COST-EFFECTIVENESS OF EVEROLIMUS COMBINATION THERAPY IN PATIENTS AFTER LIVER TRANSPLANTATION FOCUSING ON CANCER RISK: A MARKOV MODEL USING REAL-WORLD DATA

Suk-Chan Jang[1], Hye-Lin Kim[2], Gi-Ae Kim[3], Young-Suk Lim[4], Eui-Kyung Lee[1]

[1]School of Pharmacy, Sungkyunkwan University, Suwon, Gyeonggi-do, Republic of Korea
[2]College of Pharmacy, Sahmyook University, Seoul, Republic of Korea
[3]Department of Internal Medicine, Kyung Hee University School of Medicine, Seoul, Republic of Korea
[4]Department of Gastroenterology, Liver Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

OBJECTIVES

- The potential of everolimus (EVR) in reducing hepatocellular carcinoma (HCC) among the patients on immunosuppressants after liver transplantation (LT) has been reported.
- Thus, we aimed to investigate whether combining EVR with standard calcineurin inhibitor (CNI) therapy affects the risk of HCC and extrahepatic cancers and assess its cost-effectiveness.

METHODS

- A time-duration matched retrospective cohort of 1,864 patients who started immunosuppressants after LT from June 2015 to February 2020 was collected from the Korean Health Insurance Review and Assessment Service.
- The clinical outcomes of the patients who received EVR with CNI therapy (EVR group) were compared with those who received CNI therapy alone (non-EVR group).
- Using these as input parameters, a Markov model was designed with the liver and infection pathway to consider coexisting diseases simultaneously (Figure 1).
- Model simulated a cohort of 10,000 55-year-old LT patients to compare the expected costs and quality-adjusted life-years (QALYs) of combining EVR over a 30-year horizon.
- The incremental cost-effective ratio (ICER) using QALY and HCC-case-avoid was calculated.

(a)

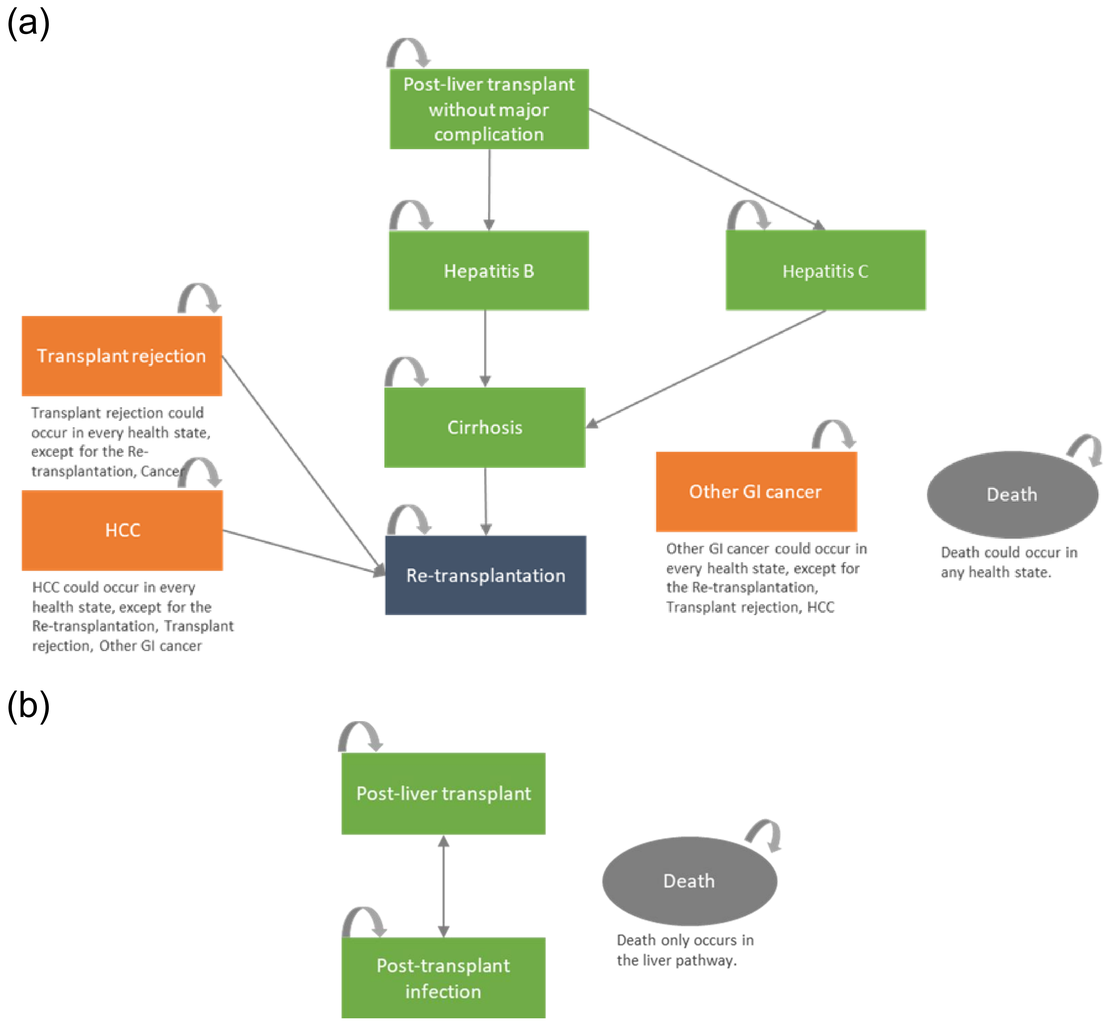

Figure 1. Structure of Markov model
(a) Liver pathway (main pathway); (b) Infection pathway

RESULTS

- During the study period, 55 and 41 patients developed HCC and extrahepatic cancers.
- The EVR group showed a lower risk of HCC (adjusted hazard ratio [aHR], 0.53; 95% confidence interval [CI] 0.30-0.94) and extrahepatic cancers (aHR, 0.30; 95% CI 0.14-0.63) compared with the non-EVR group (Table 1).

Table 1. Relative risks of cancer in EVR versus non-EVR group

Cancer type	EVR			non-EVR			Adjusted HR[a] (95% CI)
	Events	Person-years	Rate	Events	Person-years	Rate	
HCC	23	1,542	0.015	32	1,657	0.019	0.528 (0.297, 0.939)
Extrahepatic	10	1,542	0.006	31	1,657	0.019	0.301 (0.144, 0.630)
Other GI	3	1,542	0.002	11	1,657	0.007	0.248 (0.066, 0.927)

[a] Adjusted to the history of diseases, age group, sex, donor type, CCI, insurance type, and cohort entry year
CI, confidence interval; EVR, everolimus; GI, gastrointestinal; HR, hazard ratio

- The EVR group was more vulnerable to infection from one year after LT (aHR, 1.47; 95% CI 1.05-2.05) (Table 2).

Table 2. Relative risks of post-transplant infection in EVR versus non-EVR group

	EVR			non-EVR			Adjusted HR[a] (95% CI)
	Events	Person-years	Rate	Events	Person-years	Rate	
First-year	71	343	0.207	68	348	0.195	1.081 (0.773, 1.513)
Subsequent years	83	657	0.126	68	793	0.086	1.468 (1.053, 2.045)

[a] Adjusted to the history of diseases, age group, sex, donor type, CCI, insurance type, and cohort entry year
CI, confidence interval; EVR, everolimus; HR, hazard ratio

- From the healthcare system perspective, the EVR group had an ICER of USD 13,964/QALY and 54,246/HCC-case-avoid (Table 3).
- From the societal perspective considering productivity loss by premature death, the EVR group had an ICER of USD 9,694/QALY and 37,659/HCC-case-avoid.

Table 3. Base-case result of cost-effectiveness analysis

Perspective		EVR	non-EVR	Difference	ICER
Healthcare system	QALYs	9.569	8.641	0.928	
	Costs, USD	174,247	161,286	12,960	13,964/QALY
	HCC-case- avoid	0.474	0.713	0.239	
	Costs, USD	174,247	161,286	12,960	54,246/HCC
Societal	QALYs	9.569	8.641	0.928	
	Costs, USD	192,758	183,760	8,997	9,694/QALY
	HCC-case-avoid	0.474	0.713	0.239	
	Costs, USD	192,758	183,760	8,997	37,659/HCC

EVR, everolimus; HCC, hepatocellular carcinoma; QALYs, quality-adjusted life-years; USD, United States dollar

CONCLUSIONS

- Combining EVR with CNI therapy reduced the risk of HCC and extrahepatic cancers in patients who underwent LT.
- Adding EVR to CNI therapy was more cost-effective than CNI therapy alone at a socially agreed ICER threshold of USD 20,000/QALY.