Immunotherapy Updates & Patient Education

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Immune-related Adverse Events

• irAE  immune-related Adverse Event
• imAE  immune-mediated Adverse Event
• Both terms used inter-changeably
• May be a regulatory language issue

General Guidelines

• Early recognition of symptoms & frequent monitoring
• Establish correct diagnosis
  – Presentation can be subtle
  – Other causes must be ruled out
• irAEs can become severe & life threatening if diagnosis and appropriate treatment are delayed

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Management of Mild irAEs

- Primary treatment is supportive care
- Close monitoring
  - Clinical status
  - Laboratory monitoring
    - Creatinine, hepatic panel, amylase, lipase
- Multidisciplinary care may be appropriate
  - Dermatology
  - Endocrinology
  - Gastroenterology

Moderate to Severe irAEs

- High-dose steroids & treatment interruption required for more severe (grade 3) irAEs
- irAEs generally improve with high-dose steroids followed by slow taper
- The optimal dose, schedule, and course of steroids remains unclear

Late-onset irAEs

- Be aware that irAEs may come
  - Early
  - Late
    - After discontinuation of treatment
  - Any time!

Assessing irAEs

- New symptoms
- Worsening of existing symptoms
- Lab abnormalities

Pulmonary irAEs

- Pneumonitis
- Cough
  - New or worsening of existing cough
  - Dry cough
- SOB
  - Resting & ambulatory pulse ox
- CT Chest

GI irAEs

- Diarrhea
- Colitis
- Drugs cause dysregulation of GI mucosal immunity
  - Represents a distinct clinicopathologic entity, distinct from what is seen with IBD
- Decreased appetite
- Abdominal pain
- Monitor for bowel perforation
Management of GI irAEs

- Use of oral budesonide did not prevent diarrhea or colitis in a prospective, randomized, blinded study of 135 patients receiving ipilimumab therapy.
- Consider hospitalization for diarrhea not responsive to oral steroids.
  - Inadequate absorption of oral steroids due to rapid GI motility associated with diarrhea & colitis


Hepatic irAEs

- Hepatitis
- ALT, AST
- Alkaline phosphatase
- T bili

Endocrine irAEs

- Hyperthyroidism
- Hypothyroidism
- Hypophysitis
- Pancreatitis
- Type I Diabetes Mellitus

Dermatologic irAEs

- Rash
- Pruritus
- Topical steroids
  - Triamcinolone 0.1%
  - Clobetasol 0.05%
- Systemic steroids
  - Prednisone
- Antihistamines
  - Allegra 12 hr qAM & Benadryl 25mg qPM

Genitourinary irAEs

- Hematuria
- Nephritis
- CKD
- Review concomitant medications
  - Change any that are nephrotoxic
- Oral / IV hydration
- Systemic steroids
- Consult with nephrologist

Systemic Interventions

- Prednisone 1mg/kg/day
- High-dose steroids
  - Methylprednisolone 2mg/kg QD or BID
- Immunosuppressive therapy
  - Infliximab
  - Mycophenolate mofetil
Monitoring

- Once an intervention is initiated, reassessment should be done within 24 hours.
- Frequent reevaluation is recommended as irAEs symptoms & course can change rapidly, and response to interventions cannot be assumed.