1263 DERMATOLOGIC IMMUNE RELATED ADVERSE EVENT DISEASE DEFINITIONS: A MULTI-INSTITUTIONAL DELPHI CONSENSUS PROJECT PRESENTED ON BEHALF OF THE ONCODERMATOLOGY WORKING GROUP

[1]Steven Chen*, [2]Nicole LeBoeuf, [1]Kerry Reynolds, [1]Yevgeniy Semenov. *[1]MGH, Boston, MA, USA; [2]DFCI, Boston, MA, USA*

Background The accurate diagnosis and management of Dermatologic immune related adverse events (D-irAEs) from immune checkpoint inhibitors (ICI) are challenging because of the lack of specific, standardized disease definitions and severity grading criteria that capture the heterogeneity of possible manifestations of immune toxicity. However, determining the rash subtype is critical for effective treatment and future irAE risk and management.

Our group sought to develop D-irAE subtype definitions for diagnosis and severity grading developed through a modified Delphi consensus process.

Methods A working group of oncodermatologists drafted a classification system with guidance statements and disease definitions to support the work-up, diagnosis and severity grading of D-irAEs. Core diagnoses for the draft were chosen based on available literature on the presentation and frequency of D-irAEs, choosing the ten most commonly reported D-irAEs. The proposed system of diagnosis and severity grading was then reviewed by a panel of dermatologists, oncologists, oncodermatologists and irAE subspecialists. A modified Delphi consensus process was used, with 2 rounds of anonymous ratings by panelists and 2 virtual meetings to discuss controversial areas. Consensus based on numeric ratings was determined using the RAND/UCLA Appropriateness Method. The Delphi process was exempted by the Massachusetts General Hospital IRB.

Results The panel consisted of 34 members (of 35 invited) who accepted invitations to participate in the modified Delphi consensus process. Participants represented 16 different centers including US medical centers in the northeast (5), mid-west (2), south/southeast (5), and west (3), as well as 1 international clinicians and subject matter experts.

Over two rounds of voting, the panel identified unmet needs for D-irAE disease definitions and reached consensus on a variety of statements related to D-irAE, including the proposed approach (figure 1), typical timing, and other important factors in the work up of these immune toxicities. A standard work up was also proposed and found to be in agreement for all potential D-irAEs (median 8, range 6-9) (figure 2). Finally, the disease definitions, work up considerations, and diagnostic criteria for 10 predeterminted D-irAE subtypes were developed and reached consensus.

Conclusions By properly identifying the patient's D-irAE, the clinician is able to tailor treatment and understand implications about the patient's cancer therapy and toxicities. The proposed system herein allows for a standard algorithm for work-up and investigation that may lead to a core D-irAE diagnosis. We are hopeful that the implementation of said system in clinical trials will allow for more granular adjudication of data.

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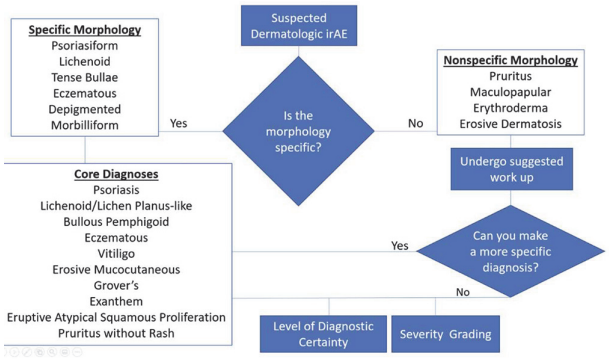

Abstract 1263 Figure 1 Proposed algorithm for D-irAE workup toward core diagnosis

Abstract 1263 Table 1 Standard work up proposedProposed standardized work up for all potential D-irAEs

STANDARD D-IRAE WORK UP
Common:
1. Full skin exam by an experienced clinician
2. Full skin exam by a board-certified dermatologist
3. Skin biopsy for H&E
4. Laboratory evaluation to assess of evidence of systemic hypersensitivity reaction (CBC with differential, CMP, UA).
Possible:
1. Skin biopsy for direct immuno-fluorescence
2. ELISAs for Bullous Pemphigoid antibody titers
3. ANA, ENA if photo-sensitivity component is noted
Uncommon/Usually Unnecessary:
For certain subtypes of D-irAE, there are other specific tests that may be considered. These include:
1. Joint exam
2. Indirect immunofluorescence with salt-split skin
3. Serum IL-6 levels

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