Outcome Measurement Instruments Used to Evaluate Dermatologic Adverse Events In Cancer Trials: A Systematic Review

Sheila Shaigany, MD[1,2,3], Nicole Mastacouris, MS[1], Rachel Tannenbaum, MD[1], Andrew Strunk, MA[1], Christopher Luan, MD[1], Joshua Burshstein, MD[1], Aaron Burshstein, MD[1], Richard Carvajal, MD[1,2,3], Amit Garg, MD[1,2,3], Allireza Alloo, MD[1,2,3].

[1]Northwell Health, [2]Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, [3]Northwell Health Cancer Institute

Background

- Development of targeted chemotherapies and immunotherapies for cancer treatment has led to increase in frequency of dermatologic adverse events (DAEs)
- Cancer therapy-related DAEs impact quality of life and often result in dose reductions or treatment interruptions
- Assessment of type, severity, and impact of DAEs necessitates well-developed and validated clinician-reported (ClinROM) and patient-reported (PROM) outcome measures to interpret and compare across trials
- Gaps in DAE measures limit rigorous and clinically meaningful reporting

Objective

Evaluate heterogeneity and quality of ClinROMs and PROMs used to assess mucocutaneous toxicities or DAEs to systemic cancer therapy

Methods

Study design: 2 systematic reviews

1. Dermatologic Adverse Event Measures and Heterogeneity in Implementation

Inclusion Criteria: Randomized controlled trials or observational studies published through 3/7/23 which used a physician- or patient-assessed instrument to report DAEs (hair, skin, nails, mucous membranes) as a primary or secondary outcome in patients receiving systemic chemotherapy or cancer immunotherapy

- Abstract and full text review by 2 reviewers; conflicts resolved via discussion

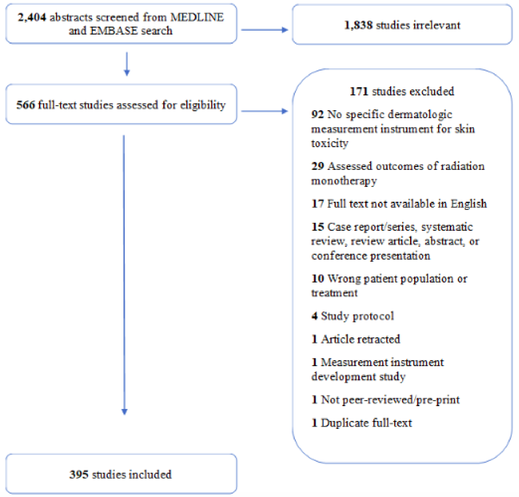
2. Psychometric Assessments and Quality Analysis of Chemotherapy Related-DAE Measures

Inclusion Criteria: Articles published through 4/12/23 using terms related to DAEs (excluding mucositis), cancer therapy, most commonly used measures (CTCAE, DLQI, Skindex (16, 17, 29), and WHO toxicity criteria), measurement properties or validation

- Included studies describing development or validation of measures in cancer patients on systemic cancer treatment
- Excluded studies using measurement instruments as an efficacy or safety outcome, or as a standard to validate a new instrument

Abbreviations: CTCAE, Common Terminology Criteria for Adverse Events. RTOG, Radiation Therapy Oncology Group. DLQI, Dermatology Life Quality Index. WHO, World Health Organization.

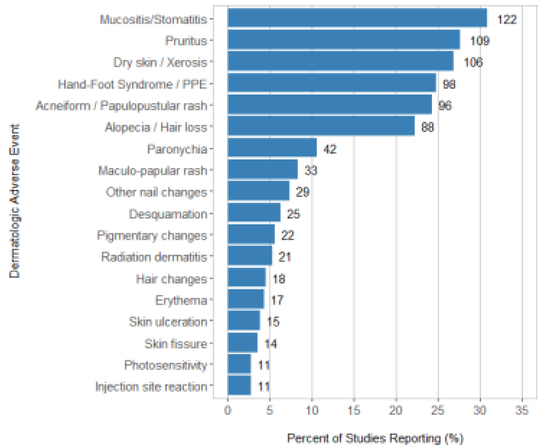
Dermatologic Adverse Event Measures and Heterogeneity in Implementation



- Identified 37 measures: 17 ClinROMs and 20 PROMs
- Among ClinROMs, CTCAE (any version) was used in 331/395 (84%) of studies reporting DAEs, followed by RTOG criteria (22/395, 5.6%), and WHO Criteria (19/395, 4.8%)
- Skin-related PROMs were infrequently used in oncology trials; only 20% of studies (79/395) reported at least one; among these, DLQI (34/395, 8.6%) and Skindex-16 (20/395, 5.1%) were most frequently utilized
- Majority of studies (322/395, 82%) reporting DAEs used one measure

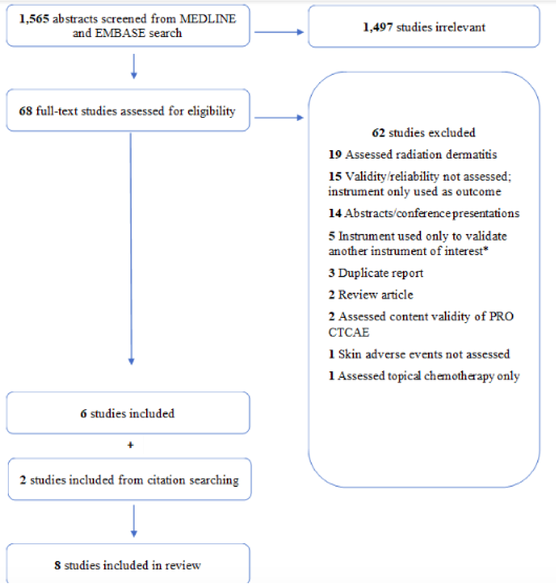
The most frequent reported descriptor of DAE was "rash" (153/395, 39%); other descriptions included mucositis/stomatitis (122/395 (31%), pruritus (109/395, 28%), dry skin/xerosis (106/395 (27%), hand-foot syndrome (98/395, 25%), acneiform eruption (96/395, 24%), and alopecia (88/395, 22%)

Figure 2. Number of studies reporting dermatologic adverse events (n=395)



Abbreviations: PPE, Palmar-Plantar Erythrodysesthesia

Psychometric Assessments and Quality Analysis of Chemotherapy Related-DAE Measures



- 8 studies included in analysis included 44 assessments of measurement properties for CTCAE, DLQI, and Skindex
- None reported measurement properties of WHO and RTOG criteria in the context of chemotherapy

- 3 assessments of construct validity of DLQI in context of chemotherapy-induced DAEs in patients with HFS
- DLQI showed moderate to high Spearman correlation (r_s = 0.61, 0.71) with the HFS-14 scale, with "very good" RoB ratings for each assessment
- Construct validity of Skindex total score (any version) in context of chemotherapy-induced DAE had 4 assessments, and Skindex subscales had 5 assessments
- There was moderate to high correlation (r_s 0.63-0.74) between Skindex-16 total and HFS-14 scales in two assessments evaluating convergent validity in patients with HFS
- Skindex-29 total score showed moderate correlations (r_s 0.61) with the Eruption Scoring System (ESS) in patients on combination chemotherapy with cetuximab
- 29 assessments of construct validity on CTCAE, specifically in acneiform rash, pruritus, xerosis, paronychia, alopecia, nail loss/onycholysis, HFS, and any other DAE
- Moderate to high correlation between CTCAE and other measures of acneiform rash and pruritus; very high for alopecia, low to moderate for pruritus

Conclusions

- There is a narrow spectrum of ClinROMs and PROMs with limited validity used in measurement of DAEs in systemic chemotherapy oncology trials
- Gaps in the current measurement of chemotherapy-related DAEs highlight an opportunity to revaluate core outcomes in trials to include rigorous assessments of mucocutaneous toxicities