Cost-Effectiveness of Recombinant Activated Factor VII in the Treatment of Intracerebral Hemorrhage over a Two-Year Managed Care Enrollment Period

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ABSTRACT

OBJECTIVES: To estimate cost-effectiveness of rFVIIa compared to standard care in treating ICH over an average MCO enrollment period of two years from a third-party payer perspective.
METHODS: A decision-analytic model estimating cost-effectiveness of rFVIIa 80mcg/kg compared to standard care in treating ICH was adapted to measure cost-effectiveness over a time horizon (enrollment period) of two years. Input parameters were obtained from clinical trial, claims data, and published literature. Cost of rFVIIa was based on wholesale acquisition cost. Costs were in 2006 US dollars. Outcomes included life-years and quality-adjusted life years (QALY). In addition, population characteristics were considered, including age (over/under 65) and gender comparisons. One-way and multivariable sensitivity analyses were conducted to assess robustness.
RESULTS: Assuming a cost-effectiveness threshold of $50,000 QALY, the incremental cost-effectiveness ratio (ICER) showed rFVIIa to be cost-effective compared to standard care alone ($2,924/QALY gained). Use of rFVIIa was found to be cost-effective in both the under- and over-65 populations ($532/QALY gained and $5,323/QALY gained, respectively). Results did not differ substantially across gender. Results were robust to changes in model parameters.
CONCLUSIONS: Treating ICH with rFVIIa 80mcg/kg within an MCO is cost-saving over the average patient enrollment period of two years compared to standard care. Due to potential improvements in long-term clinical outcome, treatment with rFVIIa may have an even greater positive impact in health plans with a younger population.

INTRODUCTION

- Intracerebral hemorrhage (ICH) is the deadliest form of stroke, resulting in mortality and severe disability among survivors.
- ICH events impose a significant economic burden due to intense medical resource use during acute treatment as well as the cost of long-term management of survivors.
- Currently, no drug therapies have been proven effective for treatment of acute ICH.
- Recombinant activated factor VII (rFVIIa) is currently indicated for treatment of bleeding episodes in hemophilia A or B patients with inhibitors to Factor VIII or Factor IX. A treatment that would reduce mortality and improve 90-day functional outcome would be valuable.

OBJECTIVE

To estimate cost-effectiveness of rFVIIa compared to standard care in treating ICH over an average MCO enrollment period of two years from a third-party payer perspective.

METHODS

Patient Population

Patients enter the hospital emergency room presenting with acute ICH within 3 hours of symptom-onset.
Specific patient characteristics include:

- Age distribution typical of published patient populations with ICH.
- Characteristics (ICH severity, disease history, time of arrival after onset of ICH event) similar to those observed in the clinical trial[1].
- Patient weight of 70 kilograms.

Study Design

- Short-term cost-effectiveness (CE) model was adapted from a previously developed decision-analytic model estimating the lifetime CE of rFVIIa 40, 80, or 160 mg/kg for acute ICH[2] (Figure 1).
- Short-term model estimates the CE of treatment rFVIIa 80 mg/kg relative to standard care alone over a typical US managed care enrollment period.
- Patients are followed for the first 90 days after ICH onset, and annually thereafter for the remainder of the two years (Figure 1).
- Model takes the perspective of a third-party US managed care payer.

REFERENCES

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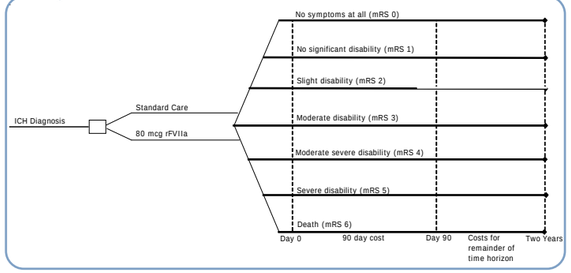
- One-time drug costs are based on wholesale acquisition costs (WAC)[3].
  -40 mcg/kg: $3,444
  -80 mcg/kg: $6,888
  -160 mcg/kg: $13,776
- Functional status, measured by modified Rankin Score (mRS) is estimated at 90 days after ICH onset, based on clinical trial data[2].
- Costs and outcomes based on functional status (defined as 90-day mRS):
- Modified Rankin Scale Categories:
  -mRS 0 (no disability)
  -mRS 1 (no significant disability)
  -mRS 2 (slight disability)
  -mRS 3 (moderate disability)
  -mRS 4 (moderate to severe disability)
  -mRS 5 (severe disability)
  -mRS 6 (death)
- Costs include: drug cost, inpatient stay, skilled nursing facility costs, and any additional medical management costs[4,5] (Table 1).
- Per-day initial hospitalization costs: $2,618 for survivors, $2,193 for those who die[6].
- Post-90 day base annual medical costs (mRS 0-2): $7,283 [6] and adjusted for higher mRS (3-5) using cost multipliers from published literature.[5]
- Mortality risk and utility weights obtained from published literature[5] and applied based on 90-day functional status (defined by mRS).

Figure 1. Model Structure



Model Assumptions

- The model assumes a permanent functional status after 90 days based on published literature[5].
- Long-term cost multipliers and death hazard ratios are based on ischemic stroke model[5] (Table 1). The model assumes that long-term costs and outcomes are based on functional status as defined by mRS.

Sensitivity Analysis

- One-way sensitivity analyses were performed on key input parameters (Figure 3).
- Parameters were varied by +/- 20%, or based on plausible range data provided in the literature[5].
- Probabilistic SA (Monte Carlo simulation with 10,000 iterations) performed on clinical efficacy rates, death hazard ratios, and cost multipliers (Figure 4).

RESULTS

Table 1. Base-Case Results: Comparison of Costs and Outcomes

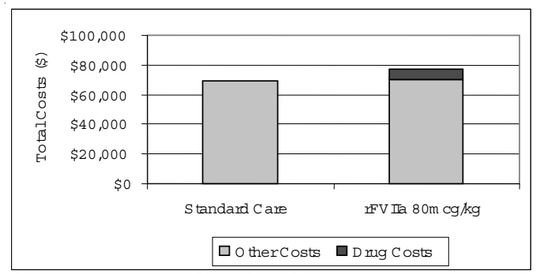
Treatment	Drug Costs	Other Costs	Total Costs	Life-Years	QALY	Incremental $/ Life-Year	Incremental $/ QALY
Baseline							
Standard Care	$0	$69,670	$69,670	1.25	0.50	N/A	N/A
rFVIIa 80mcg/kg	$6,888	$70,442	$77,330	1.45	0.76	$3,827	$2,924
Over 65							
Standard Care	$0	$67,133	$67,133	1.15	0.47	N/A	N/A
rFVIIa 80mcg/kg	$6,888	$68,479	$75,367	1.36	0.72	$6,690	$5,323
Under 65							
Standard Care	$0	$72,376	$72,376	1.34	0.53	N/A	N/A
rFVIIa 80mcg/kg	$6,888	$72,523	$79,411	1.54	0.81	$727	$532
Male							
Standard Care	$0	$69,187	$69,187	1.23	0.49	N/A	N/A
rFVIIa 80mcg/kg	$6,888	$70,069	$76,957	1.43	0.76	$4,376	$3,368
Female							
Standard Care	$0	$70,011	$70,011	1.26	0.50	N/A	N/A
rFVIIa 80mcg/kg	$6,888	$70,705	$77,593	1.46	0.77	$3,439	$2,613

rFVIIa= Recombinant activated factor VII. Table 1 illustrates the total (drug and other medical) costs per patient associated with the treatment of ICH with either rFVIIa or standard care alone. The model assumes an average patient weight of 70kg.

Two-Year Costs and Outcomes for Standard Care and rFVIIa – Overall and by Age and Gender

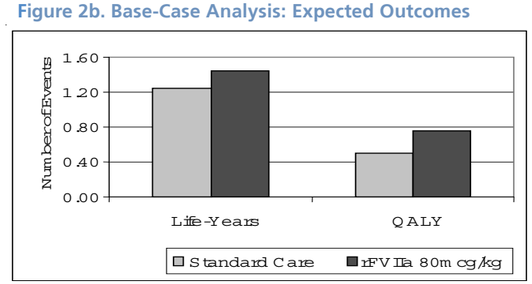
- Treatment with 80 mcg/kg rFVIIa resulted in a reduction in other medical costs compared to standard care alone (Table 1).
- rFVIIa was cost-effective compared to standard care alone assuming an acceptability threshold of $50,000/QALY
- Drug costs minimal compared to other medical costs

Figure 2a. Base-Case Analysis: Expected Costs of Treatment



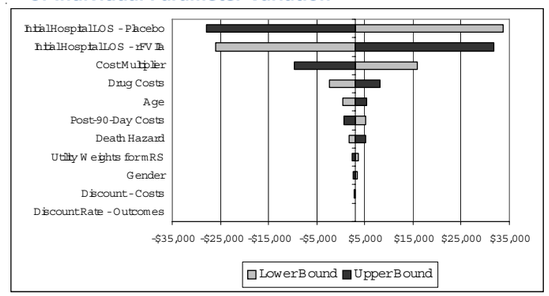
Analysis over a two-Year Time Period

Figure 2b. Base-Case Analysis: Expected Outcomes



Analysis over a two-Year Time Period

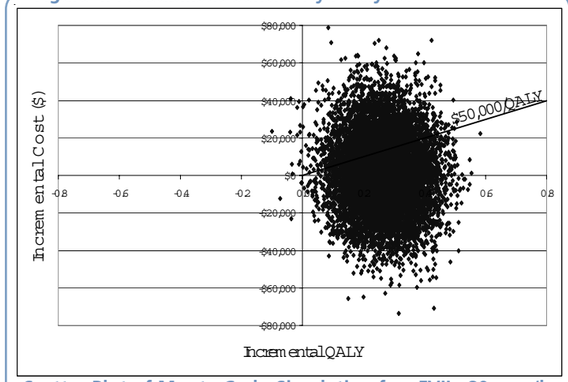
Figure 3. One-Way Sensitivity Analysis: Impact on ICER of Individual Parameter Variation



rFVIIa = Recombinant activated factor VII. LOS = length of stay. Gender represents the sensitivity analysis with male being the lower bound and female being the upper bound. Age is defined with under 65 being the lower bound and over 65 being the upper bound.

- Results are robust to realistic parameter variation
- Model most sensitive to initial hospital length of stay, 90-day functional outcome, and cost multipliers
- Age, gender, post 90-day costs, utility weights, and discount rates had minimal impact on model results

Figure 4. Probabilistic Sensitivity Analysis:



Scatter Plot of Monte Carlo Simulation for rFVIIa 80 mcg/kg vs Standard Care

- Treatment with rFVIIa 80mcg/kg was cost-effective compared to standard care in 73% of simulations, assuming a cost effectiveness threshold of $50,000/QALY (Figure 4)
- Treatment with rFVIIa 80mcg/kg dominated standard care (i.e., cost saving and more effective) in 47.3% of simulations

CONCLUSIONS

- Within the average MCO enrollment period, rFVIIa 80mcg/kg appears to be cost-effective.
- Treatment with rFVIIa more likely to have a positive impact on a younger MCO population, due to the potential gains from improved outcomes after 90 days.

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