Netupitant and Palonosetron (NEPA) is a cost-effective intervention for the prevention of chemotherapy-induced nausea and vomiting (CINV) in Singapore

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ABSTRACT

OBJECTIVES: The primary objective of this study was to assess the cost-effectiveness of NEPA compared to available treatments in Singapore hospital setting for patients receiving highly emetogenic chemotherapy (HEC). METHODS: A Markov model was developed over a 5-day time horizon that consists of the first day (acute phase) and a delayed phase (day 2-5) and was run for one cycle of chemotherapy. Payer's perspective in Singapore was adopted. Three health states were considered: complete protection (CP), complete response at best (CRB), and incomplete response. Efficacy for NEPA was response rates obtained from NETU07-07 trials. Efficacy for comparators were odds ratios compared to NEPA obtained from the Abdel-Rahman (2016) meta-analysis. Utilities of 0.90, 0.70 and 0.24 were defined for CP, CR and incomplete response, respectively. Drug costs and cost incurred to emetic events were considered in this analysis and were based on retail price in Singapore and expert opinions. RESULTS: The results of the base case analysis showed that NEPA was dominant against aprepitant (PO/IV) + ondansetron (PO), aprepitant (PO) + palonosetron (IV) and fosaprepitant (PO) + granisetron (IV) and palonosetron (IV). It was cost-effective against ondansetron (PO), with an incremental cost-effectiveness ratio (ICER) of 47 SGD per avoided emetic event and 53,244 SGD per QALY gained. Both deterministic and probabilistic sensitivity analyses (DSA & PSA) showed robustness in the results. The PSA showed that, at a willingness-to-pay threshold of 50,000 SGD, the probability of NEPA being cost-effective compared to aprepitant + ondansetron was 95.4%. In the DSA, the utility for CR was found to be the most influential parameter, although resulting in negative ICER, meaning NEPA was still dominant. CONCLUSIONS: For the prevention of CINV in patients undergoing HEC in Singapore, NEPA was more effective and less costly than the tested combination therapies, whereas it was cost-effective against ondansetron (PO/IV).

INTRODUCTION

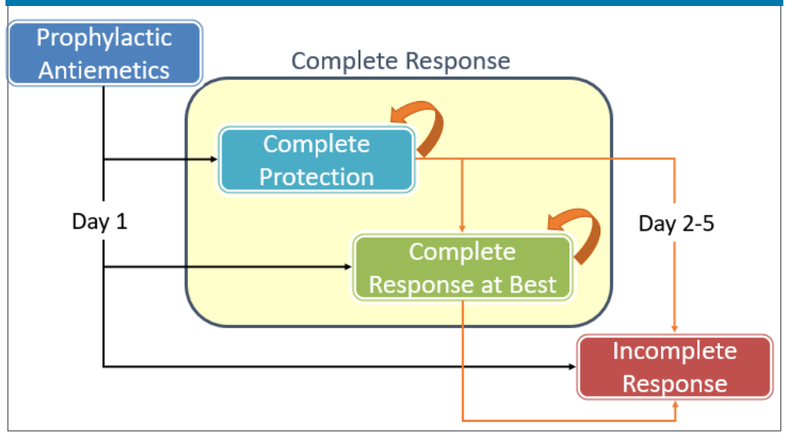
- Chemotherapy-induced nausea and vomiting (CINV) is a common and feared side-effect of chemotherapy.
- The objective was to evaluate the cost-effectiveness of the oral fixed-dose combination netupitant and palonosetron (NEPA) compared with available antiemetics to prevent CINV in patients undergoing highly emetogenic chemotherapy (HEC) in Singapore.

METHODS

Model Structure

- A three health-state Markov model, including complete protection (CP), complete response at best (CRB) and incomplete response (no CR) was constructed (**Figure 1**).
- CR was defined as no emesis no rescue medication and is composed of CP plus CRB. CP was defined as patients in CR who had no more than mild nausea. CRB was defined as CR minus CP.
- A 5-day prophylactic anti-emetic treatment period corresponding to the Singapore healthcare payer perspective, was adopted.
- A chemotherapy cycle length of 1 day was considered in the model. Cycle 1 was based on acute phase probabilities and cycles 2-5 matched the overall phase results.

Figure 1. Markov model structure



Study Population

- Cancer patients receiving prophylactic anti-emetic treatment for the management of HEC.

Model Inputs

- Efficacy data of NEPA were taken from NEPA phase III clinical trials[1] while a previously published network meta-analysis[2] was used for comparators' efficacy.
- Odds ratios (ORs) in the acute phase were not available from the meta-analysis and were thus assumed similar to the ORs in the overall phase.
- Transition probabilities were obtained by combining the response rates of CP and CR from NEPA trials and odds ratios from the meta-analysis (**Table 1**). CRB was deduced from CP and CR odds ratios.

NOTES

CINV: chemotherapy-induced nausea and vomiting; CP: complete protection; CR: complete response; CRB: complete response at best; DSA: deterministic sensitivity analysis; HEC: highly emetogenic chemotherapy; NEPA: netupitant and palonosetron; OND: ondansetron; PA: palonosetron; PSA: probabilistic sensitivity analysis; WTP: willingness-to-pay; QALD: quality adjusted life days

METHODS, CONTINUED

Utilities and Costs

- Utilities of 0.90, 0.70 and 0.24 were defined for CP, CRB and incomplete response, respectively[3-5].
- Only direct costs were considered in this analysis.
- Drug costs were based on recommended doses from international guidelines and unit costs from the Singapore National Cancer Center (NCC).
- Healthcare costs were extrapolated from Lopes et al. 2012 and inflated to 2019[6].

Sensitivity Analyses

- Deterministic and probabilistic sensitivity analyses (DSA and PSA) were performed on the model parameters to assess the impact of parameters and structural uncertainty on results. PSA parameters are shown in Table 2.

Table 1. Response rates of NEPA (95% CI) and estimated relative efficacy of the comparators

Treatment	Phase	Complete response	Complete protection
		HEC NEPA 07-07 (n=135) RR (95% CI)	
NEPA	Acute	98.5%* (96.5%-99.9%)	97.0%* (94.2%-99.9%)
	Overall	89.6%* (84.5%-94.8%)	83.0%* (76.6%-89.3%)
		Abdel-Rahman meta-analysis OR (95% CI)	
APR+OND		2.23 (0.73-5.69)	1.00 (0.90-1.10)
APR+PAL		1.46 (0.84-2.46)	1.00 (0.90-1.10)
FOS+GRA		2.27 (0.66-6.15)	1.00 (0.90-1.10)
OND (IV/PO)		4.45 (1.48-11.6)	1.00 (0.90-1.10)
PAL (IV)		3.89 (1.27-10.1)	1.00 (0.90-1.10)

* P≤0.05 *** P≤0.0001 CI: confidence interval; NA: not available; OR: odds ratio; RR: response rate
APR: aprepitant; FOS: fosaprepitant; GRA: granisetron; OND: ondansetron; PAL: palonosetron; ROL: rolapitant

Table 2. PSA parameters

Input	Distribution assumption
Cost of drug per package	Gamma
Healthcare utilisation due to CINV	Gamma
Utility value	Gamma
Clinical efficacy of NEPA	Gamma
NMA Comparative efficacy	Lognormal

RESULTS

Cost-Effectiveness Results

- NEPA was dominant against aprepitant + ondansetron (IV); aprepitant + palonosetron (IV); fosaprepitant + granisetron; and palonosetron (IV) (**Table 3**).
- NEPA was cost-effective against ondansetron (both PO and IV), with an ICER of Cost per quality-adjusted life days (QALDs) of 146 SG$, 47 SG$ per avoided emetic event, and 53,244 SG$ per QALY gained (**Table 3**).

Sensitivity Analysis Results

- A thousand simulations were computed in HEC indications (**Figure 2**).
- At a WTP (willingness to pay) threshold of SG$100,000 and higher, NEPA was the strategy with the highest probability of being cost-effective (**Figure 2**).
- In the DSA, the CR utility for NEPA in the overall phase was found to be the most influential parameter; however, while the ICER increased it still remained negative (SG$-26,737), meaning that NEPA was still dominant.

Figure 2. Probabilistic cost-effectiveness acceptability curves in Singapore

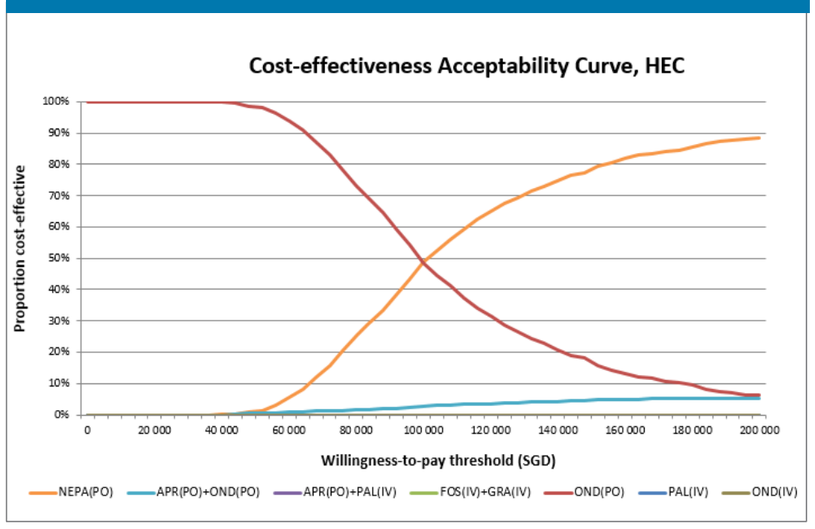


Table 3. Cost-effectiveness results of NEPA vs. comparators in HEC patients

NEPA vs. comparators in Singapore							
	NEPA	Incremental					
		APR+OND	APR+PAL	FOS+GRA*	OND* (PO)	PAL (IV)	OND* (IV)
QALDs	4.272	-0.155	-0.053	-0.16	-0.436	-0.372	-0.436
Emesis-free patients	89.6%	-10.2%	-4.1%	-10.5%	-23.7%	-20.7%	-23.7%
CINV-free patients	83.0%	-3.6%	0.0%	-3.9%	-17.1%	-14.1%	-17.1%
Total costs (SGD)	143.13	+27.63 SGD	+85.71 SGD	+48.25 SGD	-63.65 SGD	+1.07 SGD	-63.65 SGD
Costs/QALDs (SGD)	-	Dominant	Dominant	Dominant	146 SGD	Dominant	146 SGD
Costs/QALYs (SGD)	-	Dominant	Dominant	Dominant	53,244 SGD	Dominant	53,244 SGD
Cost/avoided emetic event (SGD)	-	Dominant	Dominant	Dominant	47 SGD	Dominant	47 SGD

QALD: Quality-adjusted life days; QALY: Quality-adjusted life years; SGD: Singapore dollar
APR: aprepitant; FOS: fosaprepitant; GRA: granisetron; OND: ondansetron; PAL: palonosetron; ROL: rolapitant
*Generic price

CONCLUSIONS

- The results suggest that NEPA is more effective and less costly than the tested comparators for preventing CINV associated with HEC in Singapore; whereas NEPA is cost-effective against ondansetron.
- The sensitivity analyses confirmed the robustness of these results.

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