SKIN ADVERSE EVENTS OF ANTI-CANCER TREATMENTS:

AN EXAMINATION OF DRUG-ADVERSE EVENT ASSOCIATIONS

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INTRODUCTION

Although anticancer treatments, including chemotherapies, targeted therapies, radiotherapy, and immunotherapy, are effective for treating cancer, they can be associated with significant skin toxicities, or adverse events (AEs). These can cause discomfort and may lead to discontinuation of therapies. However, a comprehensive estimation of associations between the use of cancer drugs and skin AEs is currently lacking. This study aims to investigate these associations, using a large database.

MATERIAL & METHODS

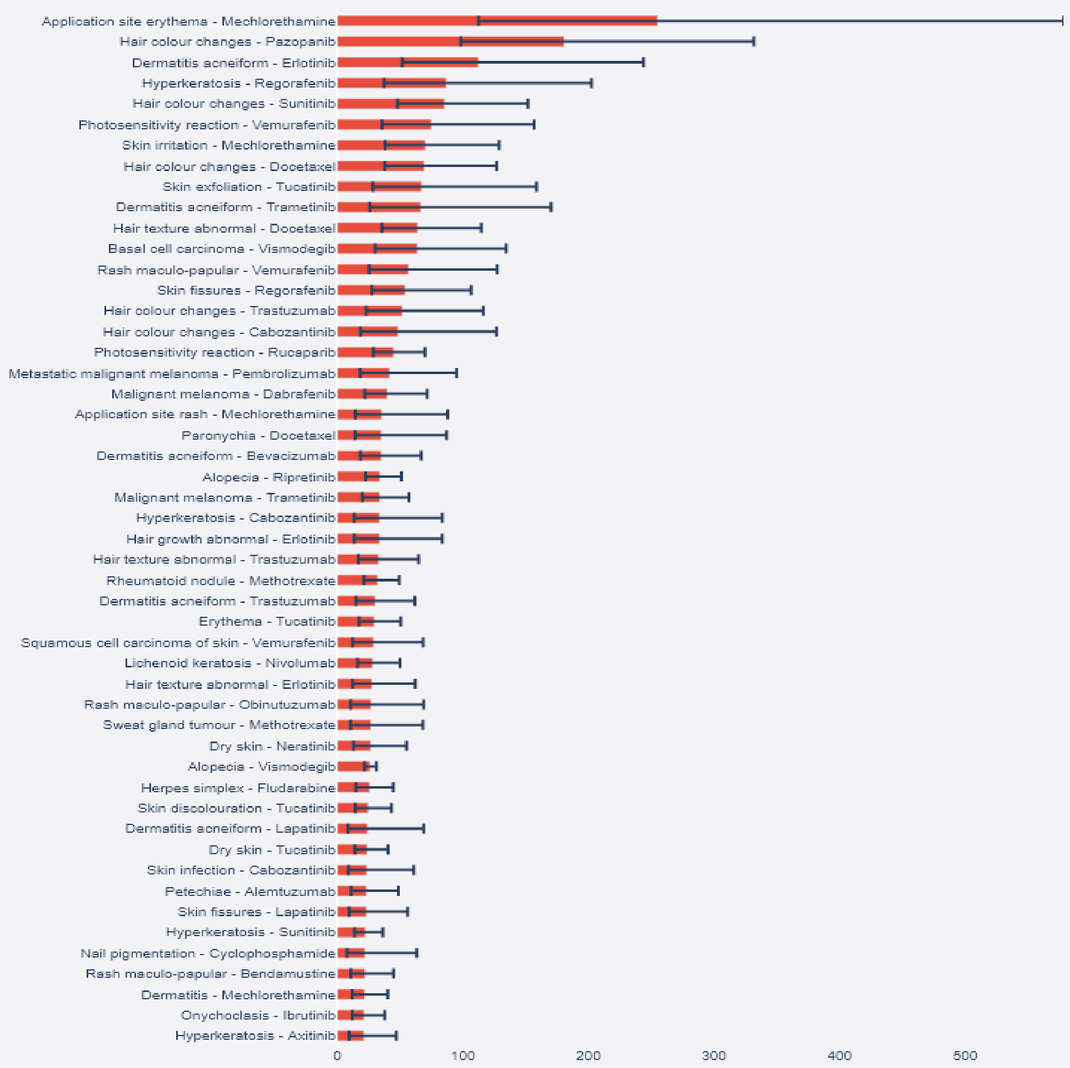
This study utilised the FDA's Adverse Event Reporting System (FAERS) database, focusing on health professional reports from January 2013 to September 2022. The database included 3,399,830 reports involving 3,084 drugs across all therapeutic areas and 16,348 AEs. A matching model using the nearest neighbour technique to identify 10 control reports for each case report based on cosine similarity of demographic and AE severity factors was used to minimise false positives and negatives. Bonferroni correction was used to handle false positives due to multiple comparisons.

RESULTS

Anticancer drugs were identified in the database (n=212). There were 10,698 anticancer drug-skin AE pairs, of which 676 had significant reporting odds ratios (ROR) >1, comprising 113 drugs and 144 AEs. The minimum ROR was 1.25, and 50% of associations displayed a ROR >10. *Figure 1* presents the top 50 drug-skin AE associations by ROR. Rash was significantly associated with 51 drugs and dry skin with 28 drugs.

Methotrexate was associated with 34 different AEs (among these, 7 were also statistically considered an indication of treatment), mechlorethamine with 33, and the anti-BRAF vemurafenib with 24 AEs. Targeted therapies were present in 49%, chemotherapies in 35.9%, and immunotherapies in 11% of pairs, respectively (*Figure 2*). Multikinase inhibitors were present in 21.8% of pairs involving a targeted therapy (*Figure 3*), and antimetabolites in 33.3% of those involving chemotherapy. Considering the relative weight of skin AEs on the tolerance profile of drugs, these AEs were present on average in 11% of the reports, with a maximum of 51% for mechlorethamine.

Figure 1: Top 50 drug-AE association by Reporting Odds Ratio (ROR)*



*Excluding associations with infinite RORs & those with fewer than 10 positive control reports

Figure 2: Distribution of significant drug-AE association by type of anti-cancer therapy

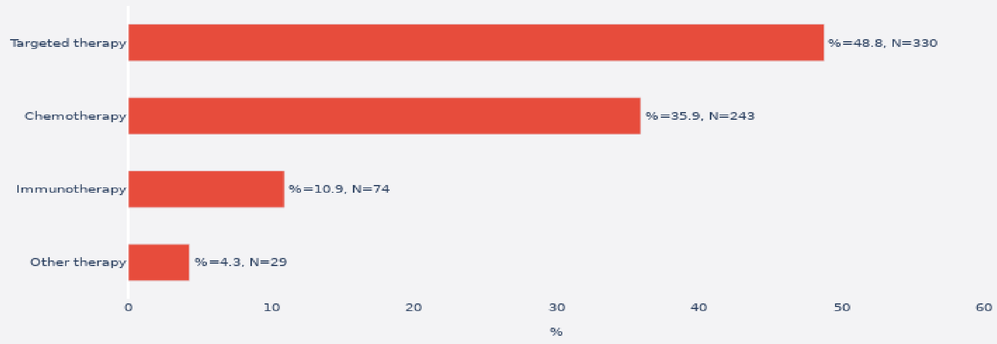
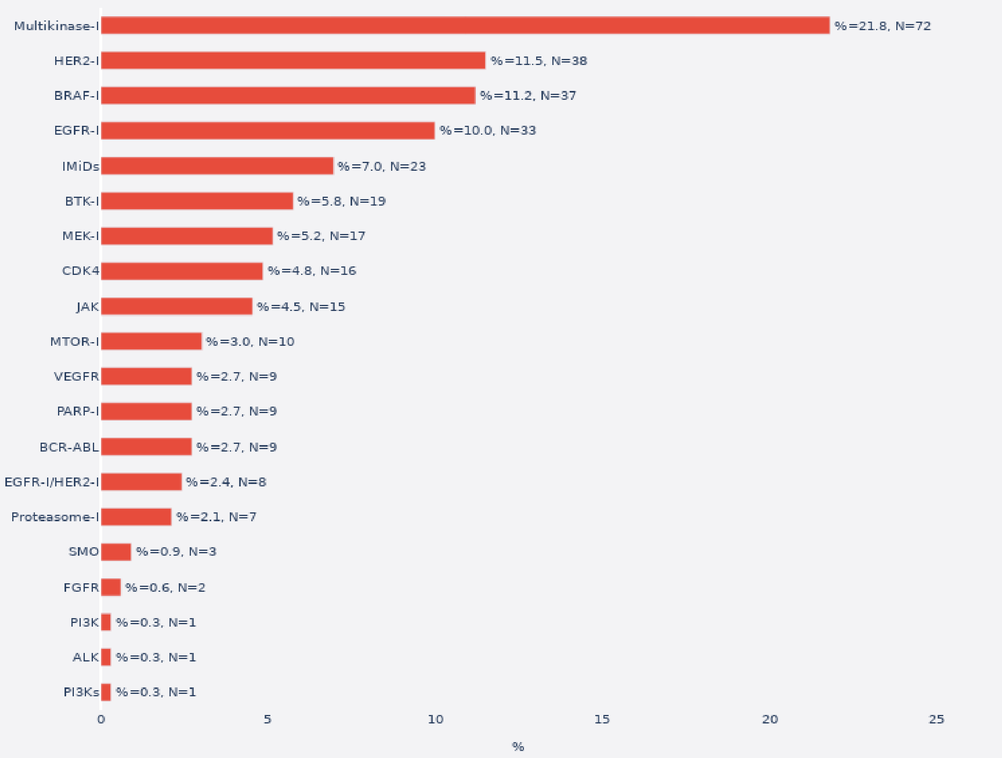


Figure 3: Distribution of significant drug-AE pairs by targeted therapy



CONCLUSION

This study used a large database to examine the associations between anticancer drugs and skin AEs. 113 anticancer drugs were identified as significantly associated with skin AEs, with rash and dry skin as the most reported AEs. Targeted therapies were most frequently associated with skin AEs, followed by chemotherapies. Methotrexate and mechlorethamine had the greatest number of associations. Some associations could be partially explained by the fact that certain anti-cancer drugs are also used to treat dermatological diseases or are administered transdermally. These data do not allow the assessment of skin AE incidence with anticancer drugs as they are likely under-reported, but the results enable quick identification of signals of skin toxicity after the introduction of new treatments. They also highlight the importance of monitoring skin AEs in patients undergoing anticancer treatments.

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