Effectiveness and Safety of Apixaban, Low-Molecular Weight Heparin, and Warfarin Among High-risk Subgroups of Venous Thromboembolism Patients with Active Cancer

Poster

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Introduction

- Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is a leading cause of morbidity and death in cancer patients receiving outpatient chemotherapy.[1]
- Cancer-associated VTE carries a high risk for recurrent VTE events and major bleeding (MB), which further increases among some high-risk subgroups of patients.[2,3]
- Clinical trials and real-world studies have assessed DOACs including rivaroxaban, edoxaban, and apixaban vs. low-molecular-weight heparin (LMWH) for the treatment of cancer-associated VTE.[4,5,6,7] However, there is limited real world evidence for apixaban for the treatment of VTE in cancer patients.

Objective

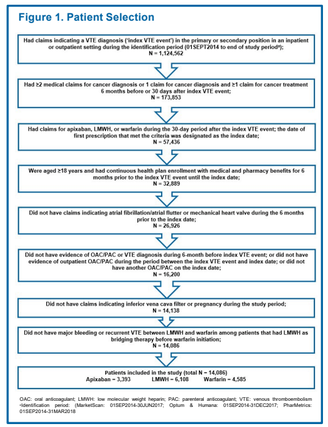
- To compare the risk of recurrent VTE and MB among VTE patients with active cancer within 6 months of initiating apixaban, LMWH, or warfarin stratified by cancer type, cancer treatment, and VTE characteristics.

Methods

Study Population

- For this study, data were pooled from four US claims databases: IBM® MarketScan® Commercial Claims and Encounter and Medicare Supplemental and Coordination of Benefits Database (“MarketScan”), IQVIA PharMetrics Plus™ (“PharMetrics”), Optum Clinformatics™ Data Mart (“Optum”), and Humana® Research Database (“Humana”).
- Patients with a primary or secondary VTE diagnosis during the identification period (MarketScan: 01 September 2014 – 30 June 2017; Optum & Humana: 01 September 2014 – 31 December 2017; PharMetrics: 01 September 2014 – 31 March 2018) were identified. The first VTE diagnosis was designated as the index VTE event.
- Patients were required to have ≥ 2 diagnoses for cancer or 1 cancer diagnosis and 1 claim for a cancer treatment (e.g., chemotherapy, radiation, cancer-related surgery) in either the 6 months prior to, or 30 days after the index VTE event.
- Patients aged ≥18 years who were prescribed apixaban, LMWH, or warfarin within 30 days following the index VTE event and had continuous enrollment in their health plan for at least 6 months prior to the index VTE event were selected.
  - **LMWH Cohort:** Patients who had LMWH within 30 days following the index VTE event and used it for ≥14 days without another anticoagulant during the period between the index VTE event and 14 days after LMWH initiation.
  - **Warfarin Cohort:** Patients with a warfarin claim within 30 days after the index VTE event without a claim for any other anticoagulant (except for LMWH as a bridging therapy) between the index VTE event and the warfarin prescription date. Patients who used LMWH as a bridging therapy (≤14 days prior to warfarin initiation) were also included.
  - **Apixaban Cohort:** Patients who initiated apixaban within 30 days after the index VTE event without a claim for any other anticoagulant between the index VTE event and apixaban initiation.
- The first prescription was designated as the index date. Additional inclusion and exclusion criteria are shown in Figure 1.

Figure 1. Patient Selection



OAC: oral anticoagulant; LMWH: low molecular weight heparin; PAC: parenteral anticoagulant; VTE: venous thromboembolism *Identification period: (MarketScan: 01SEP2014-30JUN2017; Optum & Humana: 01SEP2014-31DEC2017; PharMetrics: 01SEP2014-31MAR2018

Methods (continued)

- Patients were followed from the day after the index date until the earliest of: index therapy discontinuation, switch to another oral anticoagulant (OAC), initiation of new parenteral anticoagulant (PAC) treatment, death, study end, health plan disenrollment or the end of 6 month period.

Study Variables

- Demographic and clinical characteristics were captured in the 6 months prior to and on the index date. Baseline variables included: demographics, VTE-related variables, cancer-related variables, Deyo-Charlson comorbidity index (CCI) score, comorbidities, and medication use.
- Recurrent VTE or MB events were identified based on hospitalization with VTE or MB as the first listed diagnosis during the follow-up. Hospitalization for VTE occurring within 7 days of the index VTE event was not considered as a recurrent VTE event.

Statistical Analysis

- Treatment cohorts were balanced using stabilized inverse probability treatment weighting (IPTW).
- The risk of events were evaluated using Cox proportional hazards models.
- The following subgroup analyses were conducted in the post-IPTW population:
  - Metastatic diagnosis (Yes/No)
  - Cancer treatment (Yes/No)
  - Chemotherapy (Yes/No)
  - Upper and lower gastrointestinal (GI) cancer (Yes/No)
  - VTE event type (DVT / PE with or without DVT)
- Statistical significance (P<0.10) of the interaction between the subgroup strata and treatment were evaluated.

Results

- A total of 3,393 apixaban, 6,108 LMWH, and 4,585 warfarin patients were identified (Figure 1).
- After IPTW, all patient characteristics were balanced (Table 1). In the overall population, apixaban had a lower risk of recurrent VTE and MB vs. LMWH. Warfarin had a similar risk of recurrent VTE and MB vs. LMWH. Apixaban had a lower risk of recurrent VTE and a similar risk of MB vs. warfarin (Figure 2).

Table 1. Baseline Characteristics Among VTE Cancer Patients in the IPTW Population

	Apixaban Cohort N = 3,393	LMWH Cohort N = 6,108	Warfarin Cohort N = 4,585
Age, Mean (SD)	64.6 (12.6)	63.7 (13.2)	64.23 (12.9)
Sex, n (%)			
Male	1,621 (47.8%)	2,869 (47.0%)	2,171 (47.3%)
Female	1,772 (52.2%)	3,237 (53.0%)	2,412(52.6%)
CCI score, Mean (SD)	2.0 (2.0)	2.0 (2.1)	1.9 (2.0)
Cancer Metastasis, n (%)			
No	1,666 (49.1%)	2,936 (48.1%)	2,241 (48.9%)
Yes	1,727 (50.9%)	3,172 (51.9%)	2,344 (51.1%)
Cancer-related Treatment, n (%)			
No	833 (24.6%)	1,386 (22.7%)	1,091 (23.8%)
Yes	2,560 (75.4%)	4,722 (77.3%)	3,494 (76.2%)
Chemotherapy, n (%)			
No	1,254 (37.0%)	2,213 (36.2%)	1,696 (37.0%)
Yes	2,139 (63.0%)	3,895 (63.8%)	2,889 (63.0%)
Upper and Lower GI cancer, n (%)			
No	2,867 (84.5%)	5,114 (83.7%)	3,893 (84.9%)
Yes	526 (15.5%)	994 (16.3%)	692 (15.1%)
VTE Event Type, n (%)			
PE with/without DVT	1,455 (42.9%)	2,503 (41.0%)	1,942 (42.4%)
DVT only	1,938 (57.1%)	3,605 (59.0%)	2,643 (57.6%)

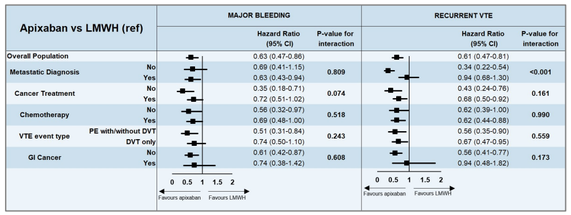
CCI: Charlson comorbidity index; DVT: deep vein thrombosis; GI: gastrointestinal; IPTW; inverse probability treatment weighting; LMWH: low-molecular weight heparin; PE: pulmonary embolism; SD: standard deviation; VTE; venous thromboembolism

Results (continued)

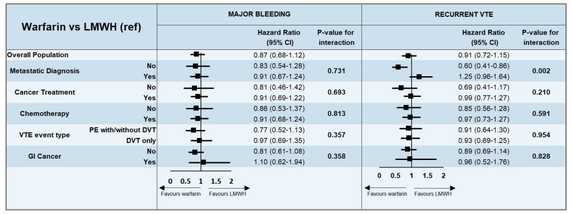
- Analyses stratified by metastatic diagnosis, cancer treatment, chemotherapy, VTE event type, and GI cancer show generally consistent results across the subgroups and with those of the overall population (Figure 2).
- There was a significant interaction in cancer treatment strata: apixaban trended towards a lower risk of MB vs. LMWH with or without cancer treatment; however, patients without cancer treatment had a larger difference vs. patients with cancer treatment.
- Two significant interactions were observed in metastatic diagnosis strata: apixaban and warfarin had a lower risk of recurrent VTE vs. LMWH in patients without a metastatic diagnosis whereas apixaban and warfarin had similar risk of recurrent VTE vs. LMWH in patients with a metastatic diagnosis.

Figure 2. Hazard Ratios of Recurrent VTE and Major Bleeding Among VTE Cancer Patients Initiating Apixaban, LMWH, or Warfarin in Post-IPTW Population

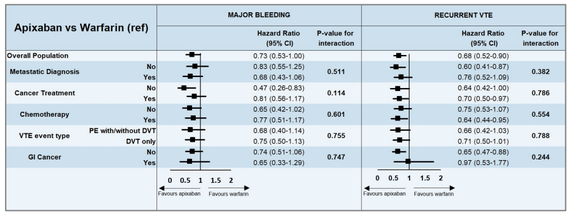
A) Apixaban vs LMWH



B) Warfarin vs LMWH



C) Apixaban vs Warfarin



CI: confidence interval; DVT: deep vein thrombosis; GI: gastrointestinal; LMWH: low-molecular weight heparin; PE: pulmonary embolism; VTE: venous thromboembolism

Limitations

- As with all observational retrospective analysis, this study could only examine associations rather than causal relationships.
- Given the lack of clinical information in claims data, cancer stage, laboratory test results (such as international normalized ratio values and serum creatinine/creatinine clearance levels), and biomarkers (such as body weight) were not available.
- The commercial databases used do not have complete death information for the patients; hence, we could not evaluate mortality and fatal recurrent VTE among this population. Mortality may be a competing risk in this population.
- In addition, the results may not be generalizable to the entire US VTE population, since we did not include uninsured patients or patients with governmental insurances such as CMS Medicare, Medicaid, and Veterans Affairs.

Conclusions

- **Across these high-risk subgroups of cancer patients with VTE, apixaban generally had a lower risk of recurrent VTE and MB vs. LMWH and lower risk of recurrent VTE compared to warfarin. Warfarin patients generally had a similar risk of recurrent VTE and MB vs. LMWH.**
- **Despite a couple of significant interactions between treatments and metastatic diagnosis, findings across the high-risk subgroups of VTE cancer patients were generally consistent with the overall population results.**

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Disclosures

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