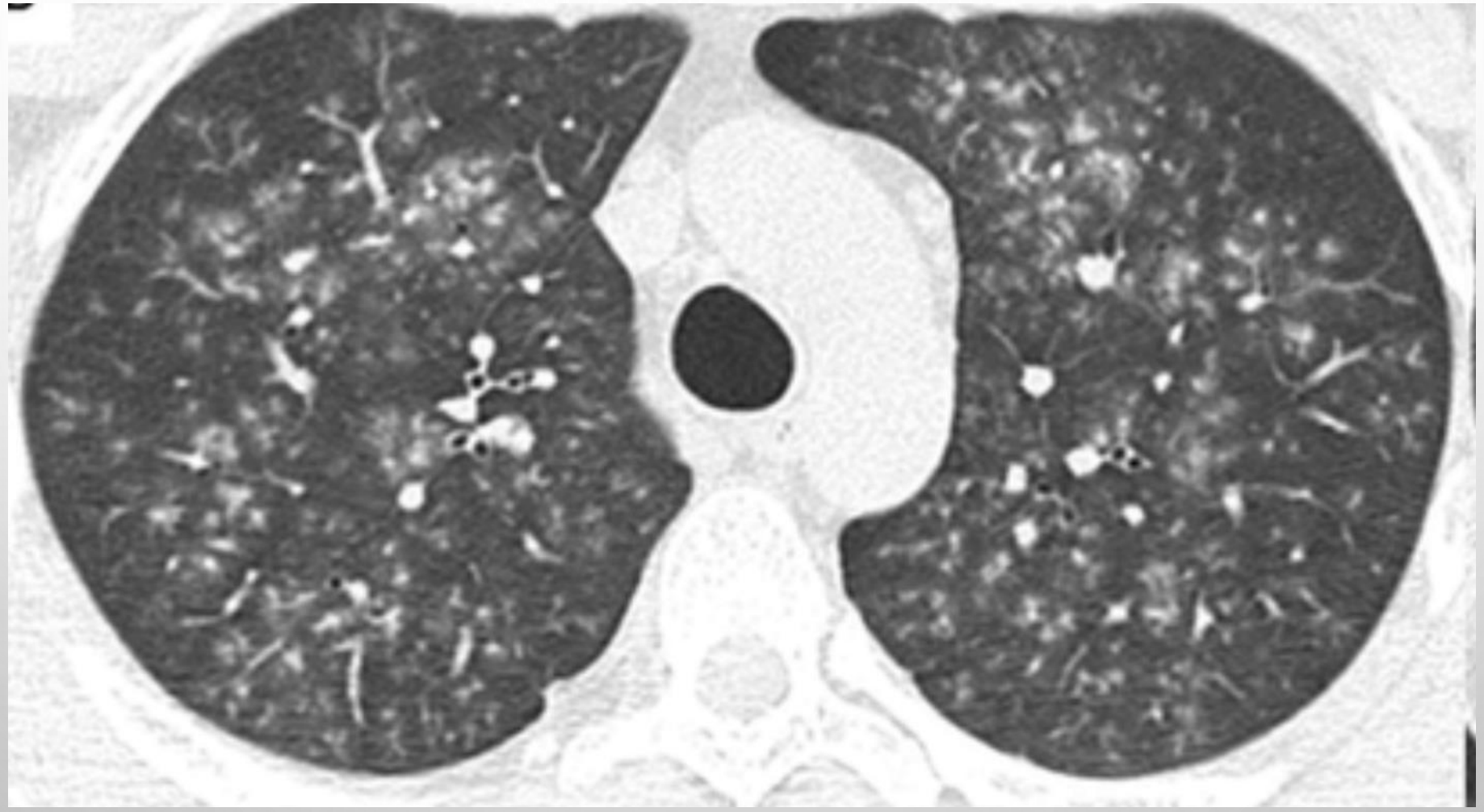
Physical examination showed diffuse maculopapular to vesicular lesions with an erythematous halo with crusting.

He didn’t reveal a previous chickenpox history. Chest radiography demonstrated multiple bilateral micronodular and reticulonodular opacities, diffuse throughout the lungs.



CT scan revealed the existence of multiple well and ill-defined nodules,

diffusely dispersed throughout both lungs .



Laboratory exams showed on arterial gasometry severe hypoxemia (PaO 2 = 45mmHg, pH = 7.48, SaO2 = 82%)

CBC:

WBC:3000 (55 PMN 38 LYM)

Hb: 11.2

Plt:130000

BUN: 46 Cr:0.7

AST:16 ALT: 21

Patients with compromised immune systems generally have worse symptoms and complications.

The vesicular rash can become more severe with enlarged vesicles that can become hemorrhagic.

Immune system impairment is one of the major risk factors of developing varicella pneumonia as a complication. Without a competent immune system, the disease process can quickly develop into adult respiratory distress syndrome followed by overall respiratory failure.

Once the patient is experiencing respiratory failure and must be mechanically ventilated, the mortality rate of varicella pneumonia jumps from about 30% to almost 50% in spite of treatment course.

Overall, complication with varicella pneumonia is the leading cause of death in patients with varicella.

What is the recommendation for the screening strategy used to detect infectious diseases before chemotherapy?

TABLE 1

Screening process according with geographic area

	Latin America	North Africa and Middle East	Asia	Sub-Saharan Africa
Human immunodeficiency virus	x	x	x	x
Hepatitis	x	x	x	x
Human T-cell lymphotropic virus-1	x	x	x	x
Strongyloides stercoralis	x	x	x	x
Schistosoma spp.	x*		x*	x
Parasites in feces	x	x	x	x
Treponema infection	x	x	x	x
Latent TB infection	x	x	x	x
Toxoplasmosis	x	x	x	x
Chagas disease	x			
Dimorphic fungi	x		x*	x
Leishmania	x	x	x	x
Malaria	x†		x†	x†

*Apply to specific areas within the region.
†Apply for patients living for more than 1 month in a malaria-risk area.

ASTMH
AMERICAN SOCIETY OF TROPICAL MEDICINE & HYGIENE
THE AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE
official Journal of the American Society of Tropical Medicine and Hygiene

What are the recommended routine preventative vaccinations for adults with cancer?

Vaccination of Adults With Cancer: ASCO Guideline

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DOI https://doi.org/10.1200/JCO.24.00032

ABSTRACT

ASCO Guidelines provide recommendations with comprehensive review and analyses of the relevant literature for each recommendation, following the guideline development process as outlined in the ASCO Guidelines Methodology Manual. ASCO Guidelines follow the ASCO Conflict of Interest Policy for Clinical Practice Guidelines.

Clinical Practice Guidelines and other guidance ("Guidance") provided by ASCO is not a comprehensive or definitive guide to treatment options. It is intended for voluntary use by providers and should be used in conjunction with independent professional judgment. Guidance may not be applicable to all patients, interventions, diseases or stages of diseases. Guidance is based on review and analysis of relevant literature, and is not intended as a statement of the standard of care. ASCO does

ACCOMPANYING CONTENT

Appendix

Data Supplement

Accepted January 11, 2024

Published March 18, 2024

Evidence-Based Medicine Committee approval: December 14, 2023

Recommendation	Evidence Quality	Strength of Recommendation
1.1. Clinicians should determine vaccination status and ensure that adults newly diagnosed with cancer and about to start treatment are up to date on seasonal vaccines as well as age- and risk-based vaccines (see Tables 2-4)	Moderate	Strong
1.2. Vaccination should ideally precede any planned cancer treatment by 2-4 weeks. However, nonlive vaccines can be administered during or after chemotherapy or immunotherapy, hormonal treatment, radiation, or surgery	Moderate	Strong

What additional vaccinations and revaccinations are recommended for adults undergoing hematopoietic stem cell transplantation, CD19 CAR-T treatment, or B-cell–depleting therapy?

2.1. Complete revaccination starting 6-12 months after hematopoietic stem-cell transplant should be offered in order to restore vaccine-induced immunity. Live and live attenuated vaccines should be delayed for at least 2 years and only given in the absence of active GVHD or immunosuppression. COVID-19, influenza, and pneumococcal vaccines can be administered as early as 3 months after transplant	Moderate	Strong
2.2. Adults with hematopoietic malignancies receiving CAR-T therapy directed against B-cell antigens (CD19, BCMA) should receive influenza and COVID-19 vaccine no sooner than 3 months after the completion of therapy. Nonlive vaccines should be administered no sooner than 6 months after completion of therapy	Very Low	Weak
2.3. Adults who receive B-cell–depleting therapy should be revaccinated for COVID-19 only, no sooner than 6 months after completion of treatment	Moderate	Strong
2.4. Long-term survivors of hematologic malignancy with or without active disease or those who have long-standing B-cell dysfunction or hypogammaglobulinemia from therapy or B-cell lineage malignancies should receive the recommended nonlive vaccines even though the response may be attenuated	Moderate	Strong

What additional vaccinations are recommended for adults with cancer who are traveling outside the United States?

3.0. Adults with solid and hematologic cancers traveling to an area of risk should follow the CDC standard recommendations for the destination	Moderate	Strong

Note. Hepatitis A, intramuscular typhoid vaccine, inactivated polio, hepatitis B, rabies, meningococcal, and nonlive Japanese encephalitis vaccines are safe

What are vaccination recommendations for household and close contacts of adults with cancer?

4.0. It is recommended that all household members and close contacts, where feasible, be up to date on vaccinations	Moderate	Strong

TABLE 2. Recommended Immunizations for Adults With Cancer

Vaccine	Recommended Age	Schedule
Influenza[a]	All ages	Annually
RSV	60 years and older	Once
COVID-19	All ages	As per the latest CDC schedule for immunocompromised[17]
Tdap or Td[b]	19 years and older	One dose of Tdap, followed by Td or Tdap booster every 10 years
Hepatitis B	19-59 years: eligible 60 years and older: immunize those with other risk factors[c]	For adults 20 years and older, use high antigen (40 μg) and administer as a three-dose Recombivax HB series (0, 1, 6 months) or four-dose Engerix-B series (0, 1, 2, 6 months)[18]
Recombinant zoster vaccine	19 years and older	Two doses at least 4 weeks apart
Pneumococcal vaccine	19 years and older	One dose PCV15 followed by PPSV23 8 weeks later OR One dose PCV20[d]
HPV	19-26 years: eligible 27-45 years: *shared decision making*	Three doses, 0, 1–2, 6-months

HIV, chronic liver diseases, intravenous drug use, sexual risk factors, incarcerated individuals.

Zoster vaccine

the most optimal humoral and cellular responses are expected when the vaccine is administered immediately after a cancer diagnosis and before the initiation of immunosuppressive treatments. The interval between the two RZV doses can be reduced to 4 weeks to achieve early protection.

Zoster vaccine

Patients who have experienced herpes zoster should receive the vaccine to prevent future episodes. There is no specific waiting period before immunization, as long as the acute episode has resolved.

Finally, the duration of clinical protection from RZV is unclear at this time and vaccination should not influence the duration of antiviral prophylaxis with certain therapies (eg, proteasome inhibitors).

TABLE 3. Recommendations for Other Vaccines That May be Indicated for Adults With Cancer and Coexisting Health Conditions

Vaccine	Type	Other Risk Factor	Recommendation
Haemophilus influenzae type b vaccination (Hib)	Nonlive	Anatomic asplenia	For elective splenectomy: one dose at least 14 days before splenectomy (preferred)
		Functional asplenia	One dose if previously did not receive Hib
Hepatitis A vaccination	Nonlive	Chronic liver disease, HIV, MSM, homelessness, injection or noninjection drug use, occupational exposure, travel	Two-dose series HepA or three-dose series HepA-HepB
Meningococcal vaccination[a]	Men ACWY (nonlive)	Anatomic or functional asplenia, complement component deficiency, complement inhibitor (eg, eculizumab, ravulizumab), Travel, Occupational, Military recruits, Residential living for college students	Two-dose series MenACWY-D Frequency: 8 weeks apart Revaccinate every 5 years if risk remains
	Men B (nonlive)	Anatomic or functional asplenia (including sickle cell disease), persistent complement component deficiency, complement inhibitor (eg, eculizumab, ravulizumab) use, occupational (microbiologists), pregnancy, MSM outbreak setting	Two-dose primary series MenB-4C at least 1 month apart Or three-dose primary series MenB-FHbp at 0, 1-2, 6 months Revaccinate every 2-3 years if risk remains
IPV	Nonlive	Travel Community risk (eg, wastewater detection of vDPV)	Single booster
MMR	Live	No evidence of immunity: HIV (CD4 >200 for 6 months), HCP, outbreak setting, travel	Contraindicated with cancer treatment and other immunocompromising conditions
Varicella	Live	Postexposure	Contraindicated with cancer treatment and other immunocompromising conditions
MVA (Monkeypox)	Live (replication-deficient)	Postexposure, Occupational exposure (laboratory worker), high risk	Safe to administer in persons with HIV or those on immunosuppressive therapies
Monkeypox and smallpox (ACAM2000)	Live		Contraindicated with cancer treatment and other immunocompromising conditions

TABLE 4. Other Vaccine Recommendations for Previously Unimmunized Adults With Cancer

Vaccine	Recommended doses[a]
IPV	Complete three-dose series
Tdap	One dose of Tdap followed by one dose of Td or Tdap at least 4 weeks later, and a third dose of Td or Tdap 6-12 months later
Hepatitis A	Perform serologic assessment for past infection. If negative, vaccinate as per Table 3
Hepatitis B	Perform serologic assessment for past infection. If HBsAg is negative, vaccinate as per Table 2
Varicella MMR	Cannot be given to immunocompromised patients. Patients with solid tumors receiving chemotherapy, immunotherapy, or radiation should be assumed to be immunocompromised For solid tumors, vaccines may be considered at least 4 weeks before cancer treatment initiation and wait at least 3 months after completion

NOTE. Adapted from CDC Adult Immunization Schedule By Medical Condition and Other Indication.[15]

Abbreviations: HBsAg, Hepatitis B surface antigen; IPV, inactivated poliovirus vaccine; MMR, measles, mumps, and rubella; Td, tetanus and diphtheria; Tdap, tetanus, diphtheria and pertussis.

[a]Timing of recommended doses: Start immunization before chemotherapy when possible. Measurement of the immune response to decide on repeating doses after treatment completion can be considered. Delay vaccination for 6 months after B-cell depletion for indicated vaccines. See separate recommendations for patients undergoing stem-cell transplant or chimeric antigen receptor T-cell therapy.

A two-dose series of varicella vaccines administered 1 month apart may be given to varicella-seronegative patients without a history of primary varicella, no sooner than 2 years after HSCT and in the absence of GVHD, no systemic immunosuppressive use for least a year, and no receipt of IVIG for 8-11 months.

There are currently no data regarding the efficacy of RZV for protection against varicella in seronegative HSCT patients although it was shown that vaccination could induce both humoral and cellular immune responses after solid organ transplantation in seronegative patients.

What post-exposure preventive are recommended if an immunocompromised person contact with someone with chickenpox?

Strategy	*Pre-Transplant*	*Post-Transplant*	Dosing	Comments
Immunoprophylaxis				
VZV immunoglobulin (VZIG, VariZIG™)	YES, if seronegative (Evidence II-1)	YES, if susceptible (Evidence II-1)	**VariZIG** 125 units/10 kg body weight in single IM dose (Max dose is 625 units, min 125 units)	• VariZIG is only available through IND protocol† • Must be given as soon as possible – no efficacy if given more than 96 hours post-exposure • Not 100% effective in clinical studies of preventing VZV, so close observation is suggested • If varicella develops, patient should be treated with antiviral therapy
IV immunoglobulin (non-specific IVIG)	Consider, if VZIG or VariZIG not available (Evidence III)	Consider, if VZIG or VariZIG not available (Evidence III)	**IVIG** 400 mg/kg IV single dose	• Amount of anti-VZV antibodies in IVIG is variable, and should only be considered if VZV specific immunoglobulin therapy is not available

Antiviral Prophylaxis				
Acyclovir‡ (and pro-drugs)	Consider, if VZIG or VariZIG not available or in addition to immunoprophylaxis (Evidence III)	Consider, if VZIG or VariZIG not available or in addition to immunoprophylaxis (Evidence III)	**Acyclovir** 800 mg PO four times daily(**adults)** 20 mg/kg PO four times daily **(maximum 800 mg four times a day, ≥ 2 yrs of age)** OR **Valacyclovir** 1 gram PO three times daily **(adults)**	• Given 7-10 days after exposure for 7 days • Alternatively, some experts recommend dosing being given days 3-22 after exposure (or till day 28 if given immunoprophylaxis) • Caution with patients with underlying renal dysfunction as dosing may need to be reduced • IV acyclovir is recommended in children <2 yrs of age [10 mg/kg IV every 8 hours] or those who cannot tolerate oral therapy • Valacyclovir is only recommended for children 2 to <18 years of age and has not been studied as a prophylactic agent in children post-SOT

What is your recommendation for a prophylaxis regimen during chemotherapy in this patient?

ANTIMICROBIAL PROPHYLAXIS BASED ON OVERALL INFECTION RISK IN PATIENTS WITH CANCER

See Antibacterial Agents (FEV-A) for dosing, spectrum, and specific comments/cautions

Overall Infection Risk in Patients with Cancer[a]	Disease/Therapy Examples	Antimicrobial Prophylaxis
Low	• Standard chemotherapy regimens for most solid tumors • Anticipated neutropenia* <7 days	• Bacterial - None • Fungal - None • Viral - None unless prior herpes simplex virus (HSV) episode
Intermediate	• Autologous hematopoietic cell transplant (HCT) • Lymphoma[c] • Multiple myeloma[c] • Chronic lymphocytic leukemia (CLL)[c] • Purine analog therapy (ie, fludarabine, clofarabine, nelarabine, cladribine) • Anticipated neutropenia* 7–10 days • Chimeric antigen receptor (CAR) T-cell therapy	• Bacterial - Consider fluoroquinolone prophylaxis during neutropenia[d] • Fungal - Consider prophylaxis during neutropenia and for anticipated mucositis (INF-2); consider *Pneumocystis jirovecii* pneumonia (PJP) prophylaxis (NF-6) • Viral - During neutropenia and longer depending on risk (INF-3, INF-4, INF-5) • See Immune and Targeted Treatments (INF-A 11 of 13)
High[b]	• Allogeneic HCT including cord blood • Acute leukemia ▸ Induction ▸ Consolidation/maintenance • Alemtuzumab therapy • Moderate to severe graft-versus-host-disease (GVHD) • Anticipated neutropenia* >10 days	• Bacterial - Consider fluoroquinolone prophylaxis during neutropenia[d] • Fungal - Consider prophylaxis during neutropenia (INF-2); consider PJP prophylaxis (INF-6) • Viral - During neutropenia and longer depending on risk (INF-3, INF-4, INF-5) • Length of prophylaxis depends on immune reconstitution.

*Neutropenia: ≤500 neutrophils/mcL or ≤1000 neutrophils/mcL and a predicted decline to ≤500/ mcL over the next 48 hours.

PREVENTION OF HERPES SIMPLEX VIRUS (HSV) AND VARICELLA ZOSTER VIRUS (VZV) REACTIVATION OR DISEASE

See Antiviral Agents (FEV-C) for dosing, spectrum, and specific comments/cautions

For CMV prophylaxis, see INF-4. For HBV, HCV, and HIV prophylaxis, see INF-5. For general vaccine recommendations, see INF-7.

Overall Infection Risk in Patients with Cancer[a]	Disease/Therapy Examples	Minimum Duration of Antiviral Prophylaxis
Low	• Standard chemotherapy regimens for solid tumors	No prophylaxis unless prior HSV episode; if needed, treat during active therapy including periods of neutropenia
Intermediate	• Autologous HCT • Lymphoma • Multiple myeloma • CLL[b] • Purine analog therapy (eg, fludarabine)	HSV prophylaxis[j] • Consider during active therapy and possibly longer depending on degree of immunosuppression VZV prophylaxis[j] • Consider for at least 6–12 months after autologous HCT
High	• Acute leukemia	HSV prophylaxis during active therapy including periods of neutropenia[j]
	• Proteasome inhibitors	VZV prophylaxis during active therapy including periods of neutropenia[j]
	• Alemtuzumab therapy • Allogeneic HCT • GVHD requiring significant escalation of immunosuppression	HSV prophylaxis[j] • Minimum of 2 months after alemtuzumab and until CD4 ≥200 cells/mcL VZV prophylaxis[j] • Prophylaxis should be considered for at least 1 year after allogeneic HCT

What treatment do you recommend for this patient?

- Antiviral ?
- IVIG ?
- Antibiotic ?
- Corticosteroids ?

Acute Varicella	**Acyclovir** 10 mg/kg IV every 8 hours	Evidence II-2	• IV therapy can be changed to oral therapy once the patient has significantly improved • Careful monitoring of renal function is needed while on IV therapy, and dosing should be adjusted for renal insufficiency
Herpes Zoster Disseminated or Invasive Disease or Herpes zoster ophthalmicus or Ramsay-Hunt syndrome/Herpes zoster oticus	**Acyclovir**‡ 10 mg/kg IV every 8 hours	Evidence II-2 or III*	• In disseminated disease IV therapy should be given for at for at least 7 days, but may need to be given for longer in patients with extensive involvement or CNS disease • Ophthalmology consultation is recommended for patients with ophthalmic involvement • Consideration for switch to oral therapy dependent on patient's clinical status

Published in final edited form as:
Am J Transplant. 2009 December ; 9(Suppl 4): S108–S115. doi:10.1111/j.1600-6143.2009.02901.x.

Intravenous Immunoglobulin (IVIG) can be used in Varicella Zoster Virus (VZV) infections, primarily as a post-exposure prophylaxis (PEP) for immunocompromised individuals when Varicella-Zoster Immune Globulin (VZIG) is unavailable.

It can also be an adjuvant therapy, combined with antiviral medications like acyclovir, for treating severe VZV infections in immunocompromised patients to help suppress the virus, although it's not a guaranteed preventative measure for all such patients.

What is bacterial co-infection in varicella pneumonia?

Bacterial co-infection is a significant complication of VZV (varicella-zoster virus) pneumonia, particularly in immunocompromised individuals and the elderly, increasing the risk of severe outcomes such as septic shock and acute respiratory distress syndrome.

Early recognition of bacterial co-infection is crucial for identifying at-risk patients and initiating prompt, aggressive treatment with antibiotics to improve prognosis and prevent mortality.

Steroids' role in varicella-zoster virus (VZV) pneumonia complex and not generally recommended, although some limited, early studies suggested they might improve oxygenation and reduce mortality in life-threatening cases, particularly in immunocompetent adults.

However, more recent studies indicate steroids can increase the risk of ICU-acquired infections and may not significantly impact overall mortality.

Therefore, steroid use in VZV pneumonia remains a clinical decision with no current official guidelines, pending further randomized controlled trials to establish their true efficacy and safety.

The patient received antiviral treatment acyclovir (10 mg/kg/8 hours) intravenously, combined with oxygen therapy via nasal cannula on 5 L/ min , prednisone 60mg per day and levofloxacin 500 mg per day for 5days. and intravenous immunoglobulin was started 2 days after prednisone.

The evolution was favorable with obtaining apyrexia after 4 days of treatment, improvement of dyspnea with correction of hypoxemia on the eighth day of treatment.

When do we start the next course of chemotherapy?

Thanks for Your Attention