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# Adverse drug reactions associated with tyrosine kinase inhibitors in cancer patients: A retrospective cross-sectional study

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# **ABSTRACT**

Background: Tyrosine kinase inhibitors (TKIs) demonstrate superior efficacy over conventional chemotherapy but are associated with various adverse drug reactions (ADRs) that can compromise therapeutic efficacy and patient adherence. Objectives: This study analyzed the ADRs associated with tyrosine kinase inhibitors (TKIs) prescribed for cancer patients undergoing treatment at the Oncology Department of Nhan Dan Gia Dinh Hospital. Methods: A retrospective cross-sectional study was conducted using outpatient records and TKI prescriptions collected from treatment encounters from June 2024 to June 2025. Results: Among the 449 TKIcontaining prescriptions reviewed, 416 (92.7%) were associated with at least one ADR, while 33 prescriptions (7.3%) reported no ADRs. The most prevalent toxicities involved gastrointestinal (59.2%), skin and subcutaneous tissue disorders (58.6%), and hepatobiliary disorders (30.7%). Serious adverse events included interstitial lung disease (8.9%) and cardiac disorders (2.4%). Other observed ADRs were eye and general disorders (e.g., fatigue). Regarding concurrent toxicity (N = 416), 69.5% of cases involved 1-3 ADRs, while 23.2% experienced more than 3 ADRs. This high frequency of ADRs per TKI prescription reflects the complexity of the toxicity profile and the significant risk of patients facing concurrent adverse effects during targeted therapy. Conclusion: The use of TKIs in cancer patients is associated with a high prevalence of ADRs, primarily manifesting as gastrointestinal, skin, and subcutaneous tissue disorders, hepatobiliary disorders. These findings underscore the importance of careful monitoring and management of ADRs to optimize treatment efficacy. Furthermore, the frequent occurrence of concurrent ADRs necessitates a comprehensive pharmacovigilance approach. Early detection and proactive management of these toxicities are crucial to maintain treatment adherence and preserve the quality of life for cancer patients.

**Keywords:** oncology, targeted therapy, tyrosine kinase inhibitors, adverse drug reactions

#### 1. INTRODUCTION

Adverse drug reactions (ADRs) associated with tyrosine kinase inhibitors (TKIs) are common and often multifaceted, reflecting both the targeted and off-target effects of these agents. The most frequently reported adverse drug reactions include skin and subcutaneous tissue disorders such as hand-foot skin reaction (HFSR), rash, xerosis, and paronychia; gastrointestinal sym-ptoms like diarrhea, nausea, and stomatitis [1]. Occasionally, hepatobiliary disorders, fatigue, and decreased weight are other common systemic side effects experienced by many patients [2]. While most ADRs are mild to moderate and manageable with supportive care or dose adjustments, severe toxicities can occur, including interstitial lung disease (ILD), cardiac disorders, and severe eye disorders. Blood and lymphatic system disorders like neutropenia and thrombocytopenia are also reported, especially with certain TKIs like sorafenib, imatinib [3]. Understanding the characteristic ADRs profile of specific TKIs is essential for optimizing patient management, improving adherence to therapy, and minimizing morbidity associated with treatment. Given the growing recognition of TKI-associated ADRs and the existing gaps in their clinical characteristics, this study was conducted to evaluate the ADRs among patients treated with tyrosine kinase inhibitors in the Oncology Department of Nhan Dan Gia Dinh Hospital.

#### 2. OBJECT AND METHOD

## 2.1. Object

A retrospective cross-sectional study was

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conducted using outpatient records and TKI prescriptions collected from treatment encounters from June 2024 to June 2025. It was approved by the Ethics Committee of Hong Bang International University under Decision No. 995/QĐ-HIU dated September 6, 2024, and was authorized to be conducted at Nhan Dan Gia Dinh Hospital.

#### 2.2. Method

A total sampling technique was employed. All eligible TKI prescriptions and medical records of cancer patients treated with TKIs at Nhan Dan Gia Dinh Hospital during the study period were retrieved. Inclusion criteria comprised prescriptions with cancer receiving TKIs therapy within the specified timeframe. Exclusion criteria were limited to records with missing essential data, preventing valid ADR assessment. Consequently, 449 records were eligible for the final analysis.

# 2.3. Data collection and definition of variables

- Demographic and clinical characteristics: Age, sex, body mass index (BMI), cancer diagnosis, stage of disease, and comorbidities.
- Treatment details: Information on the specific TKI regimen (type of drug, initial dosage, dosage modifications), duration of therapy, and concomitant medications.
- ADR-related variables: For every suspected ADR, we recorded the date of onset, clinical manifestations, laboratory abnormalities, management strategies (e.g., dose reduction, temporary interruption, or discontinuation), and

the outcome of the reaction.

#### 2.4. ADRs assessment criteria

The identification and classification of ADRs were conducted based on clinical symptoms, physical examinations, and laboratory findings extracted from medical records. The assessment followed a standardized two-step protocol:

- Causality assessment: The relationship between TKIs and suspected ADRs was evaluated using the Naranjo probability scale. Only events classified as "definite," "probable," or "possible" were included in the study.
- Classification: ADRs were coded and categorized by System Organ Class (SOC) using the Medical Dictionary for Regulatory Activities (MedDRA) terminology to ensure consistency in reporting.

# 2.5. Statistical Analysis

Data analysis was performed using SPSS Statistics 27.0 version. Descriptive statistics were used to summarize patients' characteristics, and categorical variables were expressed as frequencies and percentages. Continuous variables were presented as means ± standard deviations (SD) or medians with interquartile ranges (IQR). To identify factors associated with TKI-induced ADRs, the Chi-square/Fisher test, Logistic Regression were employed for categorical variables. A p-value of < 0.05 was considered statistically significant.

#### 3. RESULTS

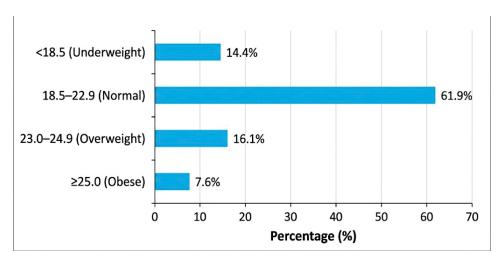


Figure 1. BMI characteristics in the study population

Comment: The majority of the study population fell within the normal weight range (61.9%). Underweight

status was observed in 14.4%, while overweight and obesity accounted for 16.1% and 7.6%, respectively.

Table 1	Raseline	demograph	nic and	nrescription	characteristics
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Characteristics	Frequency (n)	Percentage (%)					
	Age group (years)						
18 - 59	266	59.2					
≥ 60	183	40.8					
	Sex						
Male	253	56.3					
Female	196	43.7					
	Prescription duration						
≤ 14 days	171	38.1					
15 - 30 days	278	61.9					
Total	449	100.0					

Comment: Analysis of the 449 TKI prescriptions indicated that patients in the 18 - 59 age group constituted the majority (59.2%), whereas the elderly group (≥ 60 years) accounted for 40.8%. Regarding sex distribution, male patients represented a higher proportion (56.3%)

compared to females (43.7%). Notably, the majority of prescriptions were dispensed for a duration of 15 to 30 days (61.9%), aligning with outpatient prescribing regulations for chronic conditions. Meanwhile, short-term prescriptions ( $\leq$ 14 days) accounted for 38.1%.

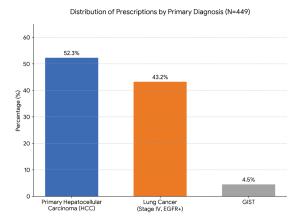


Figure 2. Distribution of study population by primary diagnosis

Comment: Primary Hepatocellular Carcinoma (HCC) was the predominant diagnosis, accounting for more than half of the study population (52.3%). Patients diagnosed with Stage IV EGFR-positive

Malignant Neoplasm of Lung constituted the second largest group at 43.2%, while Gastrointestinal Stromal Tumors (GIST) accounted for a minority of cases (4.5%) in the study population.

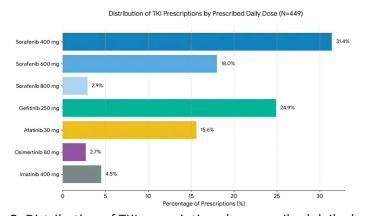


Figure 3. Distribution of TKI prescriptions by prescribed daily dose

Comment: The majority of the study population received sorafenib, which constituted 52.3% of the total 449 TKI prescriptions analyzed. This finding aligns with the pathological characteristics of the study population, where Primary Hepatocellular Carcinoma (HCC) was the predominant diagnosis, accounting for 52.3% of the study population.

Sorafenib prescriptions were distributed across three dosing levels, with the 400 mg dose being the most frequent (31.4%), followed by 600 mg (18.0%) and 800 mg (2.9%). Regarding other TKIs, gefitinib 250 mg accounted for 24.9%, followed by afatinib 30 mg (15.6%), imatinib 400 mg (4.5%), and osimertinib 80 mg (2.7%).

**Table 2.** Characteristics of the number of drugs and active substances per treatment encounter

Characteristic	Q2	Q1	Q3	(Q2 (Q1 - Q3))	Min-Max
Number of drugs per treatment encounter	4.00	4.00	7.00	4.00 (4.00 - 7.00)	2 - 20
Number of active substances per treatment encounter	6.00	4.00	10.00	6.00 (4.00 - 10.00)	2 - 28

Note: Q2 (Median): The 50th percentile, Q1 (1st Quartile): The 25th percentile, Q3 (3rd Quartile): The 75th percentile, IQR (Interquartile Range): The range between Q1 and Q3 (Q3 - Q1), representing the middle 50% of the data

Comment: The results indicated that the median number of drugs per treatment encounter was 4 (IQR: 4-7), while the median number of active substances was 6 (IQR: 4-10). The maximum number reached 20 drugs and 28 active substances per treatment encounter, whereas the minimum recorded was 2 drugs.

**Table 3.** Prevalence of ADRs in the study population

ADRs	Frequency (n)	Percentage (%)
No ADRs reported	33	7.3
ADRs occurred	416	92.7
Total	449	100.0

Comment: Based on the Naranjo probability scale, the causality assessment for all identified ADRs was classified as "probable" or "possible". Among a total of 449 prescriptions containing TKIs reviewed, 416 prescriptions reported ADRs, accounting for 92.7%, while 33 prescriptions had no ADRs recorded, representing 7.3%.

**Table 4.** Distribution of the number of ADRs per affected prescription

Number of ADRs	Frequency (n)	Percentage (%)
1 to 3 ADRs	312	69.5
> 3 ADRs	104	23.2
Total	416	92.7

Comment: Among the 416 prescriptions that reported ADRs, most (69.5%) involved only 1 to 3 ADRs. However, a notable proportion (23.2%) showed poly-ADRs, with more than 3 ADRs occurring in a single treatment encounter.

**Table 5.** Prevalence of ADRs stratified by TKI agents

TKIs	Total Prescribed (N)	ADRs Occurred (n)	Prevalence (%)
Gefitinib	112	111	99.1
Sorafenib	235	231	98.3
Afatinib	70	66	94.3
Imatinib	20	8	40.0

TKIs	Total Prescribed (N)	ADRs Occurred (n)	Prevalence (%)
Osimertinib	12	0	0.0
Total	449	416	92.7

Comment: Among the 416 prescriptions reporting the occurrence of adverse drug reactions (ADRs), sorafenib was the most frequently suspected agent, accounting for 231 cases (55.5%). gefitinib was the second most commonly implicated drug with 111 cases (26.7%), followed by afatinib with 66 cases (15.9%). Imatinib contributed a smaller proportion,

with a total of 8 cases (1.9%). This distribution aligns with the study's pathological profile, predominantly comprising Primary Hepatocellular Carcinoma (HCC, 52.3%), followed by Stage IV EGFR-positive Lung Cancer (43.2%) and GIST (4.5%). Notably, gefitinib demonstrated the highest toxicity prevalence (99.1%), slightly exceeding sorafenib (98.3%).

Table 6. Prevalence of ADRs observed in the study population

ADRs	Frequency (n)	Percentage (%)
Gastrointestinal disorders	266	59.2
Skin and subcutaneous tissue disorders	263	58.6
Hepatobiliary disorders	138	30.7
Fatigue	131	29.2
Blood and lymphatic system disorders	64	14.3
Eye disorders	45	10.0
Interstitial Lung Disease (ILD)	40	8.9
Other ADRs*	51	11.4
Weight decreased	34	7.6

<sup>\*</sup> Other ADRs include acute renal failure, scrotal infection, orchitis, peripheral neuropathy, cardiac disorders..., among others

Comment: Gastrointestinal disorders (59.2%) and skin and subcutaneous tissue disorders (58.6%) were the most prevalent ADRs observed in the population. Hepatobiliary disorders and fatigue also occurred frequently, affecting 30.7% and 29.2%

of the cases, respectively. Less frequently reported toxicities, such as acute renal failure, scrotal infection, and cardiac disorders, were aggregated into the "Other ADRs", which collectively accounted for 11.4% (N = 51) of the total reported events.

**Table 7.** Association between age and number of ADRs encountered

Number of ADRs, n (%)	18 - 59 years (N = 266)	≥ 60 years (N = 183)	Total (N = 449)	OR (95% CI)	p-value
≤ 3 ADRs	224 (84.2%)	121 (66.1%)	345 (76.8%)	2.73 (1.74 - 4.29)	< 0.001
> 3 ADRs	42 (15.8%)	62 (33.9%)	104 (23.2%)	2.73 (1.74 - 4.23)	< 0.001

Note: OR = Odds ratio; CI = Confidence interval; ADR = Adverse drug reaction. The Chi-square test was used to determine the p-value

Comment: Patients ≥ 60 years old had significantly higher odds of experiencing more than 3 ADRs

compared to those aged 18 - 59 years (OR = 2.73, 95% CI: 1.74 - 4.29, p < 0.001).

Table 8. Association between sex and the number of ADRs encountered

Number of ADRs, n (%)	Male (N = 253)	Female (N = 196)	Total (N = 449)	OR (95% CI)	p-value
≤ 3 ADRs	211 (83.4%)	134 (68.4%)	345 (76.8%)	2.32 (1.49 - 3.63)	< 0.001
> 3 ADRs	42 (16.6%)	62 (31.6%)	104 (23.2%)	2.32 (1.49 - 3.03)	< 0.001

Note: OR = Odds ratio; CI = Confidence interval. The Chi-square test was used to determine the p-value

Comment: A significant association was observed between sex and the frequency of ADRs. Female patients showed a significantly higher prevalence of encountering more than 3 ADRs (31.6%) compared to male patients (16.6%). Specifically, females were 2.32 times more likely to experience a higher number of ADRs (> 3 events) than males (OR = 2.32, 95% CI: 1.49 - 3.63).

Table 9. Association between treatment duration and number of ADRs encountered

Number of ADRs, n (%)	≤ 14 days (N = 171)	15 - 30 days (N = 278)	Total (N = 449)	OR (95% CI)	p-value
≤ 3 ADRs	123 (71.9%)	222 (79.9%)	345 (76.8%)	0.65(0.42 - 1.01)	0.053
> 3 ADRs	48 (28.1%)	56 (20.1%)	104 (23.2%)	0.03(0.42 - 1.01)	0.055

Note: OR = Odds ratio; CI = Confidence interval. The Chi-square test was used to determine the p-value

Comment: There was no statistically significant association observed between the duration of treatment and the number of ADRs encountered. Although the prevalence of > 3 ADRs appeared higher in the group treated for  $\leq$  14 days (28.1%) compared to the 15 - 30 days group (20.1%), this difference did not reach statistical significance (OR = 0.65, 95% CI: 0.42 - 1.01).

# 4. DISCUSSIONS

Our study highlights a substantial toxicity burden associated with TKI therapy in a real-world setting, with a striking 92.7% of prescriptions reporting at least one adverse event. This prevalence is notably high, reflecting the systemic impact of broadspectrum kinase inhibition. Furthermore, the fact that 23.2% of the population experienced poly-ADRs (more than 3) underscores the complexity of managing these patients outside of controlled clinical trials. This toxicity burden not only compromises patient quality of life but also poses a significant challenge to treatment adherence. A recent real-world analysis of TKI-treated patients with advanced cancer reported that over 80% developed toxicities in multiple organs, with gastrointestinal events in 76%, fatigue in 61.5%, and cardiovascular complications in 49%, highlighting that multi-organ toxicity rather than isolated events is the rule. In chronic myeloid leukemia cohorts, almost all patients on long-term TKIs report persistent low-grade adverse events involving several systems (e.g., musculoskeletal pain, GI symptoms, skin changes, metabolic and cardiovascular issues), which collectively impair quality of life and often drive dose reductions or treatment switches [4].

Consistent with the known pharmacological

profiles of TKIs, gastrointestinal disorders (59.2%) and skin and subcutaneous tissue disorders (58.6%) were the most prevalent ADRs observed. Hepatobiliary disorders and fatigue also occurred frequently, affecting 30.7% and 29.2% of the study population, respectively, emerging as the hallmark toxicities. This prevalence aligns with the mechanism of action of EGFR and VEGFR inhibitors, particularly the off-target inhibition of EGFR, which is highly expressed in rapidly proliferating tissues such as the epidermis and intestinal mucosa [5]. The disruption of skin and subcutaneous tissue disorders leads to the high frequency of diarrhea and skin reactions (e.g., HFSR, rash, xerosis,...) observed in this study, mirroring findings from pivotal trials like SHARP and IPASS. The SHARP trial established sorafenib as the first systemic therapy to significantly prolong overall survival in advanced hepatocellular carcinoma, improving median survival from 7.9 to 10.7 months, with a toxicity profile dominated by diarrhea, hand-foot skin reaction, weight loss, and fatigue, most of which were grade 1 - 2 and manageable with dose modification. This pattern of predominantly gastrointestinal and dermatologic adverse events aligns closely with the high rates of GI and skin toxicities observed in the present study, supporting the conclusion that the heavy use of sorafenib in this cohort is a major driver of the overall ADR burden [6]. Similarly, the IPASS trial, which compared first-line gefitinib with carboplatin-paclitaxel in EGFR-selected non-small cell lung cancer, demonstrated that gefitinib significantly improved progression-free survival in EGFR-mutated tumors while producing a distinct safety profile characterized mainly by acneiform rash and diarrhea rather than the hematologic and

neuropathic toxicities typical of platinum-based chemotherapy [7]. Although these reactions are often graded as mild to moderate, their chronic nature requires proactive supportive care to prevent dose interruptions.

Beyond skin and subcutaneous tissue disorders, hepatobiliary disorders affected nearly one-third (30.7%) of the population. Hepatobiliary disorders are well-recognized adverse effects of many tyrosine kinase inhibitors (TKIs) and range from asymptomatic lab abnormalities to severe liver injury. TKIs such as imatinib, gefitinib, erlotinib, afatinib, sorafenib, sunitinib, pazopanib, and others commonly cause elevations in ALT, AST, and bilirubin, which are usually mild to moderate and reversible but sometimes reach grade 3-4 and require dose interruption or discontinuation. Patterns of injury can be hepatocellular, cholestatic, or mixed; reported clinical syndromes include drug-induced hepatitis, cholestatic jaundice, and, rarely, fulminant hepatic failure [8, 9]. This finding highlights the liver's vulnerability as the primary site of CYP450-mediated TKI metabolism.

Of particular concern is the 8.9% prevalence of Interstitial Lung Disease (ILD) observed in our study. Interstitial lung disease (ILD) is an uncommon but serious adverse effect of several tyrosine kinase inhibitors (TKIs), especially EGFR-TKIs used in non-small cell lung cancer (NSCLC). ILD prevalence in clinical trials of EGFR-TKIs such as gefitinib, erlotinib, afatinib, and osimertinib is generally reported around 0.6-2.2%, but real-world pharmacovigilance data show a stronger safety signal, suggesting ILD may be under-recognized. A recent large database analysis of over 20,000 EGFR-TKI adverse event reports identified 660 ILD cases and found significant disproportional reporting for all EGFR-TKIs, with ILD most frequently reported for osimertinib and gefitinib. Meta-analyses and pooled safety reviews also indicate that fatal toxicities related to EGFR-TKIs are rare ( $\approx 1$  - 1.5%), but ILD is the leading cause among these fatal events [10, 11].

Similarly, while cardiovascular events were rare (2.4%), their potential severity necessitates routine ECG and cardiac function screening, especially in patients with pre-existing comorbidities. Cardiovascular events are a major

toxicity concern with many TKIs and include hypertension, arrhythmias (especially QT prolongation), heart failure, and arterial and venous thromboembolic events. The pattern and frequency vary across the TKI class. Vascular endothelial growth factor receptor (VEGFR) TKIs such as sorafenib, sunitinib, pazopanib, and axitinib are particularly linked to new-onset or worsening hypertension; meta-analyses show they increase the risk of all-grade hypertension nearly fourfold and high-grade hypertension more than fourfold compared with controls, and hypertension occurs in up to about 40% of treated patients [12]. Mechanistically, VEGFR blockade reduces nitric oxide production, increases vasoconstrictors, and causes capillary rarefaction, raising systemic vascular resistance and blood pressure. These agents are also associated with arterial ischemic events (myocardial infarction, stroke, peripheral arterial disease) and thromboembolism, with observational analyses showing higher rates of arterial occlusive events and thromboembolism versus non-TKI therapies [13]. Although our study population included only patients with HCC, EGFR-positive lung cancer, and GIST, cardiovascular-related adverse drug reactions have, in fact, been documented in realworld settings.

The occurrence and severity of ADRs associated with TKIs are not solely dependent on the drugs themselves but are significantly influenced by the individual patient's clinical condition. Several factors, including age, sex, play a pivotal role in modulating TKI toxicity risk and presentation. Additionally, factors such as age, genetic polymorphisms affecting drug metabolism, disease burden, and organ reserve contribute to the individual variability in ADR profiles. Elderly patients or those with compromised renal or hepatic function may experience intensified toxicities or altered pharmacokinetics, necessitating dose adjustments or closer monitoring. Crucially, our findings demonstrate that patient-specific factors, specifically female sex and advanced age, are strong predictors of increased toxicity risk. Conversely, treatment duration did not significantly correlate with ADR frequency. Our multivariate analysis identified female sex (OR = 2.32) and advanced age (> 60 years) as significant predictors for experiencing a higher number of ADRs. This finding is consistent with accumulating evidence in oncology pharmacovigilance, which suggests that sex-based differences in pharmacokinetics (PK) and pharmacodynamics (PD) play a crucial role. Females typically have a lower body surface area (BSA) and a higher percentage of body fat compared to males, which can alter the volume of distribution for lipophilic drugs like TKIs. Furthermore, variations in the activity of hepatic enzymes (e.g., CYP3A4) activity and glomerular filtration rates between sexes potentially lead to higher systemic drug exposure and slower clearance[14, 15].

# 5. CONCLUSIONS

This study provides comprehensive real-world evidence of the safety profile of TKI therapy, characterized by a remarkably high overall prevalence of adverse events (92.7%). While the majority of toxicities were gastrointestinal and dermatological - consistent with the class effects of EGFR and VEGFR inhibition - the study identified significant safety signals regarding hepatotoxicity and interstitial lung disease that warrant vigilant monitoring. These findings demonstrate that patient-specific factors, specifically female sex

and advanced age, are strong predictors of increased toxicity risk. Conversely, treatment duration did not significantly correlate with ADRs frequency. These results support a shift towards personalized pharmacovigilance. Clinicians should implement intensified monitoring protocols for elderly and female patients and maintain a low threshold for investigating respiratory symptoms to detect potential ILD early. Given the influence of polypharmacy and potential genetic predispositions on hepatotoxicity, the integration of comprehensive medication reviews and close monitoring of hepatic function is essential to optimize the therapeutic index of TKIs - particularly within a personalized treatment at dose optimization for individual patients. Integrating these risk factors into therapeutic decision-making is essential to optimize the balance between oncological efficacy and patient safety.

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# Các phản ứng có hại của nhóm thuốc ức chế tyrosine kinase trên bệnh nhân ung thư: Nghiên cứu cắt ngang hồi cứu

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# TÓM TẮT

Đặt vấn đề: Các thuốc ức chế Tyrosine kinase (TKIs) đã chứng minh được hiệu quả vượt trội so với hóa trị liệu truyền thống nhưng vẫn liên quan đến nhiều phản ứng có hại của thuốc (ADRs), có thể làm ảnh hưởng đến hiệu quả điều trị và sự tuân thủ của bệnh nhân. Mục tiêu: Nghiên cứu này phân tích các ADR liên quan đến thuốc ức chế Tyrosine kinase (TKIs) được kê đơn cho bệnh nhân ung thư đang điều trị tại Khoa Ung bướu, Bệnh viện Nhân dân Gia Định. Phương pháp nghiên cứu: Đây là nghiên cứu mô tả cắt ngang hồi cứu được thực hiện dựa trên hồ sơ bệnh án ngoại trú và các đơn thuốc TKI thu thập từ các lượt khám điều trị từ tháng 06 năm 2024 đến hết tháng 06 năm 2025. Kết quả: Trong tổng số 449 đơn thuốc có chứa TKI được khảo sát, có 416 trường hợp (chiếm 92.7%) ghi nhận ít nhất một phản ứng có hại của thuốc (ADR), trong khi 33 trường hợp (7.3%) không ghi nhận ADR nào. Các độc tính phổ biến nhất bao gồm rối loạn tiêu hóa (59.2%), rối loạn da và mô dưới da (58.6%) và rối loạn gan mật (30.7%). Các biến cố bất lợi nghiêm trọng bao gồm bệnh phổi mô kẽ (8.9%) và rối loạn tim mạch (2.4%). Ngoài ra, các ADR khác cũng được ghi nhận bao gồm rối loạn về mắt và các rối loạn toàn thân (ví dụ: mệt mỏi). Về tình trạng xuất hiện đồng thời nhiều độc tính (trên tập mẫu N = 416), 69.5% các trường hợp ghi nhận từ 1 - 3 ADR, trong khi 23.2% gặp phải nhiều hơn 3 ADR. Tần suất xuất hiện ADR cao trên mỗi đơn thuốc TKI này phản ánh sự phức tạp của hồ sơ độc tính cũng như nguy cơ đáng kể về việc bệnh nhân phải đối mặt với các tác dụng phụ đồng mắc trong quá trình điều trị đích. Kết luận: Việc sử dụng TKI trên bệnh nhân ung thư liên quan đến tỷ lệ mắc ADR cao, chủ yếu biểu hiện dưới dạng rối loạn tiêu hóa, rối loạn da và mô dưới da, rối loạn chức năng gan. Những phát hiện này nhấn mạnh tầm quan trọng của việc theo dõi và quản lý chặt chế các phản ứng có hại để tối ưu hóa hiệu quả điều trị. Hơn nữa, sự xuất hiện thường xuyên của nhiều ADR xảy ra cùng lúc đòi hỏi một

phương pháp tiếp cận cảnh giác dược toàn diện. Phát hiện sớm và quản lý chủ động các độc tính này là yếu tố then chốt để duy trì sự tuân thủ điều trị và bảo tồn chất lượng cuộc sống cho bệnh nhân ung thư.

**Từ khóa:** ung bướu, điều trị nhắm trúng đích, thuốc nhóm TKIs, phản ứng có hại, ADRs

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