Society for Immunotherapy of Cancer

Advances in Cancer Immunotherapy™

Immune Checkpoint Inhibitors: Monitoring

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University of Washington

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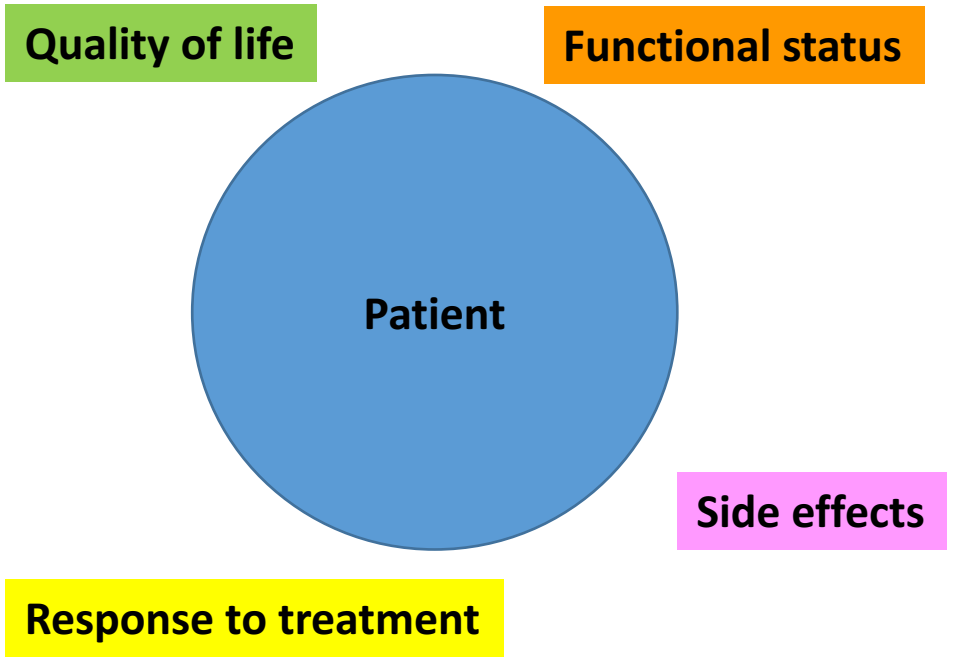
Disclosures

- Gilead Sciences (patent)
- I will be discussing non-FDA approved indications during my presentation.

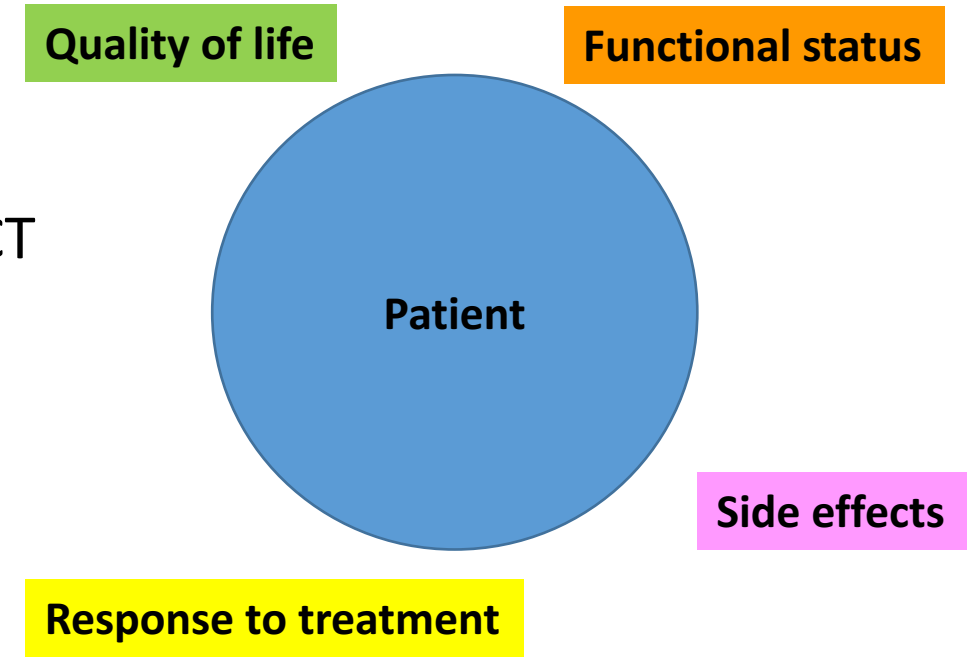
Overview

- Efficacy Monitoring
- Toxicity Monitoring



Overview

- Efficacy Monitoring
  - Recommendations
  - Pseudoprogression
  - Emerging imaging modalities: PET/CT
  - Emerging technologies: ctDNA
- Toxicity Monitoring
  - Recommendations
  - Limitations/pitfalls
  - Future directions



Efficacy monitoring: Recommendations

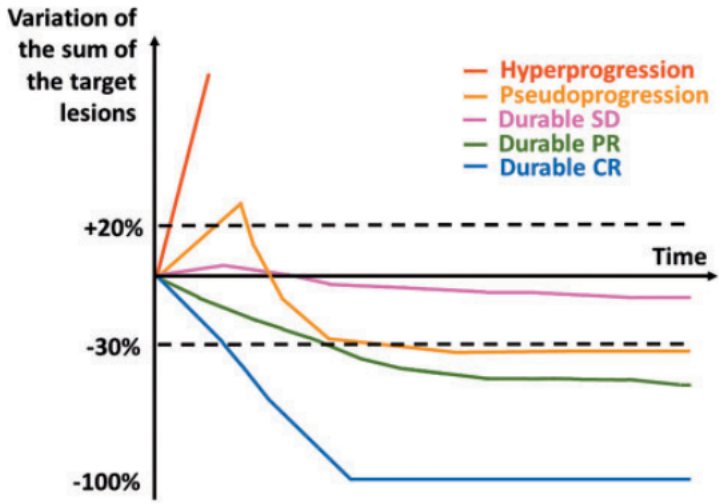
Imaging: every 6 – 12 weeks

- Cross-sectional imaging
- MRI brain if indicated

* Relevant to patients in solid tumor setting
* Other disease-specific response criteria may apply

Efficacy monitoring: Recommendations

Patterns of response



Borcoman et al. Novel Patterns of Response Under Immunotherapy. Annals Oncol 2019.

Hyperprogression

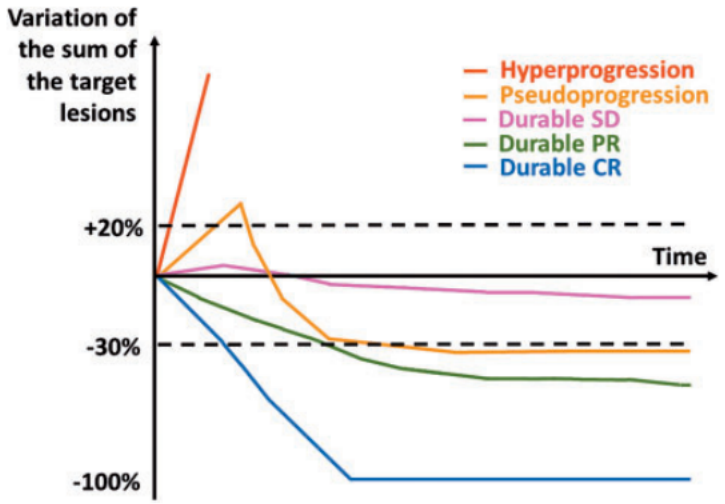
- Two-fold increase in tumor growth rate

Pseudoprogression

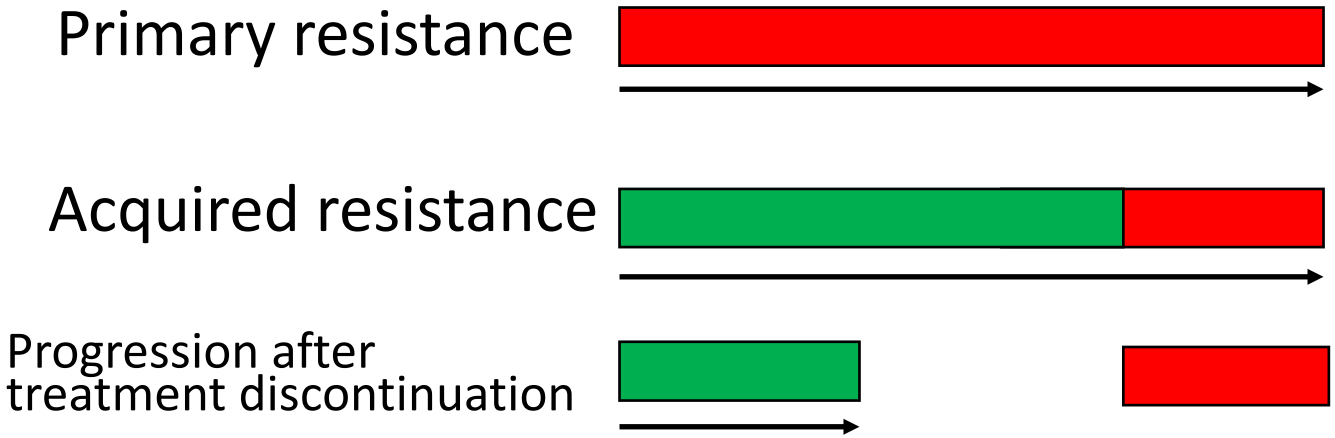
- Tumor shrinkage after initial radiological progression
- Occurs in 5 – 10% of patients receiving checkpoint immunotherapies

Efficacy monitoring: Recommendations

Patterns of response



Patterns of resistance



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Partial response, complete response, stable disease

Disease progression

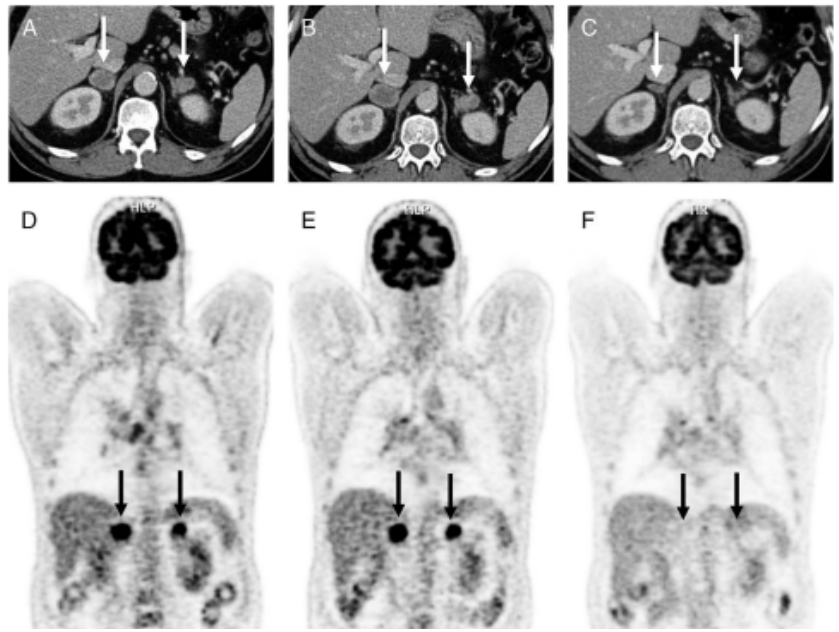
Efficacy monitoring:
Emerging imaging modalities

- PET/CT is an emerging imaging modality to assess checkpoint immunotherapy response, but requires further development
- PET/CT Changes During Chemoimmunotherapy and Radiation Therapy in Patients with Stage IV Non-Small Cell Lung Cancer (NCT04151940)

Pseudoprogression with PET/CT monitoring

CT

PET



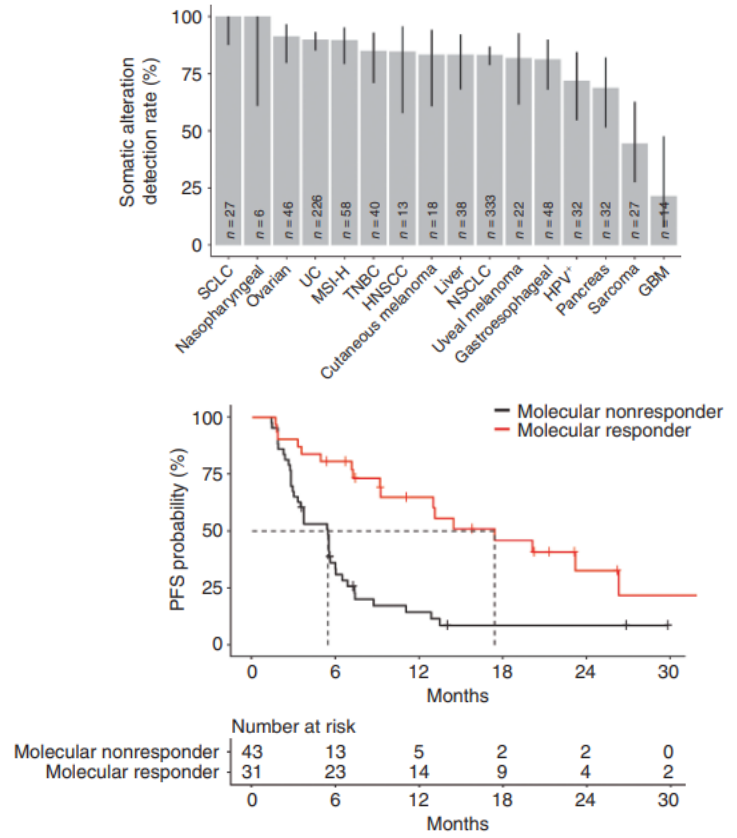
Beer et al. Comparison of RECIST, iRECIST, and PERCIST for the Evaluation of Response to PD-1/PD-L1 Blockade Therapy in Patients with Non-Small Cell Lung Cancer. Clin Nuc Med 2019.

Efficacy monitoring:
Emerging technologies-- ctDNA

- Circulating tumor DNA (ctDNA) is an emerging biomarker for identifying patients with clinical benefit from checkpoint immunotherapy
- Composite biomarkers combining multiple parameters, including ctDNA and circulating immune cell profiling, are a promising approach for predicting durable benefit

Nabet et al. Non-invasive Early Identification of Therapeutic Benefit from Immune Checkpoint Inhibitors. Cell 2020

Molecular response assessments



Zhang Q* and Luo J* et al. Prognostic and Predictive Impact of Circulating Tumor DNA in Patients with Advanced Cancers Treated with Immune Checkpoint Blockade. Cancer Discov 2020.

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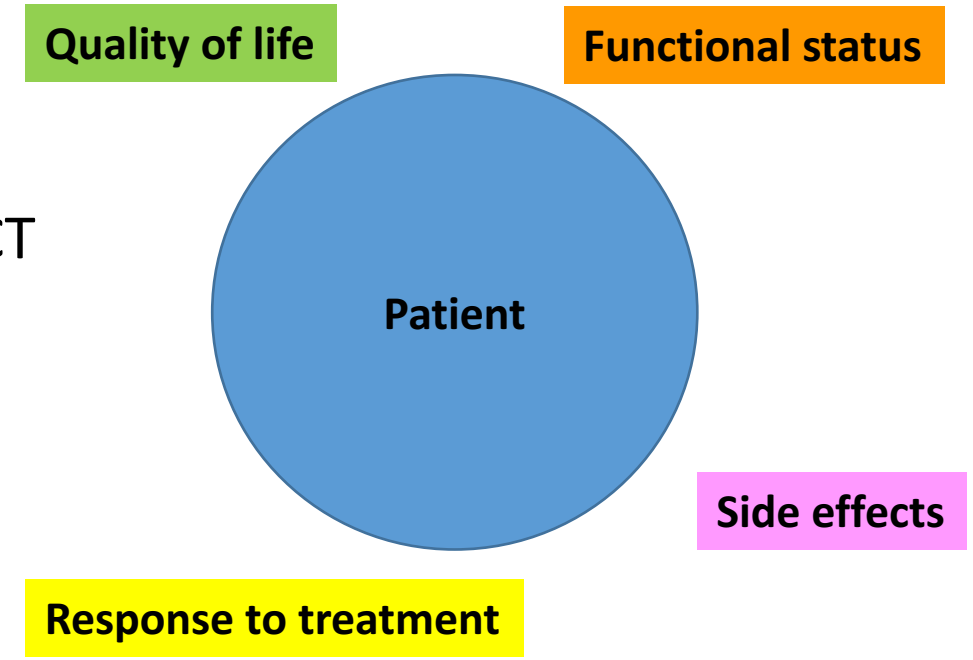
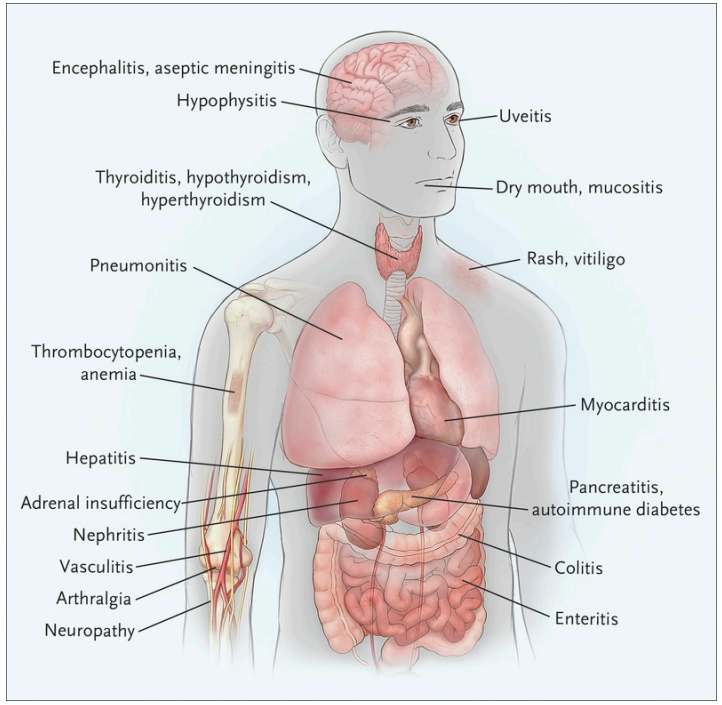


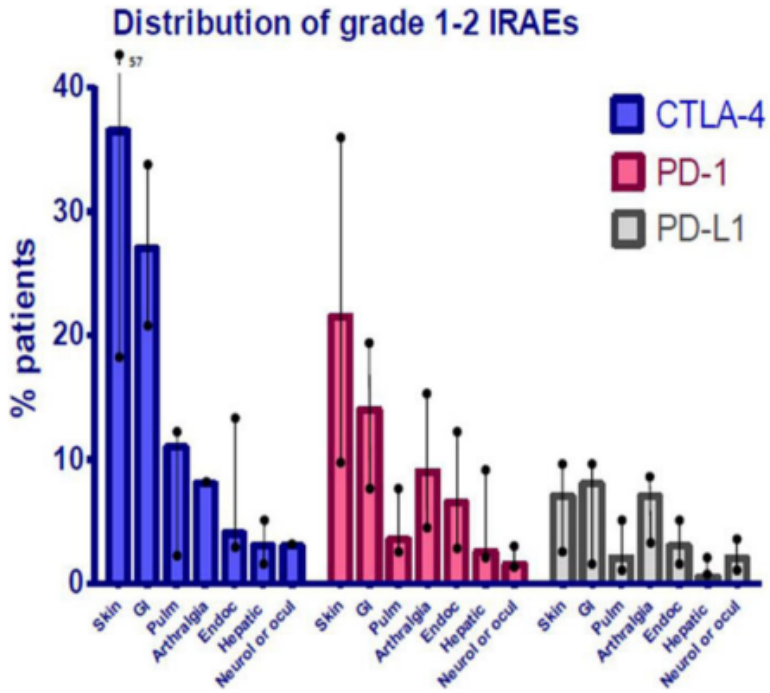
Toxicity monitoring:

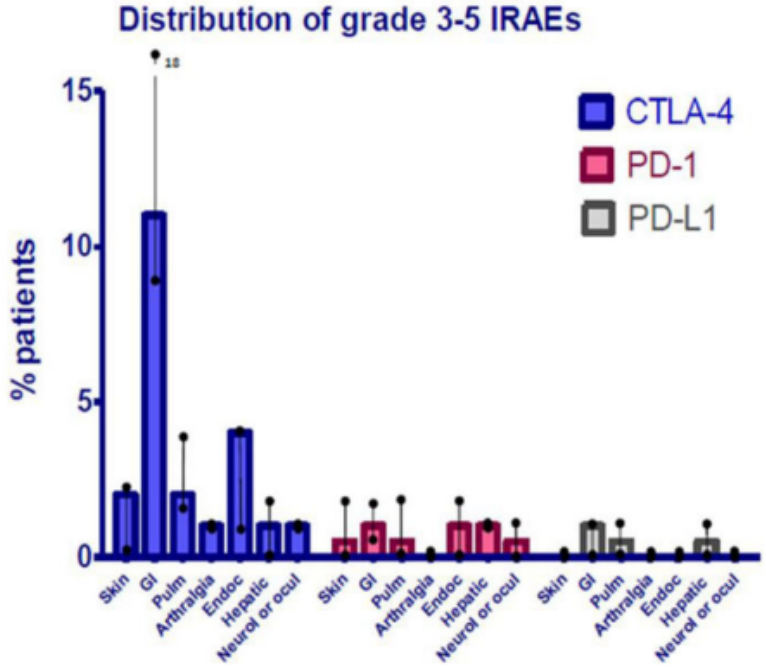
Sites of involvement



Postow et al. Immune-Related Adverse Events Associated with Immune Checkpoint Blockade. NEJM 2018.

Distribution of immune-related adverse events

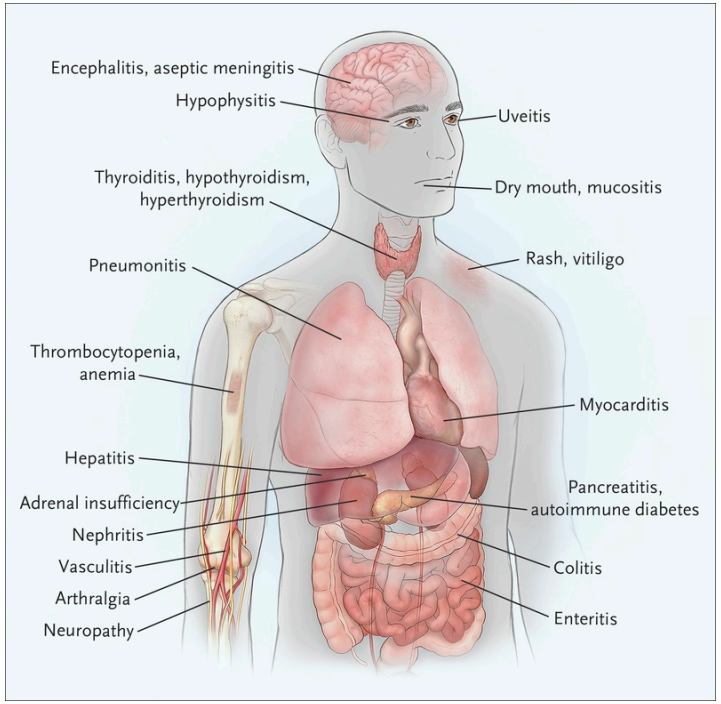




Michot et al. Immune-related adverse events with immune checkpoint blockade: a comprehensive review. Eur J Cancer 2016

Toxicity monitoring: Recommendations

Assessment pre-treatment	Monitoring frequency
Clinical: physical exam, infectious screening (HIV, hepatitis A, B, C) as indicated	At each clinic visit



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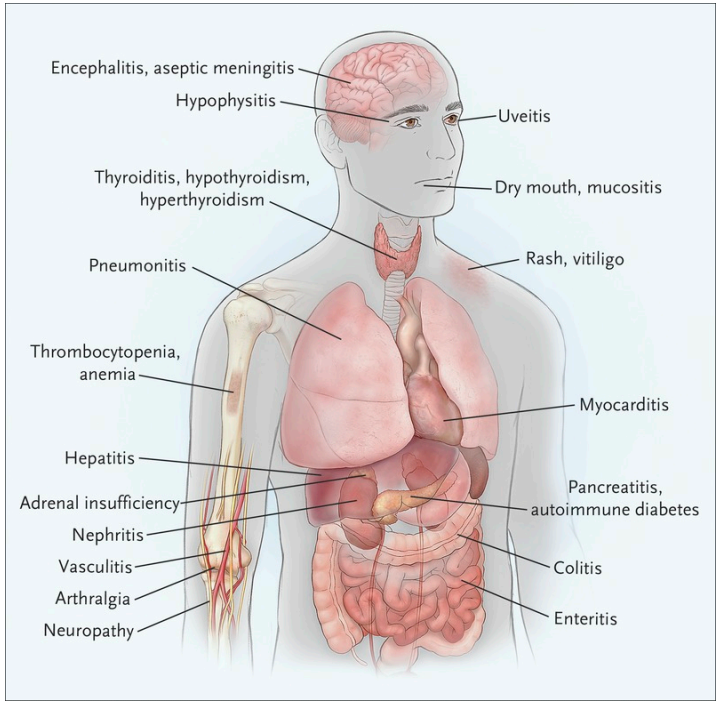

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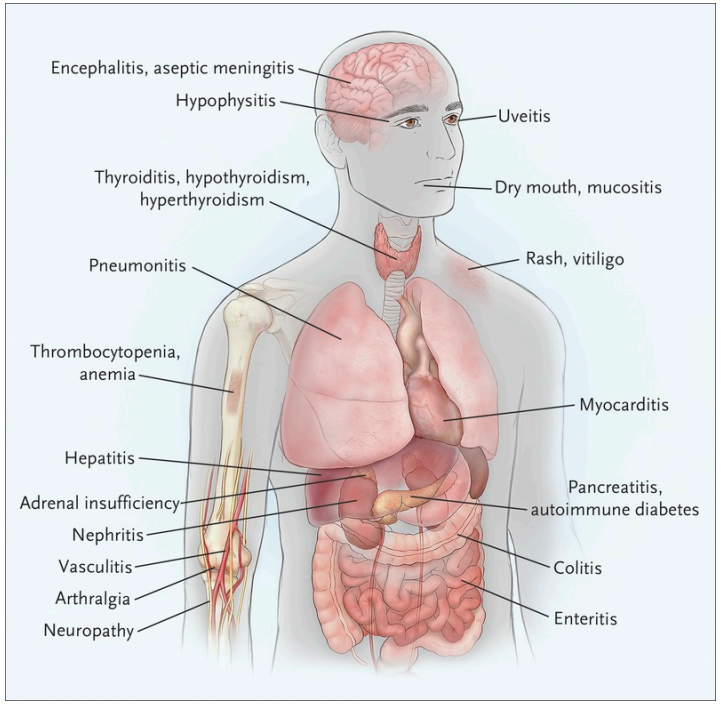

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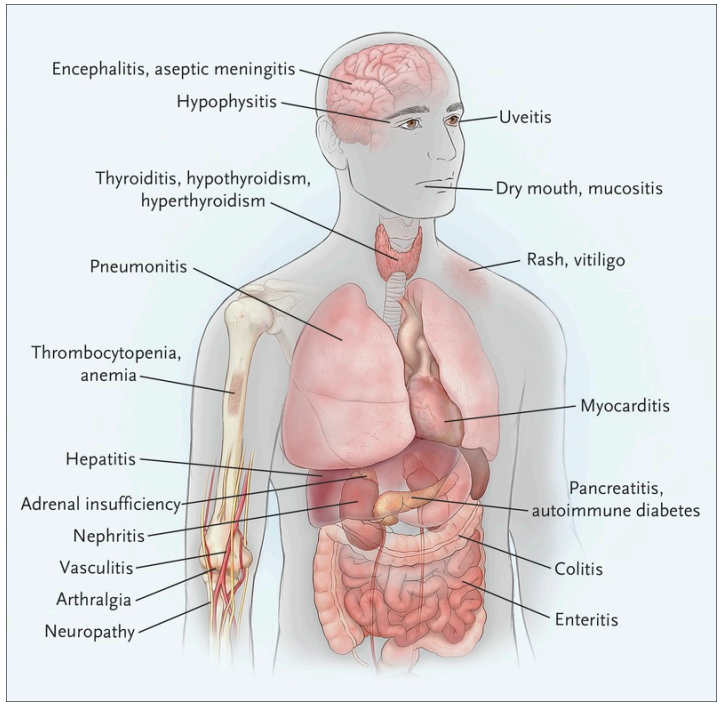

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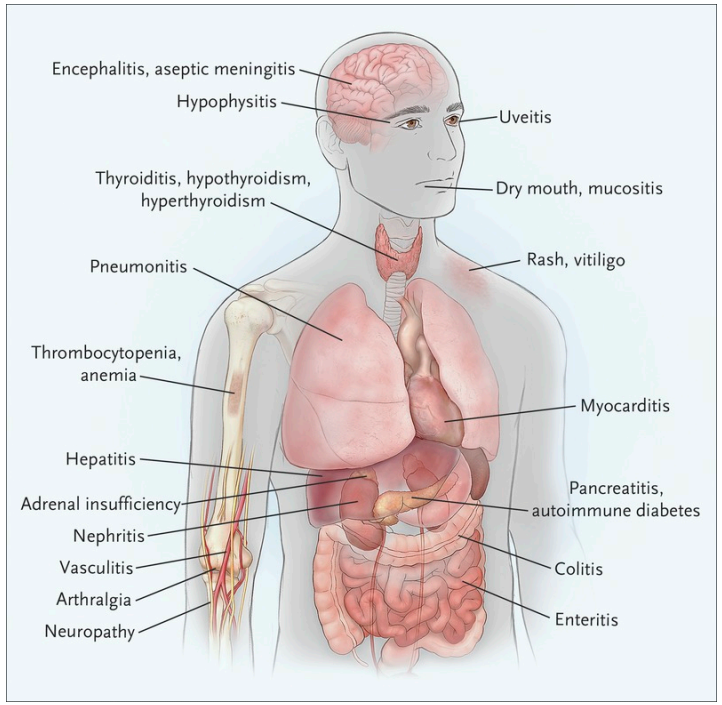

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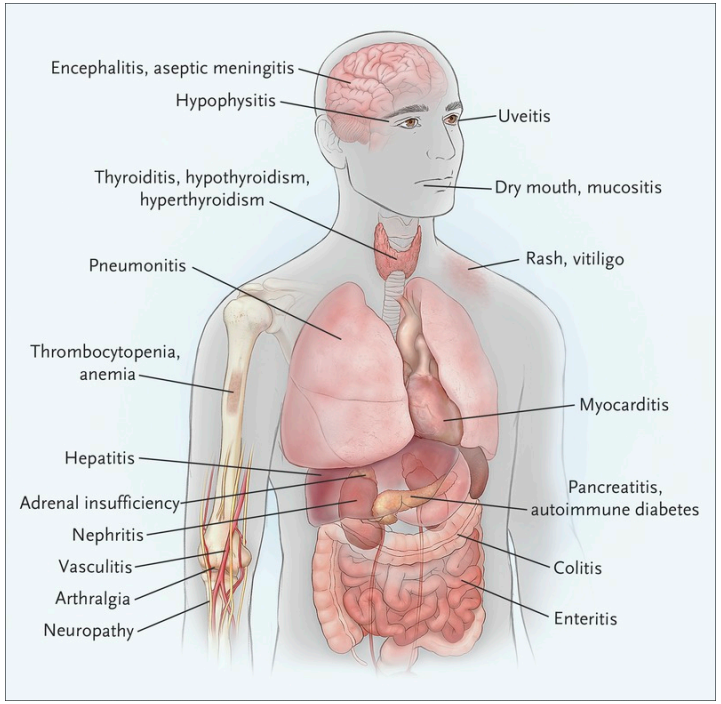

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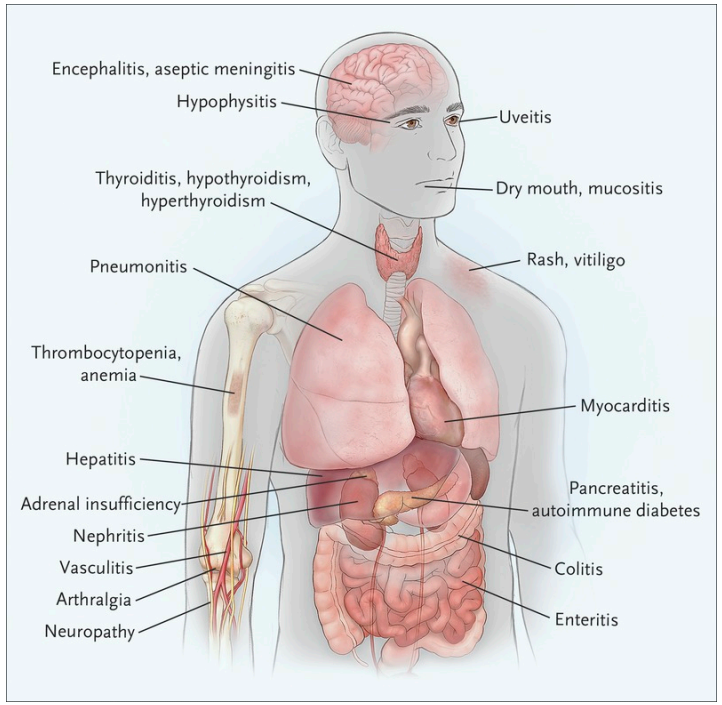

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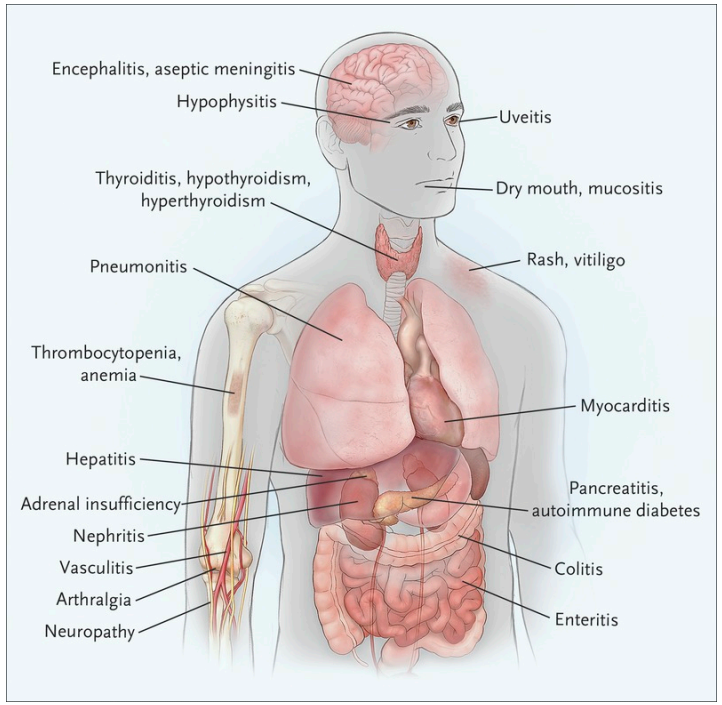

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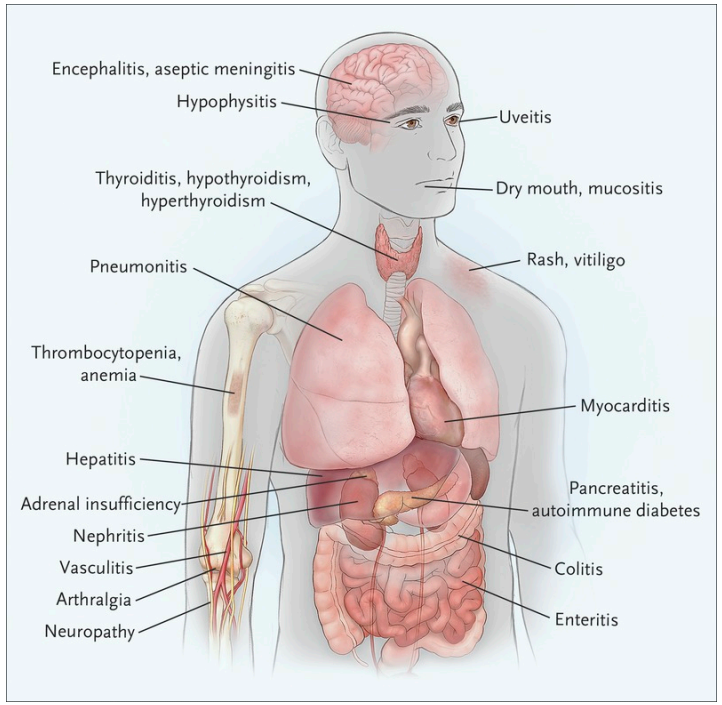

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Cardiovascular: consult cardiology as indicated; consider baseline EKG and BNP for high-risk patients	Periodic testing for those with abnormal baseline or symptoms
Pancreatic: no baseline testing	No routine monitoring if asymptomatic

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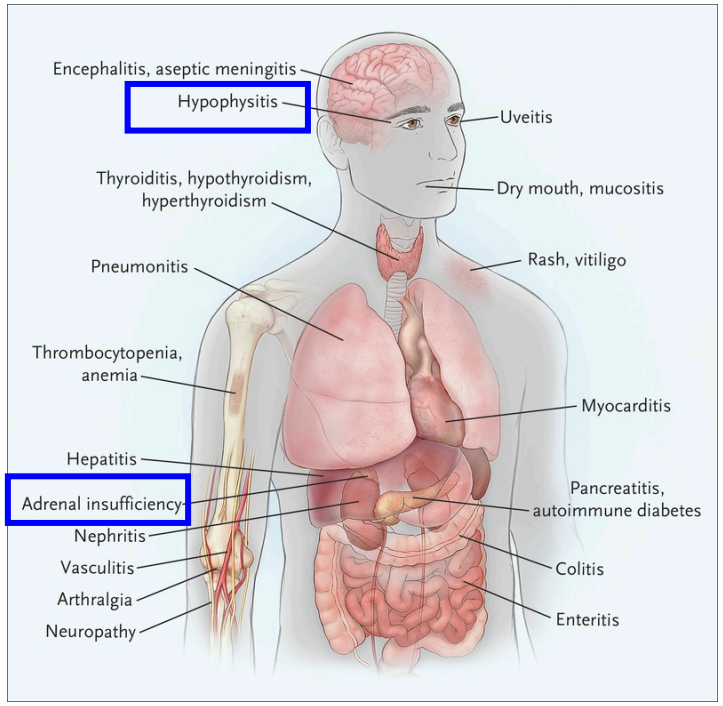
Toxicity monitoring:
Limitations/Pitfalls to interpreting cortisol



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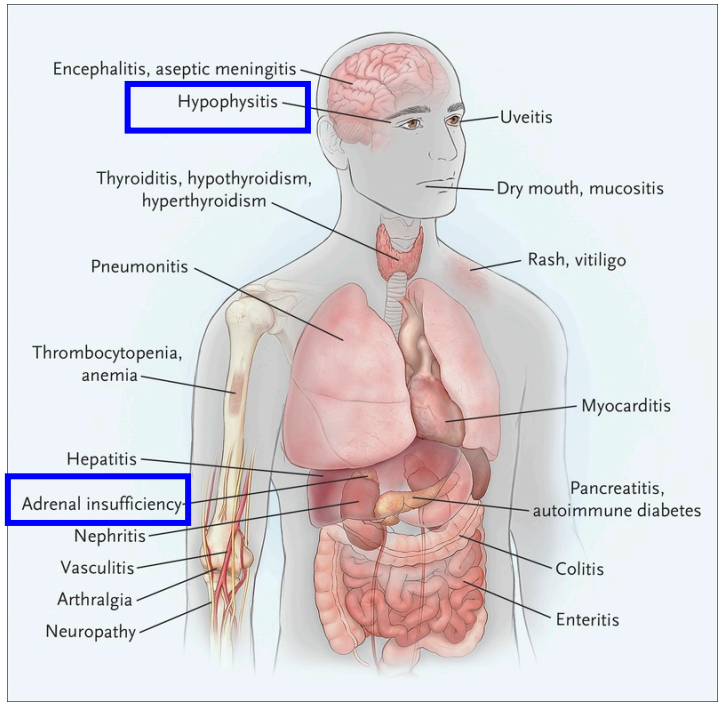

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- Cosyntropin test can be performed as indicated.
  - Early in the onset of hypophysitis, cosyntropin test can be falsely normal

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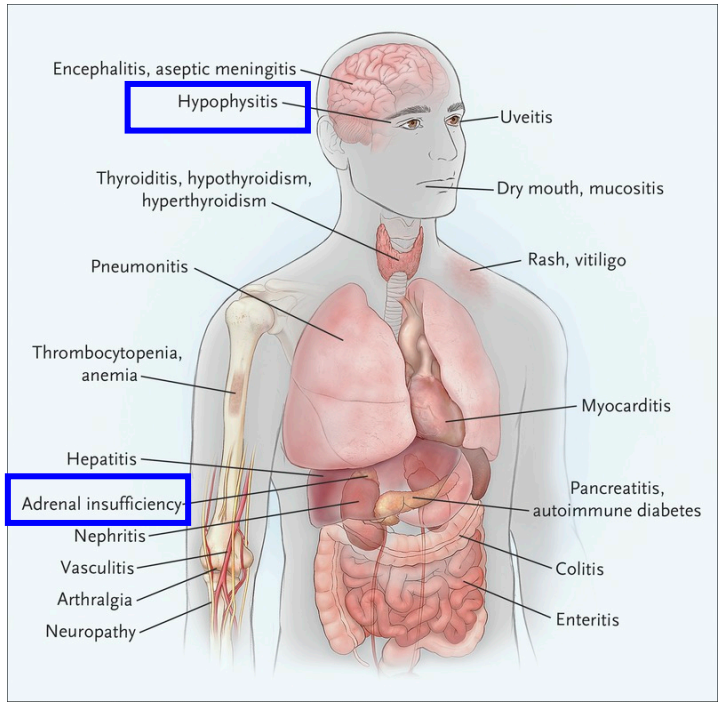

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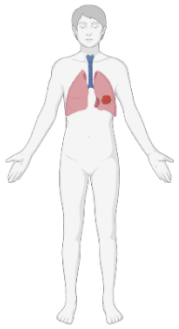
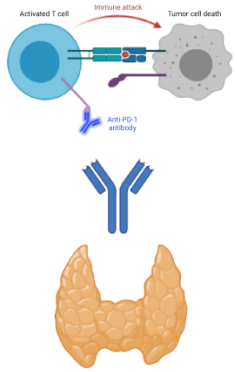
- Patients receiving steroid pre-medication as part of their treatment are expected to have a low AM cortisol level
- Cosyntropin test can be performed as indicated.
  - Early in the onset of hypophysitis, cosyntropin test can be falsely normal
- Routine surveillance with serum cortisol not recommended for treatment regimens requiring steroid pre-medications

Toxicity monitoring: Future directions





Preclinical setting	irAE prevention	irAE diagnosis	irAE treatment
Improved preclinical irAE models	Genetic biomarkers of irAE risk	Biomarkers of irAEs	Prospective irAE clinical trials
Improved mechanisms of irAEs in preclinical models	Microbial biomarkers of irAE risk	Imaging of irAEs	
Identification of novel biomarkers of irAE	Interventions to mitigate irAE risk e.g. microbial manipulation	Improved diagnostic pathways e.g. Multidisciplinary IR-Tox team	Refined treatment algorithms based on irAE mechanisms

Conroy et al. Immune-related adverse events and the balancing act of immunotherapy. Nat Commun 2022.

ICI monitoring: Take-away points

- ICI monitoring for efficacy and toxicity relies on radiologic imaging, physical exam/history, and routine labs

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- ICI monitoring for efficacy and toxicity relies on radiologic imaging, physical exam/history, and routine labs
- Hyperprogression and pseudoprogression are novel patterns of response with immunotherapy, but are infrequent
- Different biological mechanisms may be responsible for the primary versus acquired resistance
- Novel biomarkers and imaging modalities may inform future ICI monitoring strategies

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Thank you!