COST EFFECTIVENESS ANALYSIS OF DROTRECOGIN ALFA (ACTIVATED) AS A TREATMENT FOR SEVERE SEPSIS

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ABSTRACT

EFFECTIVENESS ANALYSIS OF DROTRECOGIN ALFA (ACTIVATED) AS A TREATMENT FOR SEVERE SEPSIS

INTRODUCTION : Drotrecogin alfa (activated) significantly reduced severe sepsis (SevSep) mortality at 28 days(1). According to the French budget environment, it is mandatory to evaluate its cost effectiveness ratio on a pragmatic basis using the French Intensive Care DRG(2), taking in account the maximum support during ICU stay.

METHODS : All SevSep patients in the Cub-Réa database (1997-99 period) defined according to PROWESS1 and with a hospital length of stay > 24 hours (n = 10459) were included. The baseline patients' characteristics are similar to those of the placebo group PROWESS criteria study :
Relative Risk of death with drotrecogin alfa (activated) estimated according to the observed classification into 11 néo DRG(3) groups and reach 0.8 at 28 days (28 days survival represented by the parametric function of Weibull).

Key patient data recorded : age, gender, type of admission (medical or surgical), admission mode (direct or transfer), number (1,2,3), duration and type of support (Res, Cir, Ren) and SAPS II; stratification according to these criteria; loading of the observed frequencies into a decision-tree for conditional probabilities. (Drotrecogin alfa (activated) : 7881 € ; 4 days treatment, weight 71 Kg). Calculation: Cost (C), Incremental Cost (Δ C), Effectiveness (Eff.), Incremental Eff. (Δ Eff.), Eff. ratio (Δ C/E).

CONCLUSION : The predicted Δ C/E of Drotrecogin alfa in adult SevSep patients is more favourable than the international threshold considered as acceptable (53357 €). Drotrecogin alfa is CE when including patients with all degrees of co morbidity.

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(1) Bernard G. N Engl J Med. 2001; 344: 699-70.

(2) Misset B. Réan Urg.1998; 7: 367-74.

INTRODUCTION

Drotrecogin alfa (activated) significantly reduced severe sepsis (SevSep) mortality at 28 days(1). According to the French budget environment, it is mandatory to evaluate its cost effectiveness ratio on a pragmatic basis using the French Intensive Care DRG(2), taking in account the maximum support during ICU stay.

MATERIAL AND METHODS

Patients :

All severe sepsis patients in the Cub-Rea(1) database (1997-99 period) defined according to PROWESS(1) trial and with a hospital length of stay (LOS) ≥ 24 hours (n = 10459) were included. The baseline patients' characteristics are similar to those of the PROWESS criteria study :

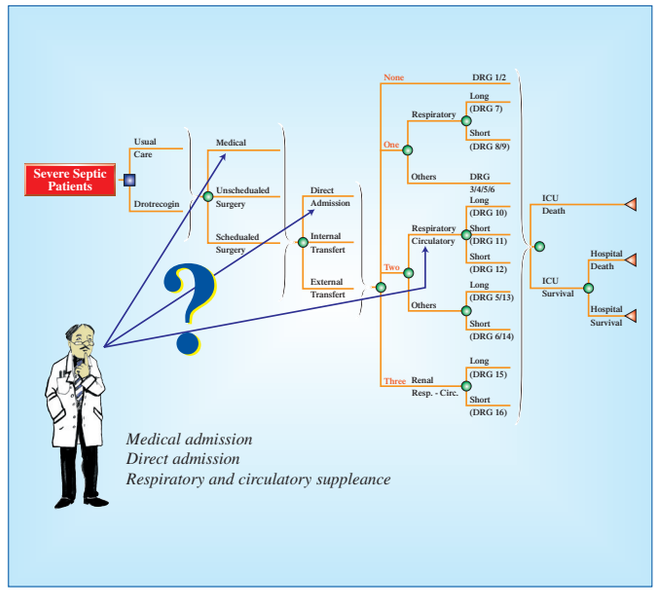
Baseline caracteristics	Cub-Réa (n = 10 459)	PROWESS placebo group (n= 840)
Age (years)	**61**	**60**
Age < 60 years (%)	**42**	**44**
SAPS II vs APACHE II	**46**	**25**
Type of organ failure (%)		
Respiratory	89	75
Circulatory	65	71
Renal	35	42
Number of organ failure (%)		
One	31	24
Two	35	32
Three	26	26
Type of organ support (%)		
Respiratory	78	78
Circulatory	65	75
Renal	18	15

French neo DRG goups :

Group	Organ support	SAPS II	Omega	Description
I	None	= 23		No support : Expected mortality < 5%
II	None	> 23		No support : Expected mortality > 5%
III	Circulatory	= 31		Circulatory failure : Expected mortality < 10%
IV	Circulatory	> 31		Circulatory failure : Expected mortality > 10%
V	Renal		Ω2+Ω3 > 90	Renal failure, no MV, high work load
VI	Renal		Ω2+Ω3 = 90	Renal failure, no MV, low work load
VII	Respiratory		Ω3 = 140	MV > 10d
VIII	Respiratory	= 33	Ω3 = 140	MV < 10d : Expected mortality < 14%
IX	Respiratory	> 33	Ω3 = 140	MV < 10d : Expected mortality > 14%
X	Respiratory and circulatory		Ω3 = 140	MV > 10d
XI	Respiratory and circulatory	= 51	Ω3 = 140	MV < 10d : Expected mortality < 48%
XII	Respiratory and circulatory	> 51	Ω3 = 140	MV < 10d : Expected mortality > 48%
XIII	Respiratory and renal		Ω3 > 140	MV > 10d + HD or HF
XIV	Respiratory and renal		Ω3 = 140	MV < 10d + HD or HF
XV	Respiratory, renal, circulatory		Ω3 > 140	MV > 10d + HD or HF
XVI	Respiratory, renal, circulatory		Ω3 = 140	MV < 10d + HD or HF

Decision tree:

Stratification according to key patient data recorded : age, gender, type of admission (medical or surgical), admission mode (direct or transfer), number (1,2,3), duration and type of support (respiratory, renal, circulatory) and SAPS II and loading of the observed frequencies into the decision-tree for conditional probabilities.



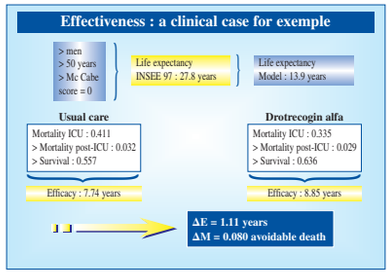
Costs calculation :

Costs estimated by subgroups and by a linear equation (nursing workload, LOS, SAPS II, living or dead status). Calculation of a incremental cost effectiveness ratio (Drotrecogin alfa (activated) price: 7 836,95 € for 4 days treatment and a mean patient's weight of 70 kg) and analysis of Monte Carlo's type).

Relative Risk of death with drotrecogin alfa (activated) estimated according to the observed classification into 11 néo DRG(3) groups and reach 0.8 at 28 days (28 days survival represented by the parametric function of Weibull).

Impact on long-term mortality :

Severe sepsis impact on long-term mortality estimated by the Mc Cabe score with 3 hypothesis for life expectancy (LE) : Unique LE of 5 years, Mc Cabe > 0 (2 years of survival), Mc Cabe = 0 (4 years LE reduction or half LE reduction *versus* whole population).



Efficiency

- Usual care
- Drotrecogin
- ΔC

• 1 •
Criteria of jugment : avoidable mortality
➥ ΔC / ΔM

• 2 •
Criteria of jugment : number of years "to live"
➥ ΔC / ΔE

RESULTS

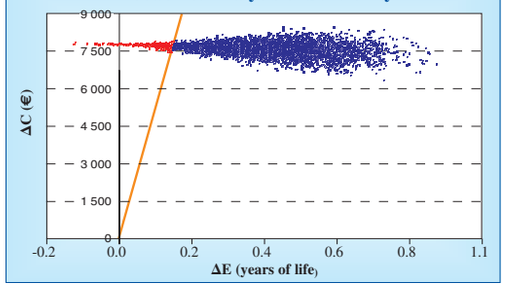
The expected cost in the model of a severe sepsis patient treated by standard care is 26 983,3 € *vs* 26 373.6 € observed from Cub-Rea. The expected cost predicted in the model of a severe sepsis patient treated by drotrecogin alfa (activated) is 34 605.90 €. The survivors LE according to the above hypothesis are 5.0, 10.6, and 6.9 years.

Corresponding effectiveness differences in favor of drotrecogin alfa (activated) are 0.33, 0.63, and 0.41 years. The cost per additional year of life saved amounts of 18 446.3 € including all degrees of severity and co-morbidity.

Incremental Cost Effectiveness Ratio

DRG Group	Strategy	Support	C (€)	Δ C	Eff.	Δ Eff.	Δ C/E
All Patients	Usual care	All type	26 983		4.6		
All Patients	Drotrecogin	All type	34 606	7 623	5.0	0.4	18 446
VII, VIII, IX	Usual care	Resp	21 383		6.6		
VII, VIII, IX	Drotrecogin	Resp	28 959	7 576	6.9	0.3	31 833
X, XI, XII	Usual care	Resp. Circ	32 565		3.6		
X, XI, XII	Drotrecogin	Resp. Circ	39 980	7 415	4.1	0.50	14 962
XV, XVI	Usual care	Resp. Circ. Ren	41 742		1.7		
XV, XVI	Drotrecogin	Resp. Circ. Ren	50 025	8 283	2.5	0.9	10 005

Probabilist Analysis of Sensibility



The sensitivity analysis shows that with an expected threshold of 53 357 €, 96.3% of the bootstrap samples are cost–effective (CE).

DISCUSSION

The differences observed in this retrospective study compared to Angus and coll.(4) findings can be explained.

First of all, standards of care change between France and US, second Angus and coll. have added additional costs for life-time healthcare costs beyond day 28.

These costs represented 50% of all cost in their work.

Assuming the same augmentation the cost per additional year live saved would be 37 690 € including all degrees of severity and co-morbidity approaching Angus and coll. findings.

CONCLUSION

The predicted cost effectiveness ratio of drotrecogin alfa (activated) in adult severe sepsis patients is much lower than the international range considered as acceptable (53 357,10 €).

Drotrecogin alfa (activated) has a cost effectiveness profile similar to, or better, than many well-accepted and common healthcare strategies.

Drotrecogin alfa (activated) is cost-effective when including patients with all degrees of co-morbidity.

Achieving this profile in practice will be dependent on careful patient selection.

For example, restriction to patients at higher risk of death will improve cost-effectiveness because the treatment effect is larger.

However, drug administration to patients with poor long-term prognosis will worsen the cost-effectiveness.

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