

# ICLIO Webinar: Immuno-Oncology: From a Community Radiologist Perspective

**Michael J. DeLeo III, MD**

Foundation Medical Partners

Southern New Hampshire Health System

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INSTITUTE  
FOR CLINICAL  
IMMUNO-ONCOLOGY



[accc-iclio.org](http://accc-iclio.org)

# Overview

- Review the four patterns of response to immunotherapy and their imaging findings.
- Review immune-related adverse events and their imaging findings.
- Dive into the role of the radiologist in caring for the patient on immune therapy.

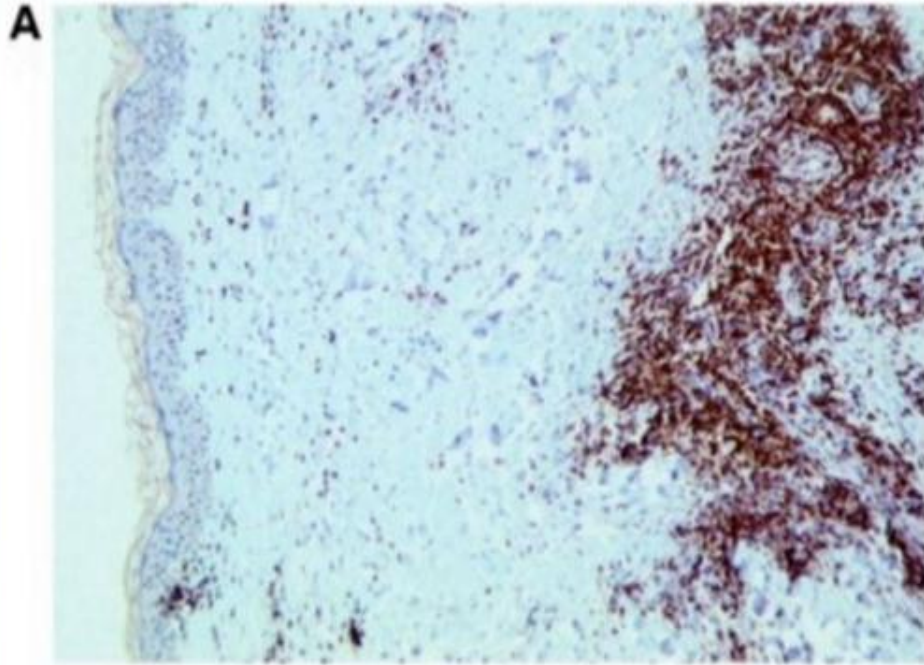
# References

- Mahony NO, McCarthy E, Johnston C; Dublin/IE. ECR 2012 Educational Exhibit. A Review of the Radiological Features of the Side Effects of Novel Immunotherapies in the Treatment of Malignancy.
- Kwak JJ, Tirumani SH, Van den Abbeele AD, Koo PJ, Jacene HA. Cancer immunotherapy: imaging assessment of novel treatment response patterns and immune-related adverse events. *Radiographics*. 2015;35:424-37.

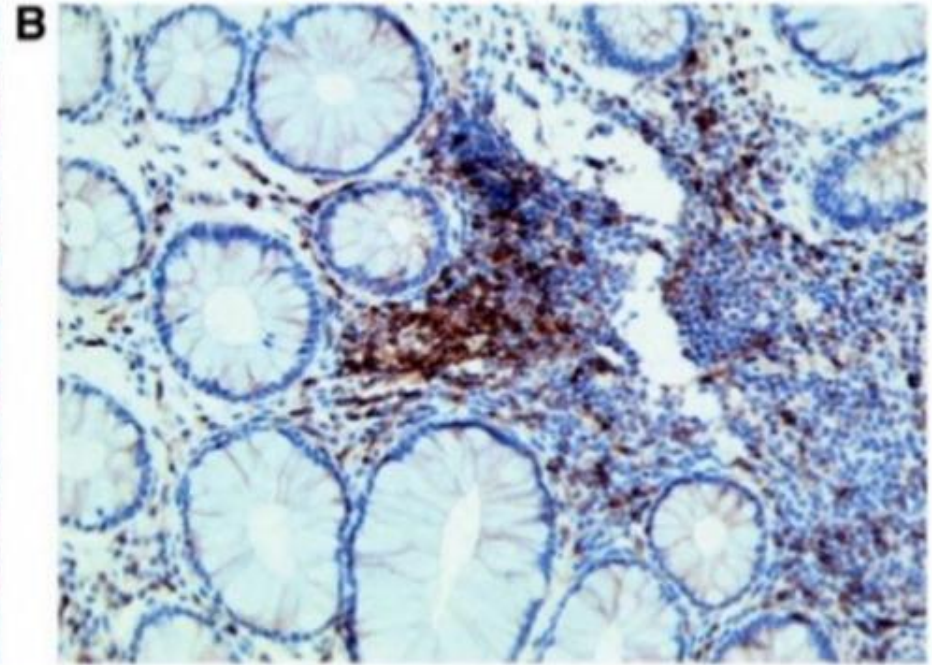
# Brief I-O Background

- Therapies that stimulate the immune system to target and kill cancer cells vs. traditional cytotoxic chemotherapeutics.
- Focus here on ipilimumab: human monoclonal antibody that blocks cytotoxic lymphocyte-associated antigen-4 (CTLA-4).
- CTLA-4 is a negative regulator of T-cell activation, so blocking CTLA-4 promotes T-cell activation and tumor targeting.

# T-cell infiltration post-CTLA-4 Ab



Skin



Bowel

Source: Sarnaik and Weber. 2009. Cancer J. 15(3)169-73.

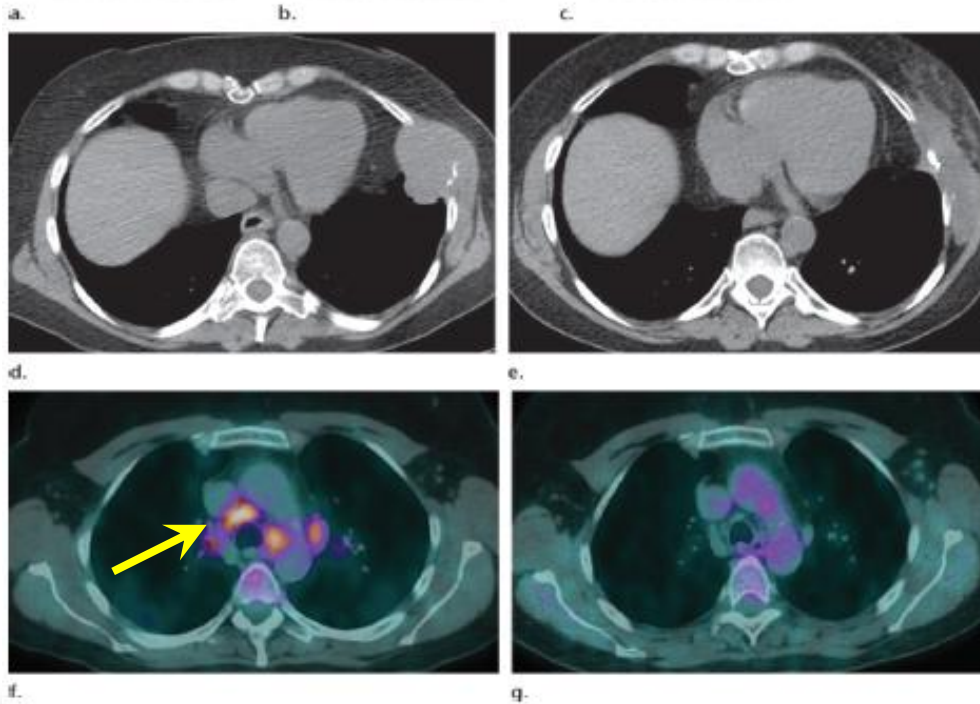
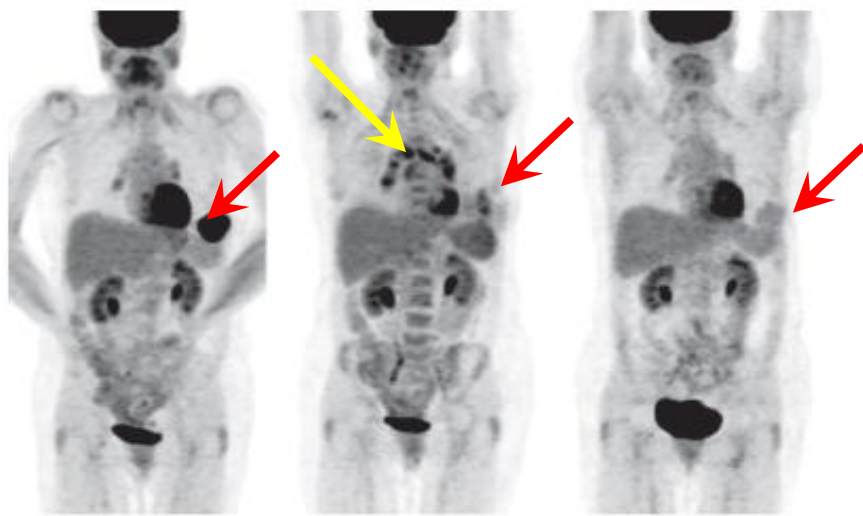
# Doctors Face a New Challenge

- Measuring response to cytotoxic chemotherapy is easy: RECIST.
- Measuring response to I-O therapy is not: Four patterns of response to active immune therapy have been characterized.
- Radiologists sit at the center of clinical decision making and must be familiar with emerging therapies.

# Patterns of Response: 1

- Decrease in size of index lesions
- No new lesions





Complete  
metabolic  
response

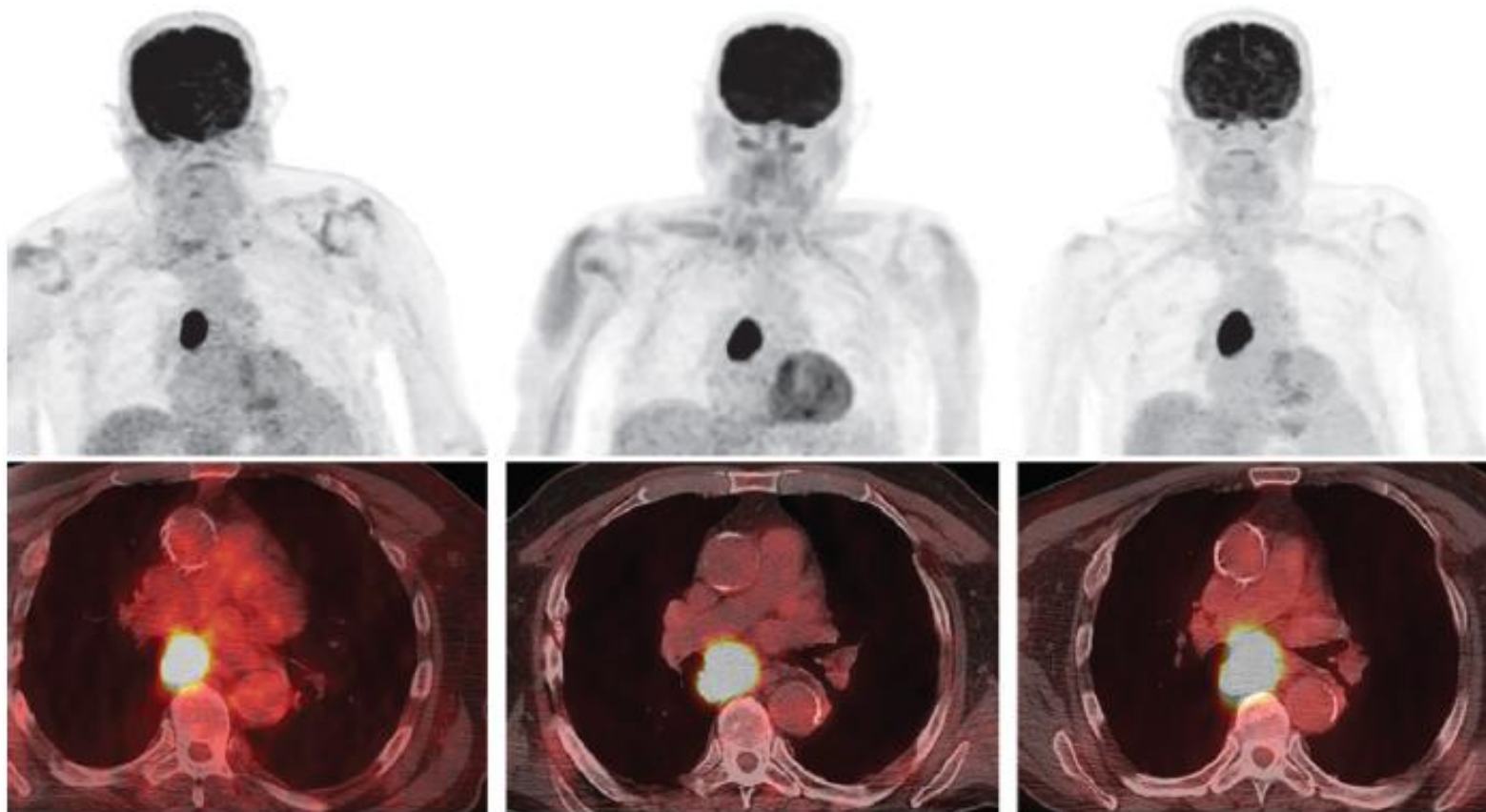
Sarcoid-like  
adenopathy,  
resolved following  
treatment (irAE)



# Patterns of Response: 2

- Clinically stable disease after completion of treatment
- Long period of disease stability followed by decreased tumor burden

# Stable Disease



2  
months

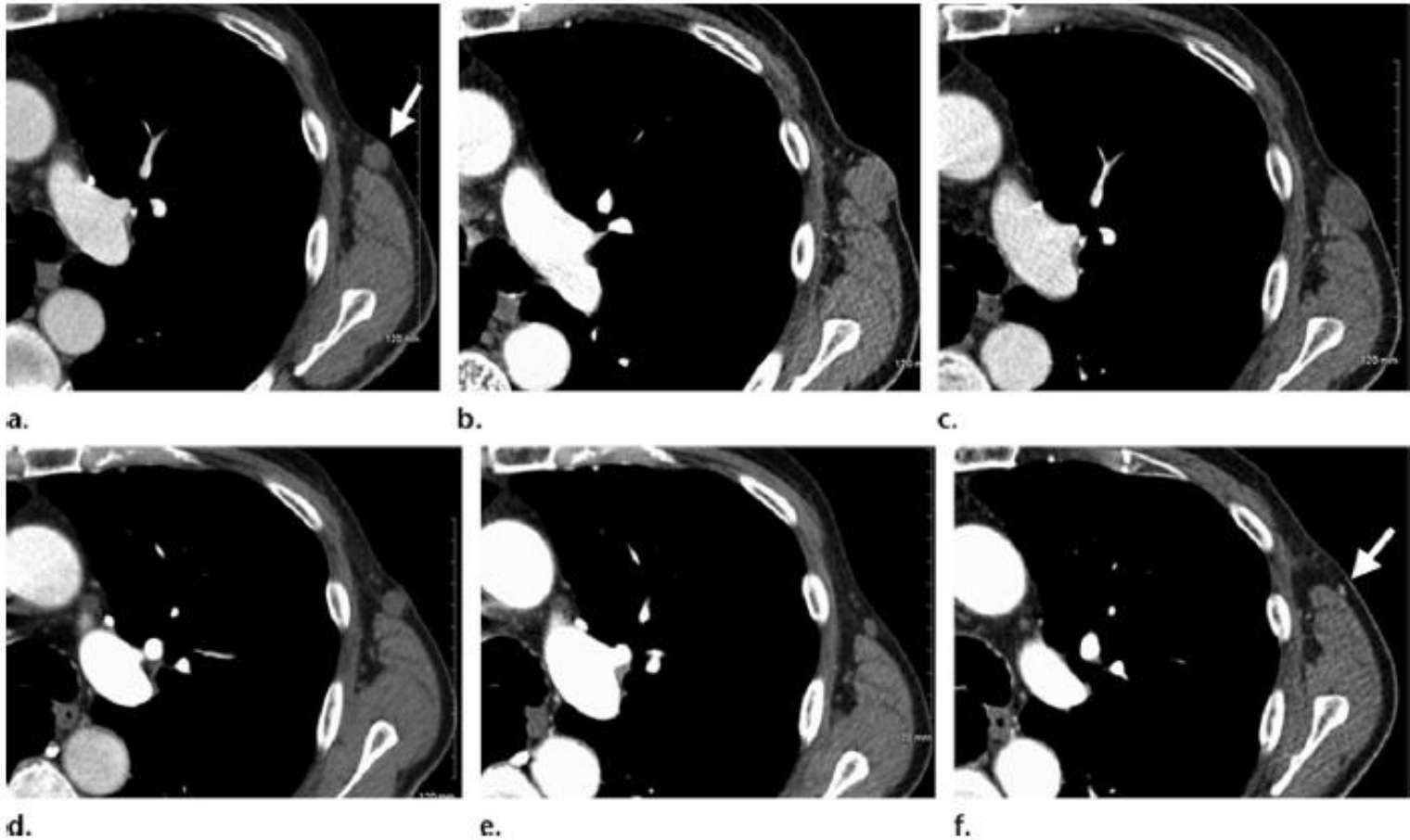
4  
months

7  
months

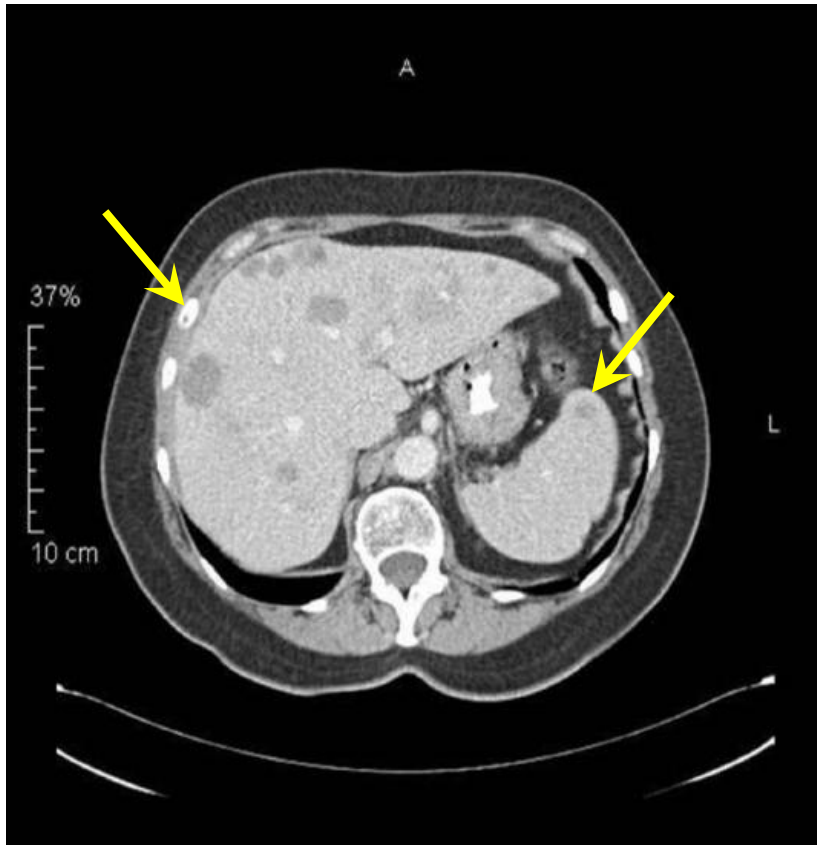
# Patterns of Response: 3

- Initial increase in tumor size followed by a decreased tumor burden
- As body mounts an immune response, see a transient increase in tumor size due to inflammatory cell infiltrates +/- edema

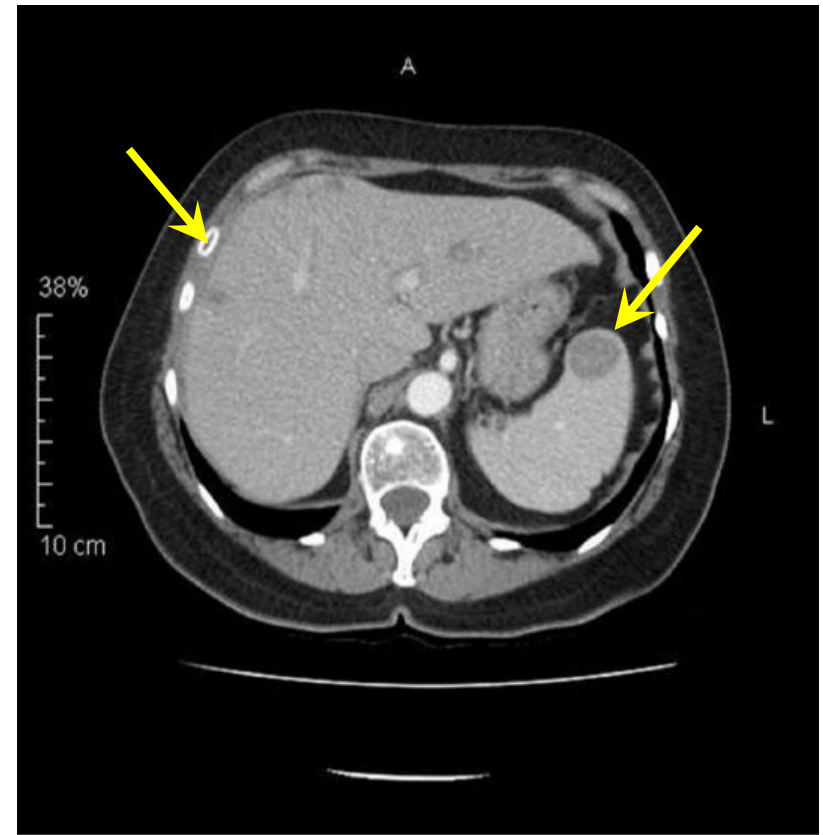
# Tumor enlargement followed by treatment response



# 67 year old woman with metastatic melanoma



Pre-ipilumamab



Post-ipilumamab

Can see a “mixed response” to active immune therapy

# Patterns of Response: 4

- New lesions after completion of treatment followed by decrease in tumor burden
  - Presumed micrometastases not previously visible
  - Due to T-cell infiltrates
  - \*Not necessarily a treatment failure. Therefore a follow-up scan, ideally of the same modality, should be performed in 4 weeks.

# Immune-Related Response Criteria

- Radiologists and other care team members must be well-versed in the new irRC.



# Immune-related response criteria

## Overall Response Using the Immune-Related Response Criteria (irRC)

Complete response (CR)	Complete disappearance of all lesions; confirmed in a repeat, consecutive assessment $\geq 4$ weeks from baseline assessment
Partial response (PR)	$\geq 50\%$ reduction in tumor burden from baseline; confirmed in a repeat, consecutive assessment $\geq 4$ weeks from baseline assessment
Stable disease (SD)	Changes in tumor burden do not meet the criteria for CR, PR, or PD
Progressive disease (PD)	$\geq 25\%$ increase in tumor burden relative to nadir (minimum tumor burden) at any time point; confirmed in a repeat, consecutive assessment $\geq 4$ weeks from prior assessment

<http://acc-iclio.org/resources/assessing-immunotherapy-response-why-irrc-matters> . Accessed 11/14/2016.

# irRC

- Initial imaging follow-up following therapy
- Follow-up imaging 4 weeks post-therapy
- Due to potential for delayed response

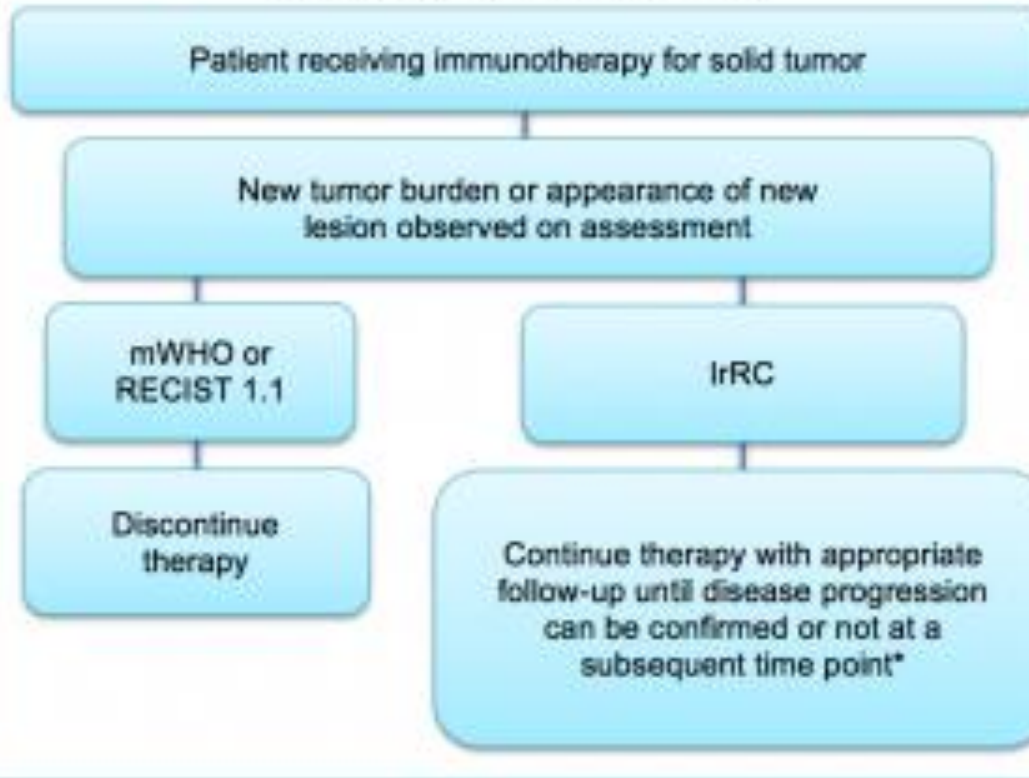
# Challenges We Face

- irRC does not specify modality
  - CT, MRI, PET/CT
- irRC does not assess tumor metabolism (PET), and PET tends to be a preferred imaging modality

# Challenges We Face

- The key clinical question, which is often impossible to differentiate, is response to therapy vs. inflammation
  - Follow-up scans when patient is clinically stable or has a clinical improvement
  - Investigation of novel PET tracers

## Simplified schematic of potential patient outcomes utilizing conventional tumor assessment metrics vs. irRC



\*Assuming immunotherapy benefits > risks (i.e. patient performance status is stable, lab values haven't significantly deteriorated, and/or moderate tumor growth)

<http://acc-icllo.org/resources/assessing-immunotherapy-response-why-irrc-matters/>. Accessed 11/14/2016.

# Challenges We Face

- With any new therapy, closely monitoring the potential adverse events (irAEs) is critical.
- Radiologists play a key role in recognizing and diagnosing immune-related adverse events.
- Radiologists must be well-versed on the imaging findings of irAEs.
- Radiologists must communicate any potential irAEs in a timely fashion.

# Immune-Related Adverse Events

- CTLA-4 irAEs:
  - GI: colitis, hepatitis
  - Skin: dermatitis
  - Endocrine: hypophysitis
- Most occur during the 12 weeks of treatment
- Median onset of irAEs:
  - Skin: 3 weeks
  - Hepatitis: 3-9 weeks
  - GI: 8 weeks
  - Endocrine: 7-20 weeks



# Immune-Related Adverse Events

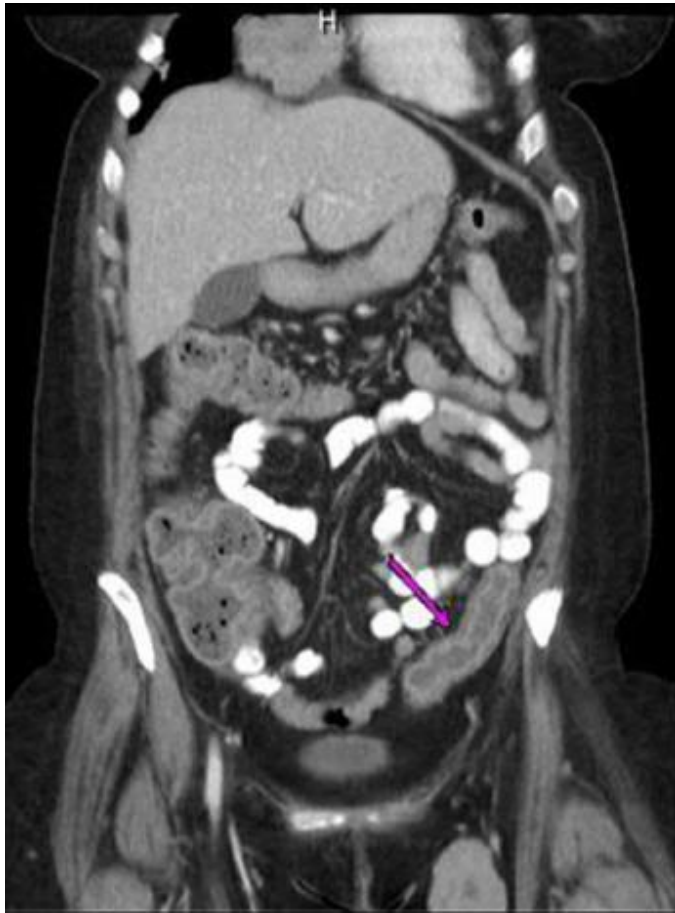
- Colitis

- Most severe and deadly irAE
- Treatment matters: steroids +/- antibiotics
- Diffuse vs. Segmental
- Diffuse: watery diarrhea, tx: steroids
- Segmental: watery + bloody diarrhea, tx: steroids + ABX

# Segmental colitis on ipilimumab



48 year old woman with abdominal pain 2 months post-ipilimumab

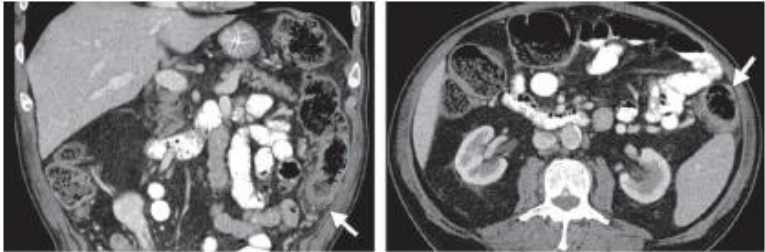


Segmental colitis



Colonic perforation

# Autoimmune colitis

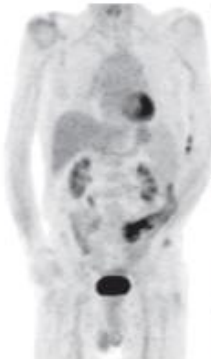
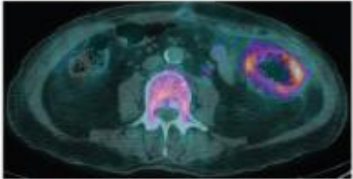


a.

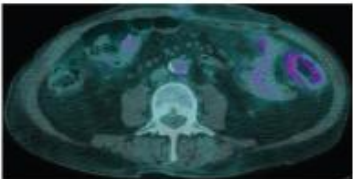
b.



c.

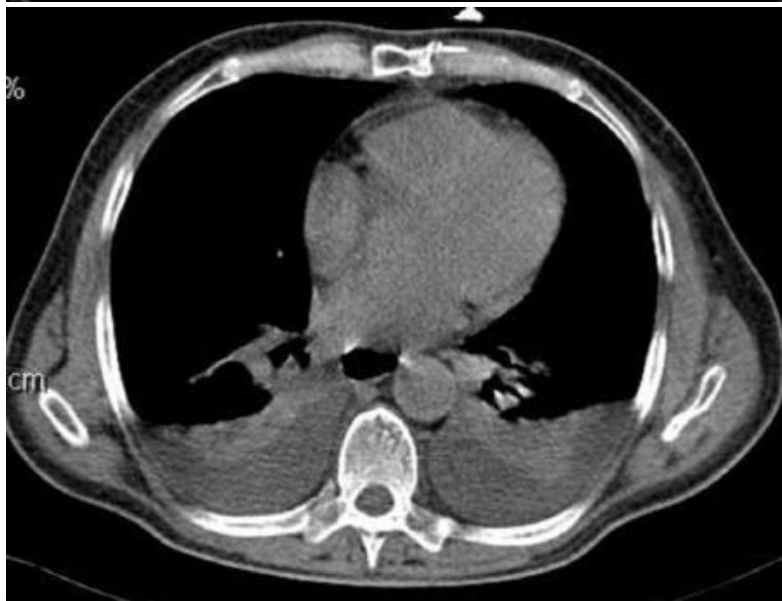
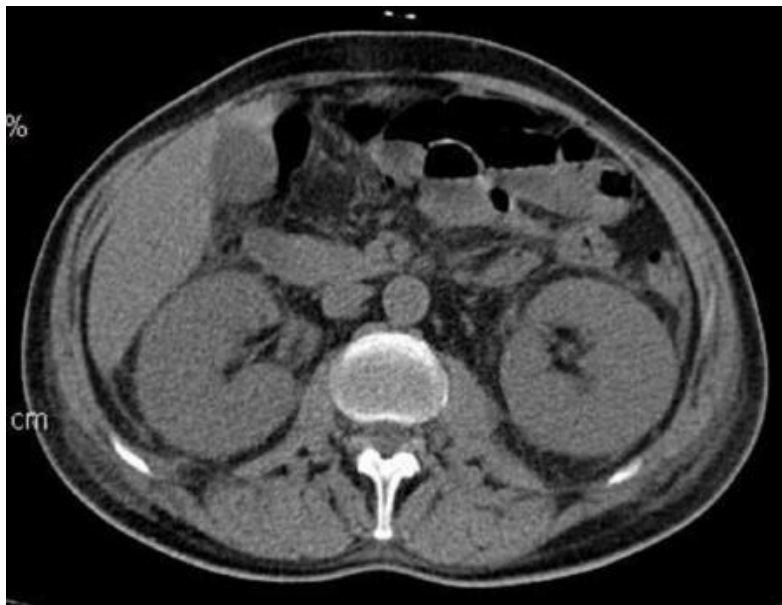


d.



# Immune-Related Adverse Events

- Hepatitis
  - Periportal edema
- Nephritis
  - Renal enlargement



Bilateral nephritis with reactive pleural effusions 2 months post-ipilimumab therapy initiation

# Immune-Related Adverse Events

- Endocrinopathies

- Hypophysitis

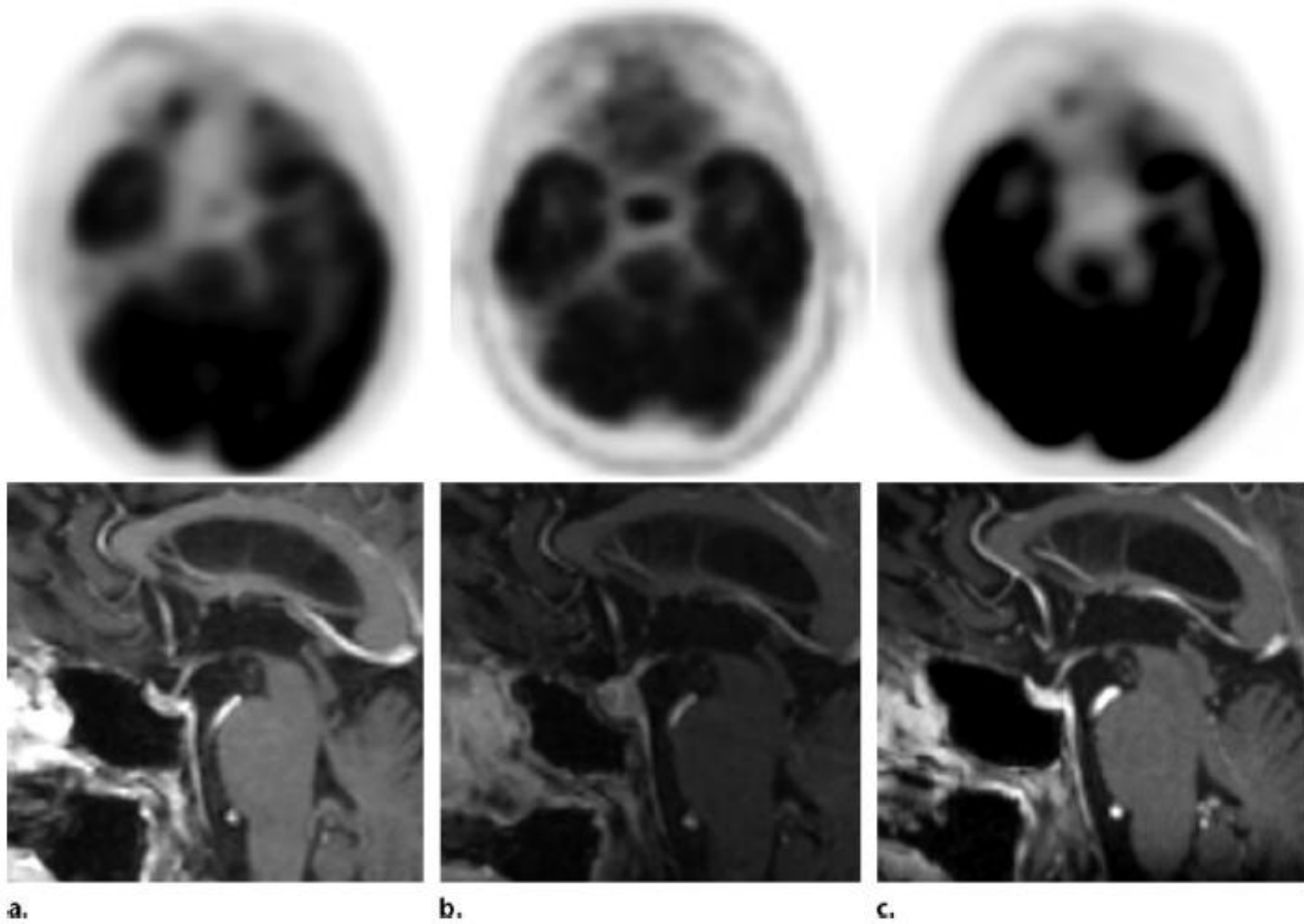
- Increased FDG avidity + pituitary enlargement
    - Should resolve / normalize following steroids

- Thyroiditis

- Findings of thyrotoxicosis on I-123 study



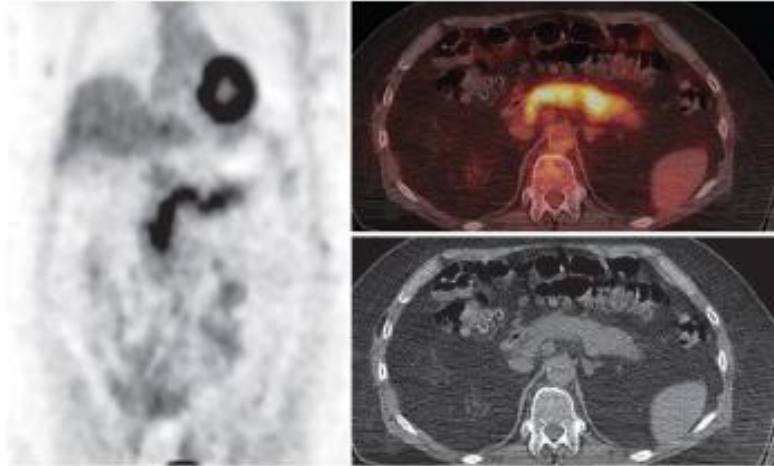
# Autoimmune hypophysitis



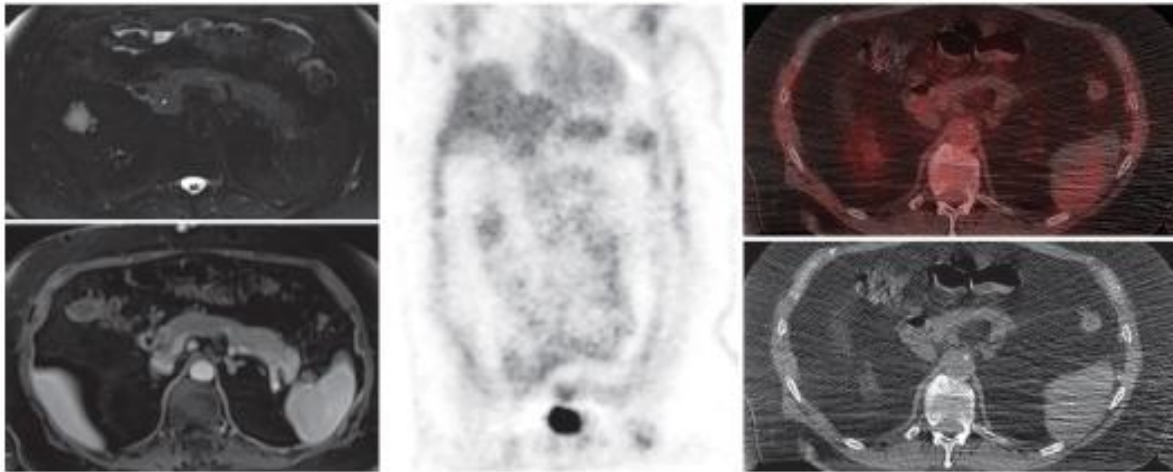
# Immune-Related Adverse Events

- Pancreatitis\*
- Myositis
- Arthritis
- Sarcoid-like reaction\*
- Vasculitis

# Autoimmune pancreatitis



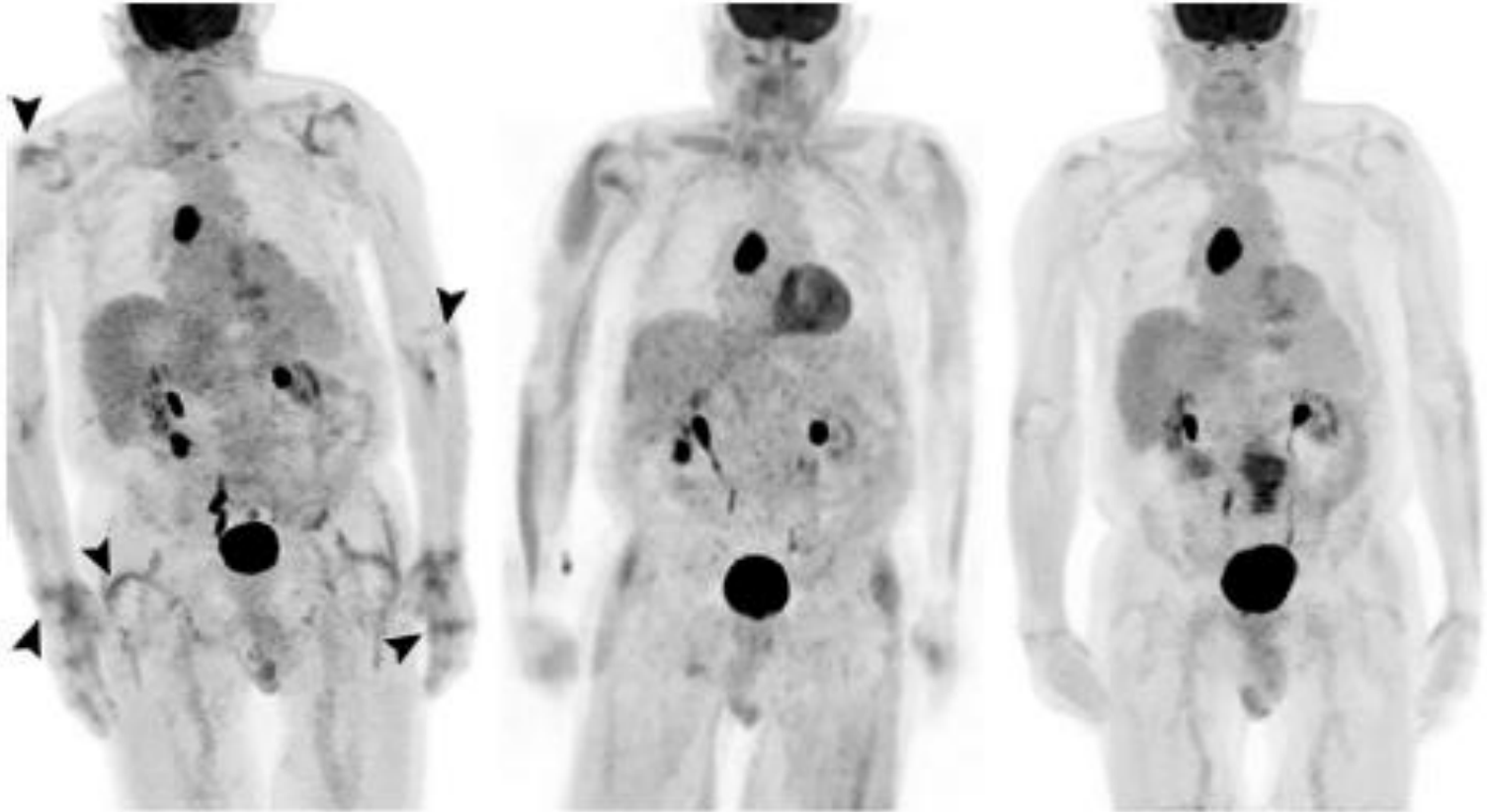
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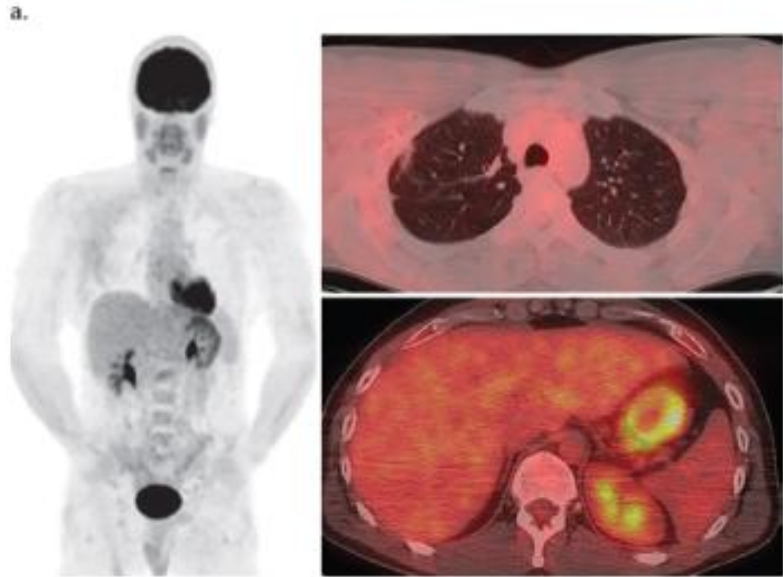
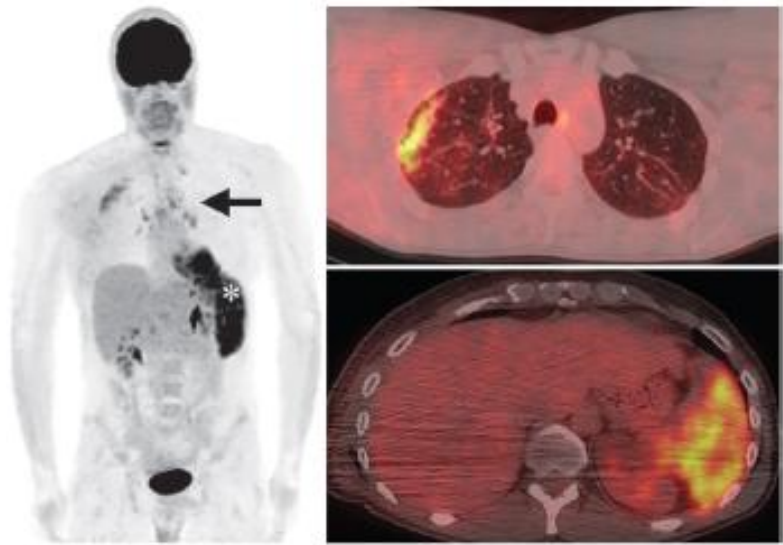


b.

c.

# Autoimmune arthritis



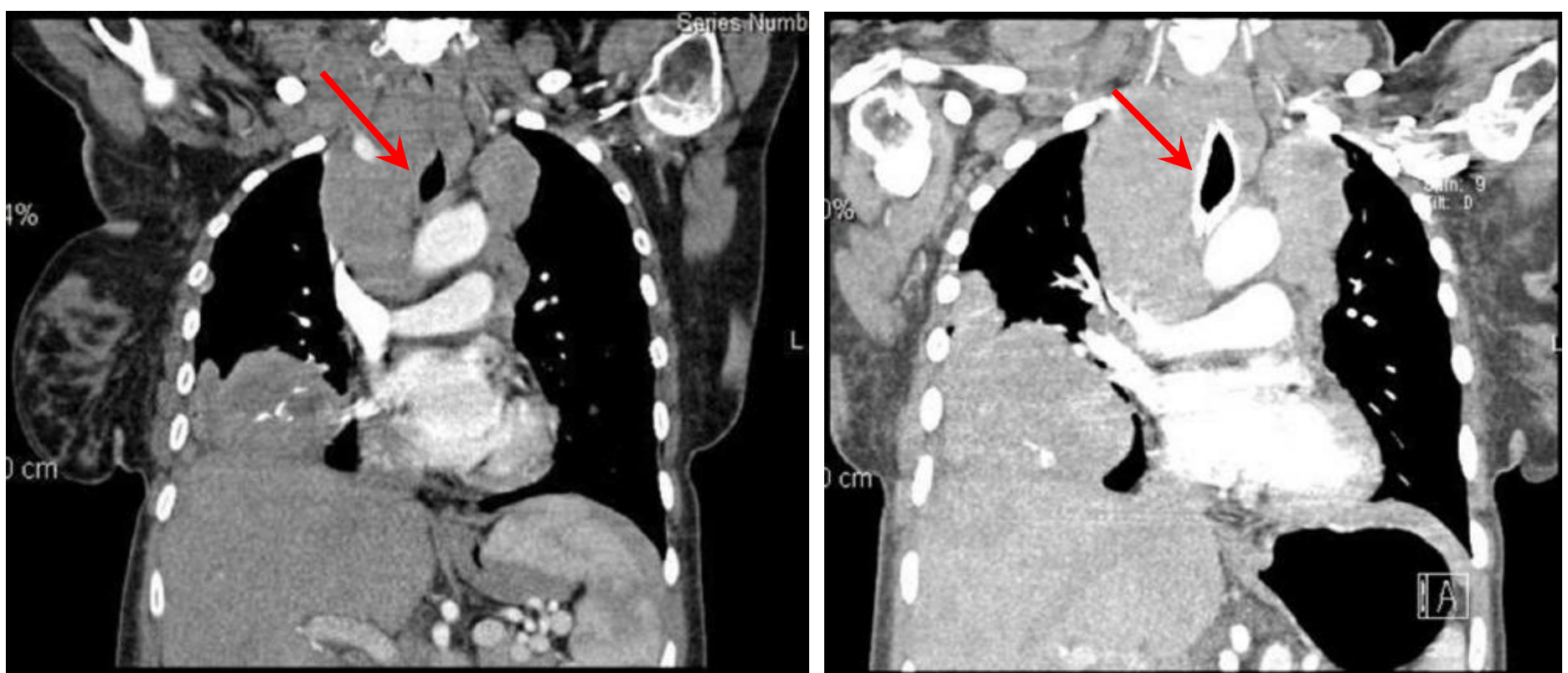


# Sarcoid-like reaction

# Immune-Related Adverse Events

- May be fewer, less severe irAEs with anti-PD-1/PD-L1 antibodies compared with anti-CTLA-4 antibodies. We will have to see...

# Flare Phenomenon



Flare phenomenon requiring tracheal stenting



# Our Experience

- Southern New Hampshire Health System (SNHHS) is a 188-bed regional health system serving about 100,000 patients a year and has a large physician network with over 500 primary/specialty providers.
- SNHHS is a clinical affiliate of Massachusetts General Hospital (MGH).
- Three MGH oncologists see patients at SNHHS.
- Patients are enrolled in clinical trials at MGH. These patients usually get their imaging at MGH.
- Patients not on trials can get their imaging anywhere.

# The Radiologist Perspective

- Oncologists, pathologists, and radiologists, should know each other well. Confidence in our colleagues is a key component of quality care delivery.
- Regular participation in multidisciplinary conferences is key.
- Important for radiologists to know what clinical trials are available to patients at your facility.

# The Radiologist Perspective

- Patient history is key: is it critical for radiologists to know when a patient is on active immune therapy as imaging studies must be interpreted in the proper clinical context.
- Oncologists and radiologists should try to come to a consensus about appropriate imaging modalities (CT / MRI / PET) and follow-up intervals. \*This may vary from practice to practice.

# The Radiologist Perspective

- In a small-to-medium sized group, consider having dedicated readers.
- All caregivers should be well-versed in both RECIST and irRC.
- What do your oncologists want in a report?

# The Radiologist Perspective

- Since only a limited number of active immune therapy agents are on the market, all caregivers should be familiar with their individual side effects, especially those that manifest on imaging studies.
- The radiologist must communicate any potential adverse event immediately to the oncology team. Some can be immediately life-threatening.

# The Radiologist Perspective

- As community hospitals partner with academic centers, the complexity of patients seen in the community is likely to increase.
- Patients may be primarily cared for in the community and travel to affiliated academic centers for clinical trials.
- Access to prior imaging studies may be a challenge.

# What does the future hold?


- As more therapies enter the market, imaging needs may change. How do we adapt?
- Can community hospitals offer the technologies needed to treat these patients?
- Concept of “steerage” in the insurance market has the potential to fragment care as patients may seek or be steered toward lower cost imaging facilities.

# Questions?



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