ICLIO National Conference

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ICLIO INSTITUTE FOR CLINICAL IMMUNO-ONCOLOGY

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Objectives

-Review treatment related toxicity and management
-Response assessment
-Other treatment decision related considerations

Toxicity and Management

Immune Related Adverse Events

- Immune mediated toxicity should be considered in the differential of any new symptom, involving any organ system
- Related to mechanism of action
- Patients must be seen prior to each treatment

Immune Related Adverse Events

- Most common immune related events with PD-1 blockade:
  - Pruritis/Rash
  - Arthralgias
  - Diarrhea
  - Elevated AST/ALT
  - Hypophysitis
- Uncommon events
  - Aseptic meningitis, AKI, episcleritis/uveitis, pancreatitis, neuropathies
- Patients should be evaluated before every dose

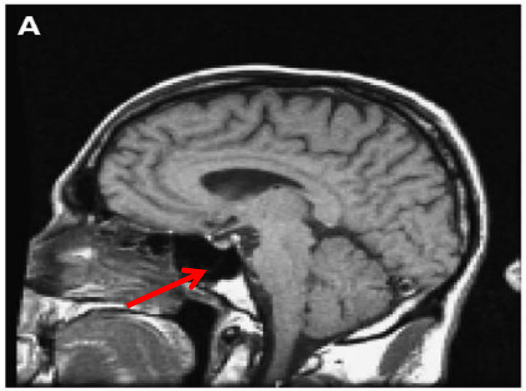
General Toxicity Management

- Emphasize communication, reporting
- Rule out alternative causes (e.g. infectious causes for diarrhea)
- Evaluate for high risk signs requiring urgent care
- Increase monitoring via phone and visits

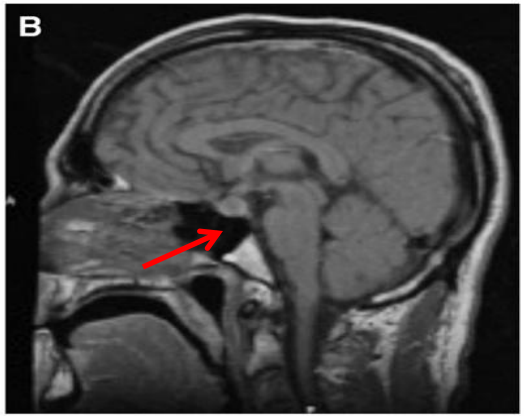
General Toxicity Management

- Treatment
  - Mild: Supportive care, increase monitoring
  - Moderate: Hold treatment, consider steroids
  - Severe: Permanently discontinue, start high dose steroids, taper over at least 4 weeks
    - Consider infliximab for refractory toxicity

Hypophysitis, Endocrinopathies



6/30/04 - Baseline (4.5 mm)



12/3/04 - Headache/fatigue (10.8 mm)

- Can present with or without severe HA
  - Differential also includes CNS mets, bleed
  - MRI with pituitary cuts
- Results in adrenal insufficiency
- Pituitary dysfunction may be permanent
- Hypothyroidism also common
  - Monitor TSH on treatment
  - Treat with replacement if indicated
  - Consultation with endocrinology

Weber JCO 2012

Adrenal Insufficiency

- Due to hypophysitis
- Rare, but risk of adrenal crisis and death if undetected
- Low threshold to consider AI early
  - Non-specific complaints
  - New severe fatigue, fevers, nausea, vomiting, low BP
- Check cortisol, ACTH, consider other pituitary axis labs
  - Physiologic dose hydrocortisone 20mg daily adequate to reverse symptoms due to AI quickly once confirmed
- Patient education after diagnosis
  - Need/timing for stress dosing, communication to providers
  - Endocrinology colleagues can help

Pneumonitis

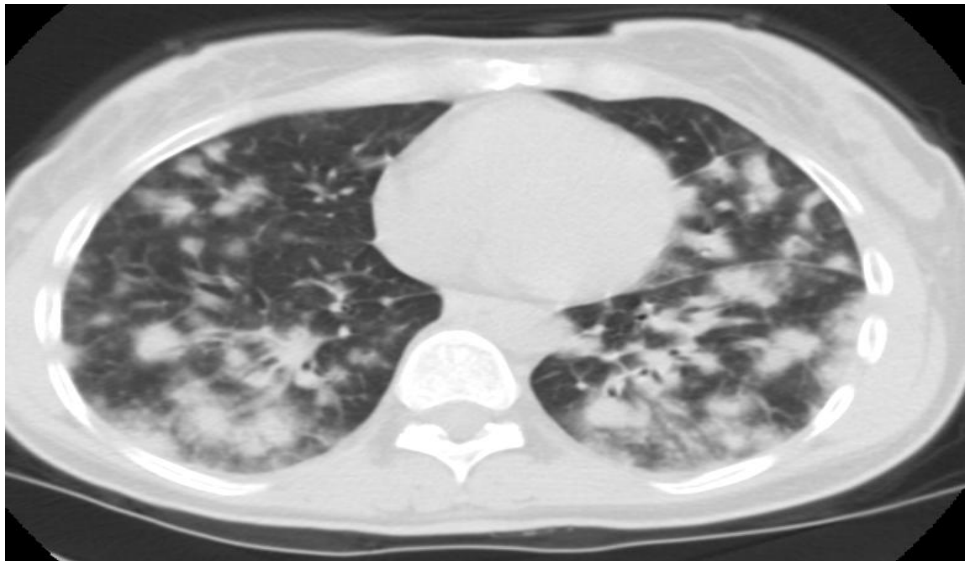


Image from Mike Postow

Pneumonitis

- Rare but potentially life threatening AE
- Radiographic only, isolated, asymptomatic
  - Can continue treatment, close observation
- Symptomatic
  - Hold treatment, initiated high dose steroids
- Severe symptoms or hypoxia
  - Hospitalize, steroids, consider bronch, pulmonary
  - Taper steroids slowly over at least several weeks
  - Consider opportunistic infectious prophylaxis

Additional Consequences of AEs

- Severe liver toxicity, rash, pneumonitis may require slow long steroid taper
  - Risk of atypical infections of immune suppression
    - PCP prophylaxis with tmp/smx
  - Risk of compression fractures
  - Several steroid related side effects

Response Assessment

- Immune related Response Criteria (irRC)
- Immune RECIST
- Practical application in clinical patient care

Response Assessment Summary

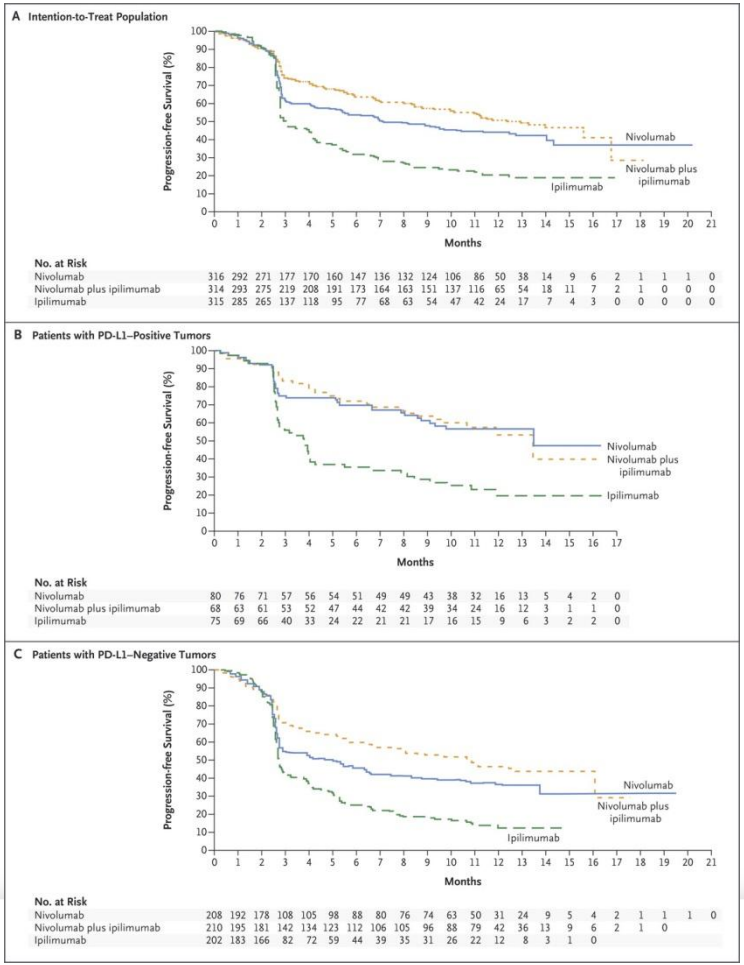
- Atypical responses observed in 6% of the 327 patients treated with pembrolizumab in KEYNOTE-001 who were followed by imaging for ≥28 weeks
- Higher rates observed with ipilimumab
- Mixed responses are not uncommon
- **In patients without clinical decline, consider repeating imaging at least 4 weeks later to confirm progression**

Wolchok ASCO 201

Dual Checkpoint Blockade

Numerically higher ORR
Awaiting OS data
Significant toxicity increase
Need predictive biomarkers
PD-L1 is not ideal

Larkin NEJM 2015



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