CPC069 Comparing oral rivaroxaban versus standard care in the treatment of symptomatic deep vein thrombosis: a patient-reported satisfaction study

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Introduction

- Treatment for deep vein thrombosis (DVT) traditionally involves initial therapy with heparin overlapping with, and subsequently transitioning to, a vitamin K antagonist (VKA) such as warfarin or acenocoumarol[1]
- The need for routine coagulation monitoring and dose adjustment with VKAs, plus the potential risk of food and drug interactions,[1,2] can be burdensome for outpatients[3]
- The link between treatment satisfaction and adherence to DVT treatment regimens is known,[4–6] and potential non-adherence to VKA therapy may impose added financial burdens on healthcare systems
- The oral, direct Factor Xa inhibitor rivaroxaban has the potential to improve patient satisfaction and adherence because: treatment does not require initial heparinization; dosing follows a fixed regimen; there is no need for routine coagulation monitoring; and food and drug interactions are minimal[7]
- In the multicentre EINSTEIN DVT trial, oral rivaroxaban was compared with subcutaneous low molecular weight heparin (enoxaparin) plus VKA (warfarin or acenocoumarol) for the treatment of acute DVT[8]
- Because of its open-label design, this study reflects real-life clinical practice and thus provides an opportunity to assess patient-reported treatment satisfaction

Objective

- To investigate patient-reported treatment satisfaction in the EINSTEIN DVT clinical trial

Methods

Patients and study design

- In EINSTEIN DVT,[8] male and female patients ≥18 years of age with confirmed acute symptomatic proximal DVT without symptomatic pulmonary embolism were randomized to receive:
  - Rivaroxaban 15 mg twice daily for 3 weeks, followed by 20 mg once daily; *or*
  - Enoxaparin 1.0 mg/kg twice daily plus VKA
    - Enoxaparin was discontinued after ≥5 days' treatment and when the international normalized ratio (INR) remained ≥2.0 for ≥2 consecutive days
- VKA dose was adjusted based on INR measurements obtained in usual care settings; the target INR was 2.5 (range 2.0–3.0)

Measuring patient-reported treatment satisfaction

- Satisfaction was evaluated from data derived from a subset of patients from seven countries (Canada, France, Germany, Italy, The Netherlands, UK and US) that included patients in both treatment arms
- Treatment satisfaction questionnaires were completed during follow-up visits and were analysed using two validated measures of treatment satisfaction:
  - Anti-Clot Treatment Scale (ACTS)
  - Treatment Satisfaction Questionnaire for Medication (TSQM) version II

ACTS

- Fifteen items representing two subscales completed at Day 15 and Months 1, 2, 3, 6 and 12:
  - Burdens (12 items)
  - Benefits (3 items)
- Treatment experiences were rated on a five-point Likert scale, ranging from 'Not at all' to 'Extremely'; higher scores indicated greater satisfaction with treatment
- Psychometric properties of the ACTS were validated using the blinded EINSTEIN DVT dataset before a comparative analysis between the treatment groups was conducted
  - Measurement properties evaluated were: acceptability; scaling assumptions; internal consistency reliability; test-retest reproducibility; aspects of validity, including known groups and discriminant validity; and exploratory responsiveness analyses
  - Overall, the ACTS Burdens and Benefits subscales met the psychometric criteria evaluated at both item level and scale level in all datasets

TSQM version II

- Eleven items representing four subscales completed at Months 1, 3, 6 and 12:
  - Effectiveness (2 items)
  - Side-effects (4 items)
  - Convenience (3 items)
  - Global satisfaction (2 items)
- Experiences of treatment satisfaction were rated on five-point and seven-point Likert scales from 'Extremely dissatisfied' to 'Extremely satisfied'
- Subscale scores were converted to a score between 0 and 100; higher scores indicated greater satisfaction with treatment
- TSQM subscales were included to allow an assessment of the construct validity of the ACTS, through hypothesized correlations between the ACTS and TSQM subscales

Statistical methods

- ACTS and TSQM were scored according to the developers' guidelines; individual subscale-specific rules were applied if <50% of ACTS questions were completed
- A prespecified repeated measures regression analysis was used to compare scores of ACTS Burdens and Benefits in the intention-to-treat population and was repeated for the four TSQM subscales
- Plots of mean values from questionnaire subscale scores for each treatment by time were created to examine the trend and shape of the score over time and to compare the difference between the two treatment groups
- Exploratory analyses of the following subgroups were included to identify any differences in responses to the ACTS and TSQM:
  - Age; sex; baseline malignancy; previous venous thromboembolism; idiopathic venous thromboembolism; immobilization at baseline; and country

Results

Patients and baseline characteristics

- A total of 1472 patients were eligible to participate; patient demographic information and clinical characteristics are shown in Table 1
- ACTS completion rates at each time point were similar (ACTS Burdens and Benefits subscales >99%)
- TSQM completion rates were lower than for ACTS (>89%), but were similar at each time point

Table 1. Demographic and clinical characteristics

	EINSTEIN DVT trial		Patient-reported treatment satisfaction substudy	
	Rivaroxaban (n=1731)	Enoxaparin/VKA (n=1718)	Rivaroxaban (n=737)	Enoxaparin/VKA (n=735)
Age, years*	55.8±16.4	56.4±16.3	56.6±16.3	57.1±15.8
Sex				
Male, n (%)	993 (57.4)	967 (56.3)	430 (58.3)	418 (56.9)
Female, n (%)	738 (42.6)	751 (43.7)	307 (41.7)	317 (43.1)
DVT, n	1708	1697 (only 1 distal)	725	723
PE, n	12	11	8	5
Cause of DVT or PE, n (%)				
Unprovoked/spontaneous	1055 (60.9)	1083 (63.0)	456 (61.9)	466 (63.4)
Recent surgery or trauma	338 (19.5)	335 (19.5)	133 (18.0)	143 (19.5)
Immobilization	265 (15.3)	260 (15.1)	103 (14.0)	105 (14.3)
Oestrogen therapy	140 (8.1)	115 (6.7)	64 (8.7)	54 (7.3)
Active cancer	118 (6.8)	89 (5.2)	58 (7.9)	37 (5.0)
Puerperium	6 (0.3)	11 (0.6)	2 (0.3)	2 (0.3)

*Mean ± standard deviation.
DVT, deep vein thrombosis; PE, pulmonary embolism; VKA, vitamin K antagonist.

ACTS Burdens subscale

- Patients in the rivaroxaban group reported higher satisfaction compared with those in the enoxaparin/VKA group over the total treatment period (least-squares mean 55.15 vs 52.57, respectively; $p<0.0001$) (Table 2)
- Patients in the rivaroxaban group showed a consistently less burdensome experience than those in the enoxaparin/VKA group over time (difference in mean ACTS Burdens scores ranged from 2.18 at Month 2 to 3.18 at Month 12) (Figure 1)
- There were differences in ACTS Burdens between subgroups, but the magnitude of the rivaroxaban treatment effect was greater than that for the subgroup effects (data not shown)

ACTS Benefits subscale

- Patients in the rivaroxaban group reported higher satisfaction compared with those in the enoxaparin/VKA group over the total treatment period (least-squares mean 11.73 vs 11.45; $p=0.0061$) (Table 2)
- Although there was no difference in mean ACTS Benefits scores at Day 15, a treatment effect became apparent from Month 2 onwards (Figure 2); the interaction of treatment effect by visit was significant ($p=0.0159$), reflecting inconsistency in patient satisfaction over visits (data not shown)
- The patient subgroup effect on ACTS Benefits showed differences between the groups; the magnitude of rivaroxaban treatment effect was greater than that for the subgroup effect, with the exception of the country-level effect (data not shown)

Table 2. ACTS Burdens and Benefits by treatment and visit (least-squares means)

	Burdens					Benefits				
	Rivaroxaban (n=737)		Enoxaparin/VKA (n=735)			Rivaroxaban (n=737)		Enoxaparin/VKA (n=735)		
Visit	n	Mean (SE)	n	Mean (SE)	Difference	n	(n=737)	n	Mean (SE)	Difference
Day 15	696	54.22 (0.25)	645	51.34 (0.26)	2.88	694	11.43 (0.10)	644	11.36 (0.10)	0.06
Month 1	674	54.85 (0.25)	645	52.34 (0.25)	2.52	669	11.55 (0.10)	643	11.37 (0.10)	0.18
Month 2	664	55.11 (0.25)	639	52.94 (0.26)	2.18	663	11.69 (0.10)	638	11.35 (0.10)	0.35
Month 3	659	55.20 (0.26)	619	52.83 (0.26)	2.37	657	11.78 (0.10)	619	11.34 (0.10)	0.44
Month 6	553	55.58 (0.26)	514	53.04 (0.27)	2.54	550	11.88 (0.11)	512	11.45 (0.11)	0.43
Month 12	92	55.99 (0.37)	87	52.81 (0.38)	3.18	91	12.37 (0.19)	87	11.49 (0.20)	0.88
Total	718	55.15 (0.23)	700	52.57 (0.23)	2.58*	718	11.73 (0.08)	700	11.45 (0.09)	0.28#

*$p<0.0001$; #$p=0.0061$.
SE, standard error; VKA, vitamin K antagonist.

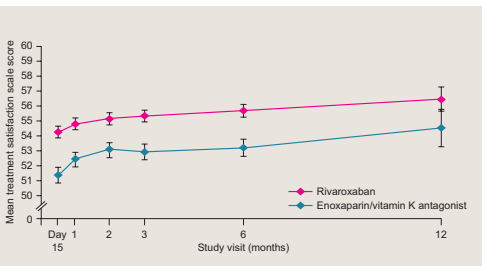

Figure 1. Mean ACTS Burdens by treatment across visits.

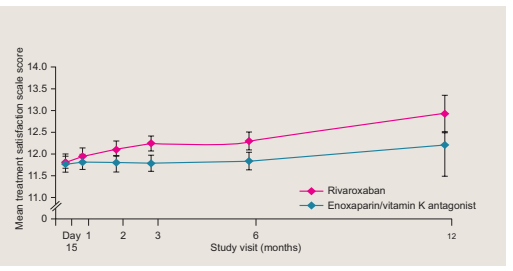

Figure 2. Mean ACTS Benefits by treatment across visits.

TSQM

- Patients in the rivaroxaban group indicated higher satisfaction than those in the enoxaparin/VKA group: higher mean TSQM subscale scores (Effectiveness, Side-effects, Convenience, Global satisfaction) were obtained across the visits, confirming results obtained in the co-primary endpoints (Figures 3–6)

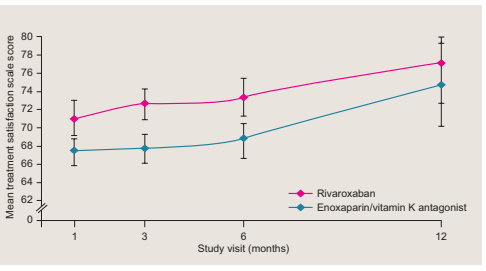

Figure 3. Mean TSQM Effectiveness by treatment across visits.

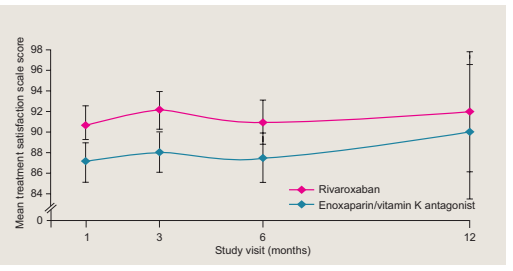

Figure 4. Mean TSQM Side-effects by treatment across visits.

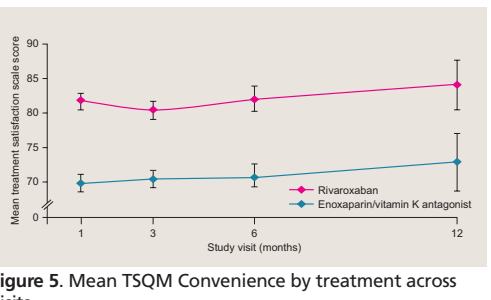

Figure 5. Mean TSQM Convenience by treatment across visits.

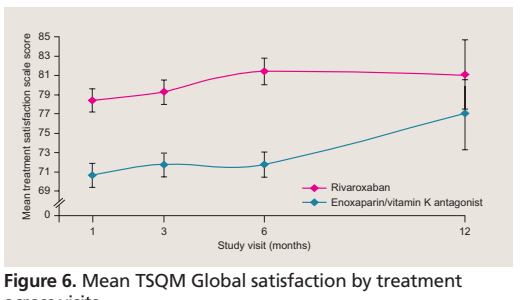

Figure 6. Mean TSQM Global satisfaction by treatment across visits.

Conclusion

- **Rivaroxaban as a single-drug regimen provided improved treatment satisfaction for patients with DVT compared with enoxaparin/VKA, particularly concerning the patient-reported burden associated with anticoagulation**

References

1. Kearon C *et al*. *Chest* 2008;133:454–545.
2. Ansell J *et al*. *Chest* 2008;133:160–198.
3. Wild D *et al*. *Expert Rev Pharmacoecon Outcomes Res* 2009;9:467–474.
4. Osterberg L, Blaschke T. *N Engl J Med* 2005;353:487–497.
5. Atkinson M *et al*. *Value Health* 2005;8:S9–S24.
6. Bharmal M *et al*. *Health Qual Life Outcomes* 2009;7:36.
7. Perzborn E *et al*. *Nat Rev Drug Discov* 2011;10:61–75.
8. The EINSTEIN Investigators. *N Engl J Med* 2010;363:2499–2510.

Disclosure of conflict of interest
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