

# Recombinant-activated factor VII as rescue for refractory haemorrhage

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## Goals

Recombinant factor VIIa (rFVIIa, Novoseven®) is indicated for treatment of bleeding in haemophilic and other patients with antibodies against factor VIII or IX. Although not licensed for other use, rFVIIa is increasingly reported as a last resort treatment in patients with refractory haemorrhages.

### Randomized Controlled Trials

Indication	Dose	n	Results
Post partum Haemorrhages	40 -120 µg / kg	12 ptes	11 good or partial responses
Blunt or penetrating trauma (> 8 CE)	200 then 100 µg / kg (2x)	301 Pts	Reduced transfusion, ARDS and MOF in subgroup. No effect on mortality
Radical Prostatectomy	20-40 µg / kg	36 Pts	Reduced transfusion needs
Partial hepatectomy (non Cirrhotics pts)	20-80 µg / kg	204 Pts	no effect
Major pelvic surgery	90 µg / kg	48 Pts	no effect
IC haemorrhage	40- 160 µg / kg	399 Pts	Dim increased in hematoma size. Dim Disabilities

## Methods

We reviewed all consecutive patients treated with rFVIIa in our hospital from March 2004 until December 2005.

Administration of rFVIIa was decided, after systematic cross-checking by the attending physician in charge of the patient and a senior haematologist of other therapeutic alternatives (correction of hypothermia, correction of acidosis, adequate substitution for all coagulation cofactors including fibrinogen and thrombocytes, embolization, surgery).

## Results

N°	Age	Source	Dosage	Bleeding	Complication	Outcome
1	53	Digestive	300 µg/kg	Stopped	Thrombosis ?	Death, day 1, from MOF
2	71	Cardiac surgery	300 µg/kg	Stopped	No	Death, day 6 from sepsis
3	20	Multiple trauma	300 µg/kg	Stopped	Thrombosis ?	Death, day 2 from brain death
4	25	Multiple trauma	300+90	Stopped	No	Death, day1 from MOF
5	25	Caesarean	300 µg/kg	Stopped	Thrombosis	Survival
6	82	Cardiac surgery	90 µg/kg	Stopped	No	Death, day 4 from MOF
7	44	ENT surgery	30 µg/kg	Stopped	No	Survival
8	33	Digestive	90 µg/kg	Stopped	No	Death, day 21 from liver failure
9	<1	Cardiac surgery	90 µg/kg	Stopped	No	Death, day 7 from MOF
10	54	Digestive	90 µg/kg	Persisted	No	Death, during surgery
11	38	Nephrectomy	90 µg/kg	Stopped	No	Survival
12	50	Aortic surgery	90 µg/kg	Stopped	No	Survival
13	76	Neurosurgery	45+45	Stopped	No	Survival
14	22	Cardiac surgery	60+60+30	Stopped	No	Death Day 3 from MOF
15	25	Multiple trauma	90 µg/kg	Stopped	No	Death from MOF

Haemorrhage stopped in all but one patients, 10 (66%) of them died. Four of 5 (80%) patients receiving very high dosage ( $\geq 300$  mcg/kg), as compared 6 of 10 (60%) of those receiving standard dose ( $\leq 90$  mcg/kg). A thromboembolic event occurred in 3 of 6 patients (50%) receiving very high dosage ( $\geq 300$  mcg/kg) of rFVIIa, as compared to none of those receiving standard dose (90 mcg/kg).

## Discussion

Very high dosages of rFVIIa initially prescribed according to preliminary recommendations were adapted to published experience. Efficacy was maintained, whereas potentially life-threatening effects were reduced.

## Conclusions

Our experience suggest that rFVIIa may be potentially useful as salvage measure in the treatment of massive bleeding. As other, we also observed that high dosage may be associated with thrombotic events which may have contributed to fatal outcome. Based on the literature and our present experience, we adapted local guidelines. These guidelines emphasize on the need of a systematic work-up for surgical, angiographic and other hematologic options before prescribing rFVIIa.