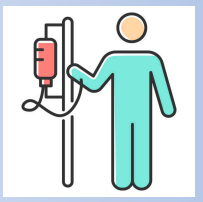
Cost-Effectiveness of Response-Adapted De-Escalation of Immunotherapy in Advanced Melanoma

Zachary Cartun[1,2]; Wolfgang G. Kunz, MD, MHBA[2]; Dirk Mehrens, MD[2]

Department of Radiology, UMass Chan Medical School, Worcester, MA[1] and Department of Radiology, Ludwig Maximilien Universität Klinikum, Munich, Germany[2]

I. Introduction

- 1/4th of US advanced melanoma patients report financial difficulties post-cancer diagnosis
- Financial burden has been identified as a significant risk factor for early mortality, particularly in healthcare systems with non-universal insurance systems – **Financial Toxicity**
- Combo Nivolumab and Ipilimumab (NIVO + IPI) immunotherapy **markedly** improves outcomes for melanoma patients (CheckMate-067 Trial (**CM**), NEJM, 2015)
- Similar progression-free (PFS) and overall survival (OS) is seen for patients with **response-adapted treatment de-escalation** (ADAPT-IT (**AI**) Phase II Trial, JCO, 2021)



Tx-Naïve Advanced Melanoma Patient

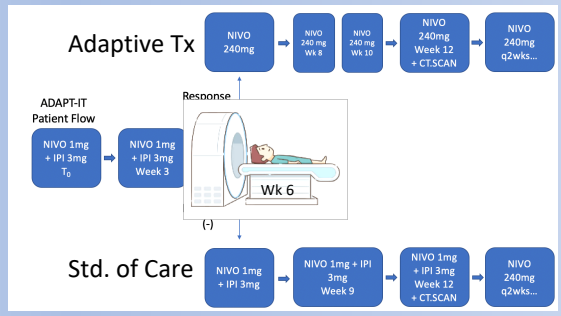


Figure 1. Adapt-IT trial patient flow

II. Objectives

1. To determine the cost-effectiveness of IPI discontinuation for patients with interim imaging-confirmed tumor response (no new index lesions AND <4% tumor growth)
2. To estimate a worst-case Willingness-To-Pay (WTP) threshold as a baseline for future studies

Model Input Parameters	Base Case Value
Monthly Costs	
Nivolumab + Ipilimumab	$63,834
Nivolumab	$15,505
2nd Line Combined Therapy	$9,548
Adverse Effects 1st Line	$341
Adverse Effects 2nd Line	$642
One Time Costs	
Progression Free Survival Exit (Surgery/Radiotherapy)	$5,651
Overall Survival Exit (Terminal Care Costs)	$16,992
Utilities	
PFD	0.8
PD	0.52
Ae Disutility/Month	0.156

Table 1. Model Input Parameters

VIII. Acknowledgements

We would like to thank the Umass Chan Dept. of Radiology for funding this work with a global radiology grant. A special thanks also to LMU Klinikum for their support.

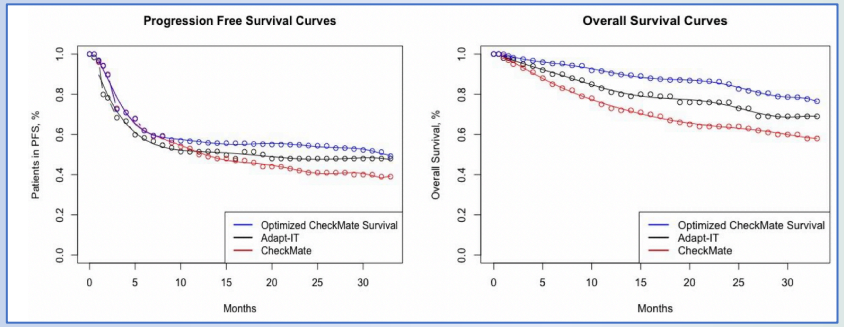


Figure 2. Model's progression free and overall survival curves

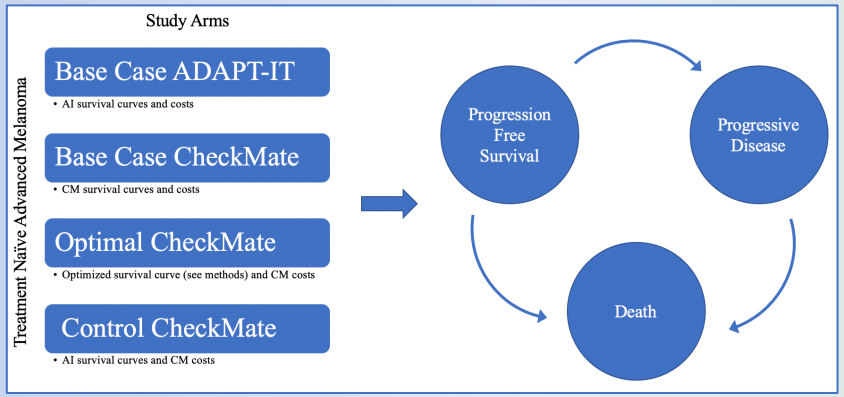


Figure 3. Partitioned Survival Analysis Model Design

III. Methods

- Survival curves derived from **AI** and **CM** trials (Treatment-Naïve Advanced Melanoma Patients) (Figure 2)
- Partitioned survival analysis computed with TreeAge decision-analysis (Figure 3)
- Drug Costs from Medicare Average Sales Prices
- Adverse Effects/adjuvant/palliative/Utility Values derived from literature
- An optimized survival arm defined by abs(AI – CM) + Max(AI,CM) per Unit Time
  - Formulated as a "Best Case" standard-of-care (SOC) scenario

Patient group	Cost ($)	IC ($)	Effect (QALY)	IE (QALY)	iNMB ($)	ICER ($/QALY)	Acceptability at WTP (%)
Base Case ADAPT-IT	418,651	-23,395	1.25	0.09	32,353	Dominant	99.64
Base Case CheckMate	442,047	(reference)	1.16	(reference)	(reference)	(reference)	0.36
Optimal CheckMate	494,144	52,098	1.37	0.20	-31,725	255,728	0.00
Control CheckMate	455,701	13,654	1.25	0.09	-4,697	152,439	0.00

Table 2. Results of cost-effectiveness analysis

IV. Results

- Base Case AI demonstrated dominant Incremental Cost-Effectiveness Ratio (ICER) and positive Incremental Net Monetary Benefit (iNMB) values (Table 2)
- Base Case AI was optimal cost-effective strategy in 99.64% of Monte Carlo simulations (Figure 4)
- **Optimized CM arm only became Cost Effective at a WTP threshold of $650,000/QALY** (Figure 5)

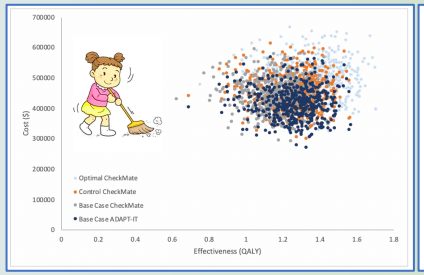


Figure 4. Probabilistic Sensitivity Analysis

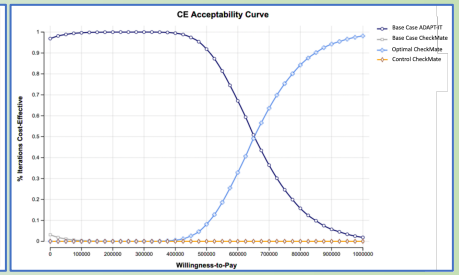


Figure 5. WTP Threshold Curves

V. Discussion

- **Cost-Effectiveness of adaptive treatment was non-inferior to even a theoretical optimal standard of care outcome**
- Immunotherapies have varying dose/effect/time ratios compared to chemotherapy
- De-escalation of multimodal treatment strategies can reduce costs based on multiple factors:
  1. Lower drug costs/costs for local therapy
  2. Lower healthcare utilization (e.g. physician or nursing time costs)
  3. Avoidance of costs in the care of adverse events,
  4. **Increased participation in the work force/productivity**

- Patient, Insurance Company, and Societal cost-effectiveness of drug de-escalation will hopefully motivate more such trials
  - **These trials are not funded by pharmaceutical companies as they are generally not in their best short term economic interests**
- Limitations: Trial data (Phase II), varying 1st-line Tx guidelines, combined cost-estimations

VII. References

1. Larkin, J., et al., *Five-Year Survival with Combined Nivolumab and Ipilimumab in Advanced Melanoma.* N Engl J Med, 2019. **381**(16): p. 1535-1546.
2. Chapman, P.B., S.P. D'Angelo, and J.D. Wolchok, *Rapid eradication of a bulky melanoma mass with one dose of immunotherapy.* N Engl J Med, 2015. **372**(21): p. 2073-4.
3. van Boemmel-Wegmann, S., et al., *Health Care Utilization and Costs Associated With Systemic First-Line Metastatic Melanoma Therapies in the United States.* JCO Oncol Pract, 2022. **18**(1): p. e163-e174.
4. Hussaini, S.M.Q., A. Gupta, and S.B. Dusetzina, *Financial Toxicity of Cancer Treatment.* JAMA Oncol, 2022.
5. Postow, M.A., et al., *Adaptive Dosing of Nivolumab + Ipilimumab Immunotherapy Based Upon Early, Interim Radiographic Assessment in Advanced Melanoma (The ADAPT-IT Study).* Journal of Clinical Oncology.
6. Kohn, C.G., et al., *Cost-Effectiveness of Immune Checkpoint Inhibition in BRAF Wild-Type Advanced Melanoma.* J Clin Oncol, 2017. **35**(11): p. 1194-1202.