Cost-effectiveness Of Tremelimumab Or Tremelimumab In Combination With Durvalumab Vs Durvalumab As Treatment Of Advanced Hepatocellular Carcinoma

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INTRODUCTION

Liver cancer is the sixth most common cancer worldwide[1]

- Hepatocellular carcinoma (HCC) accounts for approximately 80% of liver cancer cases.[2]

Although the incidence of liver cancer in the United States is declining

- 25,000 men and 11,000 women are diagnosed with liver cancer each year.[3]
- Approximately 28,000 people die from liver cancer each year.[3]

Treatments for HCC

- **Curative Treatment (for early stages of HCC)[4]**
  - Radiofrequency ablation (RFA)
  - Liver resection (LR)
  - Liver transplantation (LT)
- **Palliative Treatment (for more advanced stages of HCC)[4]**
  - Transarterial chemoembolization (TACE)
  - Transarterial radioembolization (TARE)
  - Radiation
  - Sorafenib

In October 2022, the FDA approved durvalumab in combination with tremelimumab as a treatment for unresectable HCC

- Although the clinical effectiveness of these two drugs has been established, the cost-effectiveness is unknown.

AIM

Evaluate the cost-effectiveness of Tremelimumab + Durvalumab combination compared with the Durvalumab monotherapy to treat HCC from the US payer perspective.

METHOD

Data Source	• The HCC study (NCT02519348), which focused on the safety and clinical effectiveness of Durvalumab and Tremelimumab
Study Period	• October 19, 2015 – November 6, 2020
Main Eligibility Criteria	• 18 years and older • Confirmed HCC based on histopathological findings from tumor tissues. • Immunotherapy-naïve • Have either progressed on, are intolerant to, or refused treatment with sorafenib or another approved TKI

METHOD (Cont.)

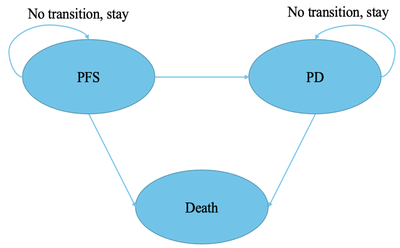
Study Groups

- Durvalumab Monotherapy (DM) (The control group)
- Tremelimumab Monotherapy (TM)
- Durvalumab & Tremelimumab Combination 1 (T75 + D)
- Durvalumab & Tremelimumab Combination 2 (T300 + D)

DM	• Dosage: 1500 mg Durvalumab • Frequency: Every 4 weeks
TM	• Dosage: 1500 mg Tremelimumab • Stage 1: Every 4 weeks for the first 7 doses • Stage 2: Every 12 weeks for the following doses
T75 + D	• Dosage: 1500 mg Durvalumab and 75 mg Tremelimumab • Stage 1: Every 4 weeks for the first 4 doses • Stage 2: 1500 mg Durvalumab for every 4 weeks for the following doses
T300 + D	• Dosage: 1500 mg Durvalumab and 300 mg Tremelimumab • Stage 1: Every 4 weeks for the first dose • Stage 2: 1500 mg Durvalumab for every 4 weeks for the following doses

Model Structure

- A Markov model with 3 discrete health states: **progression free survival (PFS), progression of disease (PD), and death** was used to assess the cost-effectiveness of TM, T75 + D, and T300 + D vs 1500 mg DM for HCC
- The model uses 60 one-month cycles because the 5-year survival rate of HCC is less than 10% [12]
- A 3% discount rate was applied to the costs and utilities at base-case analysis.（0.25% per cycle)



Assumptions

- All adverse events happened during the first cycle and the duration-adjusted disutility was subtracted from the baseline PFS utility.[5]
- The range of each parameter was based on either the reported 95% CIs in the referenced studies or determined by assuming a 25% change from the base-case value.[6]
- To calculate the dosage, a typical US patient was assumed to be 75.0 kg[6]
- In absence of cost data, the price of Tremelimumab was approximated by another CTLA-4 inhibitor, ipilimumab.[7]
- All the costs were adjusted to 2022 US dollar value.
- The willingness to pay threshold is set at $150,000/QALY.[13]

METHOD(Cont.)

Model Input

Cost

Parameters	Base-case value (range)/cycle	Distribution	Reference
Costs Input ($)			
Durvalumab	11693.25 (8769.94 – 14616.56)	Gamma	8
Tremelimumab	122328 (91746 – 152910)	Gamma	8
AE_DM	69.11 (51.83 - 86.39)	Gamma	9 & 10
AE_TM	407.17 (305.38 – 508.96)	Gamma	9 & 10
AE_T75D	55.92 (41.94 – 69.90)	Gamma	9 & 10
AE_T300D	69.804 (52.35 – 87.26)	Gamma	9 & 10
Patient with PFS	870.56 (652.64 – 1088.47)	Gamma	5
Patient with PD	1012.15 (758.84 – 1265.45)	Gamma	5
Drug Administration per Unit	329.64 (246.68 – 411.50)	Gamma	5
Subsequent Treatment per Person	119837.67 (89878.25 – 149797.08)	Gamma	5
Terminal Care per Person	8732.08 (6985.44 – 9979.73)	Gamma	5
AE: Adverse Events			

Utilities and Subsequent Treatment Proportion

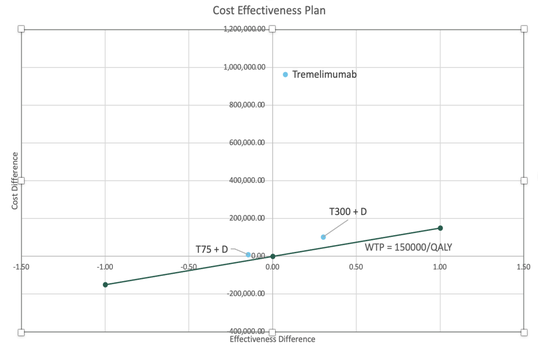
Parameters	Base-case value (range)/cycle	Distribution	Reference
Utility Input			
Utility of PFS	0.76 (0.61 – 0.91)	Beta	2
Utility of PD	0.68 (0.54 – 0.82)	Beta	2
Disutility of Rash	0.16 (0.11 - 0.20)	Beta	5
Disutility of Fatigue	0.12 (0.093 - 0.14)	Beta	10
Disutility of Diarrhea	0.10 (0.082 - 0.12)	Beta	10
Subsequent Treatment Proportion			
Durvalumab	35.6% (26.7% - 44.5%)	Beta	11
Tremelimumab	31.9% (23.9% - 39.9%)	Beta	11
T75 + D	38.1% (28.6% - 47.6%)	Beta	11
T300 + D	42.7% (32% - 53%)	Beta	11

RESULTS

Patients Demographic and Clinical Characteristics

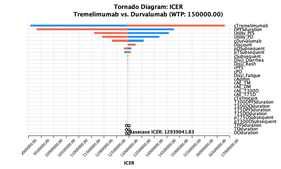
	DM (n = 104)	TM (n = 69)	T75 + D (n = 84)	T300 + D (n = 75)
Median age, years (range)	64.5 (32 – 89)	62.0 (37 – 81)	61.5 (28 – 82)	66.0 (26 – 86)
Sex, male, No.(%)	92 (88.5%)	57 (82.6%)	70 (83.3%)	65 (86.7%)
Race and Ethnicity. No.(%)				
White	35 (33.7%)	26 (37.7%)	30 (35.7%)	27 (36.0%)
Black	10 (9.5%)	2 (2.9%)	5 (6.0%)	4 (5.3%)
Asian	55 (52.9%)	39 (56.5%)	47 (56.0%)	44 (58.7%)
Hispanic or Latino	5 (4.8%)	4 (5.8%)	5 (6.0%)	4 (5.3%)
Others	4 (3.8%)	2 (2.9%)	2 (2.4%)	0
BCLC Score, No.(%)				
A	1 (1.0%)	2 (2.9%)	1 (1.2%)	1 (1.3%)
B	9 (8.7%)	13 (18.8%)	17 (20.2%)	13 (17.3%)
C	80 (76.9%)	42 (60.9%)	57 (67.9%)	58 (77.3%)
Unknown or missing	14 (13.%%)	12 (17.4%)	9 (10.7%)	3 (4.0%)

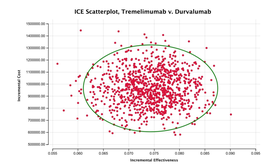
Base Case Analysis

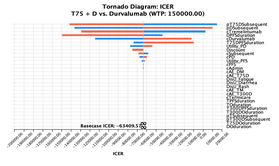


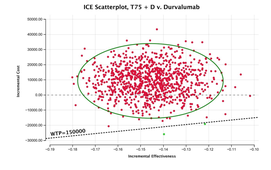
RESULTS (Cont.)

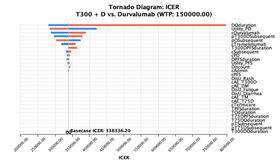
Sensitivity Analysis

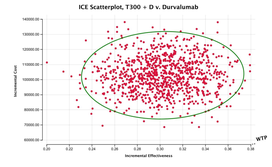




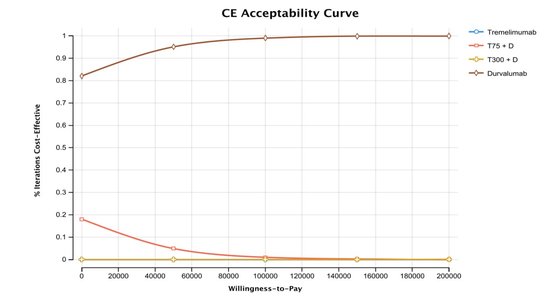








CE acceptability curve



DISSCUSIONS & LIMITATIONS

- The CEA is most sensitive to the change of the **cost of tremelimumab, the subsequent treatment proportion, and the overall survival duration of the DM group** for TM, T75 +300, and T300 +D group, respectively.
- The cost of tremelimumab has been replaced with the price of ipilimumab, suggesting a potential upcoming modification.
- The high cost of tremelimumab could pose a significant obstacle to widespread utilization of this medication. This may decrease its accessibility and affordability for patients, limiting its widespread adoption as a treatment option.

CONCLUSION

- TM, T75D, and T300D are not cost-effective compared to DM.

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