

Practical Management Pearls for Immunotherapy: Gastrointestinal Complications

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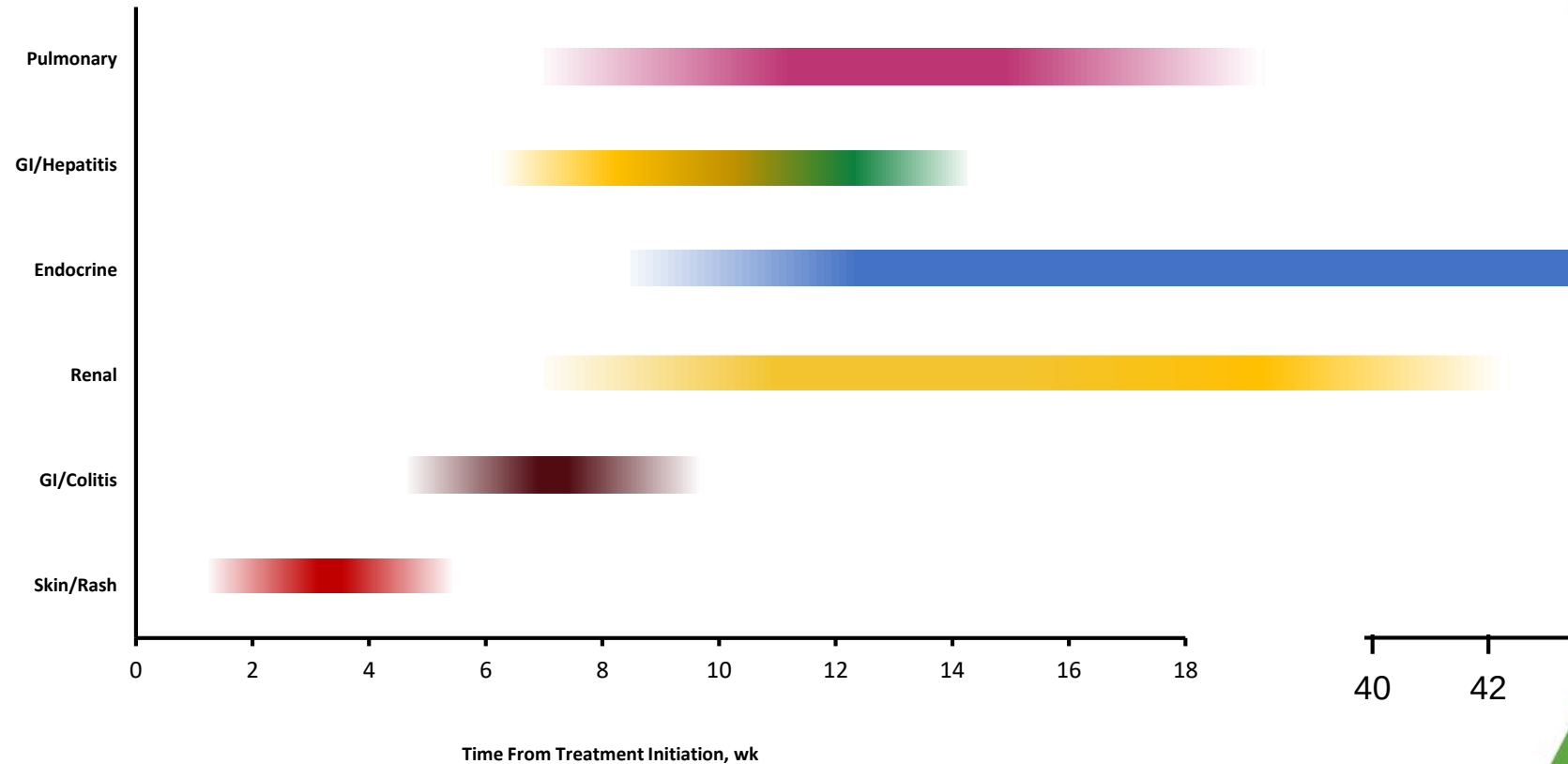
Disclosures

- Advisory Board: Merck, Iovance
- Stock: Pfizer

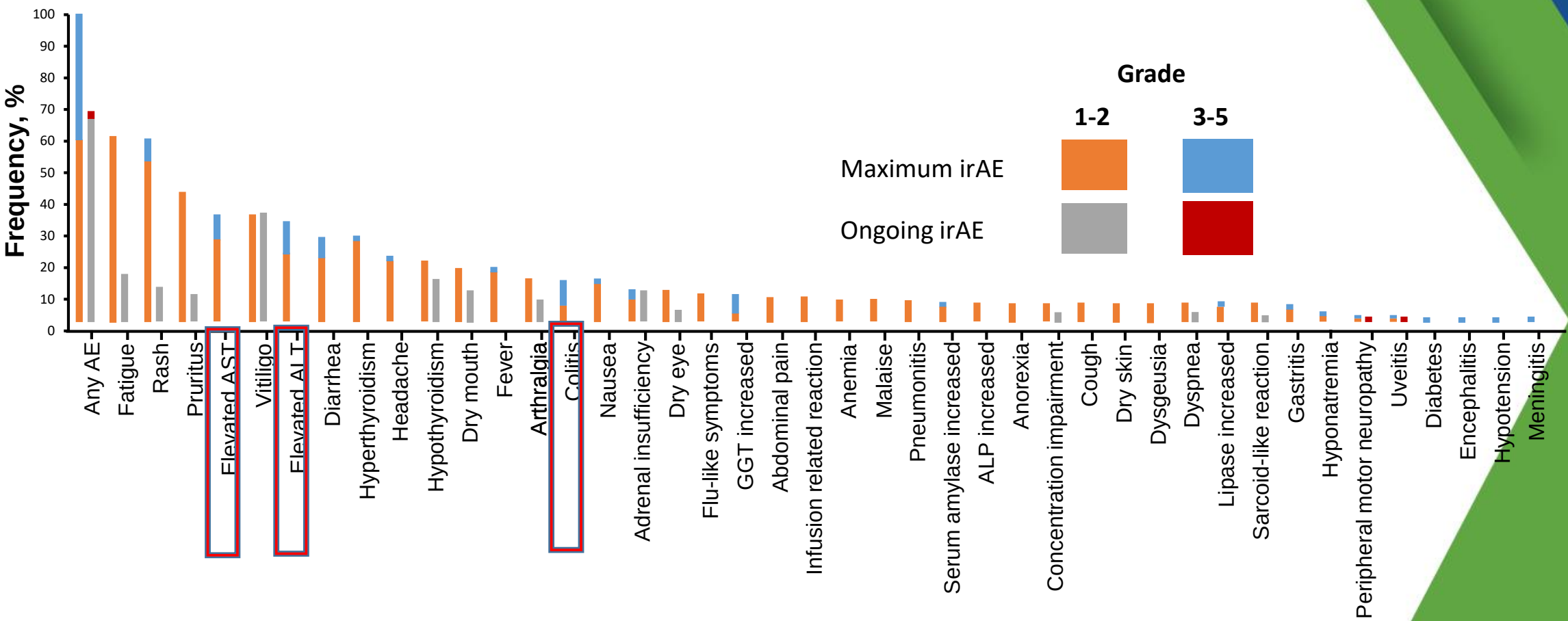
Gastrointestinal Complications

- 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



Rozeman EA et al. *Nat Med.* 2021;27:256-263.

Gastrointestinal Complications: Colitis

- Diagnosis:

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

Grade 1	Grade 2	Grade 3	Grade 4
<4	4-6	7	severe

- Gold standard=Endoscopy (flexible sigmoidoscopy/colonoscopy) with biopsy
- CT scan- less sensitive but rules out bad colitis

Treatment: Colitis

- Treatment based upon severity

Grade 1	Grade2	Grade 3	Grade 4
<4	4-6	7	>7 severe
↓ 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**

Grade 1	Grade2	Grade 3	Grade 4
<3 ULN	3-5 ULN	5-20 ULN	>20

- Rule out cholestasis (elevated bilirubin, alkaline phosphatase)
- Rule out infection (hepatitis)
- Biopsy not routinely performed

Gastrointestinal Complications: Hepatitis

- Treatment: Based upon severity transaminitis

Grade 1	Grade2	Grade 3	Grade 4
<3 ULN	3-5 ULN	5-20 ULN	>20



Observe



Prednisone



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



Prednisone

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