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

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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


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

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

Can see a “mixed response” to active immune therapy

Post-ipilumamab
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

<table>
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<tr>
<th>Overall Response Using the Immune-Related Response Criteria (irRC)</th>
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<tr>
<td><strong>Complete response (CR)</strong> Complete disappearance of all lesions; confirmed in a repeat, consecutive assessment ≥ 4 weeks from baseline assessment</td>
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<tr>
<td><strong>Partial response (PR)</strong> ≥50% reduction in tumor burden from baseline; confirmed in a repeat, consecutive assessment ≥ 4 weeks from baseline assessment</td>
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<td><strong>Stable disease (SD)</strong> Changes in tumor burden do not meet the criteria for CR, PR, or PD</td>
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<tr>
<td><strong>Progressive disease (PD)</strong> ≥25% increase in tumor burden relative to nadir (minimum tumor burden) at any time point; confirmed in a repeat, consecutive assessment ≥ 4 weeks from prior assessment</td>
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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

Patient receiving immunotherapy for solid tumor

New tumor burden or appearance of new lesion observed on assessment

mWHO or RECIST 1.1

Discontinue therapy

IrRC

Continue therapy with appropriate follow-up until disease progression can be confirmed or not at a subsequent time point*

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

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
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
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 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.
• 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?
Thank you for participating in the ICLIO e-Course. Presentation slides and archived recording will be available at accc-iclio.org