Comparative analysis of Safety of Targeted NSCLC Therapies using the FDA Adverse Event Reporting System (FAERS), differing experiences of Healthcare Providers (HCP) from EU vs US

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APPERTURE
FOCUSED VALUE

BACKGROUND

- Lung cancer remains the leading cause of cancer-related death worldwide, with non-small cell lung cancer (NSCLC) accounting for approximately 85% of lung cancer cases
- Advances in biomarker testing and the incorporation of targeted therapies into treatment guidelines have significantly improved outcomes for patients with NSCLC
- Compared with the United States, high variability in biomarker adoption is observed in the EU, likely due to further fragmentation of the market[1]
- This could, in turn, lead to varied safety outcomes between the two regions
- Therefore, to investigate this, we characterized and compared adverse events reported by healthcare professionals for each NSCLC targeted therapy class between the US and the EU

METHODS

- The FDA Adverse Event Reporting System database from Q1 2020 to Q1 2025 was utilized to perform this descriptive study
- All **NSCLC** drugs approved by the FDA were identified and categorized into their respective therapeutic classes
- The FAERS dataset was deduplicated and filtered by reports submitted only by a Healthcare Professional (HCP)
- Reports from European regions were pooled together as the comparator group to the US reports and missing data on the country of reporting were removed from the analysis[2]
- Total case counts were derived for each therapeutic class and only the top 5 classes were selected for further analysis: **ALK, BRAF, EGFR, RET** and **VEGF** inhibitors
- Descriptive analysis was conducted using SQL, summarizing the demographic characteristics and categorizing the cases by the **System Organ Class (SOC)**
- A threshold of 10% of absolute difference was used to identify significant differences between the rate of an SOC in the US and the EU
- Additionally, a comparison between adverse events mapped to SOC was performed between data extracted from the Package Insert (PI) and FAERS results

CONCLUSION

- Adverse event profiles between the EU and the US were dissimilar and this difference was observed both within and across the different targeted therapies
- The reports submitted by the HCPs in the EU contained higher rates of disease-specific adverse events, whereas a large proportion reports submitted by the US HCPs contained either general disorders or were related to drug administration
- Future studies will be needed to further investigate the underlying causes of these differences

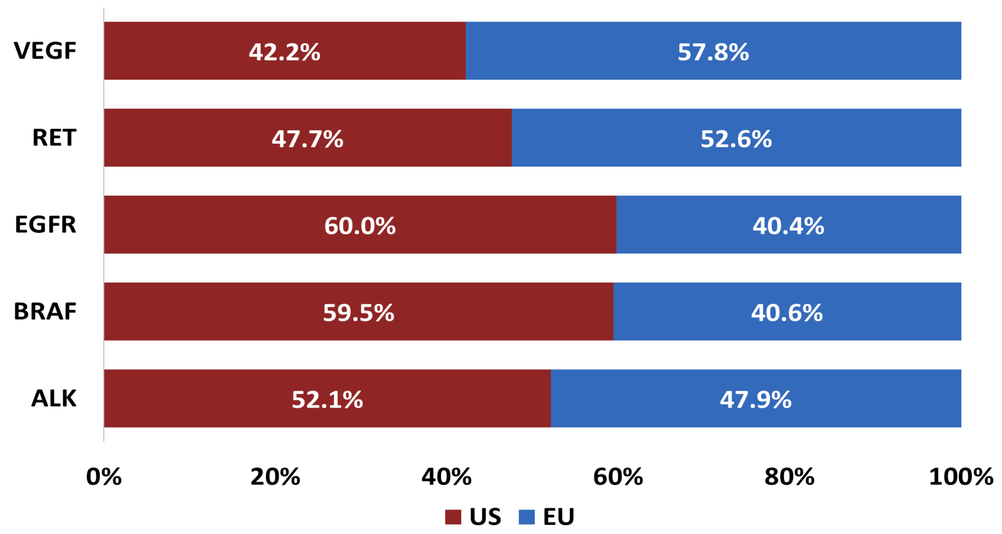
RESULTS

Table 1: Demographic characteristics of the adverse event reports reported to the FDA from 2020 to 2025

	Total (n = 46,703)	ALK inhibitors (n = 3,907)	BRAF inhibitors (n = 9,807)	EGFR inhibitors (n = 6,802)	RET inhibitors (n = 7,576)	VEGF inhibitors (n = 19,351)
Age						
<18 years	1,174 (2.51 %)	76 (1.95 %)	481 (4.9 %)	33 (0.49 %)	63 (0.83 %)	550 (2.84 %)
18-65 years	14,814 (31.72 %)	1,461 (37.39 %)	3,080 (31.41 %)	1,567 (23.04 %)	2,201 (29.05 %)	6,849 (35.39 %)
> 65 years	12,468 (26.7 %)	892 (22.83 %)	2,399 (24.46 %)	1,998 (29.37 %)	1,912 (25.24 %)	5,439 (28.11 %)
Gender						
Female	18,765 (40.18 %)	1,907 (48.81 %)	4,136 (42.17 %)	3,321 (48.82 %)	2,062 (27.22 %)	7,678 (39.68 %)
Male	18,089 (38.73 %)	1,395 (35.71 %)	4,396 (44.83 %)	1,670 (24.55 %)	4,080 (53.85 %)	6,804 (35.16 %)
Drug Role						
Primary suspect	NA	3,907 (100 %)	9,798 (99.98 %)	6,772 (99.65 %)	7,556 (99.8 %)	19,333 (99.66 %)
Outcomes						
Death	7,953 (17.03 %)	531 (13.59 %)	1,442 (14.7 %)	1,030 (15.14 %)	929 (12.26 %)	3,137 (16.21 %)
Life threatening	1,458 (3.12 %)	62 (1.59 %)	271 (2.76 %)	188 (2.76 %)	226 (2.98 %)	718 (3.71 %)
Hospitalization	10,787 (23.1 %)	775 (19.84 %)	2,491 (25.4 %)	2,092 (30.76 %)	1,509 (19.92 %)	4,834 (24.98 %)
Others	14,926 (31.96 %)	1,197 (30.64 %)	2,739 (27.93 %)	2,455 (36.09 %)	1,826 (24.1 %)	7,365 (38.06 %)

- Our analytical dataset included **46,703** unique reports from the US and EU from 2020 to 2025 for the selected five NSCLC targeted therapies *(Table 1)*
- The overall cohort was predominantly an adult population (>= 18 years) and contained similar proportion of males and females *(Table 1)*
- The proportion of HCP submitted adverse event reports was comparable between the US and the EU across all the groups *(Figure 1)*
- The **US** HCPs reported a higher rate of adverse events (>10%) in the "**General disorders and administrative site conditions**" and "**Injury, poisoning and procedural complications**" classes, except for RET inhibitors *(Figure 2)*
- In contrast, HCPs in the **EU** reported higher rates of adverse events related to organs and neoplasms, with a significantly higher rate of **"Gastrointestinal disorders"** in the VEGF cohort *(Figure 2)*

Figure 1: Distribution of HCP-reported adverse events across five drug classes between the US and the EU

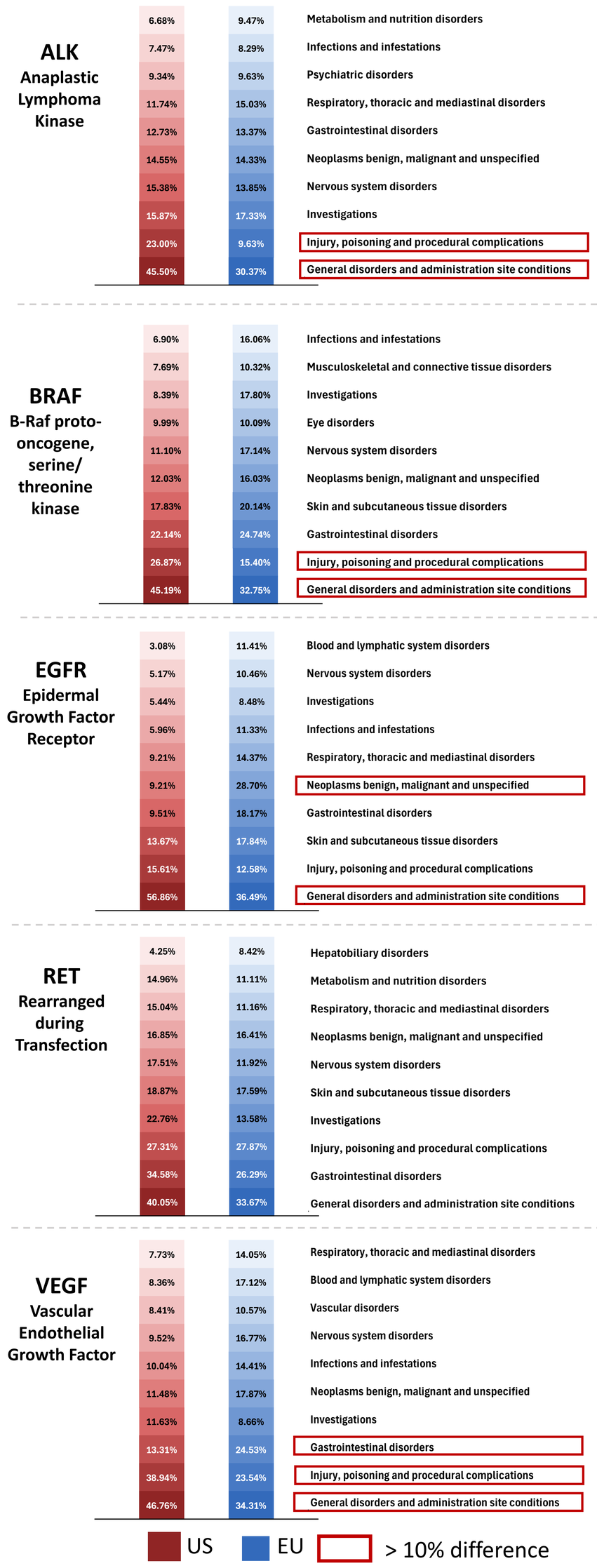


- Upon comparing data from FAERS with PI, we found significant overlaps in the SOCs for each drug class except for the **ALK group**
- **ALK** PI report mentioned higher rates of **gastrointestinal** and **hepatobiliary disorders**, while the Real-World data showed a higher rate of **general**, **respiratory**, and **nervous system disorders** in addition to other **neoplasms**
- In other groups, **general disorders** and **injury and procedural complications** were reported at a higher rate compared to the SOCs reported on the PI

LIMITATIONS

- Only reports submitted by the HCPs are reported and therefore, events reported directly by consumers were not considered in this analysis
- A large number of reports were excluded from the analysis due to missing information on the region
- Given the descriptive and exploratory design of this analysis, the conclusions drawn are preliminary and not definitive

Figure 2: Comparison of adverse event reporting rates at a system organ class level across the five targeted therapies between the US and EU



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