Systematic Review of Economic Evaluation of the First Line Treatment for Metastasis Renal Cell Carcinoma (mRCC)

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Abstact

mRCC is the unmet medical need and current treatment with interferon can yield a modest result in term of progression free survival (PFS) and overall survival (OS). Although the Food and Drug Administration has granted fast track approval for new targeted therapy for mRCC, the cost-effectiveness information of these agents is required by healthcare decision makers and providers and has been still limited. To systematically review the economic evaluation of published literature of tyrosine kinase inhibitors, mTOR inhibitors against comparator under licensed indications. The electronic databases from Pubmed, Cochrane Library and Embase were searched from 2000 to 2010. The economic evaluation studies of the first line mRCC treatments were included in the review. The total of 77 articles was retrieved and 68 articles were excluded. Nine articles were included and one was obtained from hand searching, thus ten articles were synthesized. Healthcare provider perspective and Markov model were used in all studies. Cost-utility analysis was conducted in seven studies, while cost-effectiveness analysis was performed in two studies. Treatment costs in all studies were retrieved from local published data and retrospective chart review. Eight studies showed that Sunitinib seemed to be more cost-effective compared with other targeted therapie. Bevacizumab plus interferon was considered to be less costly compared to sunitinib due to less cost of adverse event in one study. However, the implications might be used with caution due to QALY threshold and budget impact.

Key words: Economic evaluation, Renal cell carcinoma, Metastasis, First-line treatment, Systematic review

INTRODUCTION

More than 90 percents of renal tumor accounted for renal cell carcinoma (RCC). Prevalence of RCC is 2% of adult malignancies with total mortality worldwide more than 120,000 per year[1]. The global incidence and mortality is increasing with age and median age of diagnosis is around 60 years old[2]. The incidence in Thailand is 1.7 per 100,000[3]. Although the incidence is low, the burden of RCC seems to be high.

The median survival is limited once the disease progresses into metastatic stage (mRCC). mRCC is the unmet medical need and current treatment with interferon can yield a modest result in term of progression free survival (PFS) and overall survival (OS). Although the Food and Drug Administration has granted fast track approval for new targeted therapy for mRCC, the cost-effectiveness information of these agents required by healthcare decision makers and providers has been still limited. The objective of this study was to systematically review the published economic evaluation studies of tyrosine kinase inhibitors, mTOR inhibitors against comparator under licensed indications.

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MATERIALS AND METHODS

The electronic databases (i.e., Pubmed, Cochrane Library and Embase) were searched from 2000 to 2010 using searching terms as follows: (cost effectiveness) and (kidney cancer) and (sunitinib OR sorafinib, bevacizumab plus IFN OR Temsirolimus OR everolimus OR pazopanib). The economic evaluation studies of the first line mRCC treatments were included in the review.

Inclusion Criteria

The economic evaluation studies comparing both costs and outcomes related to the first line (1st line) mRCC from phase III trial were included.

Exclusion Criteria

The studies related to clinical effectiveness, safety, policy reviews or comments of the first line mRCC treatments were excluded.

RESULTS AND DISCUSSION

The total of 77 articles was retrieved and 68 articles were excluded. Nine articles were included and one was obtained from hand searching, thus ten articles were synthesized. Healthcare provider perspective and Markov model were used in all studies. A three-health state Markov model was used in one study and a five-health state Markov model was applied in three studies.

Cost-utility analysis was conducted in seven studies, while cost-effectiveness analysis was performed in two studies. There was only one study conducted using cost-minimization method assuming that both comparators had the same clinical efficacy but different in safety profile. Treatment costs in all studies were retrieved from local published data and retrospective chart review. The outcomes used were progression free survival (PFS), overall survival (OS), life years (LYs), and quality adjusted life year (QALYs) gained.

Eight studies showed that Sunitinib seemed to be more cost-effective compared with other targeted therapies with incremental cost-effectiveness ratio (ICER) ranging from US\$ 29,350 to 119,320 per QALY gained. Temsirolimus was more cost-effective compared to sunitinib with the ICER of US\$ 21,783 in poor prognosis patients. Bevacizumab plus interferon was considered to be less costly compared to sunitinib due to less cost of adverse events in one study. Parameter uncertainty was tested by using probabilistic sensitivity analysis methods.

mRCC is considered high mortality rate according to its natural history, thus 10-year time horizon was mostly used in most studies. When considering the ICER values with the willingness to pay (WTP) based on health care provider's perspective in each study, it was found that Sunitinib was considered to be not cost-effective in the UK and Thailand context, whereas it was considered to be cost-effective in the US and the Netherlands.

CONCLUSION

Treatment cost with targeted therapy in mRCC is expensive and the cost-effectiveness results of Sunitinib seemed to be varied among published literatures. Future research on the cost-effectiveness information of mRCC should be further investigated.

Table 1. Systematic review results of economic evaluation studies related to the 1st line mRCC

Study	Active drug	Comparator	Outcome Horizon	Time	Result effectiveness	Preferred cost
Mickisch et al[4]	Bevacizumab	Sunitinib	Cost of Adverse Event	NA		Bevacizumab +IFN
Tenorio et al[5]	Sunitinib, Sorfinib, Bevacizumab +IFN	IFN	ICER/PFM, ICER/OS	3 years	US$ 3767/PFS gain, US$ 5668/OS vs IFN	Sunitinib
Greenberg D[6]	Sunitinib, Sorfinib, Bevacizumab +IFN, Temsirolimus	IFN QALY	ICER/QALY Sunitinib	10 years	NIS 245,869 /	
Salinas-Escudero et al[7]	Sunitinib QALY	IFN	ICER/QALY	5 years	US$ 29,350/	Sunitinib
Godoy et al[8]	Sunitinib, Sorfinib, Bevacizumab +IFN	IFN	ICER/LYs	5 years	US$ 48,362/ LYs	Sunitinib
Munir et al[9]	Sunitinib, Sorfinib, Bevacizumab +IFN, Temsirolimus	IFN	ICER/QALY	10 years	SEK 215,415/ QALY	Sunitinib
Topibulpong et al[10]	Sunitinib, Sorfinib, Bevacizumab +IFN, Temsirolimus	IFN	ICER/QALY, ICER/LYs	Life time	Million Baht 3.669/ QALY	Sunitinib
Hoyle et al[11]	Temsirolimus	IFN-α ICER/QALY	ICER/LY, QALY	10 years	94,632 GBP/	Sunitinib
Remak et al[12]	Sunitinib	IFN-α ICER/QALY, ICER/PFS	ICER/LY, QALY	10 years	52,593 US$/	Sunitinib
Silverio et al[13]	Sunitinib, Temsirolimus	IFN	ICER/QALY	3 years	US$ 21,783/ QALY	Temsirolimus

NA= not available, IFN=Interferon, IFN- α=Interferon alfa, ICER=Incremental Cost-Effectiveness Ratio, QALY= Quality Adjusted Life Year, LY=Life Year

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