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Society for Immunotherapy of Cancer

SITC  
2017

# Variance From Evidence-Based Management of Immune-Related Adverse Events Among Healthcare Providers: Analysis of an Online Management Decision Tool

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# Presenter Disclosure Information

*Krista Marcello, BA  
Managing Editor, Clinical Care Options, LLC*

The following relationships exist related to this presentation:

*No relationships to disclose*

*The development of the resource in this presentation was made possible through unrestricted independent medical education grants supported by Merck & Co., Inc.; Merck KGaA; and Pfizer Inc.*

*There will not be discussions about the use of products for non-FDA approved indications in this presentation.*

## Background

- Immune checkpoint inhibitors are being integrated into the care of a rapidly increasing number of patients with many different tumor types
  - Profiles of toxicities, some of which are better tolerated than chemotherapy, are unique and require a specific knowledge base for optimal identification and management
  - Effective immune-related adverse event (irAE) management allows for optimal treatment and mitigates potentially serious treatment-related complications
- Many healthcare providers (HCPs) remain unfamiliar and inexperienced with managing the unique spectrum of irAEs

## Methods

- CCO developed an online management support tool designed to give clinicians easy access to balanced, evidence-based management recommendations, based on
  - Organ system affected
  - Grade/severity of irAE (CTCAE)
- Recommendations from evidence-based guidance, peer-reviewed published literature, and Dr. Weber's personal clinical experience
- 2 versions of the tool
  - Initial version: data collected from 11/9/2016 through 7/21/2017
  - Updated version: data collected from 5/10/2017 through 9/27/2017
    - Recommendations updated based on available data and guidelines
    - Added categories "rheumatologic" and "other"

## Methods

- Tool users were asked about their intended management plan before evidence-based recommendations were provided
- The current study includes an analysis of cases entered into the tool and comparison of the intended management of HCPs with the evidence-based recommendations in the tool
- Chi-square analysis was performed on the data collected from the tool for statistical significance of the variance of intended management vs evidence-based recommendations

# How to Use the Tool: clinicaloptions.com/immuneAETool

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## Managing Immune-Related Adverse Events: An Interactive Algorithm Tool

Source: Metastatic Merkel Cell Carcinoma: Insights on the Clinical Application of Immune Checkpoint Inhibitors

**Table of Contents**

**ClinicalThought**

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- MCC Immunotherapy
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**Summary Resource**

- Immunotherapy for MCC

**Interactive Decision Support Tool**

- Tool: Managing irAEs

**Interactive Tool**

Use this Interactive Algorithm Tool to enter the specifics of your patient's immune-related adverse event (irAE) and see what Jeffrey S. Weber, MD, PhD, would choose as his management approach.

With just a few clicks through pull-down menus, this Interactive Tool guides you through the management algorithm to reach an expert recommendation for each scenario based on the available data and personal experience. This tool not only educates on the best management approaches but also provides the evidence-based rationale for these approaches.

**This tool assumes your patient is receiving treatment with an immune checkpoint inhibitor and is experiencing an adverse event.** These data were compiled in April 2017 and include the opinions of our expert at that time.

Date posted: 5/9/2017

**Launch** ←

# How to Use the Tool: clinicaloptions.com/immuneAETool

**Managing Immune-Related Adverse Events: An Interactive Algorithm Tool**  
an Interactive Decision Support Tool

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## Organ System Affected by irAE

Which organ system is affected?

Please select...  

- Please select
- Gastrointestinal (colitis, diarrhea)**
- Hepatic
- Pulmonary (pneumonitis)
- Neurologic
- Dermatologic
- Renal (nephritis)
- Endocrine
- Rheumatologic (arthritis)
- Other

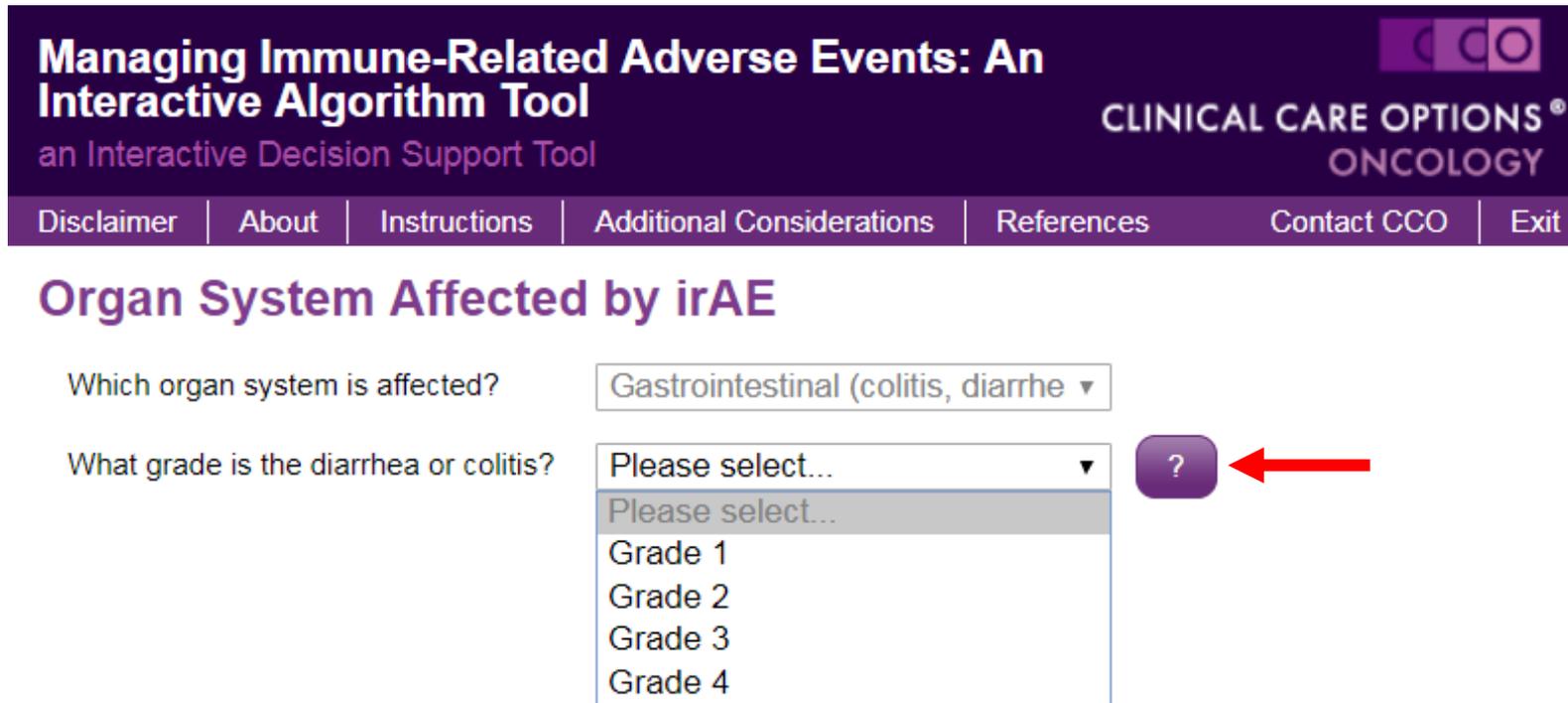
# How to Use the Tool: [clinicaloptions.com/immuneAETool](http://clinicaloptions.com/immuneAETool)

## General Information and Evidence

- irAEs reflect immune-based mechanism of action of checkpoint inhibitors.
- The rates of high-grade treatment-related AEs associated with anti-PD-1/PD-L1 agents are generally lower than those observed with anti-CTLA-4 treatment.
  - Similar incidence of irAEs reported with nivolumab, pembrolizumab, atezolizumab, and avelumab treatment.<sup>[1-5]</sup>
  - The rates of high-grade, irAEs are higher with combination of anti-PD-1 and anti-CTLA-4 antibodies vs monotherapy.<sup>[1,3]</sup> Similar rates of grade 3/4 irAEs with anti-PD-1 and anti-PD-L1 therapy have been reported across tumor types.<sup>[6-12]</sup>
  - Most grade 3/4 irAEs occur during the first 12-14 weeks of treatment, with characteristic timing.<sup>[13]</sup>
- The kinetics of onset of irAEs, particularly with ipilimumab, follow a predictable pattern but may vary when these agents are combined with other therapies.<sup>[14]</sup>
  - Skin-related toxicities occur first.

Close

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## Organ System Affected by irAE

Which organ system is affected?

What grade is the diarrhea or colitis?  ?

- Please select...
- Grade 1
- Grade 2
- Grade 3
- Grade 4

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## Organ System Affected by irAE

Which organ system is affected?

Gastrointestinal (colitis, diarrhe ▼

What grade is the diarrhea or colitis?

Grade 3 ▼



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# How to Use the Tool: [clinicaloptions.com/immuneAETool](http://clinicaloptions.com/immuneAETool)

## Recommendations

-Consider permanent discontinuation of therapy (or eliminate ipilimumab from the combination regimen, if the patient was receiving combination immune checkpoint blockade)

-Consider hospital admission

-1.0-2.0 mg/kg/day IV methylprednisolone or equivalent

-Add prophylactic antibiotics for opportunistic infections if steroids are used for > 30 days

-Consider endoscopy; check C. difficile titres and cultures

**Follow-up:** If symptoms improve, continue steroids until grade  $\leq 1$ , then taper over at least 1 month

**If symptoms persist > 3 days or recur after improvement:** Add infliximab 5 mg/kg/day (if no contraindication, and should not be used in cases of perforation or sepsis)

**Comments:** Patients receiving > 4-6 wks of steroids require *Pneumocystis carinii* prophylaxis. Patients on IV steroids may be switched to an equivalent dose of oral corticosteroids (eg, prednisone) at start of tapering or earlier, once sustained clinical improvement is established. Lower bioavailability of oral corticosteroids should be considered when switching.

Next



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## Impact

How did this irAE tool affect your management plans?

Please select... ▼

I used this tool to get expert recommendations on:

Please select... ▼

- Please select...
- A hypothetical patient case
- A specific patient in my practice

Consider, please summarize the

ENTER COMMENTS HERE...

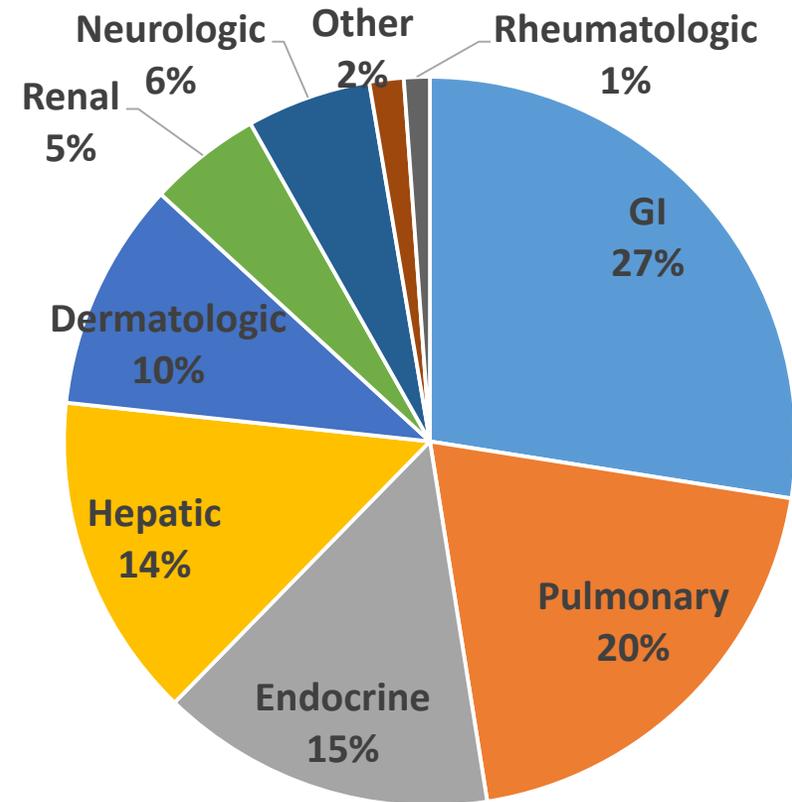
Please leave us a comment below on the utility of this tool and ways to improve it.

Enter comments here...

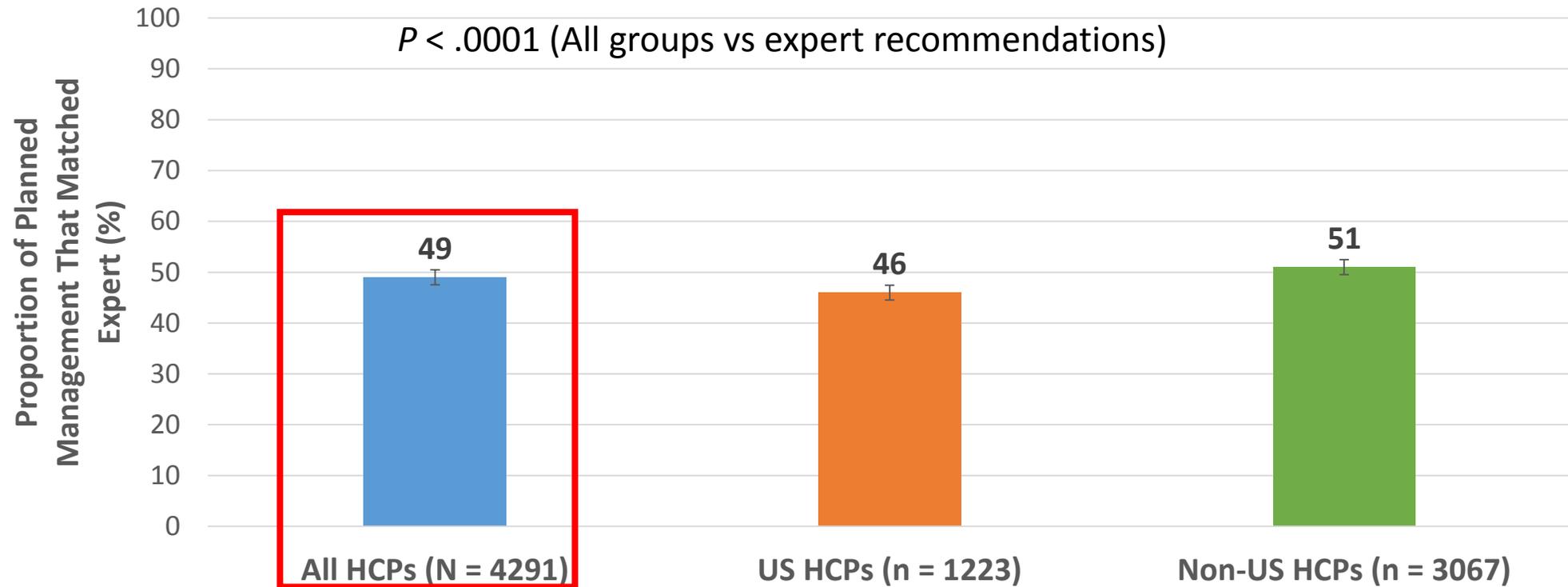
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## Cases Entered Into Tool by Organ System

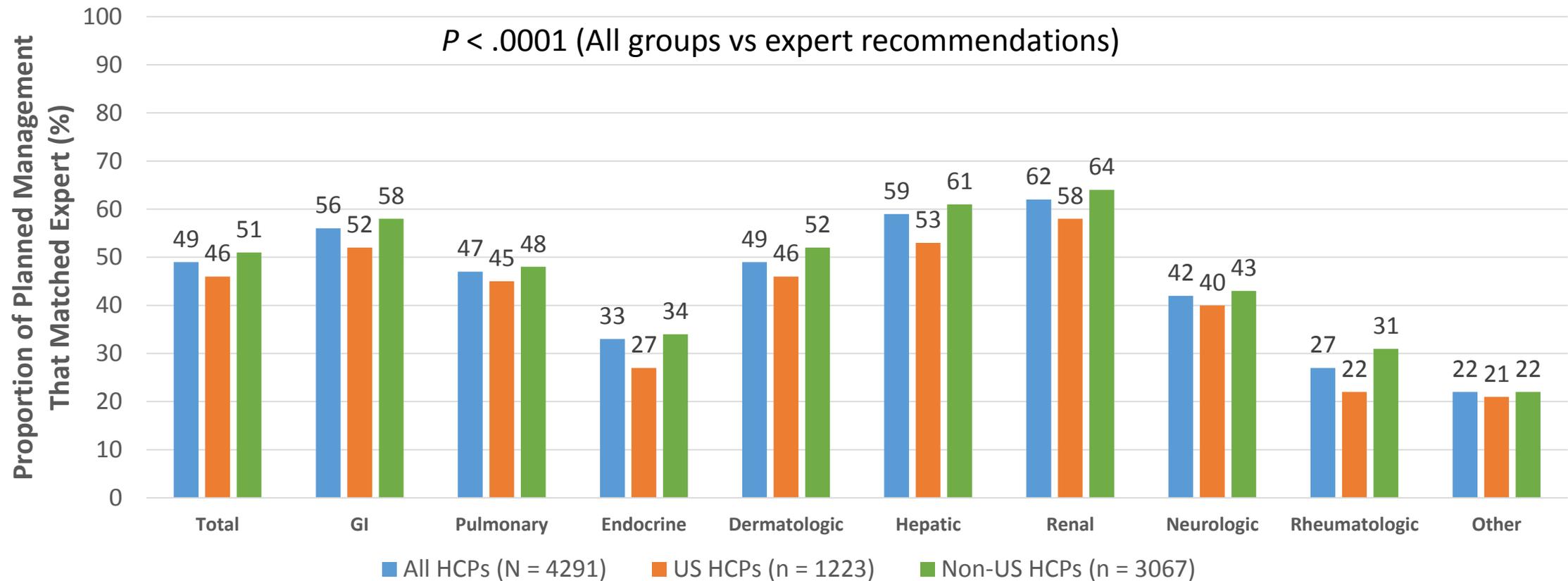
- In total, 4291 cases were entered into the tool by HCPs
- The most frequently entered cases were of GI origin (27%), followed by pulmonary (20%)
- “Rheumatologic” and “other” were added to the most recently updated tool and thus had the fewest cases



# Planned Management of HCPs Compared With Evidence-Based Recommendations: Overall Cases Entered (N = 4291)

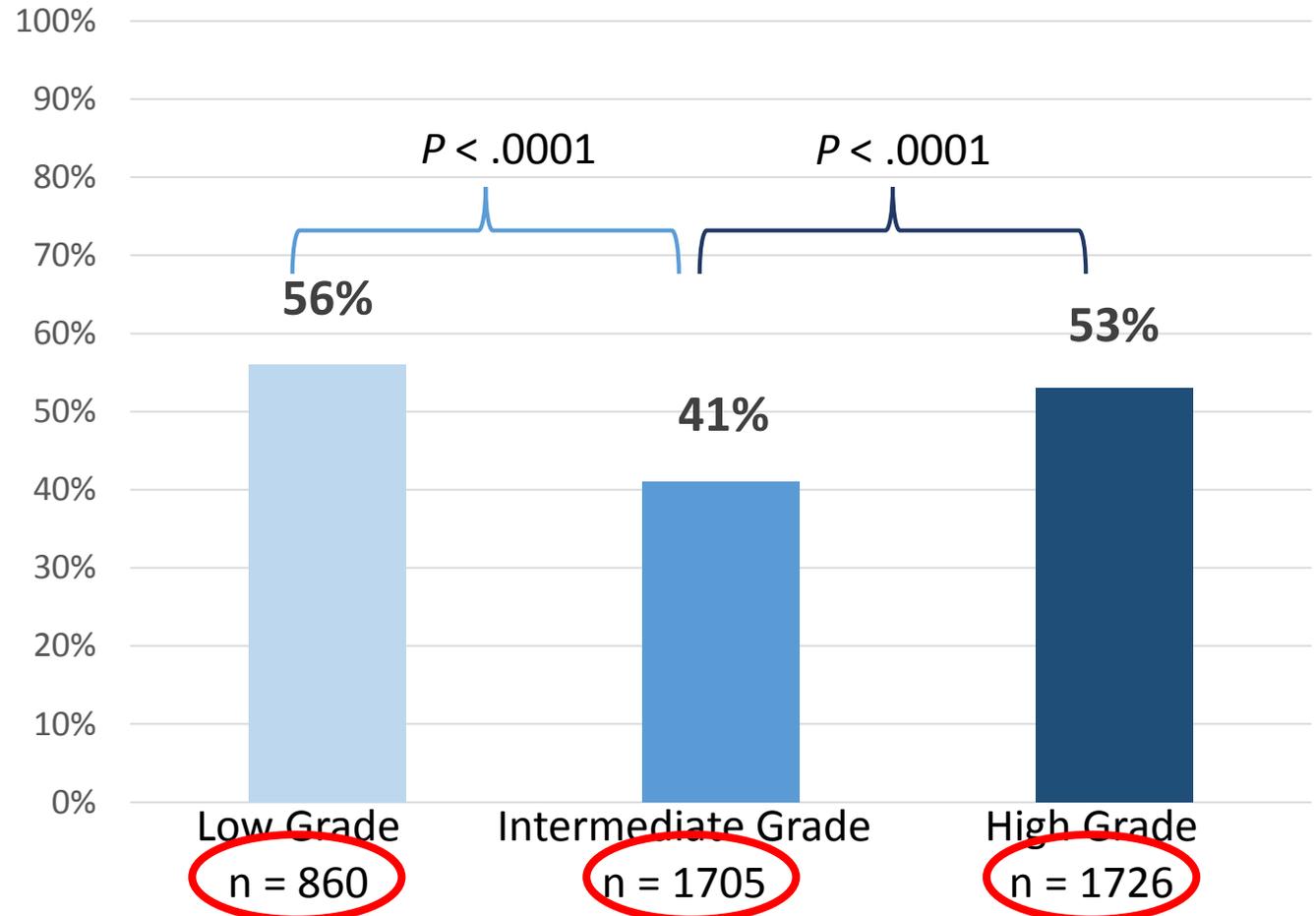


# Planned Management of HCPs Compared With Evidence-Based Recommendations: Overall Cases Entered (N = 4291)



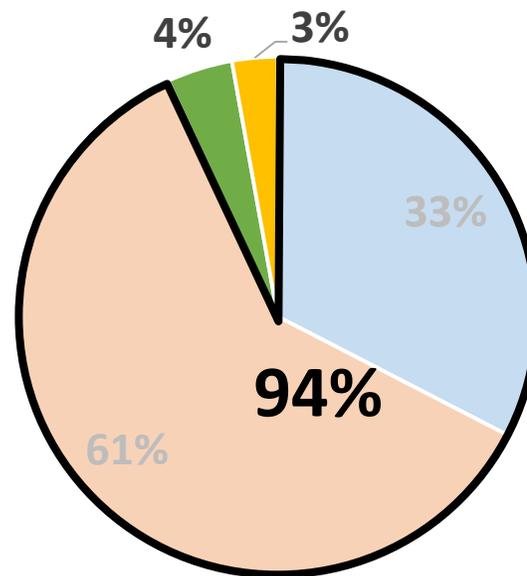
# Planned Management of HCPs Compared With Evidence-Based Recommendations by Symptom Grade (N = 4291)

- Greatest variance between initial HCP management plan and evidence-based recommendation occurred with intermediate-grade events
- HCPs used the tool to research management of intermediate- and high-grade events twice as often as low-grade events



# Impact of the Tool on Practice

- Of participants who answered the impact survey (n = 957):
  - **94%** indicated that the tool recommendations either confirmed or changed their management plan
  - **30%** were using the tool to manage a specific patient in their clinic



- Changed management plan
- Increased confidence in management plan
- Still undecided on how to manage
- Disagree with expert recommendation

## Lessons and Take-home Messages

- Despite available data, product inserts, and guidance on manufacturer Web sites, our analysis suggests many clinicians are not optimally managing irAEs associated with immune checkpoint inhibitor use
  - Overall, 49% of HCPs using the tool selected an initial management plan that matched evidence-based recommendations (46% US HCPs, 51% non-US HCPs;  $P < .0001$ )
  - Variance between HCP intended management and evidence-based recommendations was significant in each organ system
  - Lower concordance observed with intermediate vs low- or high-grade events
- A fair, balanced, evidence-based online irAE management tool is an important clinical resource that might improve patient care and safety
- The irAE tool will be updated regularly:  
[clinicaloptions.com/immuneAETool](https://clinicaloptions.com/immuneAETool)

# Acknowledgments

- Jeffrey S. Weber, MD, PhD
- Colleagues and coauthors at Clinical Care Options
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