Thrombosis Research 135 (2015) 281–288

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Regular Article

Patient-reported treatment satisfaction with oral rivaroxaban versus standard therapy in the treatment of pulmonary embolism; results from the EINSTEIN PE trial☆

Martin H. Prins [a,*], Luke Bamber [b], Stefan J. Cano [c], Maria Y. Wang [d], Petra Erkens [a], Rupert Bauersachs [e], Anthonie W.A. Lensing [b]

[a] Maastricht University Medical Centre, 6200 MD Maastricht, The Netherlands
[b] Bayer Pharma AG, Wuppertal, Aprather Weg 18a, 42096 Wuppertal, Germany
[c] Peninsula College of Medicine and Dentistry, Plymouth, PL6 8BU, UK
[d] Bayer HealthCare, Montville, NJ, 13342, USA
[e] Max Ratschow Clinic for Angiology, Grafenstraße 9, 64283 Darmstadt, Germany

ARTICLE INFO

Article history:
Received 26 September 2014
Received in revised form 3 November 2014
Accepted 11 November 2014
Available online 18 November 2014

Keywords:
Anti-Clot treatment scale
Coagulation inhibitor
Pulmonary embolism
Rivaroxaban
Treatment satisfaction
Venous thrombosis

ABSTRACT

Introduction: Rivaroxaban is an oral, direct Factor Xa inhibitor, approved for the treatment of pulmonary embolism (PE) and deep vein thrombosis (DVT) and the secondary prevention of recurrent PE and DVT as a fixed-dose, monotherapy regimen that does not require initial heparinisation, routine coagulation monitoring or dose adjustment. Approval in this indication was supported by results from EINSTEIN PE, a large, randomised, open-label study that compared rivaroxaban with enoxaparin/vitamin K antagonist (VKA) therapy in patients with acute symptomatic PE with or without DVT.

Materials and Methods: Patient-reported treatment satisfaction was evaluated in a predefined subanalysis of EINSTEIN PE to enable monitoring and optimisation of patient-reported outcomes and, therefore, patient compliance. As part of EINSTEIN PE, 2,397 patients in seven countries were asked to complete a validated measure of treatment satisfaction, the Anti-Clot Treatment Scale (ACTS) throughout the duration of treatment (up to 12 months).

Results: Patients reported greater satisfaction in the rivaroxaban treatment arm as compared with the enoxaparin/VKA treatment arm. Treatment with rivaroxaban was reported as being significantly less burdensome than enoxaparin/VKA therapy, and the benefits of treatment were significantly greater.

Conclusion: Rivaroxaban treatment resulted in improved treatment satisfaction compared with enoxaparin/VKA in PE patients, particularly in reducing patient-reported anticoagulation burden.

© 2014 Published by Elsevier Ltd.

Introduction

Pulmonary embolism (PE) is a life-threatening manifestation of venous thromboembolism (VTE) [1–4]. The estimated annual incidence of PE is approximately 69 per 100,000 and the associated mortality risk is greater than 20%, with 65% of deaths occurring within 1 hour [3,5,6]. The risk of mortality may persist at a rate of 5% for up to 12 months [7]. Although the incidence of deep vein thrombosis (DVT) is approximately twice that of PE, PE accounts for the majority of the 30-day case fatality rate in patients with VTE [1]. In addition to a high rate of mortality, PE can be associated with recurrent VTE or secondary complications [5,7]. Rates of recurrent VTE are equally high for both PE and proximal DVT, particularly in the first 6–12 months after diagnosis (hazard rate of ~20 per 1,000 person-days) [8]. However, recurrent VTE typically presents as PE after an initial PE (in ~60% of cases) and as DVT after an initial DVT (~80%); therefore, recurrent VTE after an initial PE is associated with a two- to threefold increased risk of mortality compared with recurrent VTE after DVT [7]. Secondary complications after PE include chronic thromboembolic pulmonary hypertension, which in some cases can lead to progressive right ventricular failure [9]. Considering the potential for serious complications and the risk of mortality with recurrent PE, it is unsurprising that PE patients may be treated for

Abbreviations: ACTS, Anti-Clot Treatment Scale; DVT, deep vein thrombosis; HR, hazard ratio; ITT, intention-to-treat; LMWH, low molecular weight heparin; LS, least-squares; NOAC, non-VKA oral anticoagulant; PE, pulmonary embolism; SD, standard deviation; SE, standard error; TSQM II, Treatment Satisfaction Questionnaire for Medication version II; VKA, vitamin K antagonist; VTE, venous thromboembolism.

☆ Financial support: The study was supported by Bayer Pharma AG.

* Corresponding author at: Department of Clinical Epidemiology and Medical Technology Assessment, Maastricht University Medical Centre, 6200 MD Maastricht, The Netherlands. Tel.: +31 43 3875559.

E-mail addresses: mh.prins@maastrichtuniversity.nl (M.H. Prins), luke.bamber@bayer.com (L. Bamber), stefan.cano@pms.ac.uk (S.J. Cano), maria.wang@bayer.com (M.Y. Wang), rupert.bauersachs@klinikum-darmstadt.de (R. Bauersachs), anthonie.lensing@bayer.com (A.W.A. Lensing).

http://dx.doi.org/10.1016/j.thromres.2014.11.008
0049-3848/© 2014 Published by Elsevier Ltd.

longer than DVT patients [10,11], even though guideline recommendations suggest equal treatment lengths [12].

Standard therapy for PE in haemodynamically stable patients consists of treatment with low molecular weight heparin (LMWH) overlapping with and followed by a dose-adjusted vitamin K antagonist (VKA), such as warfarin [12]. Limitations with VKA treatment include the need for regular monitoring of the anticoagulation effect, drug–drug interactions and dietary restrictions, and the initial parenteral administration of LMWH can delay discharge of patients from hospital or increase healthcare utilisation [13–16]. Given the link between patient treatment satisfaction and adherence, the limitations associated with standard therapy may impact upon adherence to therapy [17]. As the patient perspective becomes increasingly recognised for its importance and impact on outcomes, further examination of the treatment experience from the patient perspective is warranted [17,18].

Non-VKA oral anticoagulants (NOACs) may overcome some of the limitations observed with the current standard of care. Rivaroxaban and apixaban are direct Factor Xa inhibitors approved in the EU and US for the treatment of acute DVT and PE and the prevention of recurrent VTE in adults [19–22]. Dabigatran, a direct thrombin inhibitor, is also approved in the EU and US for this indication in adult patients who have been treated with a parenteral anticoagulant for 5–10 days [23,24]. The direct Factor Xa inhibitor edoxaban has completed phase III testing for VTE treatment in patients who had initially received heparin [25], and has received its first approval for this indication in Japan [26]. Recently, the updated European Society of Cardiology (ESC) guidelines recommended rivaroxaban, dabigatran and apixaban as alternatives to parenteral/VKA anticoagulation for acute-phase treatment of patients at an intermediate-low risk of early mortality from PE (Class I, Level B). Rivaroxaban, dabigatran and apixaban are also recommended as alternatives to conventional therapy for patients who require extended anticoagulation (>3 months) (Class IIa, Level B) [27].

In contrast to the trials examining dabigatran, apixaban and edoxaban [25,28–30], which included combined DVT and PE patient populations, the EINSTEIN PE trial of rivaroxaban focused on a specific population of patients with PE (with or without DVT) [31]. The results from EINSTEIN PE demonstrated that fixed-dose monotherapy with rivaroxaban was non-inferior to standard therapy (enoxaparin overlapping with and followed by a VKA) for the primary efficacy endpoint of symptomatic recurrent VTE (2.1% vs 1.8% in the rivaroxaban and standard therapy groups, respectively; hazard ratio [HR] 1.12; $P = 0.003$), and had similar rates of major or non-major clinically relevant bleeding (10.3% vs 11.4%, respectively; HR = 0.90; $P = 0.23$) and adverse events [31]. Rivaroxaban therapy was associated with a significantly lower rate of major bleeding compared with standard therapy (1.1% vs 2.2%, respectively; HR = 0.49; $P = 0.003$) [31]. In addition to offering a favourable safety profile, rivaroxaban does not require dietary modifications, routine measurement of anticoagulant effect, dose adjustments or bridging with heparins [31–33].

NOACs, including rivaroxaban, have the potential to reduce treatment burden and improve overall patient satisfaction. Indeed, in the EINSTEIN DVT study [34], a study of identical design to EINSTEIN PE that enrolled patients with DVT without concurrent PE, rivaroxaban was associated with significantly greater treatment satisfaction than standard therapy [35]. This study employed the use of the Anti-Clot Treatment Scale (ACTS), a 15-item, patient-reported instrument of satisfaction with anticoagulant treatment [36]. As in EINSTEIN DVT, treatment satisfaction was a predefined outcome in the EINSTEIN PE study, and here we compare the burdens and benefits of rivaroxaban as an oral fixed-dose regimen, versus dual-drug standard of care in patients with PE enrolled in the EINSTEIN PE study.

Materials and Methods

We investigated patient-reported treatment satisfaction in the EINSTEIN PE study [31], a randomised, open-label, event-driven, non-inferiority study including patients who had acute symptomatic PE with or without DVT. Rivaroxaban (15 mg twice daily for 21 days, and 20 mg once daily thereafter) was compared with enoxaparin (1.0 mg/kg twice daily for ≥5 days) overlapping with and followed by dose-adjusted VKA (target international normalised ratio 2.0–3.0). The intended treatment duration–3, 6 or 12 months–was determined at the discretion of the attending physician [31].

Patient-reported treatment satisfaction was assessed as an exploratory outcome of EINSTEIN PE in a subset of unselected patients from seven participating countries. Patients were asked by the study investigators to complete two measures of treatment satisfaction during follow-up visits: the anticoagulation treatment-specific ACTS and the generic Treatment Satisfaction Questionnaire for Medication version II (TSQM II) [36,37].

The clinical protocol and any changes were reviewed and approved by the Institutional Review Board at each study site and written informed consent was obtained from all patients. The trial was sponsored by Bayer HealthCare and Janssen Research & Development. Bayer HealthCare analysed the data. The study was conducted in line with Good Clinical Practice and was supervised by the EINSTEIN Steering Committee.

Patients

The EINSTEIN PE study involved male and female patients ≥18 years of age enrolled between March 2007 and March 2011 [31]. Patient-reported satisfaction was evaluated at fixed intervals in a subset of patients from the global study drawn from participating countries (Canada, France, Germany, Italy, the Netherlands, the US and the UK). All patients in the intention-to-treat population were eligible for inclusion in the treatment satisfaction substudy.

Measures

As part of the patient follow-up, each participating site asked patients to complete country-specific translations of the two treatment satisfaction questionnaires (Supplementary Table 1). The principal analysis used patient responses to the anticoagulation-specific ACTS questionnaire [36], and supportive analysis was provided by the generic TSQM II [37] for the purposes of construct validation, owing to it being a widely used and translated generic patient-satisfaction measure with published psychometric validation data [37,38].

The ACTS has been validated previously as a measure of treatment satisfaction, specifically for anticoagulants. It consists of 15 items divided into two subscales: the ACTS Burdens scale consisting of 12 questions and the ACTS Benefits scale of three questions. The questionnaire includes two additional 'global' questions [36], which were not included in the calculation of the relevant scale score. The previously published psychometric measurement properties for the ACTS include: acceptability; scaling assumptions; internal consistency reliability; test–retest reproducibility; aspects of validity, including known groups and discriminant validity; and exploratory responsiveness analyses [36]. Treatment experience was rated from 'Not at all' to 'Extremely' for each item using a five-point Likert scale. The items were coded in order that higher scores indicated greater satisfaction; the Benefit items were scored 1–5, whereas the Burden items were scored 5–1. The total scores are summed in each subscale to give an ACTS Burdens score ranging from 12 to 60 and ACTS Benefits score ranging from of 3 to 15. Six fixed intervals for evaluation of the ACTS were used (day 15, and 1, 2, 3, 6 and 12 months), and, overall, the psychometric criteria evaluated for both item level and scale level, in all datasets, were met for both the ACTS Burdens and Benefits subscales. In accordance with the developers' guidelines for ACTS, completion of <50% of the ACTS questions resulted in a missing scale, whereas in cases of a completion rate of >50%, individual subscale-specific mean imputation was applied.

The generic TSQM II was evaluated at 1, 3, 6 and 12 months alongside the ACTS questionnaire to provide a benchmark for validation purposes

Download English Version:

https://daneshyari.com/en/article/6000706

Download Persian Version:

https://daneshyari.com/article/6000706

Daneshyari.com