Abstract P6072 – Table 1. Characterization of Bleeding Events

	Major Bleeds				CRNM Bleeds			
	Reduced Dose		Full Dose		Reduced Dose		Full Dose	
	Betrixaban (N=730)	Enoxaparin (N=725)	Betrixaban (N=2986)	Enoxaparin (N=2991)	Betrixaban (N=730)	Enoxaparin (N=725)	Betrixaban (N=2986)	Enoxaparin (N=2991)
# Bleeds	10 (1.4%)	5 (0.7%)	15 (0.5%)	16 (0.5%)	25 (3.4%)	5 (0.7%)	69 (2.3%)	34 (1.1%)
Results in death	1 (10.0%)	0	0	1 (6.3%)	0	0	0	0
Severity								
Mild	0	0	1 (6.7%)	2 (12.5%)	10 (40.0%)	1 (20.0%)	29 (42.0%)	16 (47.1%)
Moderate	4 (40.0%)	3 (60.0%)	5 (33.3%)	4 (25.0%)	9 (36.0%)	3 (60.0%)	34 (49.3)	12 (35.3%)
Severe	4 (40.0%)	2 (40.0%)	8 (53.3%)	7 (43.8%)	6 (24.0%)	1 (20.0%)	5 (7.2%)	5 (14.7%)
Life Threatening	2 (20.0%)	0	1 (6.7%)	3 (18.8%)	0	0	0	0
Requires or Prolongs Hospitalization	6 (60.0%)	1 (20.0%)	6 (40.0%)	5 (31.3%)	4 (16.0%)	2 (40.0%)	7 (10.1%)	6 (17.6%)
Requires Medical Intervention	7 (70.0%)	2 (40.0%)	10 (66.7%)	9 (56.3%)	10 (17.2%)	3 (60.0%)	25 (43.1%)	20 (58.8%)
Study Drug Interrupted	1 (10.0%)	0	2 (13.3%)	0	5 (20.0%)	1 (20.0%)	11 (15.9%)	3 (8.8%)
Study Drug Withdrawn	7 (70.0%)	3 (60.0%)	9 (60.0%)	12 (75.0%)	13 (52.0%)	2 (40.0%)	38 (55.1%)	21 (61.8%)

% total bleeds is based on number of subjects in each group. All other % are based on # bleeds in each group.

jects with creatinine clearance <30mL/min, the received 40mg of betrixaban or 20mg of enoxaparin. Descriptive statistics of location, severity and clinical consequences of major and CRNM bleeding are reported according to dose and treatment arm.

Results: Overall, 46 major and 133 CRNM bleeding events occurred. The most frequent site for major bleeding was gastrointestinal (59%) and intracranial (20%). One fatal bleed occurred in each treatment arm. For CRNM bleeding, the most common were hematuria (21%), epistaxis (13%), and gastrointestinal (13%). There were no differences in the severity or clinical consequences of bleeding events between the treatment arms. Although betrixaban resulted in an increase in CRNM bleeding, 87% were mild or moderate, 63% resolved without medical intervention, did not increase or prolong hospitalization or result in more interruption or withdrawal of study drug, compared to enoxaparin.

Conclusion: The severity and clinical sequelae of major and CRNM bleeding were similar between betrixaban and enoxaparin treatment arms.

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P6073

Increased major bleeding risk with use of topical miconazole agents among users of oral anticoagulation: A population-level safety study

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Background: Summary of product characteristics discourages antifungal miconazole oral gel in warfarin users due to an enhanced anticoagulant effect. Disturbingly, case reports have described bleeding incidents with topical miconazole applied together with warfarin, but also in rivaroxaban users.

Purpose: We assessed potential adverse drug effects of commonly used over-the-counter antifungal topical miconazole among patients on oral anticoagulation.

Methods: In Danish nationwide databases, we identified all patients initiated on oral anticoagulation for either venous thromboembolism or atrial fibrillation between 2012–2017. Concomitant prescribed topical miconazole treatment (oral or on the skin) during follow-up was recorded. We analyzed the risk of major bleeding (i.e. hospitalized) using a multivariable Cox regression model adjusted for age, gender, prior bleeding, hypertension, use of antiplatelets, alcohol abuse, use of non-steroidal anti-inflammatory drugs, chronic renal disease, liver disease and prior stroke.

Results: Among 234,533 patients included (mean age 69 years, 55% males), 181,719 (77%) were on vitamin K antagonists, 16,178 (7%) on apixaban, 22,353 (10%) on rivaroxaban and 14,283 (6%) on dabigatran. During a mean follow-up of 5.8 years, 12,859 (5.5%) of patients were administered topical (oral gel or external skin treatment) miconazole antifungal medication in 4 (skin treatment) to 6 (oral gel) week periods. Incidence rates of major bleeding were 2.5 (no. events 34,432) and 9.4 per 100 person-years (no. events 214) when not exposed and exposed to topical miconazole, respectively. The corresponding hazard ratio (HR) was 2.51 [95% confidence interval (CI) 2.19–2.87]. Major bleeding risks associated with use of specific oral anticoagulants and topical miconazole administrations are presented below.

Oral anticoagulation	Topical miconazole administration	Incidence rates per 100 person-years (no. events)	Hazard ratio [95% confidence interval]
Vitamin K antagonist	None	2.5 (31,373)	reference
	To the skin	6.2 (81)	1.80 [1.44-2.23]
	Oral gel	18.5 (87)	5.65 [4.56-6.97]
Any Non-Vitamin K antagonist oral anticoagulant (NOAC)	None	2.5 (3,059)	Reference
	To the skin	3.4 (29)	2.17 [1.51-3.13]
	Oral gel	10.7 (17)	2.64 [1.64-4.25]
Apixaban	None	2.6 (740)	reference
	To the skin	6.7 (6)	1.68 [0.75-3.76]
	Oral gel	13.5 (6)	3.23 [1.45-7.22]
Rivaroxaban	None	2.5 (1,120)	reference
	To the skin	9.1 (11)	2.18 [1.20-3.94]
	Oral gel	6.7 (4)	1.59 [0.60-4.25]
Dabigatran	None	2.4 (1,199)	reference
	To the skin	9.1 (12)	2.59 [1.47-4.58]
	Oral gel	12.6 (7)	3.51 [1.67-7.37]

Risk of major bleeding

Conclusions: Topical miconazole agents, especially the oral gel, were significantly associated with major bleeding complications in patients taking oral anticoagulants. Caution is advised when treating fungal infection with topical miconazole in patients on any oral anticoagulants.

P6074

Differences between hospitalised vs. outpatient management amongst european patients with atrial fibrillation: the EORP-AF general long-term registry

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Introduction: Atrial fibrillation (AF) patients are frequently hospitalized due to both AF-related and non-AF related reasons. Also, hospitalized patients are more severely ill than those non-hospitalized. These factors can influence prescription and use of oral anticoagulant (OAC) drugs. In this analysis, we studied differences in clinical profile and use of OAC in a large contemporary cohort of European AF patients.

Methods: Baseline characteristics, use of antithrombotic drugs and clinical management between AF patients who were hospitalized vs. outpatients were studied in the EURObservational Research Programme in AF General Long-Term cohort.

Results: Among the 11096 enrolled AF patients, 5792 (52.2%) were hospitalised, while 5303 (47.8%) were outpatients. When compared to hospitalised AF patients (Table), outpatients were older, less likely female and less likely to be diagnosed with a major cardiac condition (coronary artery disease, heart failure, valvular disease, dilated cardiomyopathy; all $p<0.001$), except for hypertension which was more common in outpatients (Table). Hospitalised patients were more likely symptomatic (Table). The proportion with CHA2DS2-VASc$\geq$2 was similar ($p=0.561$), but those with HAS-BLED$\geq$3 was higher among hospitalised patients than in outpatients (19.8% vs. 14–9%; $p<0.001$). Hospitalised patients were more likely treated with vitamin K antagonist (VKA) than outpatients (52.8% vs. 47.4%; $p<0.001$). Conversely, use of non-vitamin K antagonist oral anticoagulants (NOACs) were less prevalent in hospitalised patients (31.4% vs. 38.4%; $p<0.001$). Hospitalised patients were more likely prescribed antiarrhythmic drugs (33.7% vs. 21.3%; $p<0.001$) and have procedures (pharmacological/electrical cardioversion, catheter ablation) performed (all $p<0.001$). After adjustment with multiple risk factors, regression analysis found that hospitalised patients were more likely prescribed with OAC (odds ratio [OR]: 1.61, 95% confidence interval [CI]: 1.40–1.85) and NOACs than outpatients (OR: 1.34, 95% confidence interval: 1.18–1.52).

Baseline characteristics

	Hospitalised	Outpatients	p
Age, mean (SD)	68.3 (11.8)	70.1 (10.9)	<0.001
Female	42.1%	39.1%	0.001
Hypertension	60.1%	64.7%	<0.001
Symptomatic AF	64.7%	43.6%	<0.001

AF = Atrial Fibrillation; SD = Standard Deviation.

Conclusions: Hospitalised AF patients were younger, but more burdened with concomitant comorbidities and a higher bleeding risk. After full adjustment, hospitalised patients were more likely prescribed with OAC and NOACs.