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

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Abstract and full text review by 2 reviewers; conflicts resolved. Identified 37 measures: 17

8 studies included in analysis

Moderate to high correlation between CTCAE and other measures of acneiform rash and

Skin

None reported measurement

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Majority of studies (322/395, 82%)

Excluded studies using measurement instruments as an efficacy

Gaps in the current measurement of chemotherapy

Among

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Skindex

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Construct validity of

DLQI, Dermatology Life Quality Index. WHO, World Health Organization.

Abbreviations: CTCAE, Common Terminology Criteria for Adverse Events. RTOG, Radiation Therapy Oncology Group.

Commonly used measures (CTCAE, DLQI, Skindex) were frequently utilized in oncology trials; only 20% of studies (79/395) reported at least one; among those, 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 mucosis/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%).

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

Psychometric Assessments and Quality Analysis of Chemotherapy Related-DAE Measures

• 8 studies included in analysis included 44 assessments of measurement properties in 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 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 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 0.61) with the Eruption Scoring System (ESS) in patients on combination chemotherapy with cetuximab

• 29 assessments of construct validity on CTCAE, specifically in acneform rash, pruritus, xerosis, paronychia, alopecia, nail loss/onycholysis, HFS, and any other DAE

• Moderate to high correlation between CTCAE and other measures of acneform 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 chemotheraphy-related DAEs highlight an opportunity to revalidate core outcomes in trials to include rigorous assessments of mucocutaneous toxicities

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