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Fondaparinux Versus Argatroban for Heparin-Induced Thrombocytopenia in Patients with Hematologic Malignancies

Ahmed Abbasi, MD[1]; Katherin Zambrano-Vera, MD[1]; Deepak Kataria, MD[2]; Ranjit Sah, MD[2]; Syeda Urooba Shah, MD[3]; Antonio Arciniegas Rubio, MD[4]; Ghulam Shah, MD[5]; FNU Laraib, MBBS[6]; Zeeshan Solangi, MD[2]

[1]Berkshire Health Systems, Pittsfield, MA, USA · [2]Boston Medical Center, Boston, MA, USA · [3]Jinnah Sindh Medical University, Karachi, Pakistan · [4]Brigham and Women's Hospital, Boston, MA, USA · [5]NYU Langone Medical Center, New York, NY, USA · [6]Peoples University of Medical and Health Sciences, Nawabshah, Pakistan

1 BACKGROUND

Heparin-induced thrombocytopenia (HIT) is a life-threatening prothrombotic complication of heparin exposure. It is particularly challenging in patients with hematologic malignancies, where heparin exposure is common during chemotherapy administration, central venous catheter management, transfusions and prolonged hospitalisation.

Evidence gap

Argatroban, a direct thrombin inhibitor, is widely used for anticoagulation in HIT. Fondaparinux has emerged as an alternative with easier administration and less intensive monitoring requirements. Comparative real-world data between the two agents remain limited.

Study aim

To compare thrombotic outcomes and survival between adults with HIT who received fondaparinux and those who received argatroban, using propensity score–matched cohorts drawn from a large multicentre EHR network.

2 METHODS

Data source

TriNetX Global Collaborative Network, a federated network of de-identified electronic health record data contributed by participating healthcare organisations worldwide.

Study population

Adults ≥ 18 years with an inpatient encounter and heparin exposure, followed within 5 days by a confirmed diagnosis of HIT, who then received fondaparinux or argatroban within 7 days of that diagnosis.

Outcomes & follow-up

Index date was the first qualifying inpatient heparin exposure followed by HIT. Outcomes were counted from 1 day after index with no end date: venous thromboembolism, pulmonary embolism, cerebral infarction and all-cause mortality.

Statistical analysis

1:1 propensity score matching on demographics and comorbidities. Kaplan–Meier estimates, log-rank tests and Cox models were used for time-to-event outcomes. The proportional hazards assumption held for VTE, PE and cerebral infarction, but was violated for mortality (p = 0.011).

Patient flow

Adults ≥ 18 y with inpatient heparin exposure and confirmed HIT

↓ 1:1 propensity score matching on demographics and comorbidities ↓

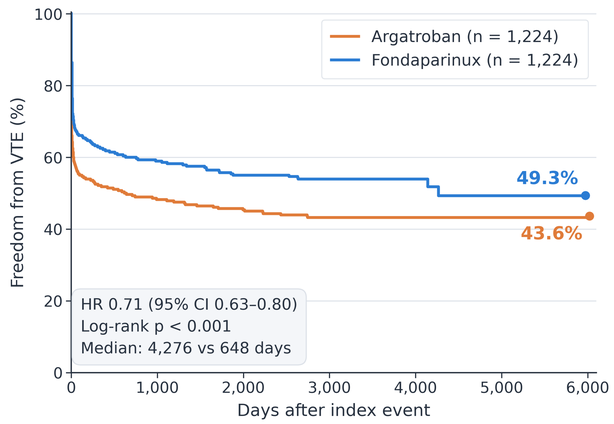
Fondaparinux	Argatroban
1,231 → **1,224 matched**	2,476 → **1,224 matched**

Table 1. Cohort characteristics after matching

Characteristic	Fondaparinux (n = 1,224)	Argatroban (n = 1,224)	Std. diff.
Age, mean ± SD, y	67.3 ± 15.1	67.6 ± 14.9	0.023
Male, n (%)	659 (53.8)	662 (54.1)	0.005
White, n (%)	909 (74.3)	922 (75.3)	0.024
Black or African American	195 (15.9)	189 (15.4)	0.013
Hispanic or Latino	45 (3.7)	35 (2.9)	0.046
Diabetes mellitus	491 (40.1)	494 (40.4)	0.005
Heart failure	541 (44.2)	543 (44.4)	0.003
Chronic kidney disease	377 (30.8)	382 (31.2)	0.009
COPD	286 (23.4)	289 (23.6)	0.006
Nicotine dependence	251 (20.5)	250 (20.4)	0.002

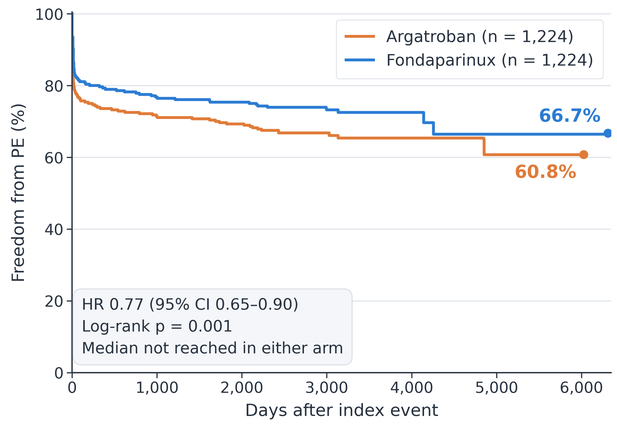
3 RESULTS

Figure 1. Freedom from VTE



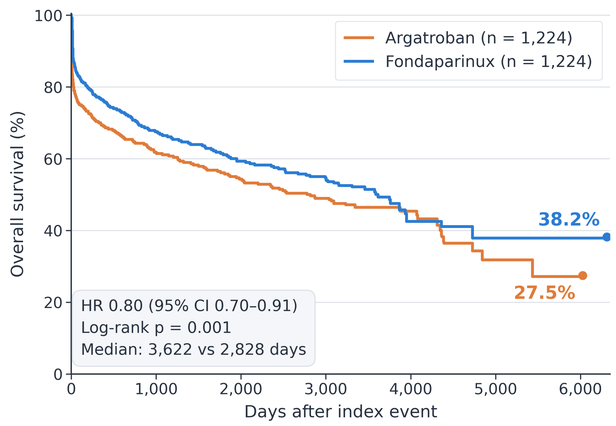
Kaplan–Meier estimates of freedom from venous thromboembolism. Median 4,276 vs 648 days.

Figure 2. Freedom from pulmonary embolism



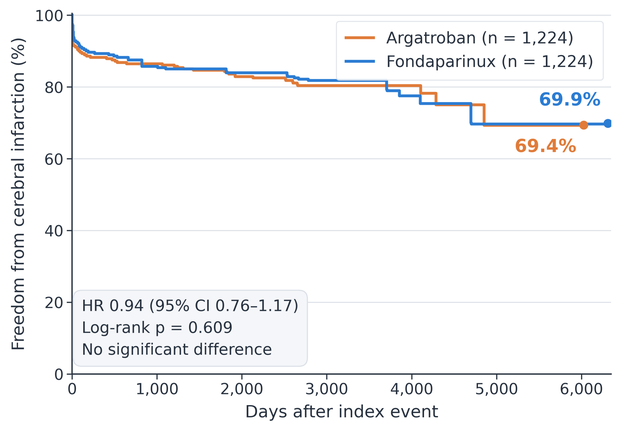
Kaplan–Meier estimates of freedom from pulmonary embolism. Median not reached in either arm.

Figure 3. Overall survival



Kaplan–Meier estimates of overall survival. The curves converge after roughly 4,000 days.

Figure 4. Freedom from cerebral infarction



Kaplan–Meier estimates of freedom from cerebral infarction. No significant difference.

Table 2. Primary outcomes in the matched cohorts

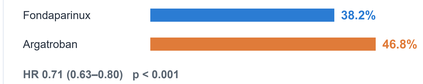
Outcome	Fondaparinux (n = 1,224)	Argatroban (n = 1,224)	Hazard ratio (95% CI)	Risk ratio (95% CI)	p value
Venous thromboembolism, n (%)	467 (38.2)	573 (46.8)	0.71 (0.63–0.80)	0.82 (0.74–0.89)	**< 0.001**
Pulmonary embolism, n (%)	262 (21.4)	318 (26.0)	0.77 (0.65–0.90)	0.82 (0.71–0.95)	**0.001**
All-cause death, n (%)	422 (34.5)	492 (40.2)	0.80 (0.70–0.91)	0.86 (0.77–0.95)	**0.001**
Cerebral infarction, n (%)	161 (13.2)	162 (13.2)	0.94 (0.76–1.17)	not analysed	**0.609**

Absolute risk differences: VTE −8.7% (−12.6 to −4.8); PE −4.6% (−7.9 to −1.2); death −5.7% (−9.5 to −1.9). Cerebral infarction was analysed by Kaplan–Meier only, so no risk ratio is reported. Venous thromboembolism and pulmonary embolism were counted as separate outcomes. p values are log-rank.

HEADLINE RESULTS

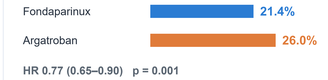
1,224 matched patients per arm

VENOUS THROMBOEMBOLISM



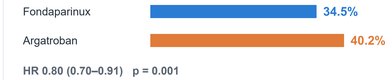
HR 0.71 (0.63–0.80) p < 0.001

PULMONARY EMBOLISM



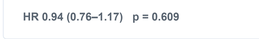
HR 0.77 (0.65–0.90) p = 0.001

ALL-CAUSE MORTALITY



HR 0.80 (0.70–0.91) p = 0.001

CEREBRAL INFARCTION



HR 0.94 (0.76–1.17) p = 0.609

4 CONCLUSIONS

Fondaparinux was associated with lower thrombotic event rates and improved survival compared with argatroban in patients with HIT.

Key findings

- Lower risk of VTE (38.2% vs 46.8%) and pulmonary embolism (21.4% vs 26.0%).
- All-cause mortality was lower with fondaparinux (34.5% vs 40.2%).
- Cerebral infarction rates were essentially identical (13.2% in both arms).
- Matching produced closely balanced cohorts — every standardised difference below 0.05.

Limitations

- Retrospective, non-randomised analysis of routinely collected EHR data.
- Cohorts were defined by HIT diagnosis and anticoagulant exposure; hematologic malignancy was not an inclusion criterion or a matched covariate.
- The proportional hazards assumption was violated for mortality; that hazard ratio is an average over follow-up.
- Residual confounding from malignancy subtype, disease burden, prior thrombosis and HIT severity cannot be excluded.

Correspondence: Ahmed Abbasi, MD (email: aabbasi@bhs1.org) · Berkshire Health Systems, Pittsfield, MA