Practical Management Pearls for Immunotherapy:
Gastrointestinal Complications

Charlotte Ariyan, MD PhD
Carol Bassok Lowenstein Chair Research
Co-Leader Melanoma DMT
Memorial Sloan Kettering Cancer Center
Disclosures

• Advisory Board: Merck, Iovance

• Stock: Pfizer
Gastrointestinal Complications

• Incidence:
  • Depends on **type** and **dose** of Immunotherapy
    • Colitis (30% Ipilimumab, 10% PD1)
    • Hepatitis 20%
    • Pancreatitis 4%
    • Gastritis/Duodenitis <5%

• Combination therapy (i.e. chemotherapy) can also cause GI toxicity....diagnosis can be difficult

• Need to be vigilant as symptoms can be vague
Timing of Toxicity of Immune Checkpoint Inhibitors

Neoadjuvant Therapy: Incidence of irAEs

- Any AE: Fatigue, Rash, Pruritus, Vomiting, Elevated AST, Elevated ALT, Diarrhea, Hyperthyroidism, Headache, Hypothyroidism, Dry mouth, Fever, Arthralgia, Colitis, Adrenal insufficiency, Dry eye, Flu-like symptoms, GGT increased, GGT increased, GGT increased, Abdominal pain, Anemia, Malaise, Pneumonitis, Serum amylase increased, ALP increased, Anorexia, Concentration impairment, Cough, Dry skin, Dysgeusia, Dyspnea, Lipase increased, Sarcoid-like reaction, Gastritis, Hyponatremia, Peripheral motor neuropathy, Uveitis, Diabetes, Encephalitis, Hypotension, Meningitis

Frequency, %

Gastrointestinal Complications: Colitis

• Diagnosis:
  • Diarrhea/abdominal pain
  • Rule out infectious causes
    • Cdiff, bacteria, parasite
  • Grading Diarrhea: # stools over baseline per NCI CTCAE V5.0

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• Gold standard=Endoscopy (flexible sigmoidoscopy/colonoscopy) with biopsy

• CT scan- less sensitive but rules out bad colitis
Treatment: **Colitis**

- Treatment based upon severity

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- BRAT diet
- oral prednisone (1mg/kg/day)
- oral prednisone (1mg/kg/day) IV methylprednisone
- IV methylprednisone (1mg-2mg/day)

Treat until symptoms grade 1, then taper steroids
No response 2-3 days: Inflixumab, Vedolizumab, fecal transplant
Caution immodium/anti-diarrhea- toxic megacolon
Gastrointestinal Complications: Hepatitis

• Diagnosis:

  • Hepatitis:
    • Elevated transaminases. ALT/AST. NCI CTCAE V5.0

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• Rule out cholestasis (elevated bilirubin, alkaline phosphatase)
• Rule out infection (hepatitis)
• Biopsy not routinely performed
Gastrointestinal Complications: Hepatitis

- Treatment: Based upon severity transaminitis

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- Observe
- Prednisone
- Prednisone (0.5-1mg/kg)
  - IV methylprednisone (1-2mg/kg)
  - Cellcept
  - Tacrolimus
  - Infliximab can have hepatic toxicity!
Gastrointestinal Complications: Pancreatitis

• Diagnosis:
  • Pancreatitis: 4% (exocrine)
    • Abdominal pain, nausea, vomiting
    • Elevated lipase (acute),
    • Diarrhea/steatorrhea/fecal fat (late)
    • CT scan
  • Pancreatitis: (1%) endocrine, more common PD1 blockade
    • DKA, elevated glucose

• Treatment: Pancreatitis
  • Observation
  • Steroids if symptoms (exocrine), possible pancreatic enzyme replacement
  • Insulin (endocrine)
Gastrointestinal Complications: Gastritis/Duodenitis

• Diagnosis:
  • abdominal pain, nausea, vomiting
  • Can be subtle- weight loss
  • Gold standard=Endoscopy (flexible sigmoidoscopy/colonoscopy) with biopsy
  • CT scan

  *High suspicion in patients with failure to thrive*

Treatment:
Steroids
Gastrointestinal Complications: Colitis

58 yo Stage IV sarcoma

CTLA-4/PD-1/Doxorubicin

Severe full body rash 2 weeks prior requiring Oral Prednisone

Presented with obstruction from intussusception from small bowel metastasis
Gastrointestinal Complications: Colitis

Patient undergoes small bowel resection
intussusception reduced- 1 foot small bowel

POD #3- severe diarrhea- >20 bowel movements x day

Infectious workup: Negative (Cdiff/cultures)

Scope with biopsy- immune colitis
Gastrointestinal Complications: Colitis

Grade 3 colitis acutely after surgery

Colitis developed in recent window of oral steroids (prednisone)

**Multidisciplinary discussion:**
Possible refractory steroid - recent course of oral prednisone

Recent bowel surgery - desire to minimize steroids

Treatment: Infliximab (steroid sparing) - rapid resolution
Summary:

• Gastrointestinal complications common

• Some symptoms vague and vigilance needs to be high

• Multi-disciplinary approach needed- especially in current era of combination treatments