Poster # PB 126

Cost-effectiveness of recombinant porcine Factor VIII (OBIZUR) for treatment of hemorrhagic events in acquired hemophilia A (AHA)

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Background

•Acquired hemophilia A (AHA) is a rare condition that occurs in 1 to 4 people per million per year.[1]

•Results of a recent prospective phase 2/3 trial demonstrated the effectiveness of recombinant porcine Factor VIII (rpFVIII) for the treatment of serious bleeds in patients with AHA.[2] However, the economic value of rpFVIII compared to recombinant activated FVII (rFVIIa) and Anti-Inhibitor Coagulant Complex (AICC) has not been previously explored.

•We conducted a cost-effectiveness analysis to compare clinical outcomes and economic value of using rpFVIII, rFVIIa, or AICC.

Methods

•We developed a discrete-event simulation (DES) model for a hypothetical cohort of 1000 AHA patients (Figure 1). The model included medication use, hospitalizations, recurrent bleeds, product switching, and thrombotic events. Individual patients were treated for their AHA related bleeding event and were tracked through their lifetime.

•Patient characteristics and model parameters were based on data from the trial[2], the EACH2 registry[3,4] (rFVIIa and AICC) and input from a clinical advisory panel of 8 hemophilia experts. All product costs were based on US ASP prices reported by Centers for Medicare and Medicaid (rpFVIII: $4.53/U; rFVIIa: $1.90/mcg, and AICC: $1.92/U). (Table 1)

•We estimated QALYs gained and total costs accrued under each treatment strategies (Table 2). Incremental QALYs and costs also were presented.

•We conducted one-way and probabilistic sensitivity analyses to assess robustness of our results to model assumptions.

Methods

Figure 1. Model structure

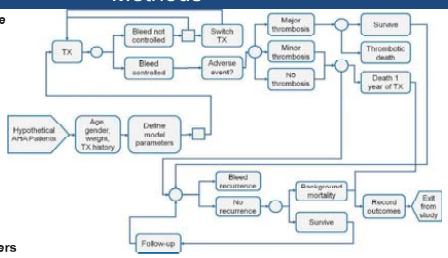


Table 1. Model parameters

	rpFVIII (n= 28)	rFVIIa (n=159)	AICC (n=60)	Distribution used to model variation	Data source
Cohort characteristics					
Age (years, median, IQR)	70 (61 - 81)	73 (15 - 91)	76 (24 - 92)	Normal	Kruse-James et al (2015); Baudo et al (2012)
Weight (median, IQR)	74 (47 – 106)	69 (40 -130)	69 (44 - 107)	Normal	Kruse-James et al (2015); Baudo et al (2012)
Human FVIII inhibitor titer (BU/mL)	48 (4 - 651)	15 (1 - 2765)	17 (0,1 - 1700,0)	Gamma	Kruse-James et al (2015); Baudo et al (2012)
Proportion (%) of patients treated as second line therapy	11 of 28 (39%)	24 of 183 (13%)	15 of 75 (20%)	Binomial	Kruse-James et al (2015); Baudo et al (2012)
Efficacy parameters					
Rates of bleed control when used as first line therapy	16 of 17 (94%)	145 of 159 (91.2%)	56 of 60 (93.3%)	Beta	Kruse-James et al (2015); Baudo et al (2012)
Rates of bleed control when used as second line therapy	8 of 11 (73%)	54 of 69 (79.4%)	54 of 69 (79.4%)	Beta	Kruse-James et al (2015); Baudo et al (2012)
Overall mortality	7 of 28 (25%)	29 of174 (16.7%)	12 of 63 (19%)	Beta	Kruse-James et al (2015); Baudo et al (2012)
Thrombotic events (TE)	0 of 28 (0%)	5 of 174 (2.9%)	3 of 63 (4.8%)	Beta	Kruse-James et al (2015); Baudo et al (2012)
Medication utilization					
Total product utilization until bleed control, Median (IQR)	1560 U/kg (100 – 12,194)	84mg (24 - 216)	30,000 U (12,000 – 56,000)	Gamma	Baudo et al (2012); Kruse-James et al (2015)
Product unit cost ($)	4.53 per Unit	1.90 per mcg	1.92 per Unit	N/A	CMS

Results

•Base case results showed bleeds were controlled in 90% (95% CI: 79-98%), 90% (95% CI: 83-96%), and 91% (95%CI: 83-97%) of patients who initiated treatment with rpFVIII, rFVIIa, and AICC, respectively (Table 2).

•Estimated discounted lifetime costs were $672,000, $264,000, and $134,000 and quality-adjusted life years (QALYs) were 6.56 (95%CI: 5.38 – 7.63), 6.77 (95%CI: 6.07 – 7.48), and 6.69 (95%CI: 5.91 – 7.50) for rpFVIII, rFVIIa, and AICC, respectively.

• Expected QALYs for rpFVIII increased to 6.92 (95%CI: 5.90 – 7.75) when we assumed similar death rate as observed for rFVIIa.

•Estimated incremental QALYs of rpFVIII compared to rFVIIa and AICC were very sensitive to the assumptions about AHA death rates under the 3 treatment strategies.

•Product unit price and utilization had the largest impact on incremental cost of rpFVIII (Figure 2).

•Probabilistic sensitivity analyses (Figure 3) suggested that probability of rpFVIII being cost-effective compared to rFVIIa or AICC is 0% at willingness to pay thresholds below $300,000 per QALYs.

Table 2. Base case results

	rpFVIII	rFVIIa	AICC
Characteristics of simulated cohorts			
Age at baseline	72.5	72.5	72.5
Weight	70.3	70.3	70.3
Proportion of patients treated as second line therapy	39%	39%	39%
Treatment outcomes in simulated cohorts			
Bleed control (% of patients)	90.2% (79.1 - 97.7)	89.7% (82.7 - 96.3)	90.8% (83.3 - 96.8)
Required treatment rounds (mean)	1.41	1.44	1.38
Switched treatment (%)	7%	8%	5%
Major thrombotic event (% of patients)	0.4%	2.3%	2.3%
Minor thrombotic event (% of patients)	0.1%	1.0%	1.2%
Death within the first year total (% of patients)	24.8%	19.8%	19.8%
Cost-effectiveness results			
Cost of treatment medications ($)	652,878	232,487	102,282
Cost of hospitalization ($)	22,643	22,561	22,184
Cost of thrombotic events ($)	103	677	718
Total cost per patient ($) and 95% CrI	672,200 (621,900 to 729,500)	263,800 (227,300 to 309,400)	133,600 (100,300 to 181,800)
QALYs gained per patient and 95% CrI	6.56 (5.38 to 7.63)	6.77 (6.07 to 7.48)	6.70 (5.91 to 7.50)

Figure 2. One-way sensitivity analysis

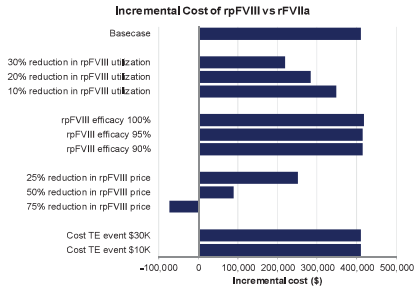
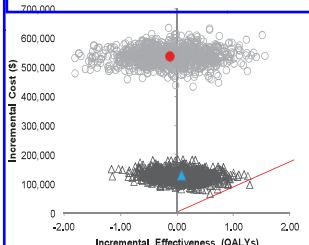


Figure 3. Probabilistic sensitivity analysis



•The probability of rpFVIII being cost-effective compared to rFVIIa would increase to 70% if rpFVIII has first year mortality rates similar to rFVIIa and if the utilization and price of rpFVIII can be reduced by 50% and 30%, respectively.

•Also, our results suggested that rFVIIa is unlikely to be cost-effective compared to AICC at any acceptable willingness to pay threshold.

The red line slope indicates the threshold equivalent to $100,000 per QALY

Conclusion

•Given comparable efficacy, AICC showed the lowest cost per treated bleed. rpFVIII becomes comparable to rFVIIa if drug utilization and price are both reduced by 50% and 30%, respectively. Overall, we found that in AHA patients who can equally likely benefit from all of these treatments, initiating treatment using AICC is the most cost-effective strategy.

•However, results should be interpreted with caution as sources from which input data were drawn may not be comparable due to differences in methodology, and differences in AHA severity and co-morbidities. Unlike patients in EACH2 registry, patients in rpFVIII trial were treated for life-threatening or limb-threatening bleeds after failing on bypassing agents. This might have affected comparability of efficacy, mortality, and utilization rates across treatments. Our conclusion can change if additional evidence emerges about lower utilization rates and unit price for rpFVIII. Ultimately, optimal treatment choice for managing acute bleed in AHA will depend on complex factors in the actual clinical setting such as patient treatment history, co-morbidities, and product availability.

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Coagulation Factors and Inhibitors

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1. **Anchor Name: poster price of rpFVIII** *[Samira Massachi]*

2. **Anchor Name: Poster price for N7** *[Samira Massachi]*

3. **Anchor Name: AH is costly to treat** *[Samira Massachi]*

4. **Anchor Name: Treatment outcomes in siluated cohorts** *[Agency Switzerland m.waldis@fatzerimbach.ch]*

5. **Anchor Name: (/page1/table2)** *[WMUS (Mannu Saroha)]*

6. **Anchor Name: Probabilistic sensitivity analysis** *[Agency Switzerland m.waldis@fatzerimbach.ch]*