

# Case of Multiple IrAE

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# Disclosures

**Advisory Board:** Array BioPharma, Aduro, BMS, Incyte, Merck, NewLink Genetics, Novartis

**Honoraria:** BMS and Merck

**Institutional Support:** RGenix, Infinity, BMS, Merck, Array BioPharma, Novartis

# 67 year old man with metastatic mucosal melanoma and brain metastases

6/14/18: Started nivolumab (1mg/kg) + ipilimumab (3mg/kg)

Had a rash after dose 1-- triamcinolone cream.

7/5/2018: Dose 2 of nivolumab + ipilimumab

Fever, tachycardia, and fatigue

# Fever, tachycardia, and fatigue

7/10/2018: Presented to a local Emergency Department with a fever of 101 degrees Fahrenheit and HR 140.

Labs notable for AST 240 (37 is nl); ALT 185 (55 is nl); bilirubin and alkaline phosphatase normal. CBC normal.

Admit for monitoring?

Hydrate, NSAIDs for fever, discharge with close LFT  
follow-up?

Evaluate for other irAE?

Fever, tachycardia, and fatigue

EKG showed atrial fibrillation at 140

Patient was admitted

TSH 0.02 (0.60 is lower limit of nl)  
Free T4 4.45 (up to 1.9 is nl)



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Start anti-thyroid medication for hyperthyroidism (methimazole or propylthiouracil)?

Start steroids for hyperthyroidism and LFTs?

Start beta blockade for symptomatic tachycardia?

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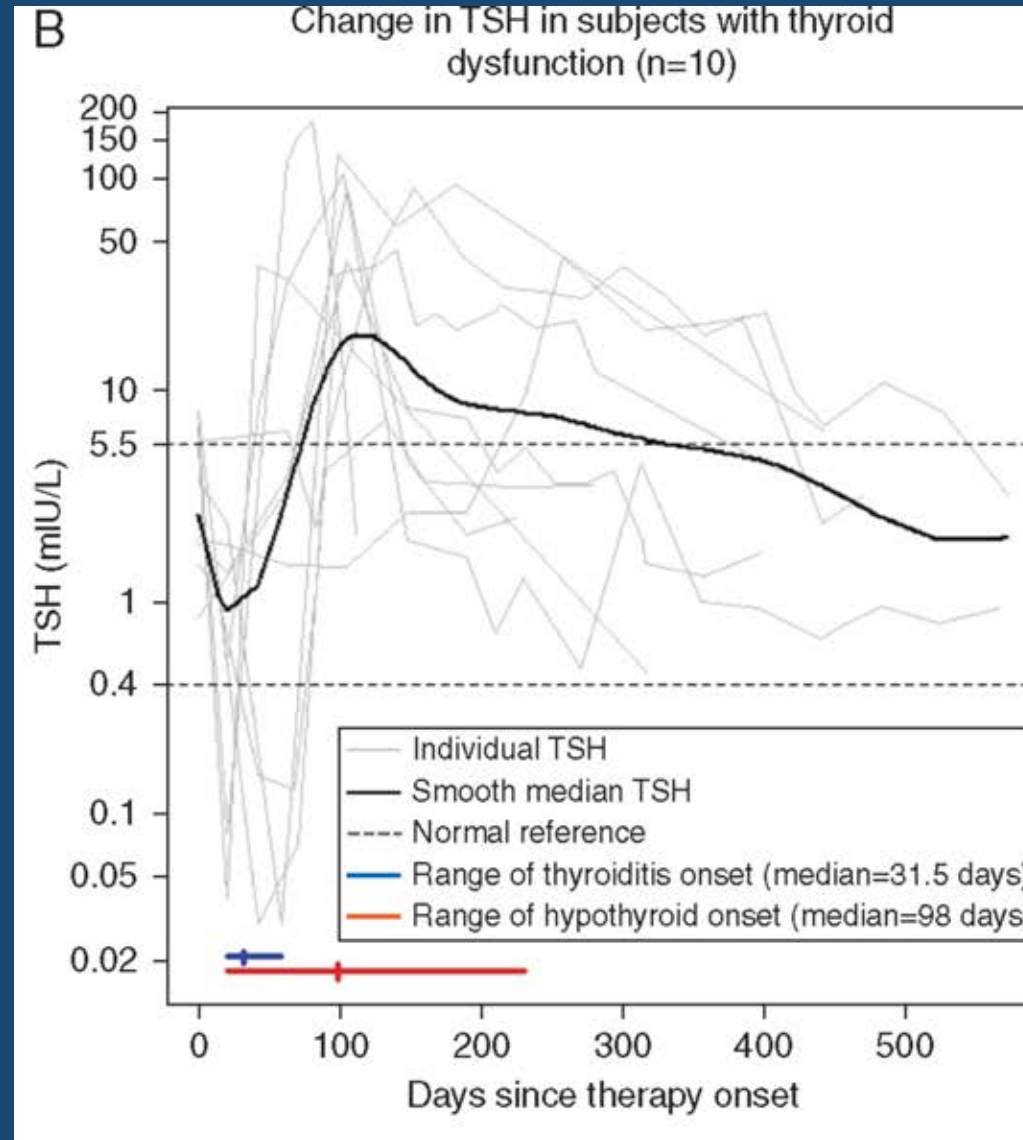
Start anti-thyroid medication for hyperthyroidism  
(methimazole or propylthiouracil)?

Start steroids for hyperthyroidism and LFTs? Pred 40

Start beta blockade for symptomatic tachycardia?

Propranolol

# Often hyperthyroid (thyroiditis) then hypothyroid



Atrial fib and LFTs resolved, tapered  
from steroids over 3 weeks

Atrial fib and LFTs resolved, tapered  
from steroids over 3 weeks

Mid-August 2018:

Epigastric abdominal pain and nausea without diarrhea

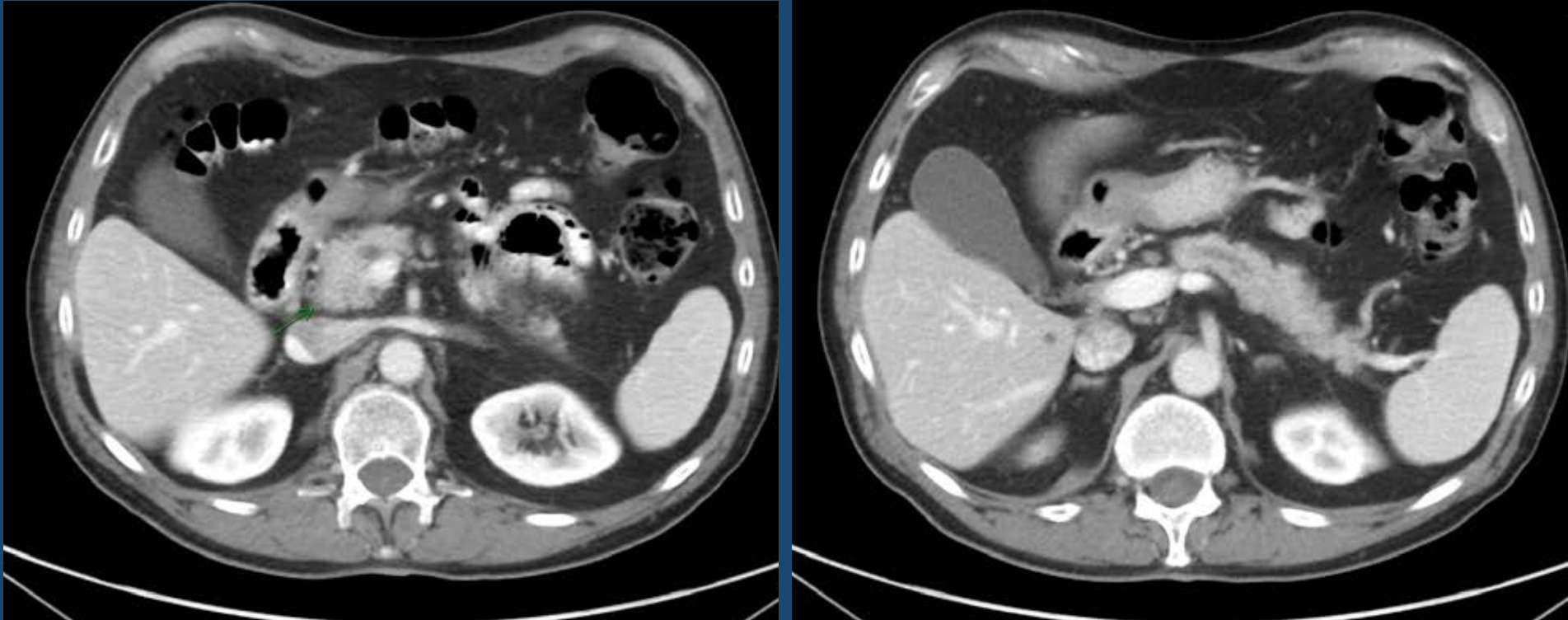
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Epigastric abdominal pain and nausea without diarrhea

Steroid induced gastritis?

Recurrence of hepatitis?

Atrial fib and LFTs resolved, tapered  
from steroids over 3 weeks



Amylase and lipase elevated 8x upper limit of normal

# Immunotherapy related pancreatitis

Steroids increased to 70mg daily

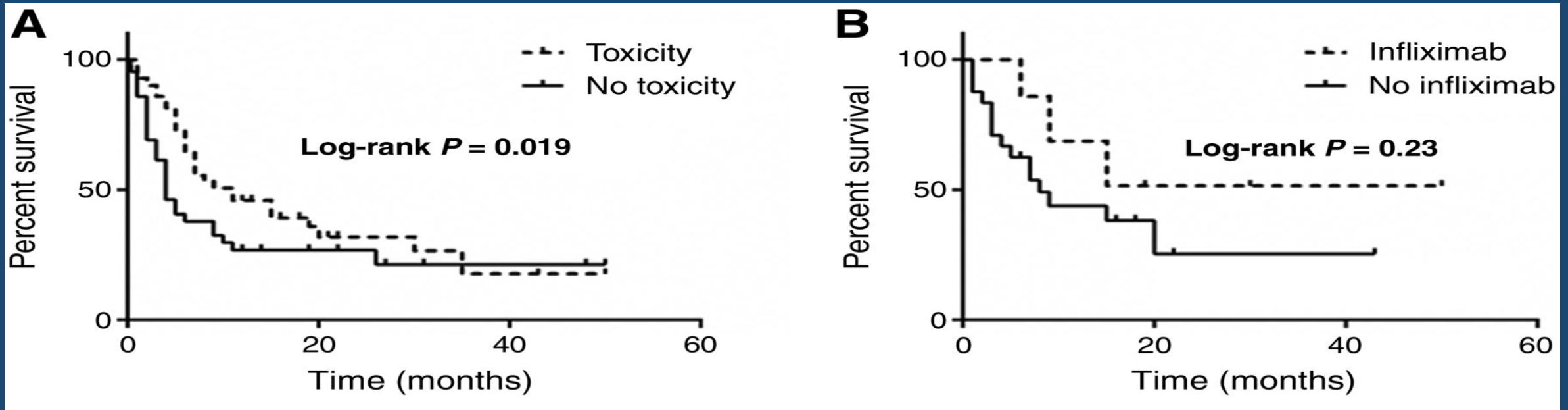
Hyperglycemia to 200s requiring metformin

8/29/18 Infliximab #1 (5mg/kg) and steroids weaned

9/12/18 Infliximab #2 (5mg/kg)



# Infliximab does not seem to affect efficacy of ipilimumab



Retrospective study of 113 patients

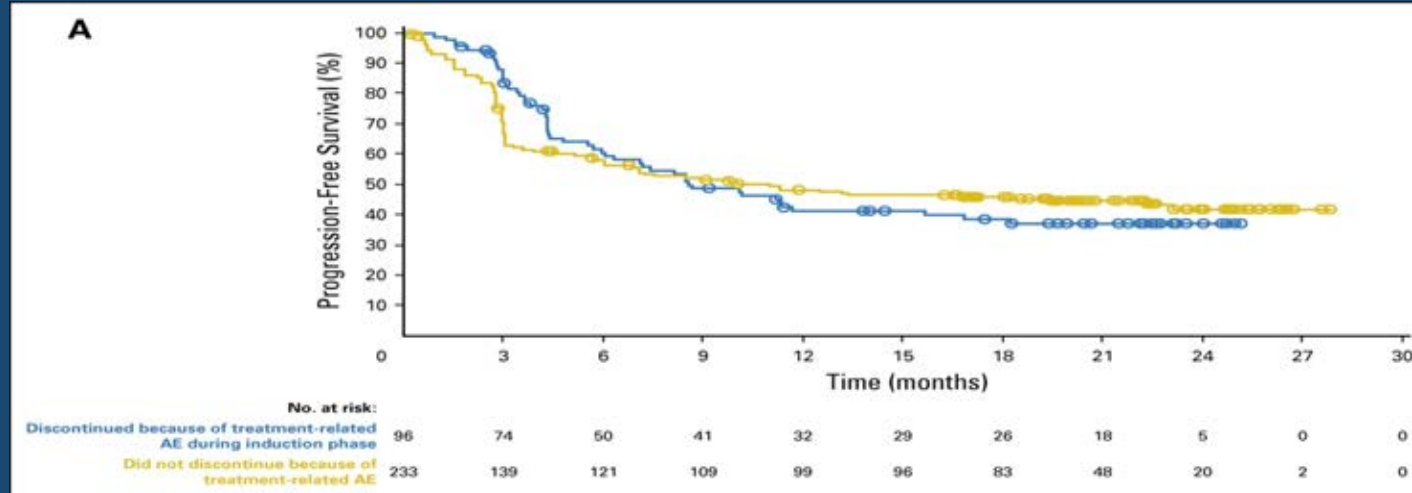
32 patients with diarrhea (19 patients Grade  $\geq 2$  diarrhea)

29 patients received steroids

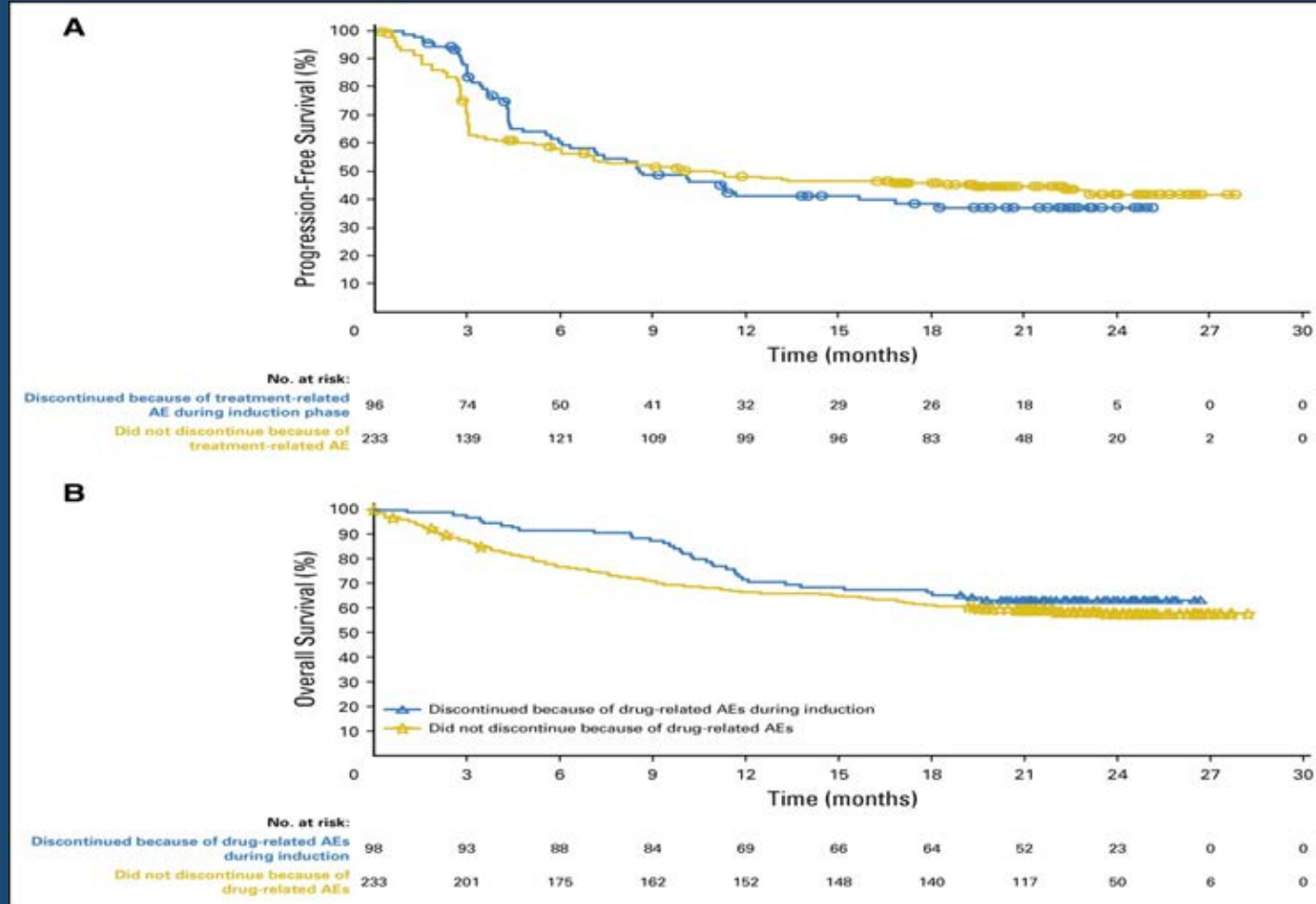
7 patients had infliximab

Arriola et al. *Clin Cancer Res* 2015

Outcomes look similar in patients who discontinue due to toxicity vs. those who continue treatment longer



# Outcomes look similar in patients who discontinue due to toxicity vs. those who continue treatment longer



# Summary of Case

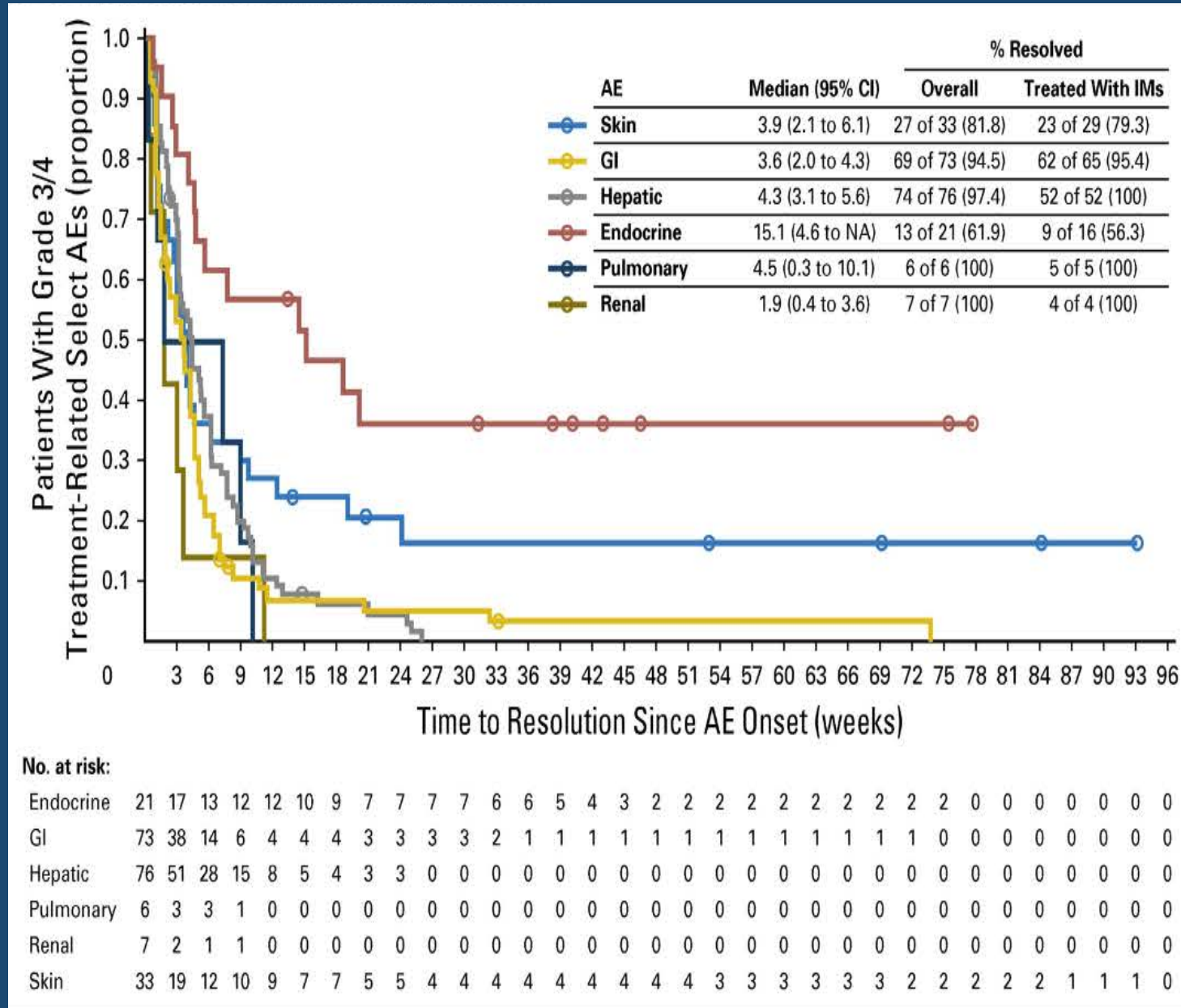
- Many organs can be involved and watch for new irAE on steroid taper
- Transient immunosuppression does not hurt immunotherapy benefit (except maybe prednisone >7.5mg daily in hypophysitis)
- Unclear how much immunotherapy is needed for benefit

# Thank you!



# Back-up Slides

# Most side effects resolve



Sznol et al.  
*Journal of Clin  
 Oncol* 2017