

Single-dose Recombinant Activated Factor VII for the Treatment of Joint Bleeds in Hemophilia Patients With Inhibitors

Amy D. Shapiro, MD

Dr. Shapiro is Medical Director of the Indiana Hemophilia and Thrombosis Center in Indianapolis, Ind.

Address correspondence to:
Amy D. Shapiro, MD
Indiana Hemophilia and Thrombosis Center
Indianapolis, IN 46260
Phone: 317-871-0000
Fax: 317-871-0010
E-mail: ashapiro@ihhc.org

Abstract: Increasing evidence suggests that a single dose of 270 µg/kg recombinant activated factor VII (rFVIIa) may be a convenient, safe, and effective alternative to the repeat-dose regimen for hemophilia patients with inhibitors. Three recent trials investigating on-demand treatment (Kavakli et al 2006, Santagostino et al 2006, and Young et al 2008) lend further weight to earlier reports demonstrating that a single dose of 270 µg/kg rFVIIa is as effective as a repeat-dose schedule of 3 x 90 µg/kg rFVIIa in producing hemostasis, reducing the need for additional hemostatic medications, and improving pain and mobility in joints affected by hemarthroses. The single-dose regimen is advantageous as it may reduce both the difficulties caused by the need for repeated venous access and the interruption of daily activities associated with repeat dosing. Safety data from these three trials, along with those from a fourth study investigating the prophylactic use of 270 µg/kg rFVIIa, also demonstrate no additional or altered safety profile associated with single-dose treatment. These findings suggest that a single dose of 270 µg/kg rFVIIa is as safe and effective a hemostatic regimen as the standard lower, more frequent dose regimen and provides comparable bleeding control in hemophilia patients with inhibitors. The single-dose 270 µg/kg rFVIIa regimen utilized similar product consumption to the 3 x 90 µg/kg rFVIIa treatment regimen.

Recombinant activated factor VII (rFVIIa; NovoSeven, Novo Nordisk) is the only recombinant bypassing therapy available for on-demand treatment of hemorrhagic events in hemophilia patients with inhibitors.¹⁻⁸ The agent binds to the surface of activated platelets in a dose-dependent manner, leading to direct activation of factor X and subsequent generation of a thrombin burst in the absence of factor VIII or factor IX and despite the presence of inhibitory antibodies.¹ High doses of rFVIIa increase the activation of platelets and the initial thrombin burst at the site of injury, resulting in a more stable clot with increased resistance to fibrinolysis.⁹⁻¹¹

Keywords

hemophilia, inhibitors, recombinant activated factor VII, single-dose

The standard-dose regimen for the treatment of spontaneous or surgical bleeds in hemophilia patients with inhibitors utilizes a dose of 90 µg/kg every 2–3 hours until hemostasis is achieved.¹² This regimen effectively controls up to 92% of mild-to-moderate bleeding episodes, with an average of 2.2 injections required to achieve hemostasis.⁶ In this study, a single dose of rFVIIa 90 µg/kg has been shown to be effective in treating 29% of bleeding episodes.⁶ However, repetitive dosing presents practical challenges as it requires repeated venous access and potential interruption of daily activities. A single-dose regimen that provides equivalent control could therefore represent an attractive alternative for patients with poor venous access and those with frequent target-joint bleeds,^{13–15} and it could potentially reduce the bleed volume, preserve venous access, minimize interruption of patients' lives, and improve both patient compliance and ease of home treatment.

An increasing body of clinical evidence also suggests that a single dose of rFVIIa (>200 µg/kg) may be a more convenient, safe, and equivalent hemostatic alternative to the repeat-dose regimen.^{11,13,15–17} This article reviews the efficacy data from three trials designed to evaluate single-dose rFVIIa treatment in hemophilia patients with inhibitors (Kavakli et al,¹⁸ Young et al,¹⁹ and Santagostino et al¹³) and discusses these data in the context of current literature on single-dose rFVIIa therapy. Safety data from these studies, and from a fourth trial evaluating secondary prophylaxis with rFVIIa in inhibitor patients (Konkle et al²⁰), are also reviewed.

Efficacy of Single-dose rFVIIa: Clinical Trials

*The Kavakli Study (Study 1510)*¹⁸

In this multicenter, double-blind, crossover trial, patients with hemophilia and inhibitors were randomly assigned to treat a first hemarthrosis with a single dose of 270 µg/kg rFVIIa or three single doses of 90 µg/kg rFVIIa at 3-hour intervals in a home treatment setting (Table 1). Efficacy was evaluated using a new, previously unvalidated, global treatment response rating tool (GTRS). Patients rated their pain and mobility (“positive” or “negative”) at 1, 3, 6, and 9 hours after the first injection according to predefined criteria. Treatment outcome was then classified as “effective” (6 or more positive scores for each bleeding episode) or “ineffective” (5 or fewer positive scores, or if additional medication was required to produce hemostatic control within 9 hours of the first dose of rFVIIa). Treatment “preference” was defined as effective treatment with one regimen and ineffective treatment with the other, whereas patients with equally effective or ineffective treatments were classified as having “no preference.”

Treatment was effective for 13 of 20 (65%) patients using the single dose of 270 µg/kg and for 14 of 20 (70%) patients using the 3 × 90 µg/kg dose regimen. There was no statistically significant “preference” between the two regimens (21% for both) among patients treated with 270 µg/kg versus 90 µg/kg for their first bleed. Overall, the need for additional medication for hemostatic control was similar between the regimens: 2 of 21 (9.5%) and 3 of 21 (14.3%) patients for the 270 µg/kg and 3 × 90 µg/kg dose groups, respectively, and was consistent with previous studies.⁶ Within 1 hour of the first rFVIIa dose, pain was reduced in more patients receiving 270 µg/kg (94%) than in patients receiving 3 × 90 µg/kg (85%). Improvements in mobility of the affected joint were similar between the two regimens (85% and 84%, respectively).

The new GTRS system aimed to standardize definitions of effective hemostasis by combining subjective pain relief with objective measures of joint mobility.¹⁸ As such, it is far more stringent than the purely subjective assessment tools utilized in most earlier studies to evaluate response to treatment in hemophilia patients. Given the strict definitions of efficacy used in this new scoring system, it was expected that the success rates obtained would be lower than those obtained previously using simpler, less stringently defined scales. Importantly, however, these data reflect similar overall hemostatic efficacy with single-dose rFVIIa compared with the repeat-dose treatment regimen.¹⁸ It should be noted that, to date, the GTRS system is not validated.

*The Young Study (Study 2068)*¹⁹

This randomized, multicenter, double-blind, crossover study evaluated two dose schedules of rFVIIa and one open-label dose of activated prothrombin complex concentrate (aPCC; FEIBA [Factor Eight Inhibitor Bypassing Activity], Baxter; Table 1) in the treatment of consecutive hemarthrosis in patients with hemophilia and inhibitors.¹⁹ All joint bleeds were eligible for inclusion, including target joints. Efficacy was assessed by requirement for additional infusion of hemostatic therapy (including aPCC and rFVIIa) within 9 hours of the first administration of trial product, and by use of the GTRS system, first utilized by Kavakli and colleagues.¹⁸

The percentage of patients requiring additional hemostatic agents after 9 hours was significantly lower in the 270 µg/kg rFVIIa group than in the aPCC group (8.3% vs 36.4%; $P=.032$).¹⁹ This result may have been influenced, in part, by study design. Patients in the rFVIIa treatment arms received three injections regardless of whether they received rFVIIa 270 µg/kg or 90 µg/kg. Having already been exposed to three infusions of hemostatic product, patients in the rFVIIa treatment arms could have, con-

Table 1. Overview of Recent Clinical Trials Investigating Single-dose rFVIIa Regimens*

Study	Indication	Main Objectives	Study Design	Dosage Regimens	Primary Efficacy Endpoint
Kavakli et al ¹⁸	Hemostatic treatment (joint bleeds) of pediatric and adult patients with hemophilia A or B and inhibitors in a home treatment setting	Efficacy Safety	Randomized, double-blind, multicenter, crossover study	Patients (n=24) were randomized in a crossover design to treat the first joint bleed with one of the following regimens: <ul style="list-style-type: none"> • Single bolus dose of 270 µg/kg rFVIIa at time 0, followed by placebo 3 and 6 hours after initial dose (n=21) • Single bolus dose of 90 µg/kg rFVIIa at time 0, and at 3 and 6 hours after initial dose (n=21) The second joint bleed was treated with the alternative dose regimen	Global treatment outcome, based on patient self-assessment of pain and mobility
Young et al ¹⁹	Hemostatic treatment (joint bleeds) of pediatric and adult patients with hemophilia A or B and inhibitors in a home treatment setting	Efficacy Safety	Randomized, double-blind, multicenter, crossover study	Patients (n=42) were randomized in a crossover design to 1 of 6 treatment-sequence permutations of the following dose regimens: <ul style="list-style-type: none"> • Single bolus dose of 270 µg/kg rFVIIa at time 0, followed by placebo 3 and 6 hours after initial dose (n=24) • Single bolus dose of 90 µg/kg rFVIIa at time 0, and at 3 and 6 hours after initial dose (n=22) • Single bolus dose of 75 µg/kg FEIBA at time 0 (n=22) 	Percentage of patients achieving hemostasis without requiring rescue medication Global treatment response, based on patient self-assessment of pain and mobility
Santagostino et al 2006 ¹³	Hemostatic treatment (joint bleeds) of pediatric and adult patients with hemophilia A and inhibitors in a home treatment setting	Efficacy Safety Cost	Randomized, open-label, multicenter, crossover study	Patients (n=20) were randomly assigned to treat 4 consecutive joint bleeds with 1 of 2 rFVIIa dose regimens: <ul style="list-style-type: none"> • 90 µg/kg rFVIIa every 3 hours • Single dose of 270 µg/kg rFVIIa 	Visual Analog Scale score Patient-rated efficacy according to change in signs and symptoms
Konkle et al ²⁰	Secondary prophylaxis (bleeding) in hemophilia A or B patients with inhibitors	Safety	Randomized, exploratory, double-blind, multicenter, uncontrolled, parallel-group study	<ul style="list-style-type: none"> • 3-month observation period (n=37) • Eligible patients (n=22) randomized to a single daily dose of either 90 µg/kg rFVIIa (n=11) or 270 µg/kg rFVIIa (n=11) for 3 months • 3-month posttreatment observation period 	Number of bleeds per month during the prophylaxis period (compared with the preprophylaxis period)

*Konkle et al is not included in the efficacy analyses discussed in this article as this study uses rFVIIa for prophylaxis, rather than on-demand treatment, of bleeding episodes. It was therefore considered inappropriate to include efficacy data from this study in the efficacy analyses. However, data from this study have been used in the analysis of safety.

FEIBA= Factor Eight Inhibitor Bypassing Activity; rFVIIa=recombinant activated factor VII.

ceivably, been reluctant to receive a further injection. In addition, patients treated for bleeding within the same joint (a target joint) all received aPCC as the third treatment, which is associated with the lowest level of response. Based on this potential for bias, results obtained for rescue medication should be interpreted with caution.

Requirements for rescue medication were similar with 270 µg/kg versus 90 µg/kg rFVIIa treatments (8.3% and 9.1% of bleeding episodes, respectively). There were no significant differences between the three groups in response to treatment at 9 hours using the GTRS, with successful responses observed in 37.5% of patients receiv-

ing 270 $\mu\text{g}/\text{kg}$ rFVIIa, 54.5% of patients treated with $3 \times 90 \mu\text{g}/\text{kg}$ rFVIIa, and 27.3% of those receiving aPCC. Individual responses to pain and mobility were also similar between treatments: pain improved in 45.8%, 54.5%, and 27.3% of patients receiving 270 $\mu\text{g}/\text{kg}$ rFVIIa, $3 \times 90 \mu\text{g}/\text{kg}$ rFVIIa, and aPCC, respectively. Corresponding rates for improvement in mobility were 45.5%, 25.0%, and 22.7%.

Post Hoc Analysis of the Kavakli (1510)¹⁸ and Young (2068)¹⁹ Studies

For the purpose of this review, efficacy data from the Kavakli and colleagues and Young and associates studies^{18,19} were combined to increase the number of patients for whom data would be available for analysis, as both studies utilized the same new global treatment scale. Demographic and baseline characteristics were largely comparable between patients in both trials, with the exception of patient age: Young and associates included a higher proportion of pediatric patients (<18 years) than did Kavakli and colleagues. The Kavakli study treated all hemarthroses (including those considered severe), whereas the Young trial treated only mild-to-moderate hemarthrosis; patients experienced at least two (Young) or three (Kavakli) mild-to-moderate hemarthroses within the 12 months prior to inclusion. Both studies assessed hemarthrosis in a home treatment setting. The majority of hemarthroses were spontaneous, with traumatic hemorrhages observed most frequently among children. It should be noted that no patient was entered in both trials (Young et al was performed in the United States; Kavakli et al was performed outside the United States).

Post hoc analysis of the combined study data showed that a single dose of 270 $\mu\text{g}/\text{kg}$ rFVIIa was as effective as the $3 \times 90 \mu\text{g}/\text{kg}$ rFVIIa dose schedule, as measured by the need for additional hemostatic medication within 9 hours of study drug administration (Figure 1). There was no significant difference between the success rates with the 270 $\mu\text{g}/\text{kg}$ and $3 \times 90 \mu\text{g}/\text{kg}$ rFVIIa dose regimen for all evaluated aspects of the new GTRS algorithm (Figure 2). The somewhat lower success rates observed in the study by Young and associates¹⁹ may be attributed to lower scores for children treated with single-dose rFVIIa: success rates were 54–63% for adults treated with both rFVIIa dose regimens and for children treated with the repeat-dose schedule, but 23% for children treated with single-dose rFVIIa. The low efficacy rates among children receiving the single-dose 270 $\mu\text{g}/\text{kg}$ is of interest; a number of these patients who reported no pain at baseline and therefore no subsequent pain relief, and were thus classified as “treatment failures,” contributed to this lower efficacy rating. The efficacy rate observed may also be lower in children due to a faster clearance rate of rFVIIa

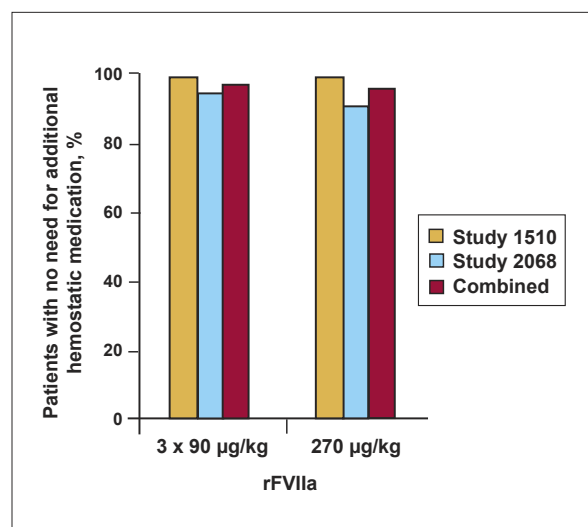


Figure 1. Proportion of patients with no need for additional hemostatic medication within 9 hours of initial recombinant activated factor VII (rFVIIa) dose (Kavakli et al [1510], Young et al [2068], and combined studies).

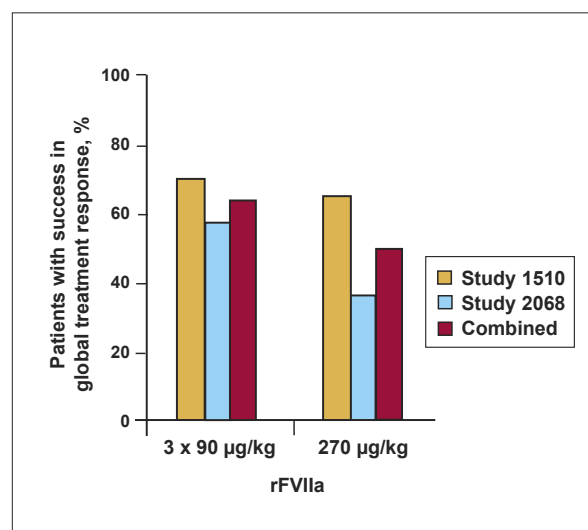


Figure 2. Global treatment response by recombinant activated factor VII (rFVIIa) dose regimen (Kavakli et al [1510], Young et al [2068], and combined studies).

compared with adults.²¹ A higher rate of traumatic, rather than spontaneous, first bleeds occurred among children in the study by Young and associates and may have contributed to the lower treatment success rates observed in this patient population, as in this type of bleed a higher variation in clearance rates has been observed.²²

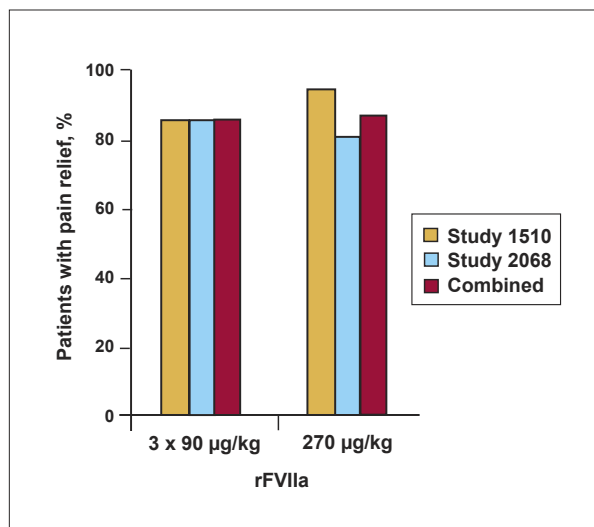


Figure 3. Pain relief at 1 hour after the initial dose by recombinant activated factor VII (rFVIIa) dose regimen (Kavakli et al [1510], Young et al [2068], and combined studies).

More than 80% of patients who reported pain at baseline experienced pain relief or a reduction in pain within the first hour of initial rFVIIa dose, and the number of patients with pain relief was comparable between the single- and repeat-dose regimens (Figure 3). Although superiority of the single-dose regimen over the repeat-dose schedule was not demonstrated, it is important to note that a high number (approximately 50%) of patients utilized analgesics after rFVIIa treatment, which may have confounded assessment of pain relief at subsequent time points.²³ In addition, a different use of analgesics in the United States versus Europe was observed. The effect of the treatment regimen on pain reduction should therefore be interpreted with caution.

Over 70% of patients reported improved mobility in the affected joint within 1 hour of initial rFVIIa administration, with similar proportions of patients in the single- and repeat-dose groups. As with pain relief, the single-dose regimen did not demonstrate superiority over the repeat-dose schedule (78% vs 88% for 270 and 90 µg/kg rFVIIa regimens, respectively). It is well established that joint mobility may not improve within the first few hours following acute hemarthrosis,²⁴ and so it is quite likely that the 1-hour data point for improved mobility does not represent the true beneficial effect of single-dose rFVIIa treatment or in fact of any specific regimen.

*Santagostino et al 2006*¹³

This multicenter, randomized, open-label, crossover trial was designed to compare the efficacy, safety, and cost of standard (3×90 µg/kg) and 270 µg/kg rFVIIa for the treatment of hemarthroses in hemophilia patients with inhibitors (Table 1). In addition to rating changes in signs and symptoms of bleeding using a visual analog scale (VAS; 0=no relief, 100=complete relief), patients also evaluated treatment as being effective, partially effective, or ineffective. Treatment was considered successful if patients achieved a VAS score of 70 or higher and if they reported definite relief of swelling, pain, and functional limitation.

No statistically significant differences were found between the 270 µg/kg and 3×90 µg/kg rFVIIa treatment regimens at any evaluated time point: success rates were 25% and 31% at 9 hours, 50% and 53% at 24 hours, and 64% and 66% at 48 hours, respectively. The reported differences in efficacy rates at the different time points are expected and in part reflect the subjective nature of the assessment method used. No differences between the 3×90 µg/kg and single-dose 270 µg/kg regimens in terms of the median number of outpatient visits (3 and 5, respectively) or days lost from school or work (0 for both) were observed.

In summary, these results demonstrate that the use of the single-dose rFVIIa regimen is as effective for the treatment of hemarthroses in hemophilia patients with inhibitors as the conventional repeat-dose regimen. The total amount of rFVIIa consumed was identical between the two dosage regimens, as were the indirect costs associated with treatment; it is important that the single-dose schedule may provide an advantage of increasing both patient convenience and the ease of home treatment, as fewer injections are required.

Single-dose rFVIIa: Supporting Evidence From the Current Literature

The findings of the trials by Kavakli and colleagues,¹⁸ Young and associates,¹⁹ and Santagostino and coauthors¹³ are supported by the following studies of single-dose rFVIIa regimens.

*Parameswaran et al 2005*¹⁵

In this retrospective analysis of data from the Hemophilia and Thrombosis Research Society database, registered bleeding episodes were categorized according to bolus rFVIIa dose range (<100, 100–150, 150–200, and >200 µg/kg per dose), with a 72-hour efficacy time point for analysis. Overall, hemostasis was achieved in 87% of 555 bleeding episodes using rFVIIa in this registry; however, the bleeding cessation rate was significantly higher for

hemorrhages treated with doses higher than 200 µg/kg rFVIIa (97%) than for those treated with any of the lower doses (84%; $P<.001$).

Kenet et al 2003¹¹

This open-label, single-center, uncontrolled study compared the efficacy of a single-dose of 300 µg/kg of rFVIIa with that of continuous infusion (CI-a: 90 µg/kg followed by 15–16 µg/kg/h; or CI-b: 180 µg/kg followed by 30 µg/kg/h) in the treatment of bleeding episodes in 3 inhibitor patients. Response to treatment was defined as definite pain relief and prevention of re-bleeding. There were 114 bleeding episodes in the 300 µg/kg rFVIIa group, 58 in the CI-a group, and 72 in the CI-b group. Eighty-two of the bleeds treated with the single-dose 300 µg/kg of rFVIIa were in target joints. Efficacy rates were higher with the single-dose 300 µg/kg of rFVIIa: 95 of the 114 (83%) bleeding episodes treated with the 300 µg/kg dose responded to a single dose, whereas approximately 91 of 130 (70%) episodes were successfully resolved using either of the continuous infusion regimens. Patients treated with the single-dose 300 µg/kg of rFVIIa protocol also reported more rapid pain relief (30–90 minutes vs 1–8 hours) and a significantly shorter duration of therapy (0–6 hours vs 4–100; $P<.001$) than those receiving continuous infusion.

Chuansumrit et al 2001¹⁶

Chuansumrit and colleagues evaluated the use of single intermediate-dose rFVIIa (150–180 µg/kg) in nine bleeding episodes in 3 patients with hemophilia and inhibitors. Treatment was considered effective if relief of pain or tenderness was reported; if a measurable decrease in swelling occurred; and if bleeding was successfully arrested. Overall, efficacy or partial efficacy was achieved in seven of nine (78%) bleeding episodes; two unresolved bleeds were successfully controlled by an additional dose given at 12 and 18 hours, respectively, after initial administration.

Cooper et al 2001¹⁷

This case report describes a patient with hemophilia B who, since the age of 8 years, demonstrated a poor response to bolus doses of rFVIIa (90–180 µg/kg) for a variety of bleeding episodes. Severe knee hemarthroses led to the development of bilateral knee flexion contractures, with eventual wheelchair confinement. Treatment of soft-tissue bleed in the left forearm with 320 µg/kg rFVIIa resulted in an excellent response, with rapidly diminished pain and a measurable reduction in the circumference of the forearm. The patient subsequently underwent intensive physiotherapy to reduce his wheelchair dependence by utilizing this high dose for prophylaxis. In addition, throughout this rehabilitative program, multiple joint,

Table 2. Treatment-emergent Adverse Events Reported in the Kavakli Study¹⁸

	rFVIIa 3 × 90 µg/kg (n=21)		rFVIIa 270 µg/kg (n=21)	
	n	E	n	E
All adverse events	6	9	6	7
Arthralgia	1	1	3	3
Joint crepitation	1	1	0	0
Hemorrhage	2	2	1	1
Nausea	1	1	0	0
Inflammation	0	0	1	1
Pain	1	1	0	0
Viral bronchitis	1	1	0	0
Headache	1	1	0	0
Tongue biting	0	0	1	1
Pruritis	0	0	1	1
Subcutaneous nodule	1	1	0	0

E=number of adverse events; n=number of patients with adverse event; rFVIIa=recombinant activated factor VII.

muscle, and miscellaneous hemorrhages were successfully treated with a single dose of 320 µg/kg rFVIIa.

Safety of Single-dose rFVIIa

Data from the studies by Kavakli and colleagues,¹⁸ Young and associates,¹⁹ and Santagostino and coauthors¹³ can be used to compare the safety profiles of the single-dose and repeat standard-dose rFVIIa regimens. A fourth study, which evaluated the efficacy and safety of single-dose rFVIIa (90 or 270 µg/kg) when used as secondary prophylaxis in inhibitor patients with high requirements for on-demand therapy, can also be utilized to assess the safety of the single-dose regimen (Table 1).²⁰

Adverse Events

In the trial by Kavakli and colleagues, adverse events occurred with similar frequency in the two rFVIIa dose groups (270 µg/kg and 3 × 90 µg/kg; Table 2).¹⁸ In the Young study,¹⁹ seven adverse events were reported in 3 patients treated with 270 µg/kg rFVIIa, and 11 adverse events in 5 patients receiving 3 × 90 µg/kg rFVIIa. All patients experiencing adverse events recovered or

stabilized, and no adverse events in either study were considered related to study drug. There were no apparent differences in the type of adverse events between the two dose regimens.

In the trial by Santagostino and coauthors,¹³ no adverse reactions were associated with the 3×90 µg/kg dose regimen, whereas two episodes of transient headache occurred in 1 patient after receiving two bolus doses of 270 µg/kg rFVIIa.

In a study in which rFVIIa was used for prophylaxis (Konkle and coworkers),²⁰ adverse events were more frequently reported during 3 months of treatment with 90 µg/kg rFVIIa (n=9) and in a 3-month pretreatment observation period for the 270 µg/kg dose group (n=9) than in the 270 µg/kg treatment period (n=8), and 90 µg/kg pretreatment period (n=8), respectively. However, no apparent treatment-dependent patterns in the number or type of adverse reactions were reported. None of the adverse events occurring among patients treated with 270 µg/kg rFVIIa was considered related to study drug, whereas five adverse events in 2 patients receiving the 90 µg/kg dose were judged to be possibly or probably related to treatment (moderate fever, headache, and vertigo [n=1]; and two episodes of allergic dermatitis [n=1]). Both patients recovered in less than 1 week.²⁰

Serious Adverse Events

No deaths or thromboembolic events were reported in these four studies, and no withdrawals due to adverse events, serious adverse events, or events considered to be possibly or probably related to the study drug were observed.

In the study by Young and associates,¹⁹ 11 serious adverse events were reported by 5 patients, including three events of hemorrhage in a nonstudy joint, two events each of infection and arthralgia, and one event each of decreased therapeutic response, back pain, pharyngolaryngeal pain, and respiratory arrest secondary to morphine administration for pain. Relationship to study drug was considered unlikely for all serious adverse reactions, and there were no trends evident with respect to age or treatment group.¹⁹

In the secondary prophylaxis study,²⁰ four serious adverse events occurred during treatment in patients receiving 270 µg/kg rFVIIa (gastrointestinal hemorrhage; pneumonia; fracture of the ulna; and a viral infection). An additional serious adverse event (infected hematoma) occurred in the posttreatment period in the patient with pneumonia. None of these serious adverse reactions was considered related to rFVIIa treatment.

The safety findings of the trials by Kavakli and colleagues,¹⁸ Young and associates,¹⁹ and Santagostino coauthors¹³ are supported by other published rFVIIa

single-dose studies. Overall, single-dose rFVIIa was well tolerated without associated thrombotic sequelae, disseminated intravascular coagulation, or death.^{11,15-17} As with all randomized controlled trials, there are insufficient patients in these trials to rule out a higher incidence of adverse events, especially in geriatric patients who may have concomitant cardiovascular risk factors.

Conclusion

The results of the recent clinical trials^{13,18-20} suggest that a single dose of 270 µg/kg rFVIIa is as effective as the repeat standard-dose regimen of 3×90 µg/kg for on-demand treatment of hemarthroses in hemophilia patients with inhibitors. In addition, the overall safety profile of the single-dose 270 µg/kg rFVIIa regimen in these trials is not altered and does not appear to present additional safety risks compared with the repeat standard-dose regimen.

A single dose of 270 µg/kg rFVIIa may be of particular benefit for patients with poor venous access, frequent target-joint hemorrhage, and needle phobia. It has also been suggested that the single-dose treatment regimen may improve patient compliance, enhance the ease of home treatment, and facilitate earlier control of hemorrhagic events.

As a result of these data, 270 µg/kg rFVIIa was recently approved by the European Medicines Agency for home treatment of mild-to-moderate hemorrhage in hemophilia patients with inhibitors.

Acknowledgment

This manuscript was sponsored in part by an unrestricted grant from Novo Nordisk A/S.

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