RIVAROXABAN

DALLA REAL LIFE INTERNAZIONALE A QUELLA ITALIANA: ESPERIENZE DAL CAMPO

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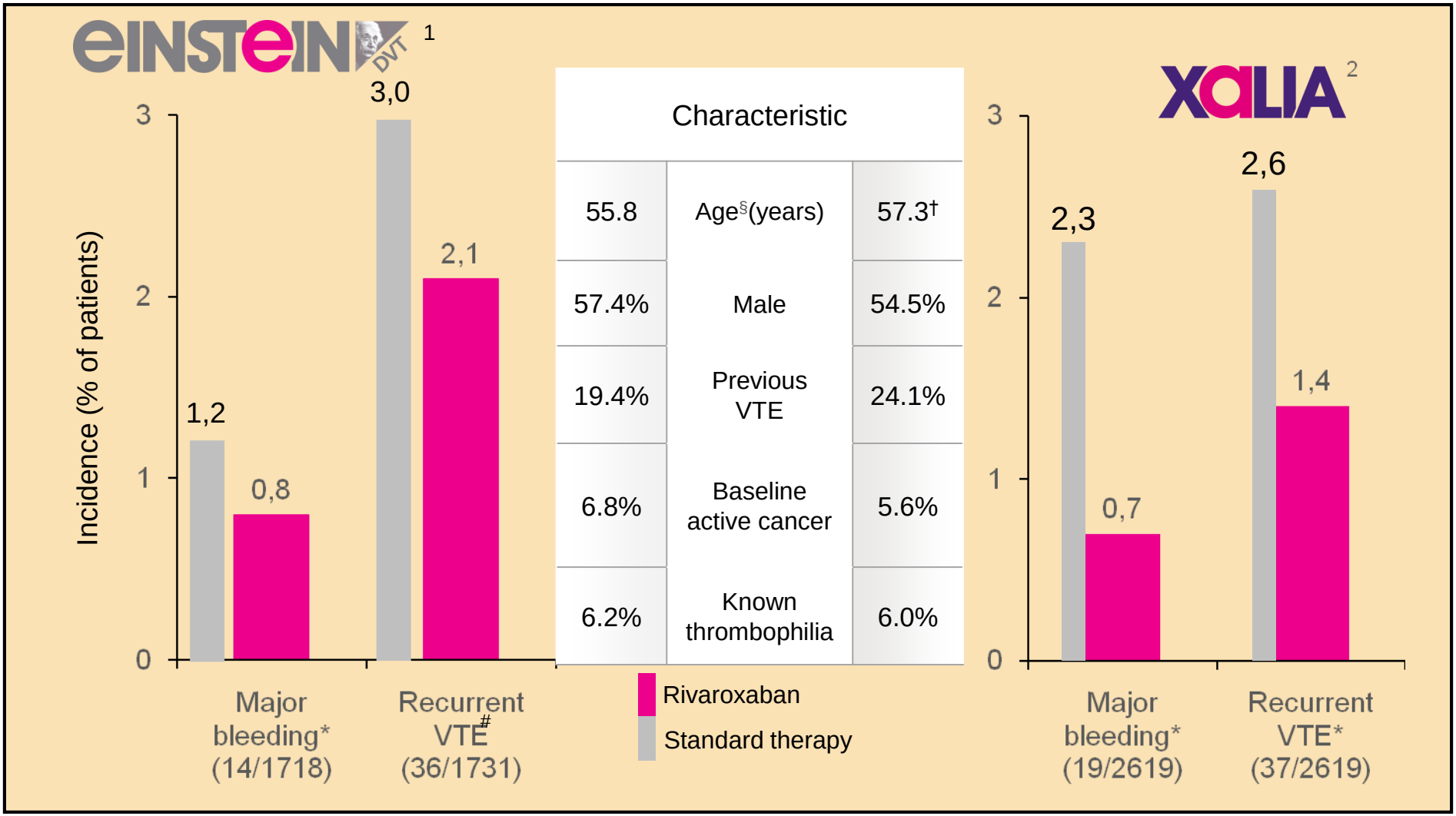
EINSTEIN DVT[1] and XALIA[2]: Rivaroxaban Outcomes



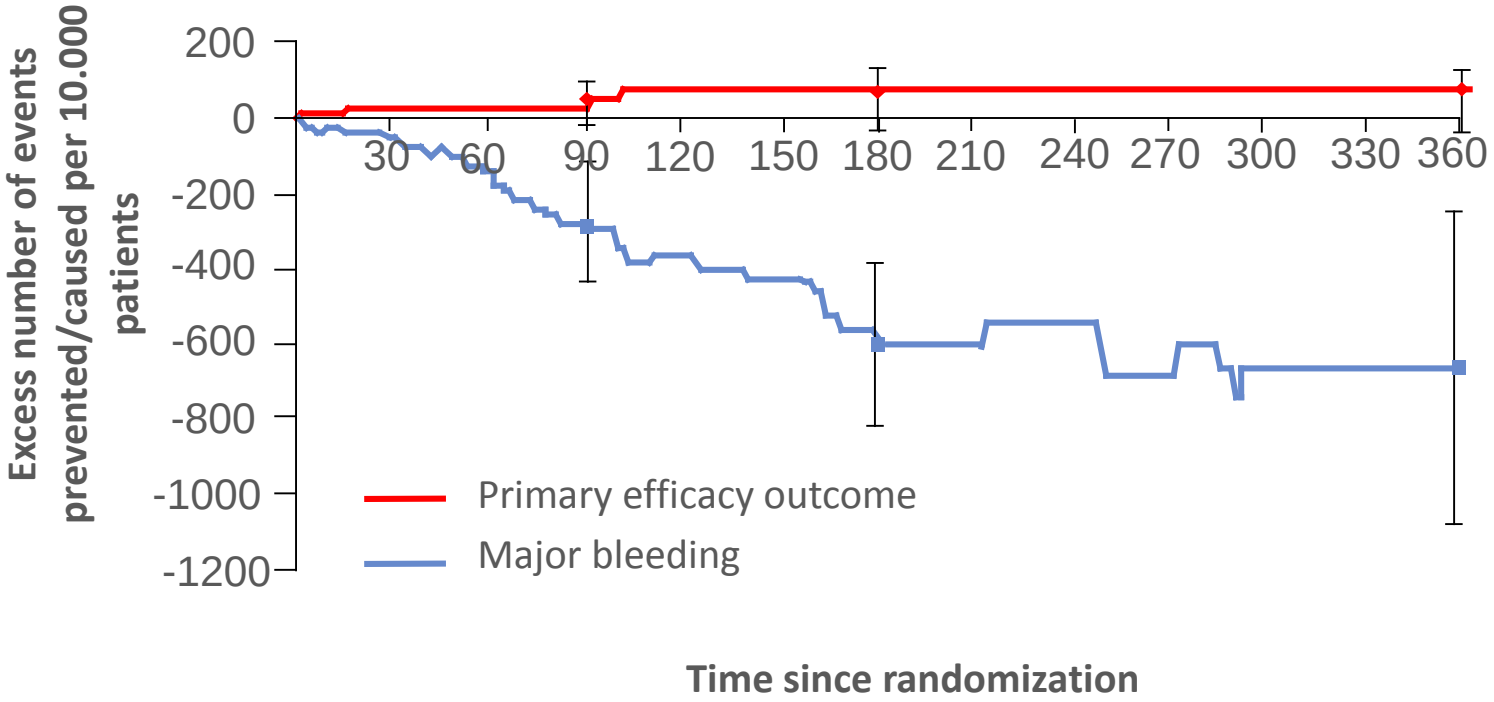
#ITT analysis; *Safety population (patients taking ≥1 dose of study drug); §mean †ASH, USA, December 2015, A894

1. The EINSTEIN Investigators, *N Engl J Med* 2010;363:2499–2510; 2. Ageno W *et al*, *Lancet Haematol* 2016;3(1):e12–e21

Long-term anticoagulation with rivaroxaban for preventing recurrent VTE: a benefit–risk analysis of EINSTEIN EXTENSION

Wells PS et al, Chest 2016; [Epub ahead of print]

Long-term anticoagulation with rivaroxaban for preventing recurrent VTE: a benefit–risk analysis of EINSTEIN EXTENSION



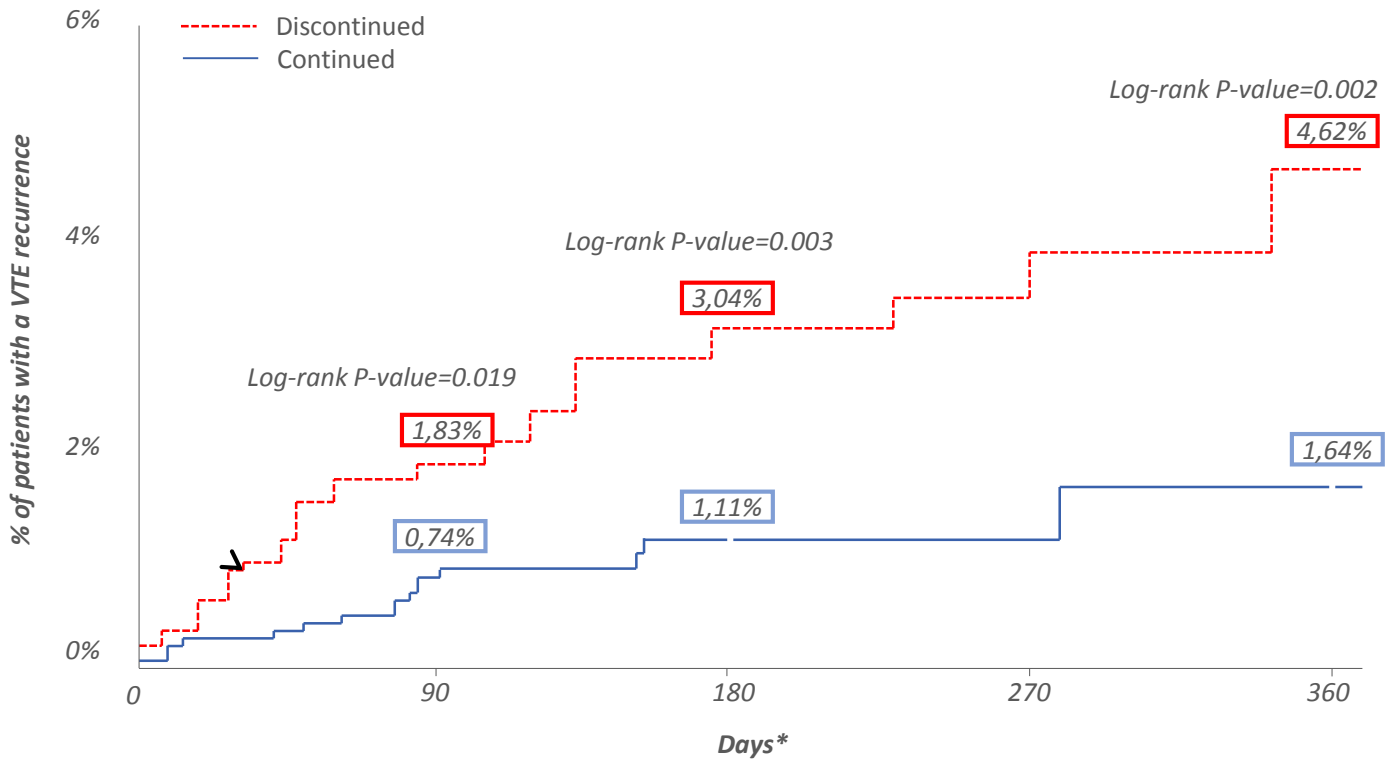
Compared with placebo, rivaroxaban prevented 3.0 times as many recurrent PE and 7.6 times as many recurrent DVT (all symptomatic) than major bleeding caused.
Of the induced major bleedings, none were fatal or in a critical organ.

Wells PS et al, Chest.2016.05.023. Epub ahead of print

Recurrence in Patients with First Unprovoked VTE who Continued vs. Discontinued Therapy

Objective: to assess the risk of VTE recurrence and major bleeding in a real-world setting of VTE patients with extended rivaroxaban treatment

Kaplan-Meier rates of VTE recurrences after 6 months of rivaroxaban therapy



*at day 0 patients had been treated with rivaroxaban for 6 months (pretreatment period)

1. Berger JS. ESC Congress, Rome, Italy, August 2016

Modifed from: CHEST 2016 Annual Meeting Abstracts

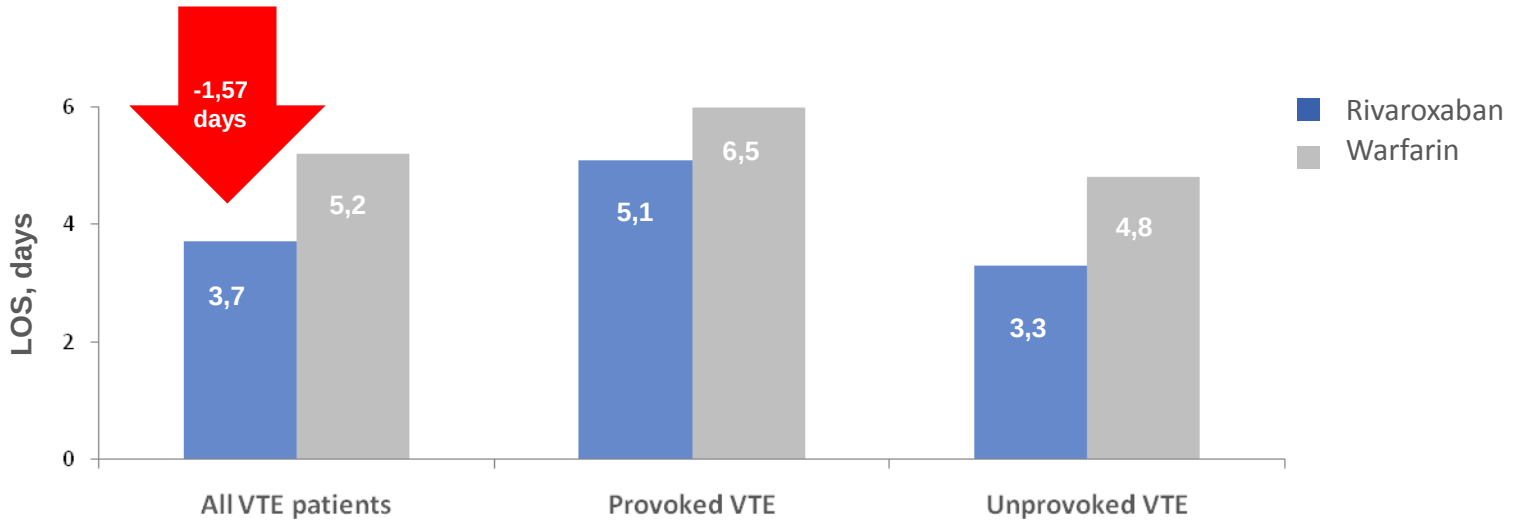
Major Bleeding Rates in Patients with First Unprovoked VTE who Continued vs. Discontinued Therapy

- No statistically significant differences (all p-values >0.05) were observed in the cumulative event rates for major bleeding between the continued and the discontinued cohort at:
  - 3 months (0.39% vs. 0.44%)
  - 6 months (0.63% vs. 1.05%)
  - 12 months (1.51% vs. 1.39%)

1. Berger JS. ESC Congress, Rome, Italy, August 2016

Shorter Hospital Stays and Lower Costs for Rivaroxaban for Venous Thrombosis Admissions

Objective: to compare hospital length of stay (LOS) and hospitalization costs among patients admitted with a primary VTE diagnosis who were initiated on oral anticoagulation therapy with rivaroxaban versus warfarin during their hospital stay.



Conclusion: this study provides evidence for clinicians to consider the potential for decreasing hospital stays and costs and simplifying treatment regimens using the rivaroxaban to treat VTE when appropriate for their patients.

Adapted from Margolis JM. J Am Heart Assoc 2016;5:e003788

Is rivaroxaban associated with shorter hospital stays and reduced costs in pulmonary embolism?

Objective:

- to determine whether rivaroxaban was associated with a reduced hospital LOS compared to parenteral bridging to warfarin in patients with PE treated outside of a clinical trial setting.
- to assess total hospital costs and readmission for recurrent VTE or major bleeding.

Outcomes in the overall PE-matched rivaroxaban and parental bridging to warfarin cohorts.

Rivaroxaban significantly reduced hospital LOS and costs compared to parenteral bridging to warfarin, without increasing the short-term risk of adverse events. This real-world result confirms those observed as part of the randomized pivotal EINSTEIN clinical trial program

Coleman CI et al, Clin Appl Thromb Hemost 2016;[Epub ahead of print]

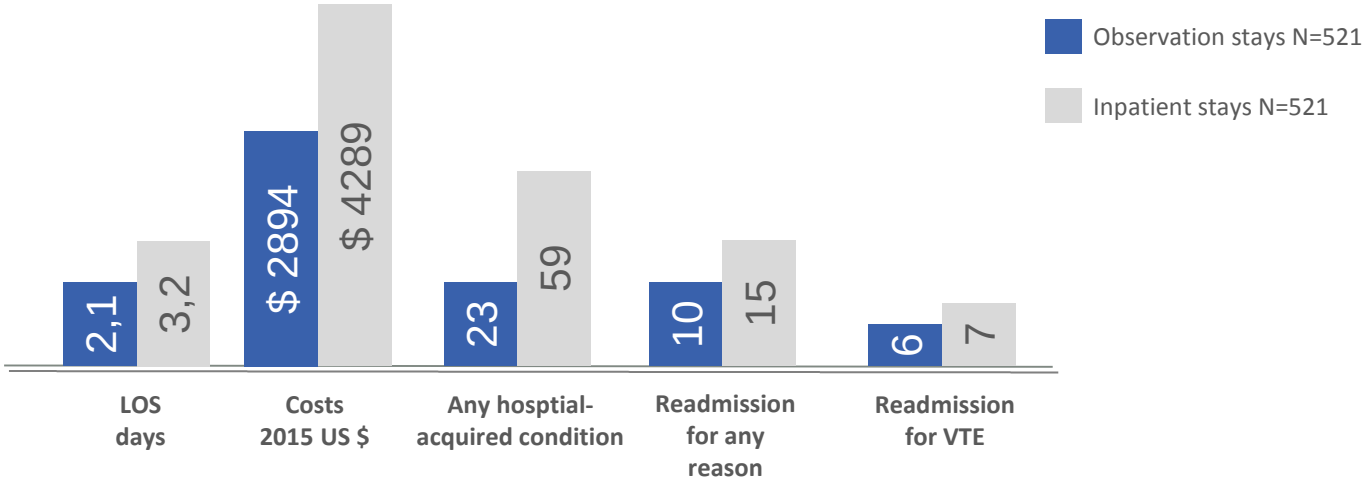
PE treated with rivaroxaban: outcomes associated with observation status versus inpatient management

Objective: to compare outcomes associated with observation vs. inpatient stays among matched PE patients treated with rivaroxaban.

Outcomes: compare

- lenght of stay (LOS)
- total costs for hospital-acquired conditions (HAC)

Outcomes of pulmonary embolism patients managed as observation or inpatient stays and treated with rivaroxaban.



Observation-managed PE patients treated with rivaroxaban experienced an ~1-day decreased LOS, less HACs (predominantly HAP) and ~$1400 lower hospital treatment costs compared to propensity-score matched inpatient-managed PE patients treated with rivaroxaban.

Modifed from: Weeda ER et al, Int J Cardiol 2016;222:846-849

Trends in LOS in acute PE over the years. What is changing in the era of DOACs?

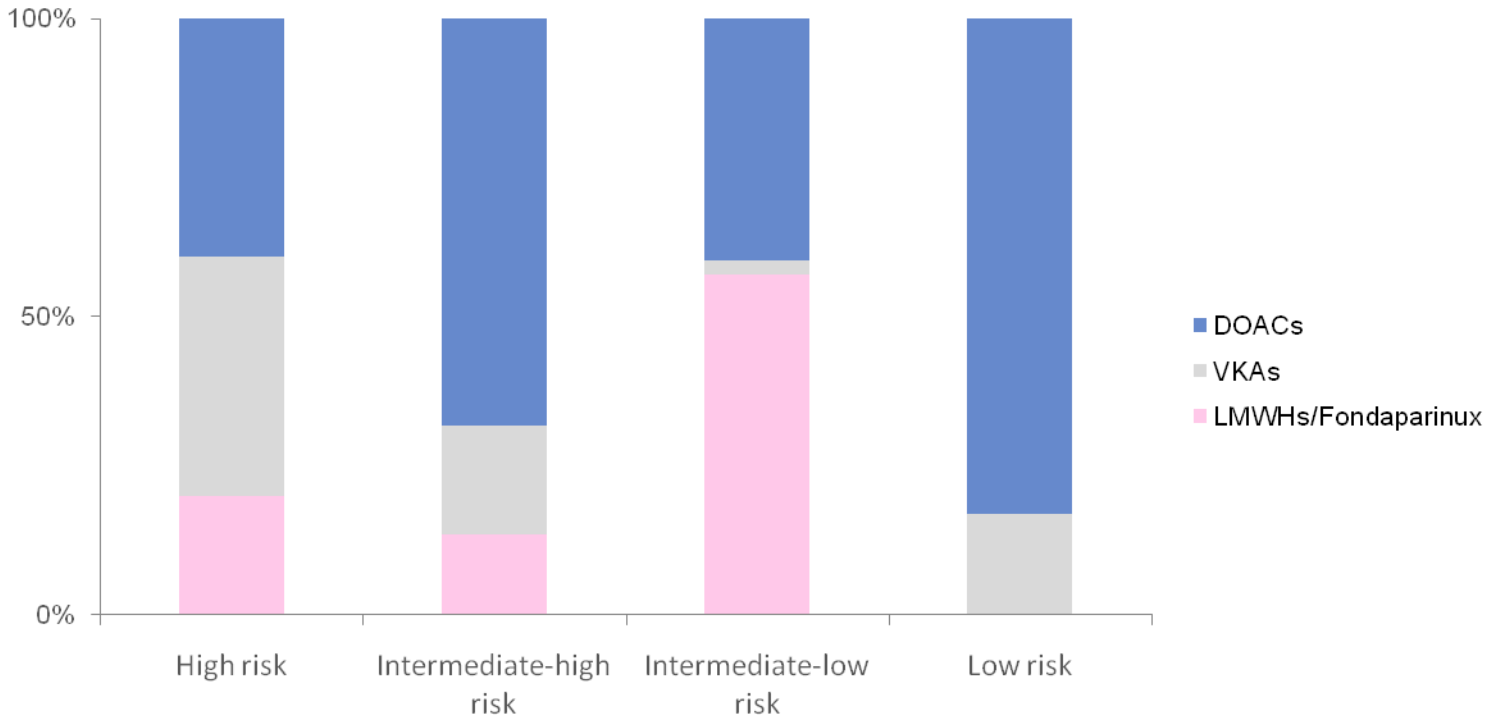
Objective: to focus on trends in length of hospital stay (LOS) over the years and on the burden of DOACs on this endpoint in patients suffering from acute PE.

	2010	2012	2014	2015	p*
Number	264	258	224	168	
Females	57,5%	55,4%	58,7%	55,9%	ns
Mean age ± (years)	76± 13	77± 11	75± 13	77± 12	ns
All-cause mortality	**15,5%**	**13,9%**	**7,7%**	**10%**	**0.038**
Mean LOS ± SD (days)	11± 6	11± 10	10± 7	9± 6	ns
Median LOS (IQR) (days)	9 (6-13)	9 (6-13)	8 (5-12)	8 (5,13)	ns
LOS distribution					
≤ 2 days	3,8%	2,8%	3,7%	2,7%	ns
≥3 or ≤ 6 days	**22,8%**	**23,5%**	**27,4%**	**27,2%**	ns
≥7 or ≤ 10 days	32,8%	34,4%	32,5%	30%	ns
≥11 days	40,6%	39,3%	36,4%	40,1%	ns

Over the years, patients discharged for pulmonary embolism reduced in number. Mean age and sex distribution were unchanged. All-cause mortality was significantly decreased (P=0.038).
Mean and median LOS were not significantly decreased over the years.

Masotti L. et al. J Cardiovasc Med 2016; [Epub ahead of print]

Anticoagulant treatment prescription according to the 2014 ESC prognostic model



In 2014 and 2015, patients with diagnosis of acute pulmonary embolism were discharged with anticoagulant treatment according ESC Guidelines. **DOACs prescribed in 40% high risk, in 68,1% intermediate-high, in 40,4% intermediate-low and 83,3% at low risk**

Masotti L. et al. J Cardiovasc Med 2016; [Epub ahead of print]

Trends in LOS in acute PE over the years. What is changing in the era of DOACs?

	DOACs	No DOACs	Total	*p*
Number	100	228	328	-
Males/Females	41%/59%	44,7%/55,3%	43,6%/56,4%	ns
Mean age ± SD (years)	77 ± 13	75 ± 13	76 ± 13	ns
Median age (IQR) (years)	80 (72-85)	77 (69-84)	78 (69-85)	ns
Mean LOS ± SD (days)	9± 5	11± 6	10 ± 6	<0.005
		VKAs 11± 6		
		LMWH/fondaparinux 11± 6		
Median LOS (IQR) (days)	7 (5-10)	10 (6-14)	9 (6-13)	<0.001
		VKAs 9 (7-14)		
		LMWH/fondaparinux 10 (5-14)		

Conclusion: DOACs are a real pharmacological option in acute pulmonary embolism, even in patients at high/intermediate-high risk.
Since the marketing of DOACs, LOS seems significantly lower in patients treated by using DOACs compared with patients treated by using the other anticoagulant molecules.
In patients prescribed DOACs, hospital costs could be dramatically saved.

Masotti L. et al. J Cardiovasc Med 2016; [Epub ahead of print]

Angiology Padova

- 239 patients treated with Rivaroxaban from march 12, 2014 to November 7, 2016 for VTE; from march 2014 only 2% of patients still treated with VKAs
- **88/239** patients to Rivaroxaban, **151** naive patien
- Rivaroxaban 20 an 15 mg 10%
- Median follow u -32)
- EOT 55 patients r 6 mts, 4 for 12 mts)
- Death: 5 patient severe heart failure)
- Great satisfactio
- 94% of patients treated immediately at home

Source: personal data on file

Angiology Padova

Subjects	239
age	57,7± 28,9
female sex	51.5%
DVT only	90%
DVT and/or PE	10%
CrCl > 80 ml/min	45%
50-80 ml/min	35%
30-50 ml/min	14%
15-30 ml/min	6%
Previous TEV	30%
Known thrombofilia	12%
Cancer	8%

Source: personal data on file

Angiology Padova
Cancer Patients

Type of Cancer

Breast cancer: 3 pts

Genitourinary cancer: 6 pts (2 prostate, 2 urinary bladder, 2 kidney)

Colorectal cancer: 1 pt

Gastric cancer: 0

Lung cancer: 2 pts

Haematologic: 6 pts

Source: personal data on file

Angiology Padova Efficacy

SUBJECTS	**239**
TOLERABILITY (ADVERSE EFFECTS) **(gastric pain, reduction of libido, 2 episodes of AST/ALT >2/increase: 20 mg ⟶ 15 mg)**	**1.6%**
SCA/ICTUS	**0%**
EFFICACY (VTE Recurrence) **(2 patients)**	**0.8%**

Source: personal data on file

Angiology Padova
Safety

ALL BLEEDINGS	**13.8%**
MINOR	**28/239 (11,7%)**
MAJOR	**5/239 (2,1%)**
Fatal	**0**
Life-threatening	**0**
Gastrointestinal	**0**
Non-fatal	**5**
haemoglobin drop > 2 g/dL	**2**
hematuria	**3**
Need to decrease dosage according to ClCr	**1.8%**
Need to decrease dosage for bleeding management	**2.0%**
Need to Switch anticoagulant therapy	**0%**

Source: personal data on file

Angiology Padova
Cancer patients

N° patients = 18

Age 68.5 years (±15.3)

- SWITCH 80% (refused to continue or intolerance to LMWH treatment)
- NAIVE 20%

Source: personal data on file

Angiology Padova
Cancer patients

SUBJECTS	**18**
TOLLERABILITY (ADVERSE EFFECTS)	**0,8%**
EFFICACY (VTE RECURRENCES)	**0%**
SCA/ICTUS	**0%**
MINOR BLEEDING	**1.2%**
MAJOR	**0**

Source: personal data on file