COMPARISON OF DERMATOLOGICAL SIDE EFFECTS ACROSS FIRST-GENERATION TYROSINE KINASE INHIBITORS

K. ALI[1], B. LI[1] and WJR. QUAN[2]
1. Department of Medicine, University of Florida- Jacksonville
2. Division of Hematology/Oncology, University of Florida-Jacksonville

UF College of Medicine Jacksonville

Introduction

Tyrosine kinase inhibitors (TKIs) continue revolutionizing cancer therapy, with recent breakthroughs in NSCLC treatment. However, TKIs have adverse effects, such as dermatological side effects, that may limit their therapeutic benefit. Retrospective data review can help understand this and result in fewer discontinuations.

Aim

This is a retrospective analysis of adverse dermatologic events (ADE) among first-generation TKIs (imatinib, gefitinib, erlotinib) using the FDA Adverse Event Reporting System (FAERS) database, which contains information on adverse event reports submitted to FDA.

Objectives

- Generate information on the dermatologic side effects of first-generation TKI
- Compare this data to other dermatologic side effects across other generations of TKI as a whole

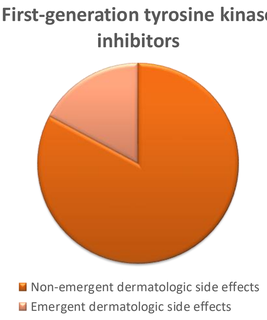
Methods

- ADE were sub-categorized into '**non-emergent**' (NE) and '**emergent**' (E), with 'emergent' including effects that would likely result in an urgent healthcare visit.
- 'Non-emergent' consisted of rash, dry skin, pruritus, alopecia, erythema, acne, and nail discoloration. 'Emergent' consisted of skin exfoliation, stomatitis, mucosal inflammation, cellulitis, drug reaction with eosinophilia and systemic symptoms (DRESS), urticaria, Stevens-Johnson syndrome (SJS), dermatitis, palmar-plantar erythrodysesthesia (PPE).
- Data for second- (bosutinib, dastinib, nilotinib) and third- (osimertinib) generation TKIs were obtained for the same data points. Statistical analysis was performed using Microsoft Excel and the Chi-square test, comparing the ADE of first-generation TKIs to other generations.

	First-Generation TKI	Other TKI	Total	Relative Risk	95% confidence interval	p-value
Non-Emergent (NE) Dermatological Side Effects	15698	9349	25047	0.97	(0.94, 0.98)	0.005
Emergent (E) Dermatological Side Effects	3251	1767	5018	1.03	(1.01, 1.06)	0.004
Total	18949	11116	30065			

Results

- In first-generation TKI, **18949 ADE** were reported, with **15698 non-emergent** (NE) and **3251 emergent** (E). Compared to second and third-generation TKI, NE's relative risk (RR) was **0.97**. For E, the RR was **1.03**.
- Both these associations had statistically significant confidence intervals (CI) and p-values. **First-generation TKI has a slightly higher association with ADE which would require urgent medical attention than other-generation TKI.** However, the overall incidence of emergent is lower compared to non-emergent. There is a lower risk of NE ADE with first-generation TKI.



Summary

First-generation TKI has a slightly higher association with ADE which would require urgent medical attention than other-generation TKI. Further studies comparing all three generations of TKI will help generate more robust data.

Discussion

FAERS relies on voluntary reporting, which can result in underreporting or misclassifying data. For example, 'rash' may be reported, but the severity of the rash may be downplayed, leading to it falling under the 'non-emergent' rather than 'emergent.'
Mild ADE may not be reported and can skew the data toward more severe cases.

References

1. U.S. Food and Drug Administration. FDA Adverse Event Reporting System (FAERS) Public Dashboard. https://fis.fda.gov/sense/app/95239e26-e0be-42d9-a960-9a5f7f1c25ee/sheet/7a47a261-d58b-4203-a8aa-6d3021737452/state/analysis

Contact: kabeer.ali@jax.ufl.edu