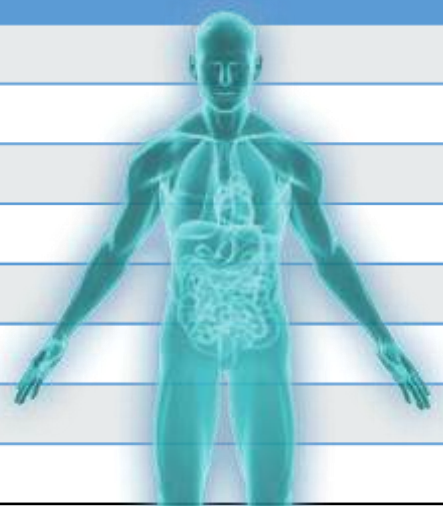
ΑΝΟΣΟΘΕΡΑΠΕΙΑ ΤΟΥ ΚΑΡΚΙΝΟΥ ΤΟΥ ΠΝΕΥΜΟΝΑ

Πνευμονική τοξικότητα της ανοσοθεραπείας και αντιμετώπισή της

Βάσσος Δημήτριος MD, MSc
Πνευμονολόγος
Επιστημονικός Συνεργάτης
Πανεπιστημίου Αθηνών
Ογκολογική Μονάδα ΄Γ ΠΠ
Γ.Ν.Ν.Θ.Α. «Η Σωτηρία»

Organs Systems Often Affected by I-O Therapy-Related AEs

I-O therapy-associated AEs target certain organ systems[1]
Skin[1–6]
Endocrine system[2,4,6,7–10]
Liver[2,6,11–12]
Gastrointestinal tract[2,6,9,13]
Nervous system[6,10,14,15]
Eyes[1,4,16–18]
Respiratory system[1,5,6,10,15,19]
Hematopoietic cells[6,9,12,20–22]



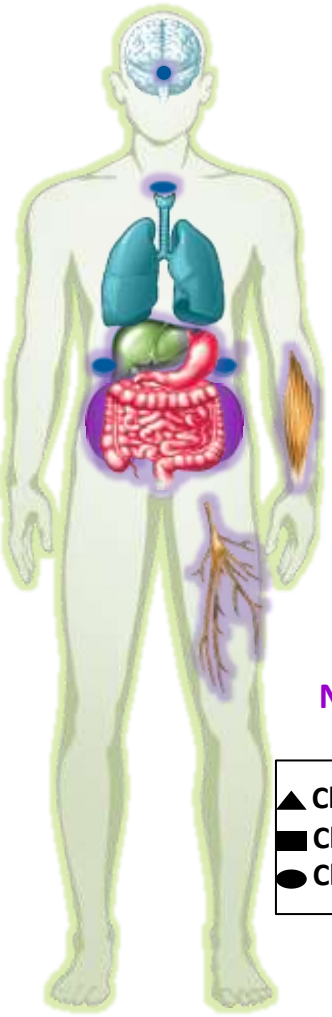
1. Amos SM, et al. *Blood.* 2011;118:499–509; 2. Phan GQ, et al. *PNAS.* 2003;100:8372–8377; 3. Rosenberg SA. *J Immunother Emphasis Tumor Immunol.* 1996;19:81–84; 4. Chianese-Bullock KA, et al. *J Immunother.* 2005;28:412–419; 5. Harris J, et al. *Med Pediatr Oncol.* 1994;22:103–106; 6. Chow LQ. *Am Soc Clin Oncol Educ Book*. 2013:280–285; 7. Bendle GM, et al. *Nat Med.* 2010;16:565–570; 8. Soni N, et al. *Cancer Immunol Immunother.* 1996;43:59–62; 9. Ronnblom LE, et al. *Ann Intern Med.* 1991;115:178–183; 10. Fraenkel PG, et al. *J Immunother.* 2002;25:373–378; 11. Lamers CH, et al. *J Clin Oncol.* 2006;24:e20–e22; 12. Roskrow MA, et al. *Leuk Res.* 1999;23:549–557; 13. Parkhurst MR, et al. *Mol Ther.* 2011;19:620–626; 14. Pellkofer H, et al. *Brain.* 2004;127:1822–1830; 15. Smalley RV, et al. *Blood.* 1991;78:3133–3141; 16. Dudley ME, et al. *J Clin Oncol.* 2008;26:5233–5239; 17. Yeh S, et al. *Ophthalmology*. 2009;116:981–989; 18. Robinson MR, et al. *J Immunother*. 2004;27:478–479; 19. Morgan RA, et al. *Mol Ther.* 2010;18:843–851; 20. Kochenderfer JN, et al. *Blood.* 2010;116:4099–4102; 21. Lin TS, et al. *J Clin Oncol.* 2010;28:4500–4506; 22. Herishanu Y, et al. *Leuk Lymphoma.* 2003;44:2103–2108.

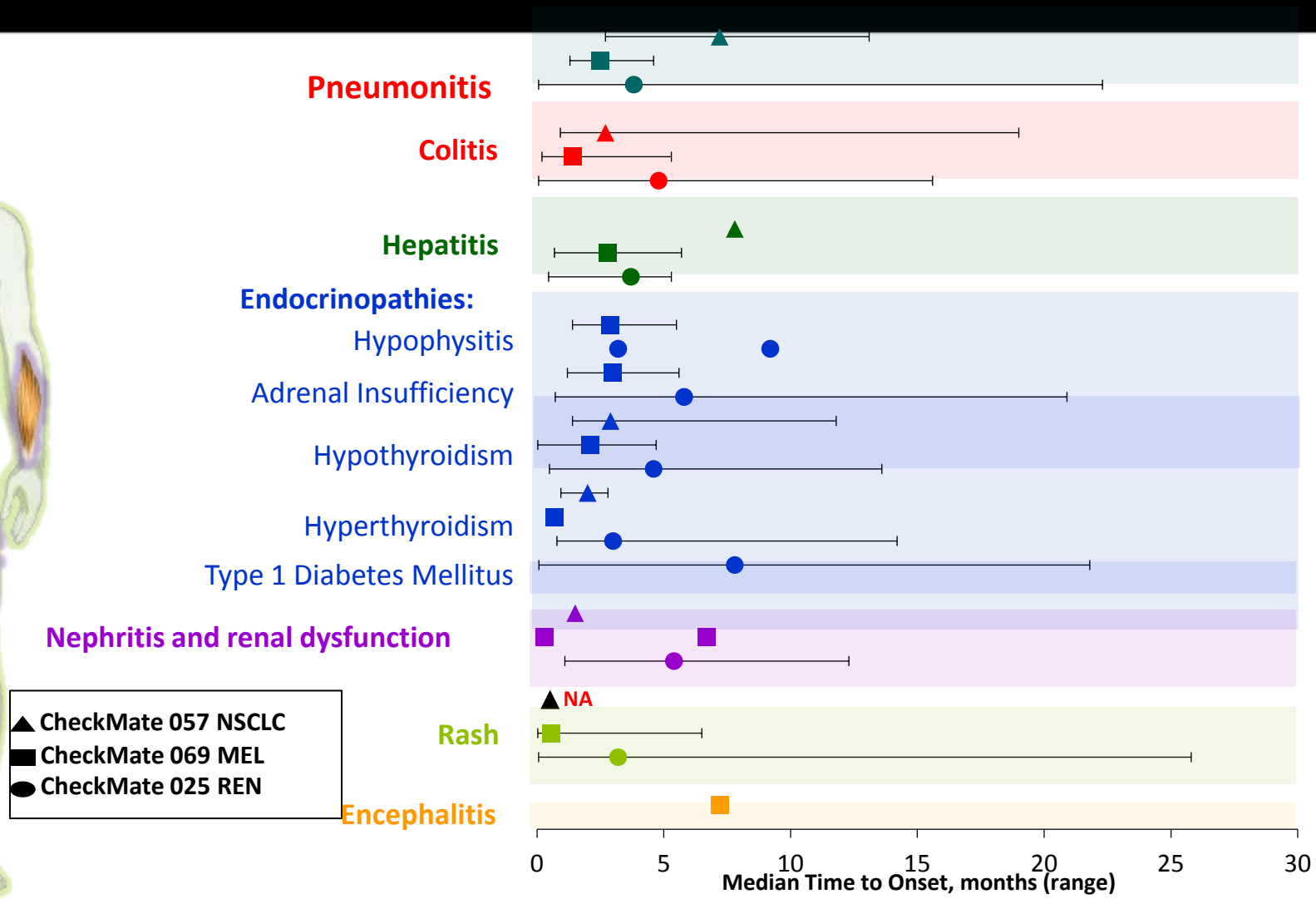
Toxicities of Checkpoint Immunotherapies

Drug	Pneumonitis	Colitis, Diarrhea (Entercolitis[a])	Rash, Pruritus (Dermatitis[a])
Ipilimumab 3 mg/kg 10 mg/kg	<1%	8%, 32-46% (7%) 16%, 49% (16%)	29-42%, 31% (2%) 50%, 45% (4%)
Nivolumab	3.1%	2.9%, 23-31%	21-40%, 17-23%, (9%)
Ipilimumab + Nivolumab	6%	26%, 52%	53%, NR (23%)
Pembrolizumab	3.4%	1.7%, 14-26%	17-24%, 11-28%
Atezolizumab	2.6%	19.7%	15%[a]

[a]Grade 3-5, immune-mediated
[b]Urothelial carcinoma
Ipiliumab prescribing information: http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/125377s073lbl.pdf
Nivolumab prescribing information: http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/125554s022lbl.pdf
Pembrolizumab prescribing information: http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/125514s012lbl.pdf
Atezolizumab prescribing information: http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/761041s000lbl.pdf

Time to Onset of Immune-Mediated Reactions Associated With Nivolumab





OPDIVO [Immune-Mediated Adverse Reactions Management Guide]. Princeton, NJ: Bristol-Myers Squibb; 2015.

REVIEW OF CURRENT DATA

Clinical Cancer Research

Home About Articles For Authors Alerts

Personalized Medicine and Imaging

PD-1 inhibitor-related pneumonitis in advanced cancer patients: Radiographic patterns and clinical course

Mizuki Nishino, Nikhil H Ramaiya, Mark M Awad, Lynette M Sholl, Jennifer A Maattala, Myriam Taibi, Hiroto Hatabu, Patrick A. Ott, Philippe Armand, and F. Stephen Hodi

DOI: 10.1158/1078-0432.CCR-16-1320 Published 17 August 2016

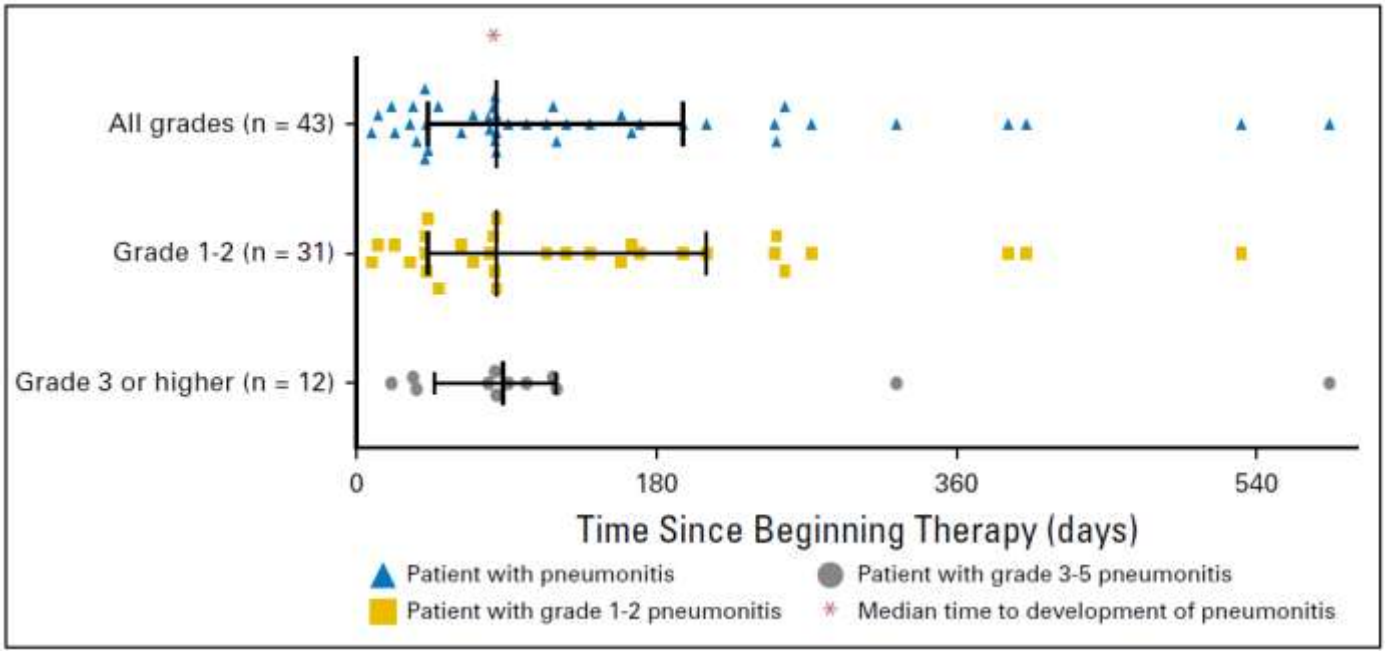
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Pneumonitis in Patients Treated With Anti–Programmed Death-1/Programmed Death Ligand 1 Therapy

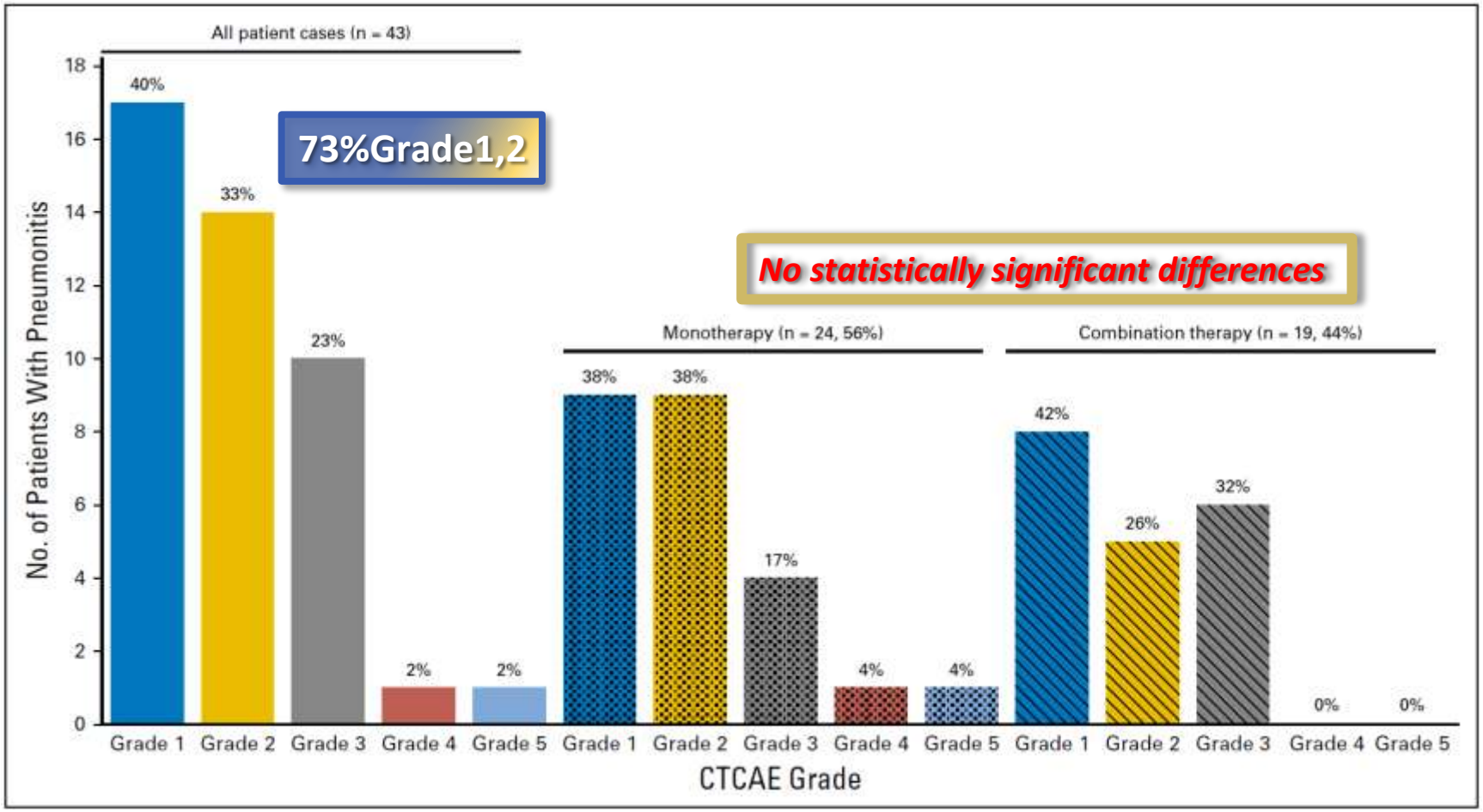
Jarushka Naidoo, Xuan Wang, Kaitlin M. Woo, Tunc Iyriboz, Darragh Halpenny, Jane Cunningham, Jamie E. Chaft, Neil H. Segal, Margaret K. Callahan, Alexander M. Lesokhin, Jonathan Rosenberg, Martin Voss, Charles M. Rudin, Hira Rizvi, Xue Hou, Katherine Rodriguez, Melanie Albano, Ruth-Ann Gordon, Charles Leduc, Natasha Rekhtman, Bianca Harris, Alexander M. Menzies, Alexander D. Guminski, Matteo S. Carlino, Benjamin Y. Kong, Jedd D. Wolchok, Michael A. Postow, Georgina V. Long, and Matthew D. Hellmann

Onset of pneumonitis

- Median time to onset of pneumonitis : 2.8 months
- Range : 9 days to 19.2 months
- Combination therapy : Median time 2.7 m
- Monotherapy : Median time 4.6 m



GRADE


All patient cases (n = 43)
No. of Patients With Pneumonitis
18
16
14
12
10
8
6
4
2
0
40%
33%
23%
2%
2%
73%Grade1,2
No statistically significant differences
Monotherapy (n = 24, 56%)
Combination therapy (n = 19, 44%)
38%
38%
17%
4%
4%
42%
26%
32%
0%
0%
Grade 1
Grade 2
Grade 3
Grade 4
Grade 5
CTCAE Grade

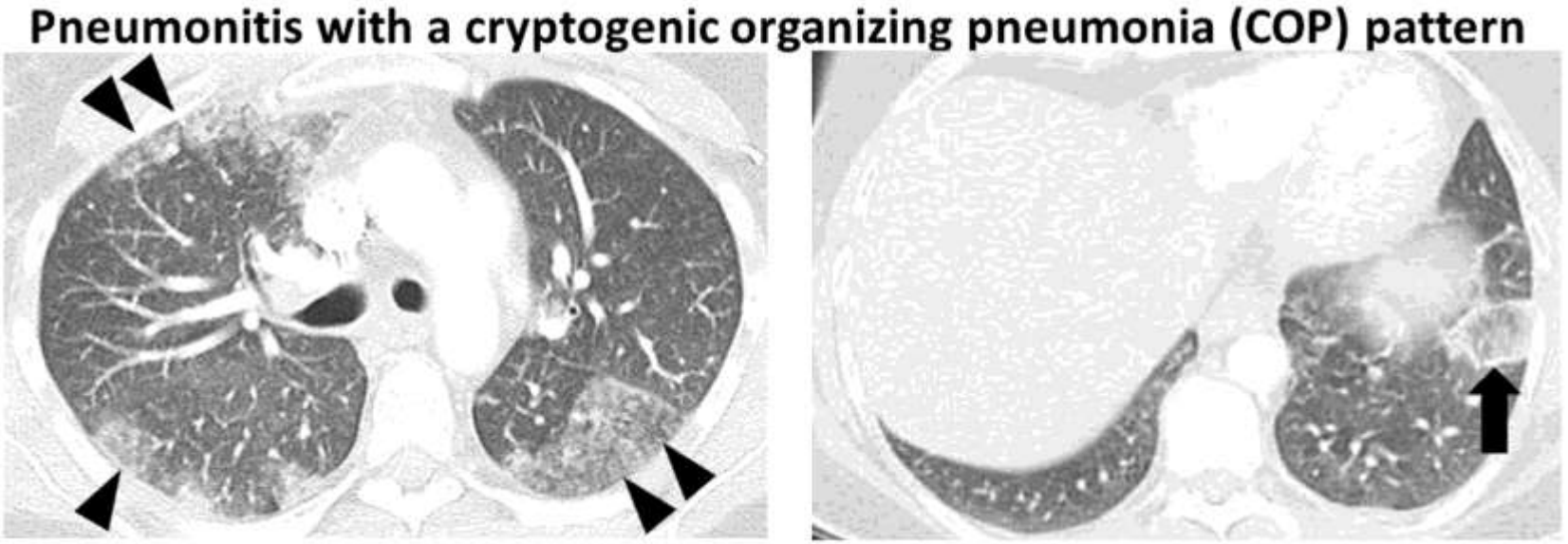
SYMPTOMS

SYMPTOMS	NO (%)
Dyspnea	23 of 43 [53%]
Cough	15 of 43 [35%]
Fever	5 of 43 [12%]
Chest pain	3 of 43 [7%]
Asymptomatic	**14 of 43 [33%]**

- 58% Additional immune-related toxicity (25 of 43)

Radiographic patterns of pneumonitis

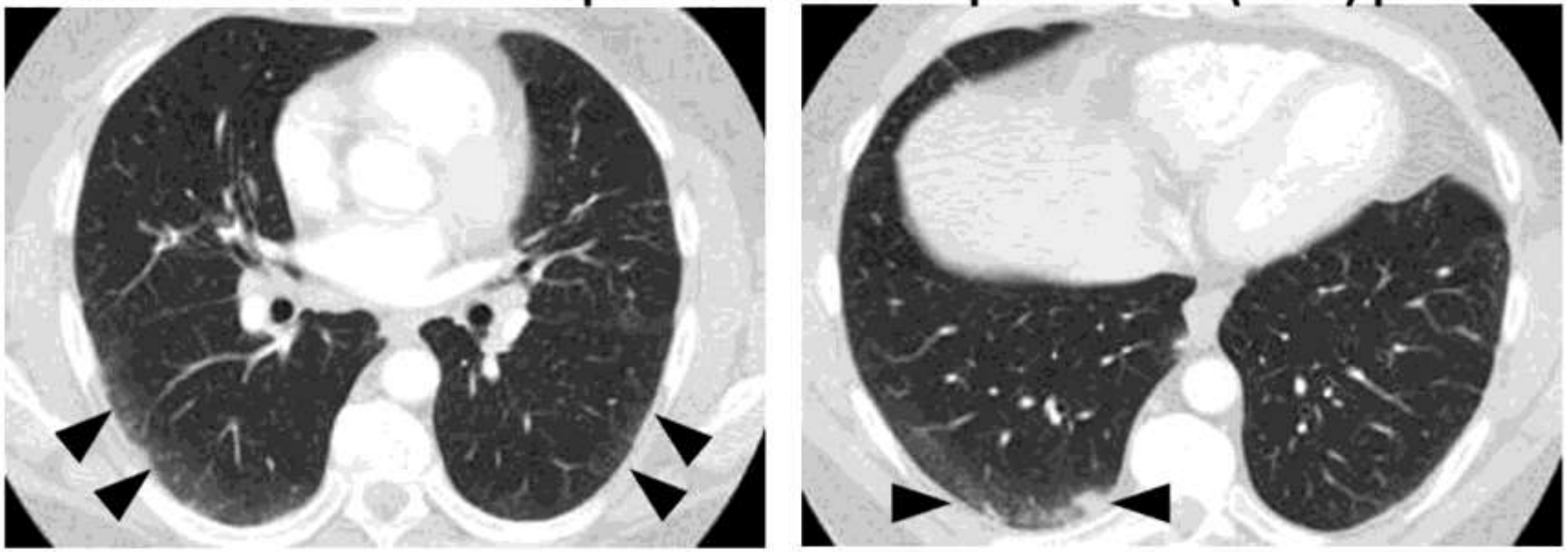
- COP Pattern – most common (65%) – Grade 2



Radiographic patterns of pneumonitis

- NSIP Pattern 15% - Grade 1

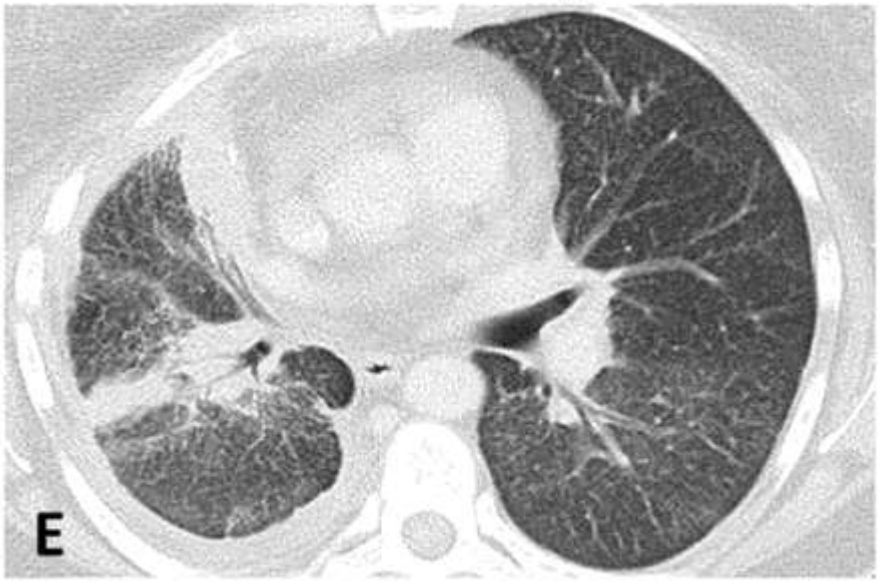
Pneumonitis with a non-specific interstitial pneumonia (NSIP) pattern

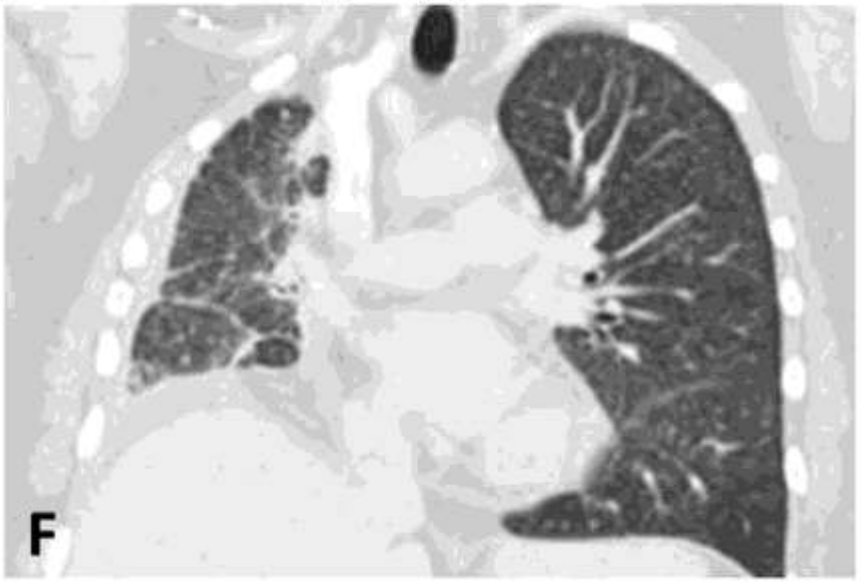


Radiographic patterns of pneumonitis

- HP Pattern 10% - Grade 1

Pneumonitis with a hypersensitivity pneumonitis (HP) pattern

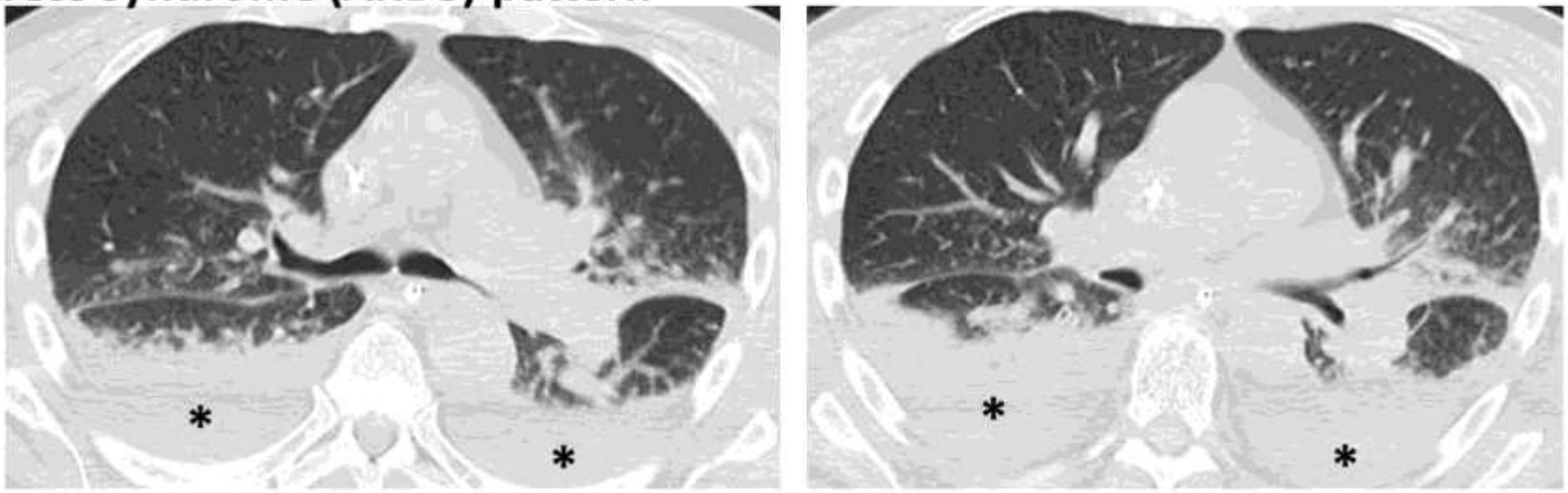




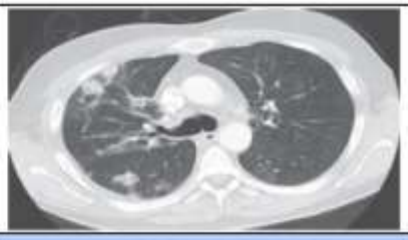
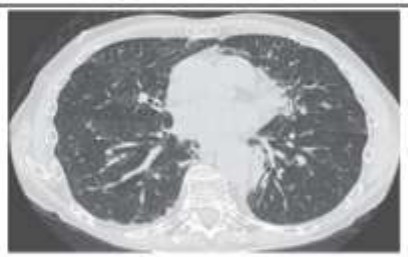
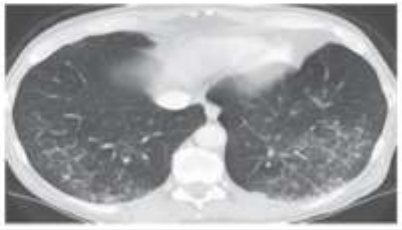
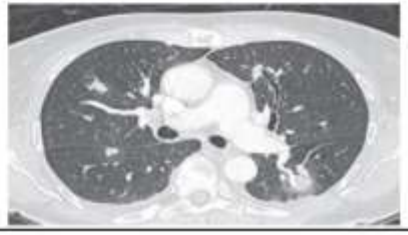
Radiographic patterns of pneumonitis

❖AIP-ARDS Pattern 10% - Grade 3

Pneumonitis with an acute interstitial pneumonia (AIP)/acute respiratory distress syndrome (ARDS) pattern



Radiologic features

Radiologic Subtypes	Representative Image	Description
Cryptogenic organizing pneumonia-like (n = 5, 19%)		Discrete patchy or confluent consolidation with or without air bronchograms Predominantly peripheral or subpleural distribution
Interstitial (n = 6, 22%)		Increased interstitial markings, interlobular septal thickening Peribronchovascular infiltration, subpleural reticulation Honeycomb pattern in severe patient cases
Hypersensitivity (n = 2, 7%)		Centrilobular nodules Bronchiolitis-like appearance Tree-in-bud micronodularity
Pneumonitis not otherwise specified (n = 4, 15%)		Mixture of nodular and other subtypes Not clearly fitting into other subtype classifications

- COP – Like Appearance most common in NSCLC
- COP – Like more likely to require treatment

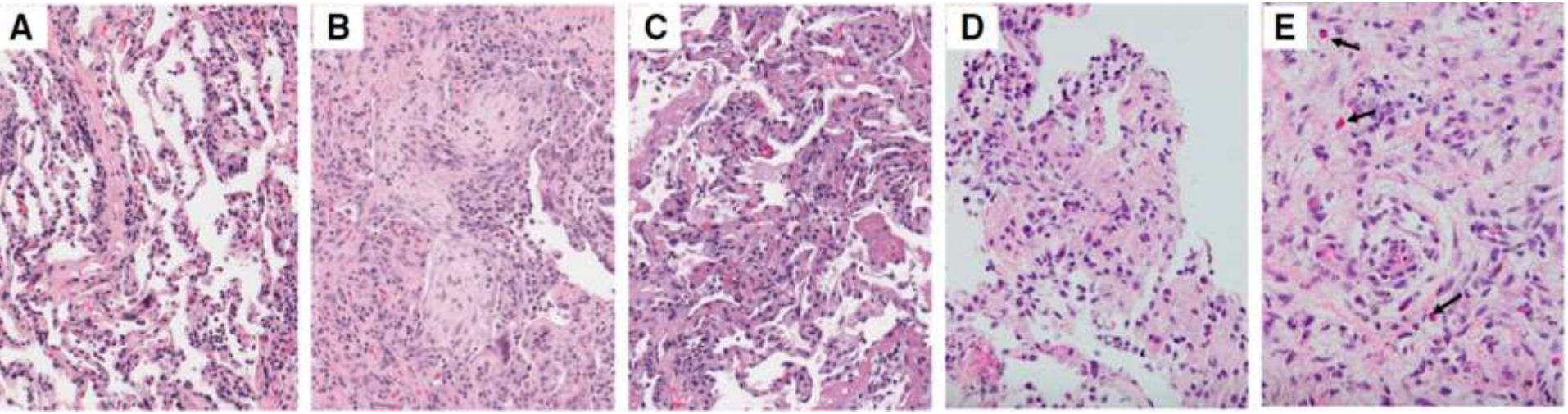
Radiologic features

Chest X-Ray

- 67% : possible pneumonitis
- 11% : possible progressive cancer
- 22% : no new radiographic abnormality

Pathologic Features

- 11 pt Biopsy (8 bronchoscopic, 2 core biopsies,1 wedge



(A) Cellular interstitial pneumonitis

(B) Organizing pneumonia

(C) Diffuse alveolar damage

(D) Poorly formed granulomas

(E) Eosinophils (arrows).

Management and outcome

Highest CTCAE Grade	Highest Treatment Required for Pneumonitis Management, No. (%)				
	Treatment Hold	Oral Corticosteroids	Intravenous Corticosteroids	Additional Immunosuppression*	Total
1	15 (83)	2 (12)	0 (0)	0 (0)	17
2	0 (0)	10 (71)	4 (29)	0 (0)	14
3	0 (0)	2 (20)	4 (40)	4 (40)	10
4	0 (0)	0 (0)	1 (100)	0 (0)	1
5	0 (0)	0 (0)	0 (0)	1 (100)	1
Total	15	14	9	5	43

PNEUMONITIS FLAIR

	Clinical Outcomes of Pneumonitis Management, No. (%)				
	Completely Resolved	Improved	Worsened	Unknown	Total
1	17 (100)	0 (0)	0 (0)	0 (0)	17
2	10 (71)	3 (21)	0 (0)	1 (8)	14
3	4 (40)	2 (20)	4 (40)	0 (0)	10
4	1 (100)	0 (0)	0 (0)	0 (0)	1
5	0 (0)	0 (0)	1 (100)	0 (0)	1
Total	32	5	5	1	43

DEATH

3 INFECTION

Abbreviation: CTCAE, Common Terminology Criteria for Adverse Events (version 4).
*Additional immunosuppression: Three patients received infliximab alone (all grade 3), and two patients received both infliximab and cyclophosphamide (one grade 3 and one grade 5).

Oral corticosteroids as maximum immunosuppression used in 14 of 17 [82%]

Median starting dose of prednisone :50 mg (range, 20 to 80 mg)

Median duration of corticosteroid: 68 days (range, 20 to 154 days)

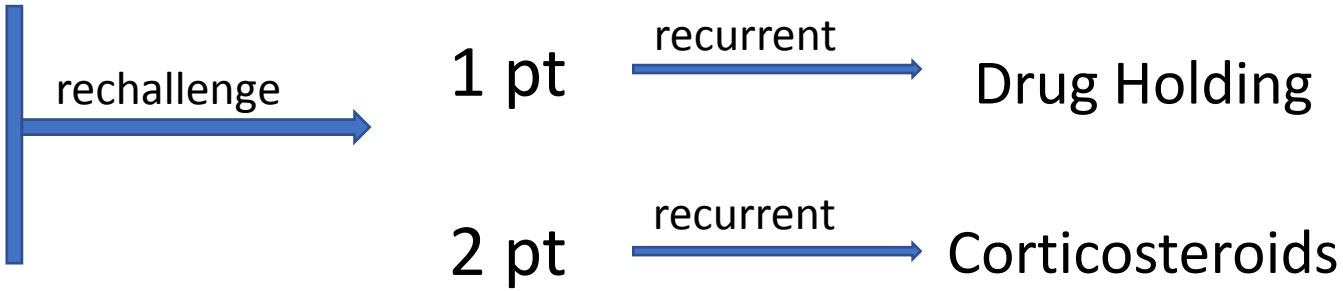
Recurrent Pneumonitis

- 11 pt recurrent during corticosteroid therapy after improvement
- 8 improved with further management
- 3 worsened/died

Rechallenge Immunotherapy

- 12/43 pt Rechallenge Immunotherapy

- 9 GR 1
- 3 GR 2



Clinical Features – Pneumonitis Outcomes

Worsening clinical outcome:

- Current vs former smokers (P = .053)
- Underlying lung conditions vs no lung conditions

- ❑ FEV1
- ❑ DLCO

→ NO ASSOCIATION

Risk factors

ORIGINAL ARTICLE

Pneumonitis in Non–Small Cell Lung Cancer Patients Receiving Immune Checkpoint Immunotherapy: Incidence and Risk Factors

Karthik Suresh, MD,[a,*] Khinh Ranh Voong, MD,[b] Bairavi Shankar, BS,[c] Patrick M. Forde, MD,[c,d] David S. Ettinger, MD,[c] Kristen A. Marrone, MD,[c,d] Ronan J. Kelly, MD,[c,d] Christine L. Hann, MD,[c,d] Benjamin Levy, MD,[c,d] Josephine L. Feliciano, MD,[c,d] Julie R. Brahmer, MD,[c,d] David Feller-Kopman, MD,[a] Andrew D. Lerner, MD,[a] Hans Lee, MD,[a] Lonny Yarmus, DO,[a] Franco D'Alessio, MD,[a] Russell K. Hales, MD,[b] Cheng Ting Lin, MD,[e] Kevin J. Psoter, PhD,[f] Sonye K. Danoff, MD, PhD,[a] Jarushka Naidoo, MBBCh[c,d]

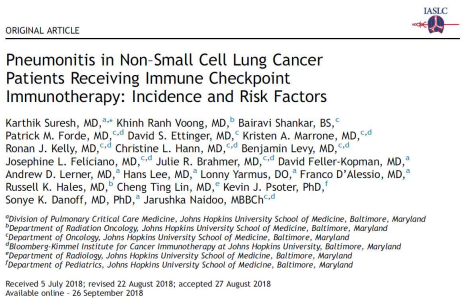
[a]*Division of Pulmonary Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland*
[b]*Department of Radiation Oncology, Johns Hopkins University School of Medicine, Baltimore, Maryland*
[c]*Department of Oncology, Johns Hopkins University School of Medicine, Baltimore, Maryland*
[d]*Bloomberg-Kimmel Institute for Cancer Immunotherapy at Johns Hopkins University, Baltimore, Maryland*
[e]*Department of Radiology, Johns Hopkins University School of Medicine, Baltimore, Maryland*
[f]*Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland*

Received 5 July 2018; revised 22 August 2018; accepted 27 August 2018
Available online - 26 September 2018

Risk factors

- Overal Incidence :19%
- Combination Therapy vs Monotherapy
- Hystology : Squamous vs Adenocarcinoma (55% lower odds)
- Seasonal Pattern (increased number of cases in winter)
- Possible role of viral infection
- Smoking Status ??? (No association n this article)
- Cancer stage (Higher rates at a lower cancer stage)
- Time of onset:

  Early → Higher Grade → Higher Mortality



ORIGINAL ARTICLE

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Karthik Suresh, MD,[a,*] Khinh Ranh Voong, MD,[b] Bairavi Shankar, BS,[c] Patrick M. Forde, MD,[c,d] David S. Ettinger, MD,[c] Kristen A. Marrone, MD,[c,d] Ronan J. Kelly, MD,[c,d] Christine L. Hann, MD,[c,d] Benjamin Levy, MD,[c,d] Josephine L. Feliciano, MD,[c,d] Julie R. Brahmer, MD,[c,d] David Feller-Kopman, MD,[a] Andrew D. Lerner, MD,[a] Hans Lee, MD,[a] Lonny Yarmus, DO,[a] Franco D'Alessio, MD,[a] Russell K. Hales, MD,[b] Cheng Ting Lin, MD,[e] Kevin J. Psoter, PhD,[f] Sonye K. Danoff, MD, PhD,[a] Jarushka Naidoo, MBBCh[c,d]

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[e]Department of Radiology, Johns Hopkins University School of Medicine, Baltimore, Maryland
[f]Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland

Received 5 July 2018; revised 22 August 2018; accepted 27 August 2018
Available online - 26 September 2018

Risk factors

RADIOTHERAPY

- KEYNOTE - 001

- Previous thoracic radiotherapy (63%)
- No previous thoracic radiotherapy (40%)

ORIGINAL RESEARCH

WILEY Cancer Medicine

Risk factors for pneumonitis in patients treated with anti-programmed death-1 therapy: A case-control study

Pengfei Cui[1,2] | Zhefeng Liu[1] | Guoqiang Wang[3] | Junxun Ma[1] | Yuanyu Qian[1] |

Prior thoracic radiotherapy					
No	37 (67.3)	96 (87.3)			
Yes	18 (32.7)	14 (12.7)	3.34	1.51-7.39	.003
Combination therapy					
No	21 (38.2)	69 (62.7)			
Yes	34 (61.8)	41 (37.3)	2.73	1.40-5.31	.003
Prior lung disease					
No	18 (32.7)	64 (58.2)			
Yes	37 (67.3)	46 (41.8)	2.86	1.45-5.64	.002

Diferential Diagnosis

Infectious pneumonia[1]	▪ Sudden onset, rapid illness progression ▪ Productive cough and fever ▪ Clinical manifestation can differ according to the etiological agent
Chronic obstructive pulmonary disease (COPD)[2]	▪ Midlife onset; slow progression ▪ History of exposure to noxious particles ▪ Dyspnea ▪ Airflow limitation
Congestive heart failure[2,3]	▪ Fine basilar crackles on auscultation ▪ Dilated heart on chest radiography ▪ Pulmonary edema ▪ Volume restriction, not airflow limitation
Chemotherapy- and/or drug-induced pneumonitis[4]	▪ Temporal association with exposure to causative agent and development of respiratory signs and symptoms
Radiation-induced pneumonitis[5]	▪ Lung fibrosis usually confined to radiation port
Tumor progression	▪ Typically associated with radiographic changes

Immune-mediated pneumonitis

- Symptoms are nonspecific and can be difficult to distinguish from other etiologies
- Diagnosis is mainly one of exclusion and requires meticulous ruling out of all other possible etiologies

The relevant clinical study protocol should always be consulted for specific study-related information.

1. Fishman MC, et al. *Pulmonary disease.* In: Fishman MC, Hoffman AR, Klausner RD, Thaler MS, eds. Medicine. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2002.
2. Celli BR, et al. *Am J Respir Crit Care Med*. 2015;191(7):e4-e27.
3. Price DB, et al. *Mayo Clin Proc*. 2010;85(12):1122-1129.
4. Matsuno O. *Respir Res*. 2012;13:39.
5. Choi YW, et al. *Radiographics.* 2004;24(4):985-997.

Tests to Confirm the Diagnosis

Imaging: Chest x-ray and CT scan[1,2]	▪ Ground-glass opacities (GGO); often seen in lung cancer patients ▪ Cryptogenic organizing pneumonia (COP)-like; commonly present in patients with melanoma ▪ Hypersensitivity-type pneumonitis ▪ Interstitial-type pneumonitis
Pulmonary function tests[3,4]	▪ Arterial oxygen saturation via oximetry ▪ Lung diffusion (DLCO) testing ▪ Spirometry
Bronchoscopy and histology	▪ Bronchoscopy with bronchoalveolar lavage and lung tissue will help distinguish infections ▪ Varied histological features[1,3,5,6]

The study-related relevant clinical study protocol should always be consulted for specific information.

1. Naidoo J. Pneumonitis with anti–PD-1/PD-L1 therapy [presentation]. ECC 2015..
2. Naidoo J, et al. ECC 2015. Abstract 503.
3. Michot JM, et al. *Eur J Cancer.* 2016;54:139-148.
4. Dosing Modification and Toxicity Management Guidelines 19 August 2016 Version.
5. Chow LQ. *Am Soc Clin Oncol Educ Book.* 2013. doi:10.1200/EdBook_AM.2013.33.e280.
6. Peng B, et al. *BMC Cancer.* 2015;15:895.

Bronchoscopy

- Bronchoscopy with bronchoalveolar lavage (BAL) is a minimally invasive, well-tolerated clinical tool
- Combined with clinical data and radiographic imaging
- Rule out other diseases (infection malignancy)
- When the clinical picture is consistent with pneumonitis, biopsy is unnecessary.
- Transbronchial biopsy may have a role to rule out other etiologies like lymphangitic spread of tumor or infection.

Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: American Society of Clinical Oncology Clinical Practice Guideline
J Clin Oncol 36:1714-1768.

CTCAE v5 Definitions

Respiratory Disorders

AE[a]	Grade 1	Grade 2	Grade 3	Grade 4
Pneumonitis	• Asymptomatic **or** • Clinical or diagnostic observations only **or** • Intervention not indicated	• Symptomatic **or** • Medical intervention indicated **or** • Limiting instrumental ADL[b]	• Severe symptoms **or** • Limiting self care ADL[c] **or** • Oxygen indicated	• Life-threatening respiratory compromise **or** • Urgent intervention indicated (e.g. tracheotomy or intubation)

	Grade 1	Grade 2	Grade 3	Grade 4
Radiographic involvement	• Confined to one lobe of the lung or < 25% of lung parenchyma	• Involves more than one lobe of the lung or 25%-50% of lung parenchyma	• Involves all lung lobes or > 50% of lung parenchyma	

[a]AEs have been selected based on those most commonly observed with durvalumab and tremelimumab monotherapy and combination regimens; [b]Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money etc.; [c]Self care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications and not bedridden.
*Grade 5 definition: death.

ADL = activities of daily living; AE = adverse event; CTCAE = Common Terminology Criteria for Adverse Events version 5

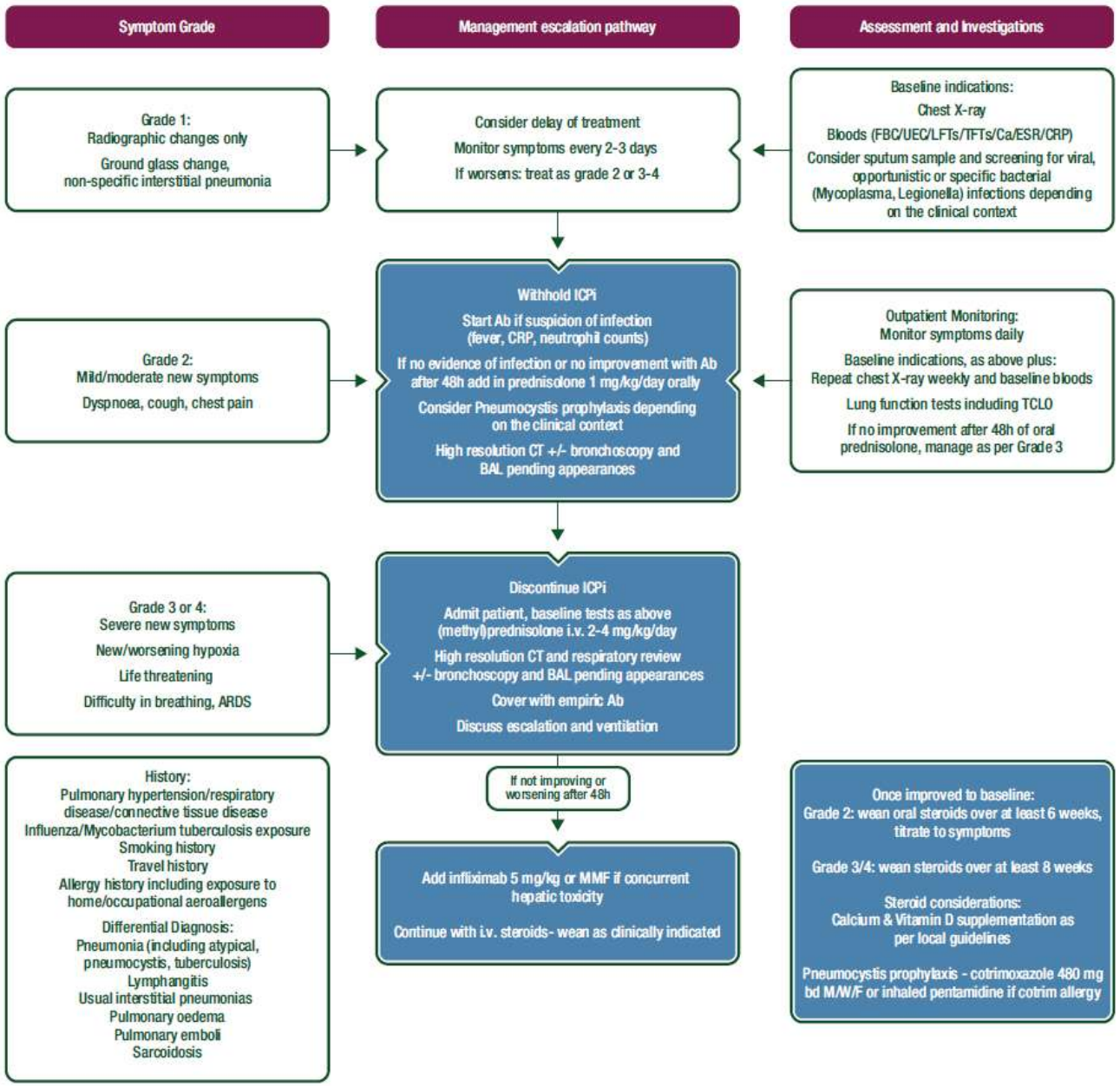
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

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

CLINICAL PRACTICE GUIDELINES

Management o
ESMO Clinical P
treatment and

J. B. A. G. Haanen[1], F. Carbonn
the ESMO Guidelines Commi



MANAGEMENT OF GRADE 1-2 PNEUMONITIS

Symptom Grade	Management escalation pathway	Assessment and Investigations
Grade 1: Radiographic changes only Ground glass change, non-specific interstitial pneumonia	Consider delay of treatment Monitor symptoms every 2-3 days If worsens: treat as grade 2 or 3-4	Baseline indications: Chest X-ray Bloods (FBC/UEC/LFTs/TFTs/Ca/ESR/CRP) Consider sputum sample and screening for viral, opportunistic or specific bacterial (Mycoplasma, Legionella) infections depending on the clinical context
Grade 2: Mild/moderate new symptoms Dyspnoea, cough, chest pain	Withhold ICPi Start Ab if suspicion of infection (fever, CRP, neutrophil counts) If no evidence of infection or no improvement with Ab after 48h add in prednisolone 1 mg/kg/day orally Consider Pneumocystis prophylaxis depending on the clinical context High resolution CT +/- bronchoscopy and BAL pending appearances	Outpatient Monitoring: Monitor symptoms daily Baseline indications, as above plus: Repeat chest X-ray weekly and baseline bloods Lung function tests including TCLO If no improvement after 48h of oral prednisolone, manage as per Grade 3

MANAGEMENT OF GRADE 3-4 PNEUMONITIS

Grade 3 or 4:
Severe new symptoms

New/worsening hypoxia

Life threatening

Difficulty in breathing, ARDS

History:
Pulmonary hypertension/respiratory disease/connective tissue disease
Influenza/Mycobacterium tuberculosis exposure
Smoking history
Travel history
Allergy history including exposure to home/occupational aeroallergens

Differential Diagnosis:
Pneumonia (including atypical, pneumocystis, tuberculosis)
Lymphangitis
Usual interstitial pneumonias
Pulmonary oedema
Pulmonary emboli
Sarcoidosis

Discontinue ICPi

Admit patient, baseline tests as above
(methyl)prednisolone i.v. 2-4 mg/kg/day

High resolution CT and respiratory review
+/- bronchoscopy and BAL pending appearances

Cover with empiric Ab

Discuss escalation and ventilation

If not improving or worsening after 48h

Add infliximab 5 mg/kg or MMF if concurrent hepatic toxicity

Continue with i.v. steroids- wean as clinically indicated

Once improved to baseline:
Grade 2: wean oral steroids over at least 6 weeks, titrate to symptoms

Grade 3/4: wean steroids over at least 8 weeks

Steroid considerations:
Calcium & Vitamin D supplementation as per local guidelines

Pneumocystis prophylaxis - cotrimoxazole 480 mg bd M/W/F or inhaled pentamidine if cotrim allergy

Re-Challenge ICIs after Pneumonitis

In Grade 1 and 2 pneumonitis we can re-challenge the drug with careful patient selection

Subjects with incidence of Grade 3 and 4 pneumonitis should be permanently discontinued from immunotherapy

JOURNAL OF CLINICAL ONCOLOGY
Official Journal of the American Society of Clinical Oncology

Total No 915

12/43 pts Re-challenge Immunotherapy

9 GR 1
Of 17pts 53%

3 GR 2
Of 14pts 21%

Initially Cortico-steroids p.o

Re-challenge

1 pt Relapsed — **Drug Holding**

2 pts Relapsed — **Corticosteroids**

Naidoo J. et al Pneumonitis in patients treated with anti PD-1/PD-L1 therapy; J Clin Oncol2016.68.2005

NCCN management of toxicity related to immunotherapies, 2016

Sarcoidosis-Like Reactions

REVIEW ARTICLE

Sarcoidosis-Like Reactions Induced by Checkpoint Inhibitors

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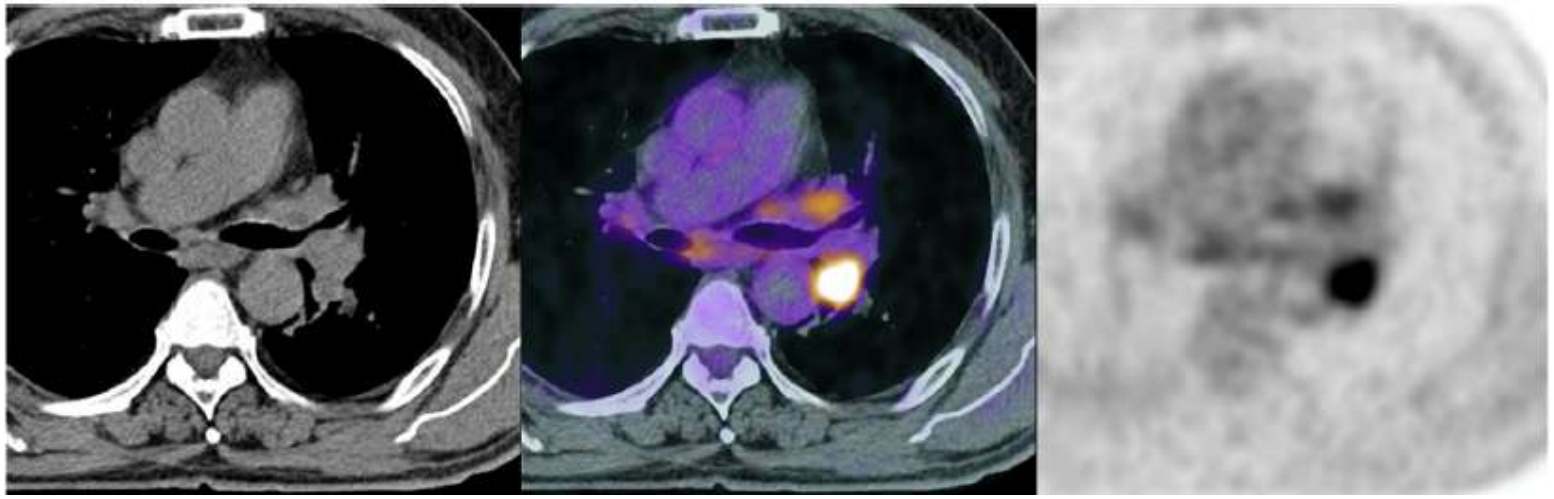
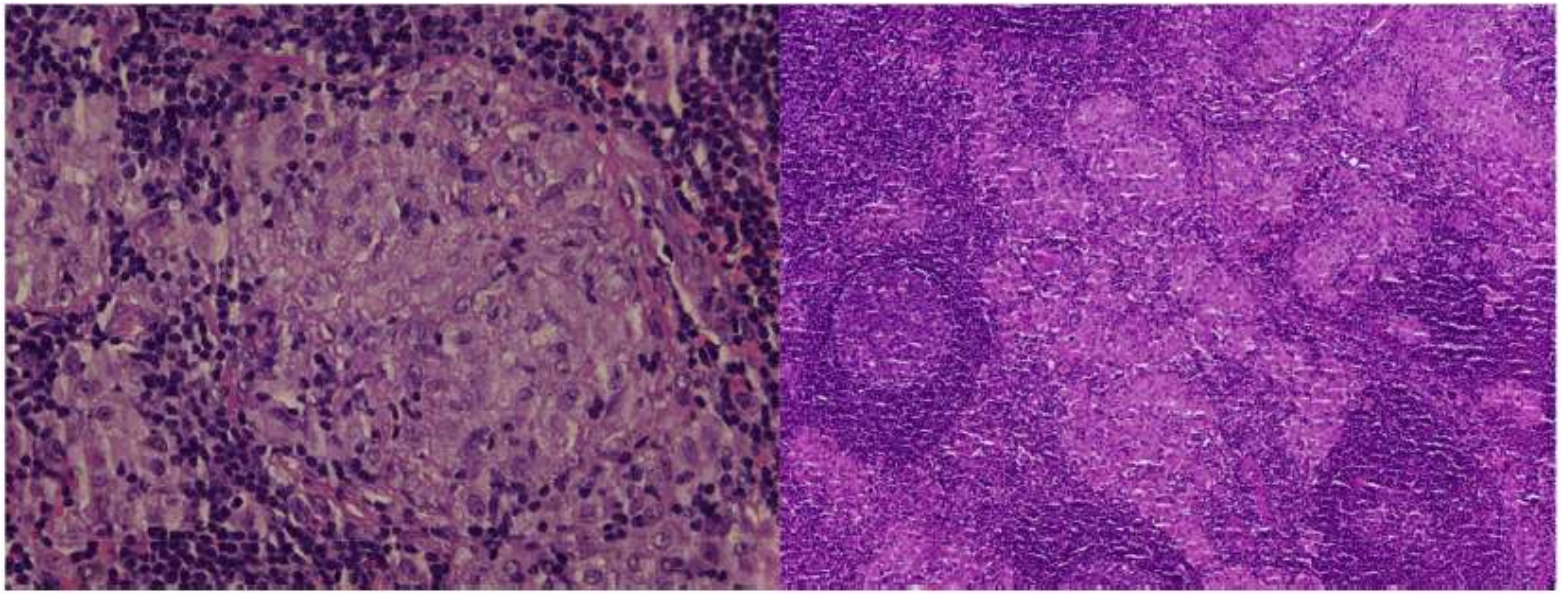
Sarcoidosis-Like Reactions

- Most common ICI : IPILIMUMAB(5%), NIVOLUMAB, PEMBROLIZUMAB(<0,5%)
- Most common underlying malignancies: Melanoma, Prostate Carcinoma, Hodgkin's lymphoma ,Uterine leiomyosarcoma, Lung Cancer
- Time of onset: 3 weeks – 2 years (≤36 weeks)
- Organ involved : Mediastinal lymph node, skin ,lung, extrathoracic lymph node, spleen, neural tissue, eye, bone
- Radiological Findings: pulmonary nodules and mediastinal lymphadenopathy, intra-abdominal lymphadenopathy, Ground-glass pulmonary infiltrates



Sarcoidosis-Like Reactions

PATHOLOGY



Identical to that of sarcoidosis
Focal infiltration by noncaseating epithelioid and giant cell granulomas
These lesions can coalesce into micronodules

Sarcoidosis-Like Reactions

MANAGEMENT

- Action not always needed

Persistent patients' symptoms: fatigue, fever, and dyspnea → initiation of corticosteroid treatment

- If checkpoint inhibitor therapy shows a significant beneficial effect against a cancer but induces a sarcoidosis-like reaction, it may be prudent to continue checkpoint inhibitor therapy and add anti-sarcoidosis therapy

- In cases of a sarcoidosis-like reaction where the checkpoint inhibitor therapy has been equivocal or ineffective, discontinuation of ICI could be considered, which should resolve the sarcoidosis-like reaction.

SUMMARISING

- **Always look and ask for side effects,**

half of patients with pneumonitis are asymptomatic and 1/3 had negative CXR

- **Always ask for HRCT** if you suspect pneumonitis

- ***Education of specialists***
- ***Specialists collaborations***
- ***Education of patients for early detection of irAE***

- **Treat Sarcoidosis-like reactions when symptoms occur –According to response to treatment**

- **More combinations potentially more side effects**