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EE603

Economic Evaluation of C5 Inhibitors in Patients with Paroxysmal Nocturnal Haemoglobinuria – A Systematic Literature Review

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INTRODUCTION

- Paroxysmal nocturnal haemoglobinuria (PNH) is a rare, progressively debilitating, life-threatening disease characterized by intravascular haemolysis and venous thrombosis. It is closely related to aplastic anaemia[1]
- PNH is believed to affect males and females in equal numbers, although some studies show a marginal female preponderance. The prevalence is estimated to be between 0.5 and 1.5 per million people in the general population[2]
- The current standard of care for patients with PNH consists of C5 inhibitors, a class of drugs that act on the complement system and have been demonstrated to improve life expectancy[3]

OBJECTIVES

Our aim was to conduct a systematic literature review (SLR) to identify and summarize model-based economic evaluations of C5 inhibitors used to manage PNH.

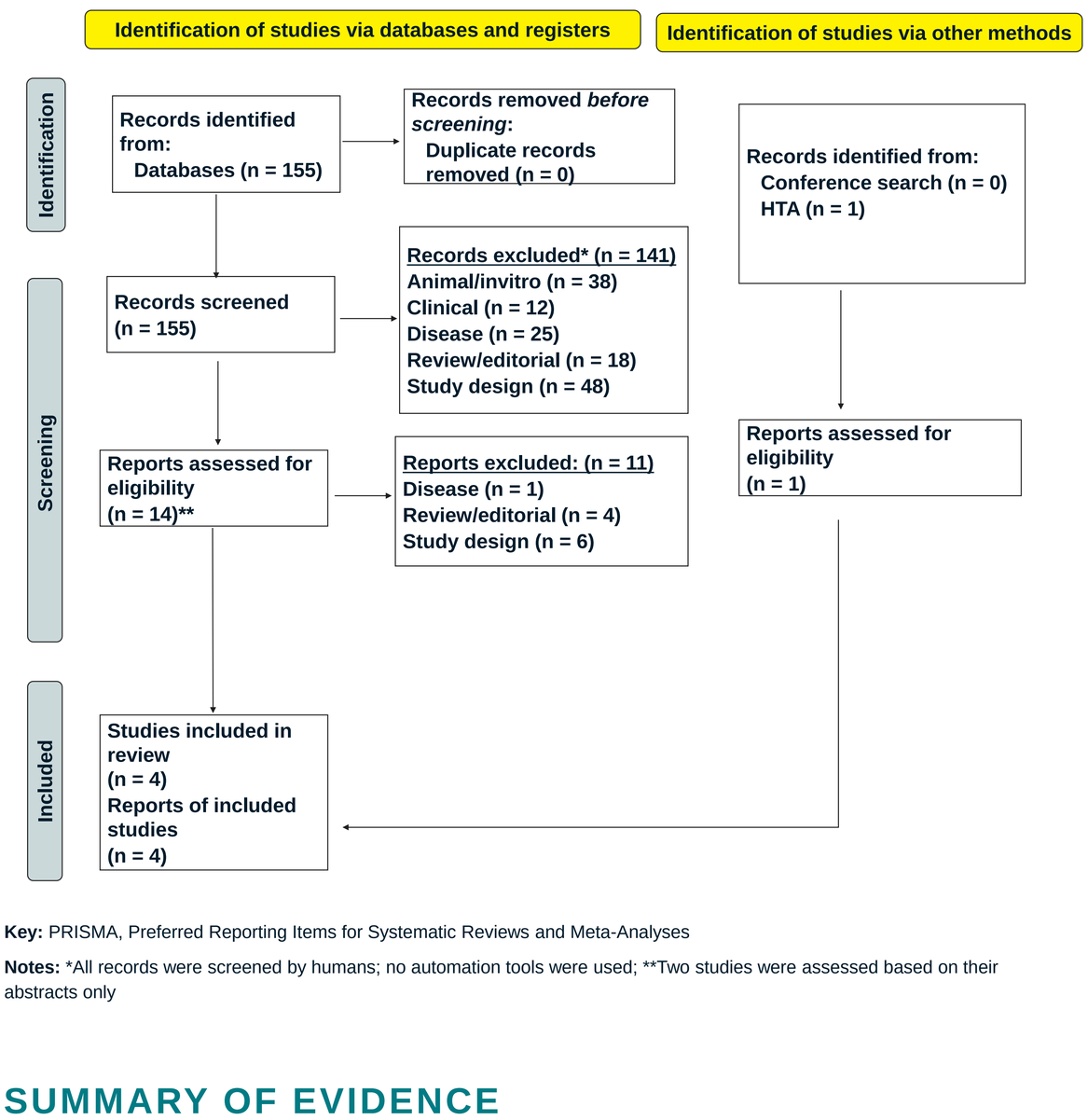
METHODS

- MEDLINE® In-Process was systematically searched, using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[4], by pairing relevant keywords to identify studies that were screened using the Population, Intervention, Comparator, Outcome, Study Design (PICOS) criteria
- Database searches were supplemented by bibliographic searches. The searches were not limited by study country or timeframe. However, searches were restricted to the English language
- Two independent reviewers performed initial screening of the title and abstract for each reference identified by the electronic database search. Two reviewers assessed each potentially relevant article. Any uncertainty regarding the inclusion of a study was checked by a third reviewer. Data were extracted by one independent reviewer and quality checked against the original source by another independent reviewer

RESULTS

Of the 156 records identified from the electronic database search, the final review included four[4-7] studies with model-based economic evaluations of C5 inhibitors in patients with PNH **(Figure 1)**

Figure 1: PRISMA flow diagram



Key: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Notes: *All records were screened by humans; no automation tools were used; **Two studies were assessed based on their abstracts only

SUMMARY OF EVIDENCE

- Of the included studies, one study each was conducted in the US, UK, Canada and Brazil assessing adult patients with PNH **(Table 1)**
- A cost–utility analysis was conducted using a Markov model in Canada, Brazil and the US; the UK model performed a preliminary cost-effectiveness analysis based on clinical evidence **(Table 2)**
- A US payer and Brazilian public health perspective was adopted in the respective studies; the economic perspective was not reported in the remaining two studies
- Three studies assessed eculizumab versus standard of care (SoC) or placebo, while one study assessed ravulizumab versus eculizumab

Table 1 : List of included economic evaluation studies

Study name	▪ Intervention ▪ Comparator	Key patient characteristics	Economic analysis	Country
Coyle et al. 2014[5]	▪ Eculizumab plus current standard of care ▪ Current standard of care	Not reported	Cost–utility	Canada
Cruz et al. 2021[6]	▪ Eculizumab ▪ Standard of care	35-year-old patients with symptomatic PNH	Cost–utility	Brazil
O'Connell et al. 2020[7]	▪ Ravulizumab ▪ Eculizumab	Adult patients with PNH	Cost–utility	US
Connock et al. 2008[8]	▪ Eculizumab ▪ Placebo and standard of care	Adult patients with PNH	Cost-effectiveness	UK

Table 2 : Key characteristics of the included studies

Study name (economic analysis type)	Model	Time horizon	Perspective	Price year	Discounting	Model health states
Coyle 2014 (cost–utility)	Markov model	NR	NR	NR	NR	NR
Cruz 2021 (cost–utility)	Markov decision model	20 years	Brazilian public health system perspective	NR	NR	NR
O'Connell 2020 (cost–utility)	Markov state-transition model	Lifetime	US payer perspective	NR	3% for both cost and life years gained	Model with 11 health states: ▪ Eight related to BTH events (with distinction between BTH events related to suboptimal free C5 inhibition versus related to CAC) ▪ Two related to mortality (natural/background and PNH-related) ▪ One related to spontaneous remission
Connock 2008 (cost-effectiveness)	Decision tree	10–15 years	NR	NR	3.5% for both cost and life years gained	▪ The model follows PNH patients who are divided into two groups: those with eculizumab and those with no eculizumab. ▪ Patients in either group may develop thrombosis, some of whom will die

Key: BTH, breakthrough haemolysis; CAC, complement-amplifying condition; NR, not reported; PNH, paroxysmal nocturnal haemoglobinuria.

KEY FINDINGS

- In Canada, the incremental cost per life year gained was CAD 4.62 million for eculizumab compared with SoC; the cost per quality-adjusted life year (QALY) gained was CAD 2.13 million
- In Brazil, the incremental cost-effectiveness ratio (ICER) for eculizumab versus SoC was BRL 10,139,542.84 per QALY. The opportunity cost of eculizumab per patient funded was 102.3 discounted QALYs
- A US comparison between ravulizumab and eculizumab favoured ravulizumab in terms of health benefits and cost savings (ICER: USD -1,000,818)
- In the UK, the ICER per life year for eculizumab versus SoC/placebo was GBP 3,211,000 and GBP 2,768,000 at 10 years and 15 years, respectively **(Table 3)**

Table 3: Results of included studies

	Canada		Brazil		US		UK	
	Eculizumab + SoC	SoC	Eculizumab	SoC	Ravulizumab	Eculizumab	Eculizumab	Placebo/SoC
QALYs	-	-	-	-	18.93	17.25		
LYG							10 years: 8.99 15 years: 12.18	10 years: 8.29 15 years: 11.08
Incremental QALYs	2.45		1.08		1.67		-	
Incremental LYG	1.13		-		-		10 years: 0.70 15 years: 1.10	
Total cost	-	-	-	-	USD 7,690,403	USD 9,363,868	10 years: GBP 2,248,000 15 years: GBP 3,044,000	10 years: 0 15 years: 0
Incremental cost	CAD 5.24 million		BRL 10,959,375.95		USD -1,673,465		10 years: GBP 2,248,000 15 years: GBP 3,044,000	
ICER	CAD 2.13 million/QALY CAD 4.62 million/LY		BRL 10,139,542.84		USD -1,000,818		10 years: GBP 3,211,000 15 years: GBP 2,768,000	

Key: ICER, incremental cost-effectiveness ratio; LYG, life years gained; QALY, quality-adjusted life year; SoC, standard of care.

DISCUSSION AND CONCLUSIONS

- The results of this SLR suggest that eculizumab may provide substantial benefits in terms of life expectancy, but at higher incremental costs, impacting its cost-effectiveness
- Ravulizumab proved to be a dominant strategy versus eculizumab, resulting in large cost savings and increased benefits. However, the cost-effectiveness of ravulizumab over eculizumab was not reported outside the US
- The results of this systematic review should be interpreted with caution because:
  - There is a dearth of economic evaluations assessing individual treatments in patients with PNH
  - There is paucity of economic modelling in PNH
  - The populations considered in the current models are too heterogeneous
- Exploring more cost-effective treatment options is warranted in future

REFERENCES

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Disclosure : Further information is available on request.

An electronic version of the poster can be viewed by scanning the QR code.

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