Association between EGFR-TKIs and venous thromboembolism among older patients with advanced non-small cell lung cancer (NSCLC)

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BACKGROUND

- VTE, which includes DVT and PE, is a significant clinical and economic burden in patients with NSCLC.
- Incidence of VTE have been reported in patients with NSCLC treated with EGFR-TKI.
- However, little is known about the risk of VTE in different generations of EGFR-TKIs.

OBJECTIVES

- To compare the risk of developing VTE after initiating 3rd- and 1st/2nd-generation EGFR-TKIs in older patients with advanced NSCLC
- To identify the risk of VTE stratified by sex, age, and race

METHODS

Data Source

- 2006-2019 Surveillance, Epidemiology and End Results (SEER)-Medicare database

Study Population

Patients were included if they:

- were older patients (≥65 years) with advanced NSCLC
- initiated EGFR-TKI between 2007-2017 (first prescription date: index date)
- continuously enrolled in both Medicare A, B and D
- did not use both 3rd- and 1st/2nd-generation EGFR-TKIs
- did not have history of VTE during 1 year prior to the index date

Key Variables

Predictor

3rd-generation EGFR-TKI: osimertinib
1st/2nd-generation EGFR-TKI: gefitinib, erlotinib, afatinib

Outcomes: Incident VTE/DVT/PE

- Crude incidence rate (no. of events/100 person-years) (Tab 1)
- Hazard ratio (the risk of VTE/DVT/PE) (Fig 2)

Subgroup

- Age (65-74 vs ≥75)
- Sex (female vs male)
- Race (white vs non-white)

Covariates

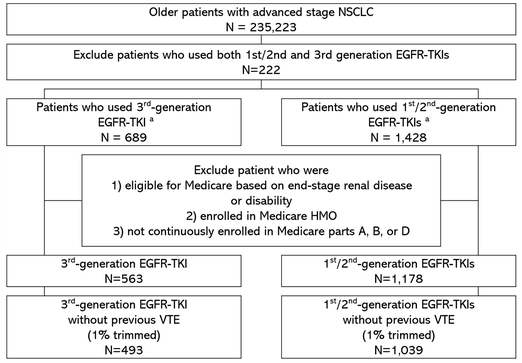
- Socioeconomic (sex, age, race, income, region, urban/rural, payer, marital status)
- Clinical (year of diagnosis, stage, histology, tumor size, radiation, surgery, other cancers, CCI, tobacco use disorder)

Statistical Analysis

Inverse probability of treatment weighting (IPTW): based on propensity score calculated from socioeconomic and clinical characteristics
Generalized linear model (Poisson distribution and log link function): Incidence rate calculation
Cox proportional hazard model: Hazard ratio calculation

RESULTS

Fig 1. Patient selection flow chart



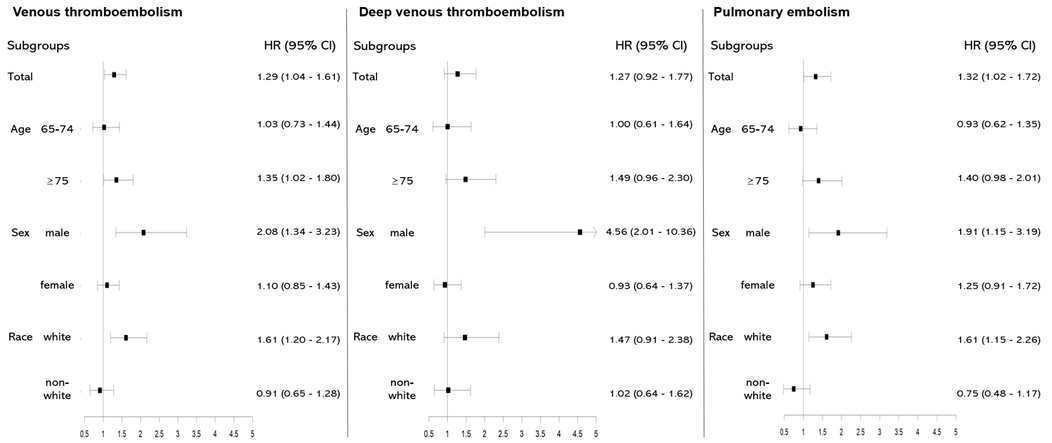
A total of 493 and 1,039 patients were included in 3rd and 1st/2nd-generation EGFR-TKI group, respectively (Fig 1).

Tab 1. Incidence rate of VTE/DVT/PE

	3rd-generation EGFR-TKI group			1st/2nd-generation EGFR-TKIs group		
	No. of events (No. of total patients) [a]	100 Person-years [a]	Incidence rate [b] (95% CI)	No. of events (No. of total patients) [a]	100 Person-years [a]	Incidence rate [b] (95% CI)
VTE	198 (1456)	1959	10.12 (8.80 - 11.63)	148 (1518)	1914	7.75 (6.60 - 9.10)
DVT	89 (1456)	2015	4.44 (3.61 - 5.46)	65 (1518)	1973	3.28 (2.57 - 4.18)
PE	136 (1456)	2007	6.77 (5.72 - 8.01)	101 (1518)	1940	5.22 (4.30 - 6.35)

Weighted crude incidence rates of VTE, DVT, and PE were higher in the 3rd-generation EGFR-TKI group (Tab 1).

Fig 2. Hazard ratio of VTE/DVT/PE



- The 3rd-generation EGFR-TKI group had a higher risk of VTE compared to the 1st/2nd-generation EGFR-TKI group (Fig 2). The risk was even higher in patients who are age ≥75, male and white.
- The overall risk of DVT was not significantly different between the two groups in the total population, but male patients treated by 3rd-generation EGFR-TKI had a significantly higher risk of developing DVT.
- There was a significantly higher risk of PE in the 3rd-generation EGFR-TKI group compared to the 1st/2nd-generation EGFR-TKIs, especially in male and white patients who did not use both 3rd- and 1st/2nd-generation EGFR-TKIs.

CONCLUSIONS

Limitations

- Our findings may not be generalizable to patients who switched from 1st/2nd-generation EGFR-TKI to 3rd-generation EGFR-TKI as they were excluded from our analysis.
- Generalizability of our findings is limited to patients aged 65 or older who are enrolled in Medicare.

Implications

- In the absence of a comparison of VTE risks across different EGFR-TKI generations, this retrospective study represents the first analysis using the U.S. population-level claims data to assess the risk of VTE among older patients with NSCLC treated with 1st/2nd-generation or 3rd-generation EGFR-TKI.
- Our findings demonstrate a higher risk of VTE associated with osimertinib use compared to 1st/2nd-generation EGFR-TKIs based on real-world data.
- Our findings underscore the importance of closely monitoring VTE in older patients treated with osimertinib.

Conclusions

- Older patients with advanced NSCLC who used osimertinib have higher risk of VTE compared to those who used 1st/2nd-generation EGFR-TKIs.
- The risk of VTE is particularly higher among osimertinib users who are male, white, and aged ≥ 75.
- Careful monitoring of VTE in patients with high risk would be required to prevent VTE.

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DISCLOSURE

This study was partially supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HI9C1328).

CCI, Charlson comorbidity index; CI, confidence interval; DVT, deep venous thromboembolism; EGFR-TKI, epidermal growth factor receptor-tyrosine kinase inhibitor; HR, hazard ratio; IR, incidence rate; NSCLC, non-small cell lung cancer; PE, pulmonary embolism; VTE, venous thromboembolism