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ETNA-VTE Europe: The Effect of Body Mass Index on 12-Month Outcomes in VTE Patients with Edoxaban

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Introduction

- Venous thromboembolism (VTE) is the third most common cardiovascular disease, affecting about 10 million people globally each year[1]
- Edoxaban, a non-vitamin K antagonist oral anticoagulant (NOAC), is approved for the treatment and secondary prevention of acute VTE in adults based on its comparable efficacy and superior safety to warfarin in a broad spectrum of patients with VTE during the Hokusai-VTE trial[2]
- During the treatment of VTE, obesity may affect the bioavailability, distribution and half-life of NOACs and, consequently, outcomes of treatment[3]
- Dose reduction of edoxaban is recommended in patients with one or more of the following clinical factors: moderate or severe renal impairment (creatinine clearance 15–50 mL/min), body weight ≤60 kg, concomitant use of certain P-glycoprotein inhibitors[4]
- ETNA-VTE-Europe (NCT02943993) was initiated in agreement with the European Medicines Agency (EMA) to assess benefits and risks of edoxaban treatment and secondary prevention of VTE with edoxaban up to 18 months in routine clinical practice[5]

Aim

- Using data from the ETNA-VTE-Europe registry, our aim was to characterise obese patients and to investigate outcomes in patients treated with edoxaban categorised by BMI

Methods

- ETNA-VTE-Europe is a single-arm, multinational, prospective, non-interventional post-authorisation safety study conducted in 310 sites in 8 European countries (NCT02943993)[5]
- A total of 2,322 patients with acute VTE treated with edoxaban were enrolled, and will be followed-up for 18 months subsequent to the index VTE
- The primary objective of ETNA-VTE-Europe was to assess the 18-month rate of symptomatic VTE recurrence in patients with VTE treated with edoxaban in clinical practice
- The co-primary objective was to assess the real-world rates of bleeding and adverse drug reactions
- This sub-study analysed outcomes in normal weight (BMI 18.5–25 kg/m^2), overweight (BMI 25–30 kg/m^2) and obese (BMI >30 kg/m^2) patients enrolled into the ETNA-VTE-Europe study
- Results for patients with BMI ≤18.5 kg/m^2 are not reported due to low patient numbers in this subgroup (n=18) and 149 patient had missing BMI data
- Patients with history of cancer, active cancer at baseline or new cancer within 6 months (182 days) after start of acute index VTE were excluded from the analysis to avoid confounding factors

Results

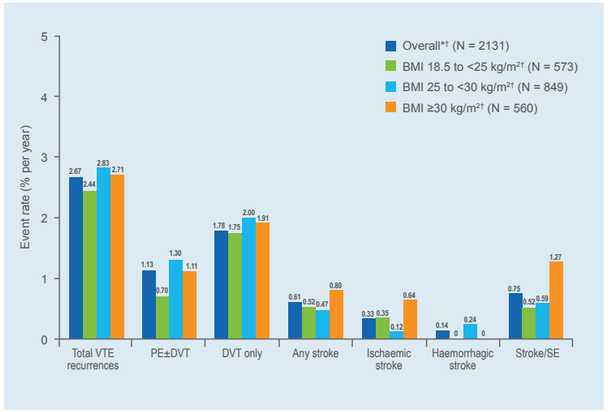
- This snapshot analysis set included 2131 patients who completed 1-year follow-up
- Of these patients, 573 were normal weight, 849 were overweight and 560 were obese (**Table 1**)
- Obese patients were more often female, had higher rates of hypertension, diabetes and prior VTE, chronic venous insufficiency and a higher eGFR than non-obese patients (**Table 1**)
- Obese patients received the 60 mg edoxaban dose more often (**Table 1**)
- At 1-year follow-up, overall VTE recurrence was 2.67% with consistent results across the range of BMI categories (**Figure 1**)
- Any bleeding was observed in 12.29% and major bleeding in 1.69% with a numerical decrease in obese patients (**Figure 2**)
- While all-cause mortality followed a U-shape association across BMI groups, there was a consistent trend for a reduced cardiovascular mortality in obese patients (**Figure 3**)

Table 1. Patient characteristics by BMI category

Patient characteristics	Overall*† (N=2131)	BMI 18.5 to <25 kg/m²* (N=573)	BMI 25 to <30 kg/m²* (N=849)	BMI ≥30 kg/m²* (N=560)
Female, n (%)	983 (46.1)	297 (51.8)	335 (39.5)	322 (51.3)
Age, years, mean ± SD	62.4 ± 16.07	61.9 ± 18.19	64.0 ± 14.93	61.9 ± 14.97
BMI, kg/m², mean ± SD	27.9 ± 5.00	22.7 ± 1.85	27.3 ± 1.37	34.2 ± 4.04
recalc. eGFR (Cockroft-Gault), ml/min, mean ± SD	95.7 ± 38.95	82.1 ± 31.85	92.3 ± 34.60	114.0 ± 44.88
Frailty (physician judgement), n (%)	261 (12.2)	75 (13.1)	106 (12.5)	75 (11.9)
Medical history, n (%)				
Hypertension	888 (41.7)	165 (28.8)	359 (42.3)	360 (57.3)
Diabetes mellitus	235 (11.0)	40 (7.0)	81 (9.5)	117 (18.6)
Chronic venous insufficiency	234 (11.0)	49 (8.6)	104 (12.2)	85 (13.5)
Bleeding history	60 (2.8)	20 (3.5)	21 (2.5)	18 (2.9)
Ischaemic stroke	52 (2.4)	14 (2.4)	22 (2.6)	15 (2.4)
History of VTE, n (%)				
Prior PE±DVT	160 (7.5)	38 (6.6)	55 (6.5)	54 (8.6)
Prior DVT	350 (16.4)	89 (15.5)	149 (17.6)	108 (17.2)
Edoxaban treatment at baseline, n (%)				
Edoxaban 60 mg	1873 (87.9)	449 (78.4)	771 (90.8)	521 (93.0)
Edoxaban 30 mg	258 (12.1)	124 (21.6)	78 (9.2)	39 (7.0)

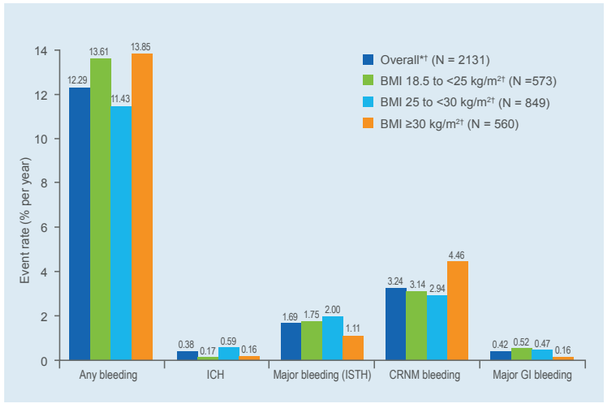
*Patients with history of cancer, active cancer at baseline or new cancer within 6 months (182 days) after start of acute index VTE were excluded from the analysis; †One hundred and forty-nine patients had missing BMI.
DVT, deep vein thrombosis; **eGFR**, estimated glomerular filtration rate; **PE**, pulmonary embolism; **SD**, standard deviation; **VTE**, venous thromboembolism

Figure 1. Annualised efficacy event rates by BMI category



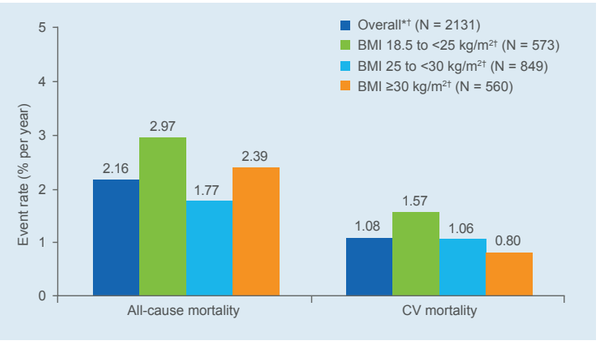
*A total of 149 patients had missing BMI
†Patients with history of cancer, active cancer at baseline or new cancer within 6 months (182 days) after start of acute index VTE were excluded from analysis; **DVT**, deep vein thrombosis; **GI**, gastrointestinal; **PE**, pulmonary embolism; **SE**, systemic embolism; **VTE**, venous thromboembolism; **SEE**, systemic embolic events

Figure 2. Annualised safety event rates by BMI category



*A total of 149 patients had missing BMI
†Patients with history of cancer, active cancer at baseline or new cancer within 6 months (182 days) after start of acute index VTE were excluded from analysis; **CRNM**, clinically relevant non-major; **GI**, gastrointestinal; **ICH**, intracranial haemorrhage; **ISTH**, International Society on Thrombosis and Haemostasis

Figure 3. Annualised mortality event rates by BMI category



*A total of 149 patients had missing BMI
†Patients with history of cancer, active cancer at baseline or new cancer within 6 months (182 days) after start of acute index VTE were excluded from analysis; **CV**, cardiovascular

Conclusions

- **Obesity does not appear to substantially affect the risks of recurrent VTE and any bleeding complications in a contemporary cohort of edoxaban-treated patients**
- **Apart from all-cause mortality following a U-shape association and CV mortality being numerically lowest in BMI ≥30, which may be due to chance, there were no appreciable differences in outcomes across the various subgroups**

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