Emergency Medicine Approach to Oncologic Emergencies

Jason Bischof, MD, FACEP
Associate Professor
Department of Emergency Medicine
The Ohio State University Wexner Medical Center

MedNet21
Center for Continuing Medical Education

The Ohio State University
Wexner Medical Center

Disclosures

- Dr. Bischof and Dr. Reynolds have no financial conflicts to report related to this presentation.
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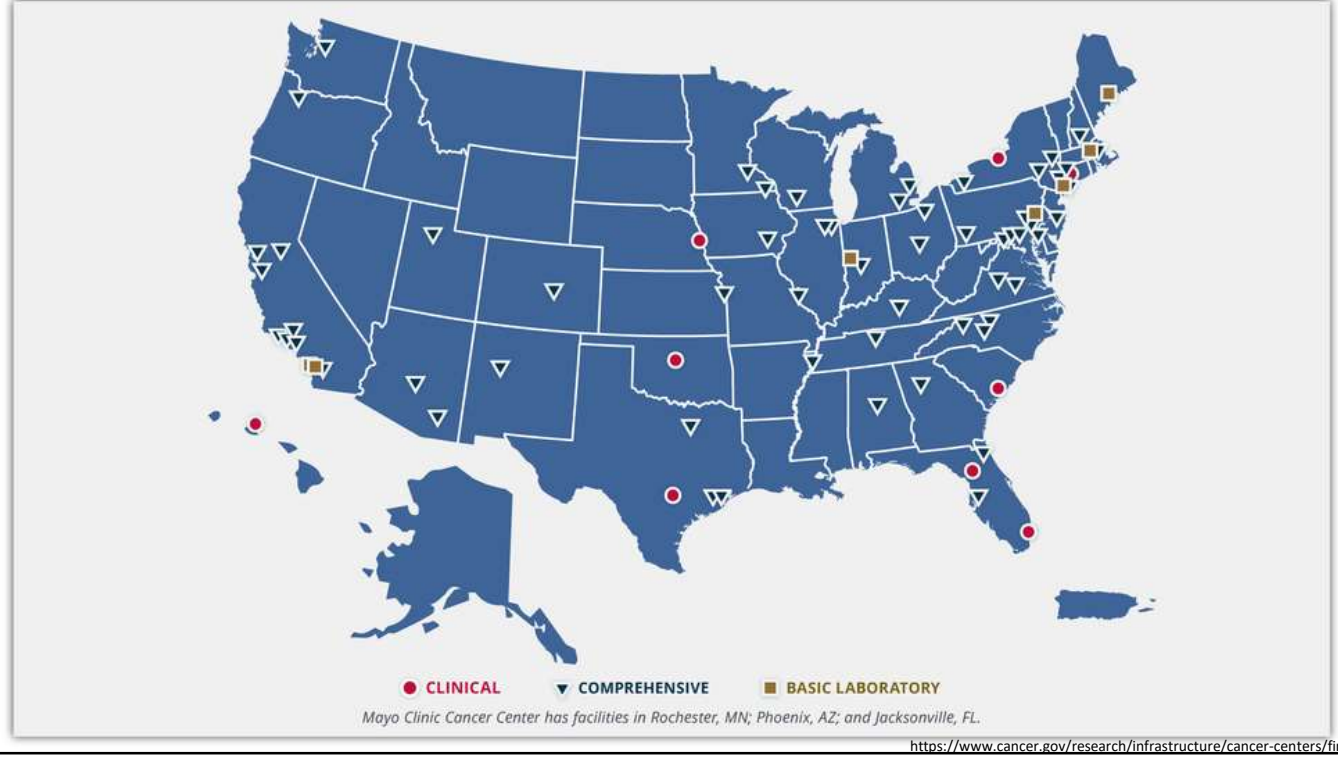
  - Beckman Coulter, PCORI, NCI, Calcimedica, Comprehensive Research Associates, Sysmex America

Objectives

1. Describe common presentations of acute oncologic emergencies and diagnostic evaluation
2. Review the management of oncologic emergencies
3. Discuss advances in oncology treatment and how to approach treatment to rapidly developing new therapies



https://www.cancer.gov/research/infrastructure/cancer-centers/find

Current state of unscheduled acute care

JAMA Oncol. 2017 Oct 12;3(10):e172450. doi: 10.1001/jamaoncol.2017.2450. Epub 2017 Oct 12.

Trends in Adult Cancer-Related Emergency Department Utilization: An Analysis of Data From the Nationwide Emergency Department Sample.

Rivera DR[1], Gallicchio L[1], Brown J[2], Liu B[1], Kyriacou DN[3], Shelburne N[1].

Author information

Abstract

IMPORTANCE: The emergency department (ED) is used to manage cancer-related complications among the 15.5 million people living with cancer in the United States. However, ED utilization patterns by the population of US adults with cancer have not been previously evaluated or described in published literature.

OBJECTIVE: To estimate the proportion of US ED visits made by adults with a cancer diagnosis, understand the clinical presentation of adult patients with cancer in the ED, and examine factors related to inpatient admission within this population.

DESIGN, SETTING, AND PARTICIPANTS: Nationally representative data comprised of 7 survey cycles (January 2006-December 2012) from the Nationwide Emergency Department Sample were analyzed. Identification of adult (age ≥18 years) cancer-related visits was based on Clinical Classifications Software diagnoses documented during the ED visit. Weighted frequencies and proportions of ED visits among adult patients with cancer by demographic, geographic, and clinical characteristics were calculated. Weighted multivariable logistic regression was used to examine the associations between inpatient admission and key demographic and clinical variables for adult cancer-related ED visits.

MAIN OUTCOMES AND MEASURES: Adult cancer-related ED utilization patterns; identification of primary reason for ED visit; patient-related factors associated with inpatient admission from the ED.

RESULTS: Among an estimated 696 million weighted adult ED visits from January 2006 to December 2012, 29.5 million (4.2%) were made by a patient with a cancer diagnosis. The most common cancers associated with an ED visit were breast, prostate, and lung cancer, and most common primary reasons for visit were pneumonia (4.5%), nonspecific chest pain (3.7%), and urinary tract infection (3.2%). Adult cancer-related ED visits resulted in inpatient admissions more frequently (59.7%) than non-cancer-related visits (16.3%) ($P < .001$). Septicemia (odds ratio [OR], 91.2; 95% CI, 81.2-102.3) and intestinal obstruction (OR, 10.94; 95% CI, 10.6-11.4) were associated with the highest odds of inpatient admission.

CONCLUSIONS AND RELEVANCE: Consistent with national prevalence statistics among adults, breast, prostate, and lung cancer were the most common cancer diagnoses presenting to the ED. Pneumonia was the most common reason for adult cancer-related ED visits with an associated high inpatient admission rate. This analysis highlights cancer-specific ED clinical presentations and the opportunity to inform patient and system-directed prevention and management strategies.

How does the Emergency Medicine Provider approach Oncologic Emergencies?

The 2022 Model of the Clinical Practice of Emergency Medicine

The 2022 revision of the EM Model notably added immunotherapy complication in addition to previous additions from the 2019 revision of the Oncology section within Category 8, Hematologic and Oncologic Disorders

- **Febrile Neutropenia**
- **Hypercalcemia of Malignancy**
- Hyperviscosity Syndrome
- Malignant Pericardial Effusion
- **Spinal Cord Compression**
- Superior Vena Cava Syndrome
- Tumor Hemorrhage
- **Tumor Lysis Syndrome**
- **Chemotherapy Complications**
- **Immunotherapy Complications**

Beeson et al. J Emerge Med. 2020 May 28;S0736-4679(20)30154-2.

Case 1

-56 yo male

-On chemotherapy for lung cancer

-Presents with chest pain, dyspnea with activity, worsening fatigue, chronic cough and right sided pleuritic chest pain.

-ED vitals: Temperature 101.7F, HR 125, RR 18, BP 138/72, Oxygen Sat 92% on RA.

-Exam: Coarse rhonchi in the right base.

What are the next steps in evaluation and treatment?

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Maegan S. Reynolds MD, FACEP, LSSBB
Associate Professor
Department of Emergency Medicine
Lead Physician, The Ohio State University Wexner Medical Center
Oncology Pod

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Case 1

Oncologic Patients with Fever

- **Question 1 – What is their ANC (Absolute Neutrophil Count)?**
- **Question 2 – Solid tumor or hematologic?**
- **Question 3 – Possible source for fever?**

- **Work-up – Blood cultures (including from line), CBC, Chem, UA/urine culture, CXR, Lactate, additional labs/imaging based on exam and malignancy**
- **Treatment – Empiric broad spectrum antibiotics (ie. cefepime +/- Vancomycin for history of MRSA or line infection)**

Febrile Neutropenia

- Single oral temperature measurement of ≥38.3°C (101°F) or a temperature of ≥38.0°C (100.4°F) sustained over a 1 hour period

And

- Severe neutropenia that is defined as an absolute neutrophil count (ANC) of <500 cells/mm^3 or expected during the next 48 hours

- Multiple etiologies including myelosuppression secondary to chemotherapy

- Treatment: *Apply National Guidelines* (Taplitz et al. J Clin Oncol. 2018)

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Case 2

-A 63 yo female

-History of metastatic breast cancer on chemotherapy

-Presents with weakness, fatigue, nausea and multiple episodes of emesis. Denies fevers, has had some constipation but denies any abdominal pain.

-ED vitals: Temp 98.6F, HR 110, RR 16, BP 105/78, O2 Sat 96% on RA

-Exam: Dry mucous membranes, mild 4+/5 diffuse weakness, and soft, non-tender, non-distended abdominal exam.

What are the next step in evaluation and treatment?

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Case 2

Question 1 – What is the etiology of the patients symptoms?

Question 2 – What are their electrolytes?

Work-up – Chemistry with Ca, Mag, Phos, LFTs, CBC, UA, consider imaging (IE. CT abd/pelv) based on exam

Results – Calcium is 14.6, Albumin 2.1, Ionized CA 1.38

Why do all of those lab values matter?

Treatment – Start IV fluids, consider Zoledronic acid, Calcitonin, etc.

Hypercalcemia

- Presentation:
  - GI symptoms, Neurologic changes, renal failure
- Severity:
  - Degree and rate of onset
- Causes:
  - Humoral: parathyroid hormone-related protein (PTHrP) secretion (80%)
  - Osteolytic (20%)
  - Vitamin D secretion
  - Ectopic PTH
- Treatment: Fluids, bisphosphonates, calcitonin, monoclonal antibody (Denosumab), avoid loop diuretics (volume dependent)

Sadiq NM, Naganathan S, Badireddy M. Hypercalcemia. [Updated 2021 Sep 11]. https://www.ncbi.nlm.nih.gov/books/NBK430714/

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Case 3

- 76 year old Male
- History of metastatic prostate cancer
- Presents with acute back pain radiating to the right leg. Onset this morning when awakening, with numbness and weakness to the right leg affecting gait. No fevers, no bowel or bladder changes, normal stools, and he denies any injuries.
- ED vitals: Temp 98.9F, HR 110, RR 16, BP 165/88, O2 Sat 99% on RA.
- Uncomfortable with L2/L3 spinous tenderness, Strength/sensation/pulses intact to upper extremities and left leg. Right leg with no edema, strong DP/PT pulses but with 3/5 weakness and numbness to the lateral and posterior thigh.

What are the next steps in evaluation and treatment?

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Case 3

Question 1 – What is the differential diagnosis?

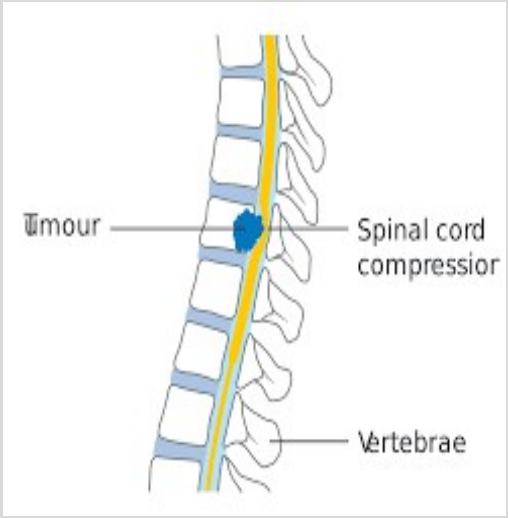
Question 2 – What imaging is needed?

Work-up – Labs – CBC, Chem, Coags, Lumbar CT vs. Emergent Lumbar MRI

Treatment – Pain control, Steroids , NSGY consult

Malignant Spinal Cord Compression

- Etiology: Primary invasion, Metastatic lesions, Pathologic fracture
- Back pain, focal neurologic deficits
- Associated with breast, lung, prostate, and kidney cancer, lymphoma and multiple myeloma
- Acute neurologic findings requires urgent MRI evaluation
- Multiple grading systems, symptom (Frankel) and imaging based (ESCC)
- Treatment: Dexamethasone 10-16mg IV, Chemotherapy/Radiation/Surgery depending on tumor type



Ropper AE, Ropper AH. N Engl J Med ;376:1358-1369
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https://www.mdanderson.org/content/dam/mdanderson/documents/for-physicians/algorithms/clinical-management/clin-management-spinal-cord-compression-web-algorithm.pdf
https://en.wikipedia.org/wiki/Spinal_cord_compression

Acute Intracranial Edema

What is the presentation for acute intracranial edema?

- Confusion, headache, vomiting, seizures

- Work-up : Emergent CT Head, plus usual altered mental status evaluation ie. Infection, electrolytes, ischemia

- Same treatment – Steroids! Plus Neuro-Oncology or NSGY

Presents in patients with primary brain tumor (GBM, neuroblastoma) or intracranial metastasis (melanoma)

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Case 4

- 19 yo male
- Recent relapse of ALL, discharged from the hospital yesterday after chemotherapy induction.
- Presents with palpitations and dehydration. He reports fatigue, nausea and vomiting, feeling that his heart is racing and he is urinating less. The patient is concerned he is dehydrated following reaction from chemotherapy.
- ED vitals: Temp 99.0F, HR 146, BP 92/54, RR 16, O2 Sat 99% on RA.
- Exam: Dry mm, delayed capillary refill, abdomen soft, non-tender and non-distended.

What is your next step in evaluation?

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Case 4

Question 1 – Any concern for arrhythmia or sepsis?

Question 2 – What are the patients electrolytes?

Work-up : EKG, cardiac monitoring, Chem with Ca, Mag, Phos, LFTs, CBC, UA, consider blood cultures or infection evaluation

Results – EKG with peaked T waves, PR depression, QRS 105
Potassium 6.2mEq/L, Phos 5.5 mg/dL, Calcium 6.1 mg/dL

What is the treatment and what additional labs?

Tumor Lysis Syndrome

- Tends to occur in rapidly dividing tumors.
- Rapid release of potassium, phosphorous, nucleic acids, and cytokines.
- Laboratory definition: ≥2 abnormal serum values or a 25% change in value of uric acid, potassium, phosphorous, and calcium.
- Treatment: fluids, allopurinol, rasburicase, serial electrolyte monitoring, dialysis
  - no role for urine alkalinization

Cairo et al. Br J Haematol. 2010 May;149(4):578-86.
Coiffier et al. J Clin Oncol . 2008 Jun 1;26(16):2767-78.

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Case 5

- 58 year old Female
- History of ovarian cancer and peritoneal carcinomatosis currently on chemotherapy
- Presents with fatigue, nausea, multiple episodes of emesis and abdominal distension. She denies fevers, she does have chronic constipation and poor appetite. She also reports progressive lower pelvic pain not controlled with home opiates.
- ED vitals: Temp 98.6F, HR 110, RR 18, O2 Sat 95% on RA, BP 102/68.
- Exam: Thin and chronically ill appearing, dry mucous membranes, lungs clear, normal heart sounds, abdomen is notably distended with a fluid wave, soft with mild lower pelvic tenderness but no guarding or rebound, and mild bilateral lower extremity edema.

What are the next steps in evaluation and what challenges are raised by this case?

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Case 5

Question 1 – What is the work-up?

Question 2 – What are the common presentations for patients undergoing chemo and what barriers to care exist?

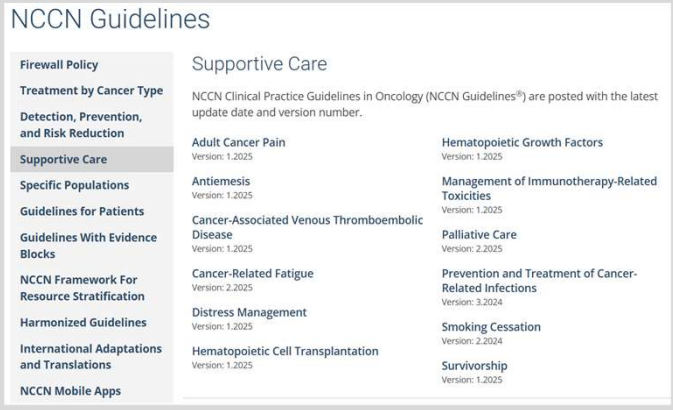
Work-up – CBC, Chem, LFTs, lipase, BNP, UA, CT Abdomen/Pelvis non-contrast

Results – CBC without neutropenia, mild AKI and hyponatremia, CT showing mild ascites and progression of disease burden

Initial Management – IVFs, anti-emetics, pain control

Chemotherapy Complications

- Supportive Care, Symptom Control
- Pain and Palliative Care Expertise
- Care Coordination for outpatient management



Case 6

- 57 year old Male
- Non squamous cell lung cancer on unknown therapy
- Presents with shortness of breath, chills and fatigue, cough. No nausea, vomiting, diarrhea, constipation. No recorded fevers, no dysuria, no penile discharge, no chest pain.
- ED vitals: Temp 97.8F, HR 92, RR 22, O2 Sat 98% on RA, and BP 138/84.
-Exam: Ill appearing, moist mucous membranes, abdomen soft, no distension or tenderness. Diffuse crackles in all lung fields.

What are the next steps in evaluation and treatment?

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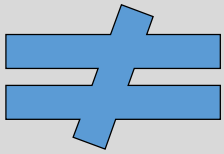
Immunotherapy



Chemotherapy

Case 6

Question 1 – What is the differential diagnosis and how much work-up is needed?

Question 2 – What is the ED treatment? Does the patient need admission?

Work-up – CBC, Chemistry, LFTs, lipase, UA, CXR, EKG, troponin, BNP, ESR, CRP

Management – Consider immunotherapy complications!

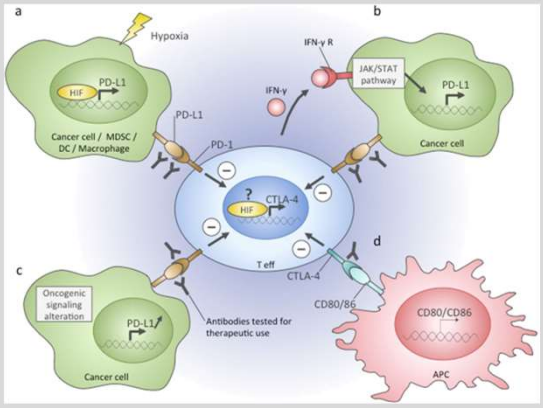
Cytokine Release Syndrome

Immunotherapy complications

- Difficulty to identify in the acute setting
- Varied complications
- Mild to severe symptoms
- Of particular concern:
  - Cytokine Release Syndrome (CRS)
  - Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)

Lee et al. Biol Blood Marrow Transplant. 2019 Apr;25(4):625-638.
https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/car-t-cell1.htm

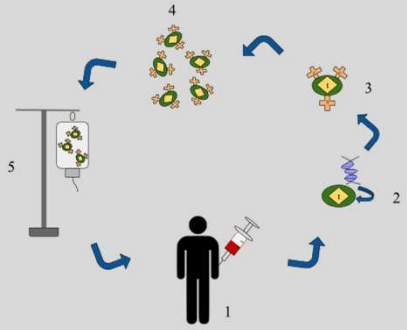
Immune Checkpoint Inhibitors (ICI)



Other Major Classes of Immunotherapy:
-Oncologic Vaccines
-Cytokines
-Viral Therapy
-Bispecific antibodies

Author: Varvara Petrova, Margherita Annicchiarico-Petruzzelli, Gerry Melino & Ivano Amelio **(CC BY 4.0)**

Chimeric Antigen Receptor T-cell Therapy (CAR-T)



https://upload.wikimedia.org/wikipedia/commons/archive/b/b6/20180611203918%21CAR_T-cell_Therapy.svg

Research Letter | Oncology

March 9, 2020

Estimation of the Percentage of US Patients With Cancer Who Are Eligible for Immune Checkpoint Inhibitor Drugs

Alyson Haslam, PhD[1,2]; Jennifer Gill, MS[1]; Vinay Prasad, MD, MPH[1,3,4]

Proportion of US patients with cancer were eligible for immune checkpoint inhibitor therapy
1.5% (2011) --> 36% (2019)

Immune Related Adverse Events (irAEs)

- All organ systems are potentially affected.
- Presentation is often delayed weeks, months and even years later.

- Eyes: Uveitis, Conjunctivitis
- Endocrine: Hypo/hyperthyroidism, hypopituitarism, hypophysitis, adrenal insufficiency
- Cardiovascular: Myocarditis, Pericarditis, Vasculitis
- Gastrointestinal: Colitis
- Musculoskeletal: Arthritis, Dermatomyositis
- Neurologic: Neuropathy, Myelopathy, Encephalitis, Myasthenia
- Respiratory: Pneumonitis, Pleuritis
- Liver: Hepatitis
- Renal: Nephritis
- Dermatologic: Rash, Vitiligo, Rash

Patil et al. Expert Rev Mol Diagn. 2018 Mar;18(3):297-305.
Haanen et al. Annals of Oncology 28 (Supplement 4): i119–i142, 2017

Common Terminology for Adverse Events (CTCAE)

Introduction
The NCI Common Terminology Criteria for Adverse Events is a descriptive terminology which can be utilized for Adverse Event (AE) reporting. A grading (severity) scale is provided for each AE term.

SOC
System Organ Class (SOC), the highest level of the MedDRA[1] hierarchy, is identified by anatomical or physiological system, etiology, or purpose (e.g., SOC Investigations for laboratory test results). CTCAE terms are grouped by MedDRA Primary SOCs. Within each SOC, AEs are listed and accompanied by descriptions of severity (Grade).

CTCAE Terms
An Adverse Event (AE) is any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure. An AE is a term that is a unique representation of a specific event used for medical documentation and scientific analyses. Each CTCAE v4.0 term is a MedDRA LLT (Lowest Level Term).

Grades
Grade refers to the severity of the AE. The CTCAE displays Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline:

- **Grade 1** Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
- **Grade 2** Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*.
- **Grade 3** Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care ADL**.
- **Grade 4** Life-threatening consequences; urgent intervention indicated.
- **Grade 5** Death related to AE.

A Semi-colon indicates 'or' within the description of the grade.

A single dash (-) indicates a Grade is not available. Not all Grades are appropriate for all AEs. Therefore, some AEs are listed with fewer than five options for Grade selection.

Grade 5
Grade 5 (Death) is not appropriate for some AEs and therefore is not an option.

Definitions
A brief Definition is provided to clarify the meaning of each AE term. A single dash (-) indicates a Definition is not available.

Navigational Notes
A Navigational Note is used to assist the reporter in choosing a correct AE. It may list other AEs that should be considered in addition to or in place of the AE in question. A single dash (-) indicates a Navigational Note has not been defined for the AE term.

Activities of Daily Living (ADL)
*Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
**Self care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.

[1] CTCAE v5.0 incorporates certain elements of the MedDRA terminology. For further details on MedDRA refer to the MedDRA MSSO Web site (https://www.meddra.org/).

https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf

VOLUME 36 · NUMBER 17 · JUNE 10, 2018
JOURNAL OF CLINICAL ONCOLOGY ASCO SPECIAL ARTICLE

Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: American Society of Clinical Oncology Clinical Practice Guideline

Julie R. Brahmer, Christina Lacchetti, Bryan J. Schneider, Michael B. Atkins, Kelly J. Brassil, Jeffrey M. Caterino, Ian Chau, Marc S. Ernstoff, Jennifer M. Gardner, Pamela Ginex, Sigrun Hallmeyer, Jennifer Holter Chakrabarty, Natasha B. Leighl, Jennifer S. Mammen, David F. McDermott, Aung Naing, Loretta J. Nastoupil, Tanyanika Phillips, Laura D. Porter, Igor Puzanov, Cristina A. Reichner, Bianca D. Santomasso, Carole Seigel, Alexander Spira, Maria E. Suarez-Almazor, Yinghong Wang, Jeffrey S. Weber, Jedd D. Wolchok, and John A. Thompson in collaboration with the National Comprehensive Cancer Network

Puzanov *et al. Journal for ImmunoTherapy of Cancer* (2017) 5:95
DOI 10.1186/s40425-017-0300-z
Journal for ImmunoTherapy of Cancer
POSITION ARTICLE AND GUIDELINES Open Access

Managing toxicities associated with immune checkpoint inhibitors: consensus recommendations from the Society for Immunotherapy of Cancer (SITC) Toxicity Management Working Group

I. Puzanov[1†], A. Diab[2†], K. Abdallah[3], C. O. Bingham III[4], C. Brogdon[5], R. Dadu[2], L. Hamad[1], S. Kim[2], M. E. Lacouture[6], N. R. LeBoeuf[7], D. Lenihan[8], C. Onofrei[9], V. Shannon[2], R. Sharma[1], A. W. Silk[12], D. Skondra[10], M. E. Suarez-Almazor[2], Y. Wang[2], K. Wiley[11], H. L. Kaufman[12†], M. S. Ernstoff[1*†] and on behalf of the Society for Immunotherapy of Cancer Toxicity Management Working Group

ESMO
Annals of Oncology 28 (Supplement 4): iv119–iv142, 2017
doi:10.1093/annonc/mdx225
CLINICAL PRACTICE GUIDELINES

Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

J. B. A. G. Haanen[1], F. Carbonnel[2], C. Robert[3], K. M. Kerr[4], S. Peters[5], J. Larkin[6] & K. Jordan[7], on behalf of the ESMO Guidelines Committee*

NCCN CLINICAL PRACTICE GUIDELINES IN ONCOLOGY

Management of Immunotherapy-Related Toxicities, Version 1.2019

John A. Thompson, MD[1,†,‡]; Bryan J. Schneider, MD[2,†,‡]; Julie Brahmer, MD, MSc[3,†,‡]; Stephanie Andrews, MS, RN, ANP-BC[4]; Philippe Armand, MD, PhD[5]; Shailender Bhatia, MD[1]; Lihua E. Budde, MD, PhD[6]; Luciano Costa, MD, PhD[7]; Marianne Davies, MSN, DNP[8]; David Dunnington, MA[9]; Marc S. Ernstoff, MD[10,‡]; Matthew Frigault, MD[11]; Brianna Hoffner, MSN[12]; Christopher J. Hoimes, MD[13]; Mario Lacouture, MD[14]; Frederick Locke, MD[4]; Matthew Lunning, DO[15]; Nisha A. Mohindra, MD[16]; Jarushka Naidoo, MD[3]; Anthony J. Olszanski, MD, RPh[17]; Olalekan Oluwole, MD[18]; Sandip P. Patel, MD[19]; Sunil Reddy, MD[20]; Mabel Ryder, MD[21]; Bianca Santomasso, MD, PhD[14]; Scott Shofer, MD, PhD[22]; Jeffrey A. Sosman, MD[16]; Momen Wahidi, MD[23]; Yinghong Wang, MD, PhD[23,‡]; Alyse Johnson-Chilla, MS[24]; and Jillian L. Scavone, PhD[24]

Cytokine Release Syndrome (CRS)

- Presents from mild to severe symptoms
  - fatigue → hypotensive shock and respiratory failure.
- Treatment: Supportive care as necessary
- Grading based on need for supportive measures

Lee et al. Biol Blood Marrow Transplant. 2019 Apr;25(4):625-638.
https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/car-t-cell1.htm

Immune Effector Cell-Associated Neurotoxicity syndrome (ICANS)

- Symptoms range from non specific neurologic symptoms (Fatigue) to Seizures, Coma and Death 2/2 cerebral edema
- Graded by alterations to mental status
- Onset typically 3-10 days after treatment
- Evaluation: Altered Mental Status evaluation + LP + MRI
- Treatment: Supportive care seizure prophylaxis ± tocilizumab ± steroids

Lee et al. Biol Blood Marrow Transplant. 2019 Apr;25(4):625-638.
https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/car-t-cell1.html

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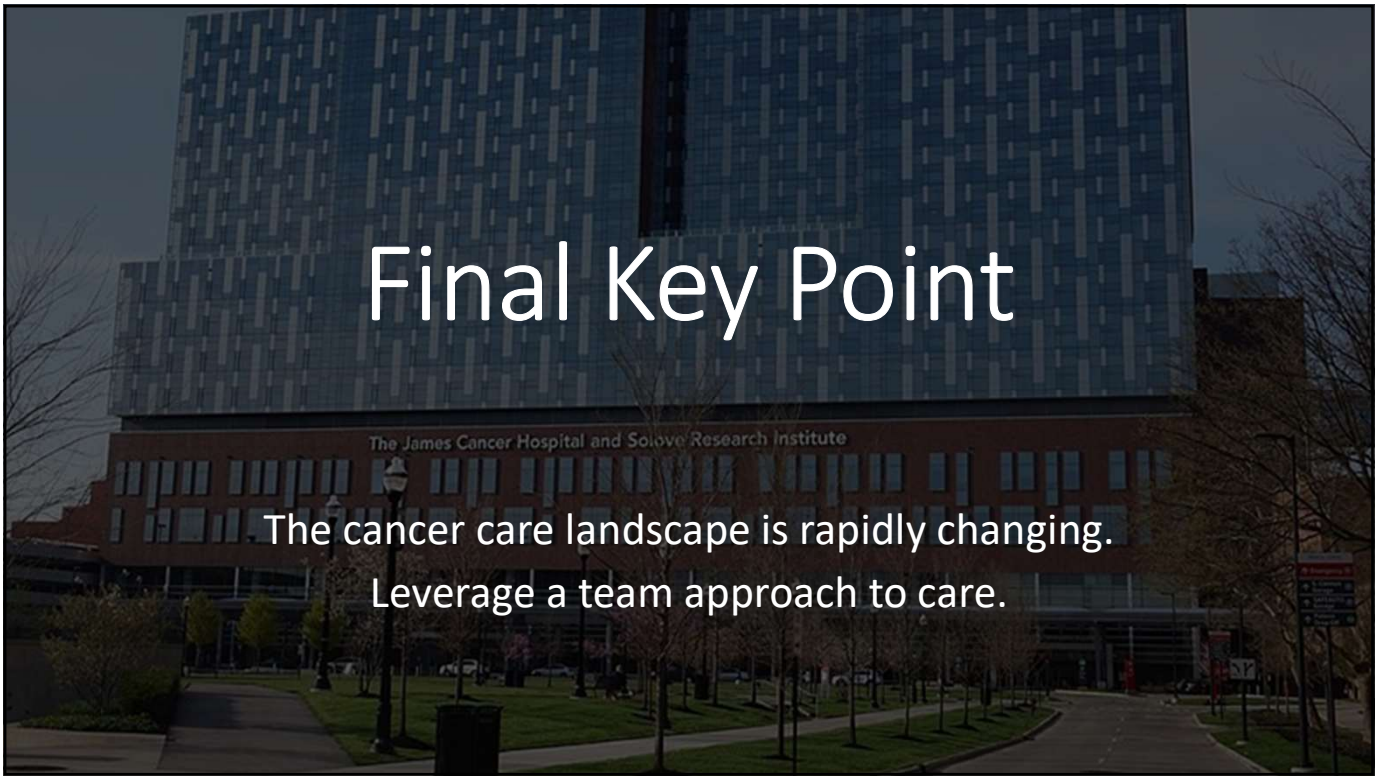

Final Key Point

The cancer care landscape is rapidly changing.
Leverage a team approach to care.