Cost-Effectiveness of Recombinant Activated Factor VII as Adjunctive Therapy for Bleeding Control in Severely Injured Trauma Patients in Germany

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Abstract

**Purpose:** The purpose of this study was to assess the cost-effectiveness of recombinant activated factor VII (rFVIIa) as adjunctive therapy for the control of bleeding in patients with severe blunt trauma injuries in Germany. The primary outcome measure was incremental cost per quality-adjusted life-year (QALY) gained.

**Materials and Methods:** We developed a cost-effectiveness model based on patient-level data from a 30 day international, randomized, placebo-controlled phase II trial. The data were supplemented with secondary data from the German Trauma Register and German life tables to estimate lifetime costs and benefits. We assumed that the non-significant difference in mortality observed in the phase II trial of 5% in favor of rFVIIa could be verified in the ongoing, much larger follow-up trauma study. We adopted the perspective of third-party payers in Germany, and included all trauma-related healthcare costs.

**Results:** The incremental cost per QALY gained with rFVIIa relative to placebo was €29,451. The probability that this was below €30,000 and €40,000 was 51% and 58%, respectively. The estimates were sensitive to the differences observed in mortality and the applied discount rate.

**Conclusions:** Based on preliminary evidence from a phase II trial, we conclude that, relative to placebo, rFVIIa may be a cost-effective therapy from the third-party payer perspective in Germany.

Key Words

Recombinant activated factor VII (rFVIIa) · Trauma · Uncontrolled bleeding · Cost-Effectiveness analysis

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Introduction

Trauma imposes a significant burden on society, accounting for nearly one in ten of all deaths [1]. Uncontrolled bleeding is a leading cause of mortality in...
trauma, accounting for 40% of trauma deaths [2].

Transfusions play a significant role in the management of coagulopathic bleeding, yet they are not always effective in correcting coagulopathy [3] and they are limited by potential side effects [4]. Recombinant activated factor VII (rFVIIa, NovoSeven™) is currently approved in most regions of the world for the treatment of bleeding in hemophilia patients with inhibitors. In the USA and Europe, rFVIIa is also approved for the treatment of FVII deficiency; additional approved indications in Europe include bleeding related to acquired hemophilia, and Glanzmann’s thrombasthenia for patients refractory to platelet transfusions.

Boffard et al. [5] recently reported the results from two multicenter, international, randomized, placebo-controlled trials, which were conducted to investigate the use of rFVIIa as an adjunctive therapy for bleeding control in patients with severe trauma. Among patients with blunt trauma who were alive at 48 h post-trauma, a significant reduction in red blood cell (RBC) units transfused was observed with rFVIIa (estimated reduction of 2.6 RBC units, \( P = 0.02 \)).

While the safety and efficacy of rFVIIa in blunt trauma patients has been demonstrated, little is known about its cost-effectiveness. The aim of this study was therefore to provide a first assessment of the cost-effectiveness of rFVIIa relative to placebo as adjunctive therapy for control of bleeding in patients with blunt trauma injuries in Germany. For our analysis, we assumed that the observed non-significant difference in mortality of the phase II study of 5% in favor of rFVIIa could be verified in the ongoing, much larger follow-up trauma study.

**Materials and Methods**

**Preliminaries**

Based on the patient-level data reported by Boffard et al. [5], we therefore undertook an economic evaluation of rFVIIa relative to placebo in patients with severe blunt trauma injuries. The primary cost-effectiveness measure was the incremental cost per quality-adjusted life-year (QALY) gained with rFVIIa relative to placebo. We adopted the perspective of a third-party payer in Germany, and included all trauma-related healthcare costs accruing to rFVIIa and placebo. A lifetime time horizon was used, and future costs and benefits were discounted at a rate of 5% [6]. All costs were measured in 2004 Euros (€).

The analysis was conducted at the patient level, using data from the intention-to-treat population of blunt trauma patients in Boffard et al. [5]. These data were limited to findings on morbidity, mortality and healthcare use up to 30 days post-trauma. In order to assess lifetime cost-effectiveness, we supplemented the patient-level data with secondary data sources: (i) a cohort of 358 patients from the German Trauma Registry [7] and (ii) life tables for the general population in Germany [8]. The structure of the economic model is shown in Figure 1.

Boffard et al. [5] detected a significant difference in the primary endpoint of their study (blood transfusions), but they observed no significant difference in mortality rates at 30 days (25% for rFVIIa versus 30%; \( P = 0.58 \)). While recognizing that rFVIIa did not have a statistically significant impact on survival, we considered our primary health outcome (lifetime QALYs) to be justified for the following reasons: (i) blood trans-