EE521

Economic Evaluation of Trastuzumab Deruxtecan for HER2+ Advanced Gastric Cancer Patients

Rahul Mudumba, MHS[1], Hui-Hsuan Chan, MHS[2], Jeromie Ballreich, PhD MHS[3]
(mudumba@usc.edu)
[1]Department of Pharmaceutical and Health Economics, Alfred E. Mann School of Pharmacy, University of Southern California, Los Angeles, CA USA
[2]CHOICE Institute, School of Pharmacy, University of Washington, Seattle, WA USA
[3]Department of Health Policy and Management, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD USA

OBJECTIVE

To evaluate the cost-effectiveness of trastuzumab deruxtecan compared to chemotherapy of physician's choice for patients with human epidermal growth factor receptor 2 positive (HER2+) locally advanced or metastatic gastric or gastroesophageal junction cancer previously treated with at least two lines of therapy.

METHODS

Model Type: Three-state partitioned survival model

Intervention: Trastuzumab deruxtecan (T-DXd) administered every 3 weeks

Comparator: Physician's choice chemotherapy (irinotecan) administered every 2 weeks

Target population: Advanced HER2+ gastric cancer patients previously treated with at least 2 lines of therapy

Model Structure: 3 mutually exclusive health states: progression-free, post-progression, death

Time Horizon: 5 years

Cycle Length: 4 weeks

Perspective: US healthcare sector

Clinical Efficacy & Modeling: The model transition parameters were populated with clinical efficacy data from the DESTINY-Gastric01 phase II randomized clinical trial [1]. To extrapolate progression and survival beyond the time horizon of the clinical trial, we digitized the published Kaplan-Meier (KM) curves to obtain estimates of individual patient data (IPD) using the WebPlotDigitizer [2].

We then reconstructed the KM curves with the IPD estimates of the chemotherapy control arm in R 4.1.3 based on the algorithm provided by Guyot et al. and fitted separate parametric models for PFS and OS to the reconstructed KM curves using various parametric distributions to determine the best fit based on Akaike information criterion (AIC) [3].

Upon selecting the best fitting parametric model to extrapolate PFS and OS for patients receiving physician's choice of chemotherapy in the control arm, we applied the hazard ratios (HRs) observed in the DESTINY-Gastric01 trial to the PFS and OS curves in this arm to derive the KM curves for the intervention arm receiving T-DXd.

Key Base Case Model Assumptions:

1. Patients are treated with either T-DXd or irinotecan as 3L+ therapy in the progression-free state indefinitely or until disease progresses.

2. Applied hazard ratios (HRs) between T-DXd and chemotherapy from the DESTINY-Gastric01 trial (0.47 and 0.59 for PFS and OS respectively) until 24 months, the length of trial follow-up [1].

3. We assume HRs regress to the midpoint of the trial HRs and 1 (0.735 and 0.795 for PFS and OS respectively) after 24 months until the model ends.

4. Model assumes that the leftover contents in single-dose drug vials are discarded after opening, leading to wastage that is paid for, based on drug label recommendations [4,5].

5. We assume that patients who progress on either T-DXd or chemotherapy are switched to palliative/end-of-life care.

Costs: Costs include drug costs extracted from CMS Average Sales Price and administrative, adverse event, and end-of-life costs derived from published literature, measured in 2023 US Dollars and discounted at 3% annually.

Outcomes: Quality-adjusted life years (QALYs), including from treatment, remissions and adverse events, were sourced from published literature and discounted at 3% annually.

Sensitivity Analysis: We conducted both probabilistic and deterministic sensitivity analysis to test model assumptions and robustness.

Scenario Analysis: We performed 3 separate scenario analyses where we assumed full treatment benefit for T-DXd, no additional benefit beyond trial, and no drug wastage.

MODEL INPUTS

Variables	Base-Case	Lower Value	Upper Value	Distribution	Reference
Clinical endpoints					
Hazard ratio for OS	0.59	0.39	0.88	Lognormal	Shitara et al. 2020
Hazard ratio for PFS	0.47	0.31	0.71	Lognormal	Shitara et al. 2020
Post-24-month HR for OS	0.735	0.695	0.94	Lognormal	Calculation
Post-24-month HR for PFS	0.795	0.655	0.855	Lognormal	Calculation
Chemotherapy objective response rate (%)	14.3	6.0	26.0	N/A	Shitara et al. 2020
T-DXd objective response rate (%)	51.3	42.0	61.0	N/A	Shitara et al. 2020
Average patient bodyweight (kg)	80	64	96	Normal	Assumption
Average patient body-surface area (m^2)	1.8	1.44	2.16	Normal	Assumption
Cost					
Dose schedule per cycle					
Chemotherapy (irinotecan)	150 mg/m^2	N/A	N/A	N/A	Label
Trastuzumab deruxtecan (T-DXd)	6.4 mg/kg	5.4 mg/kg	6.4 mg/kg	N/A	Label
Drug costs					
Irinotecan (per 100-mg vial)	$11.45	$7.72	$15.17	Gamma	base case: Medicare/ASP+6%, lower: VA big4 price
Trastuzumab deruxtecan (per 100-mg vial)	$2,716.89	$1,740.27	$3,478.53	Gamma	base case: Medicare/ASP+6%, lower: VA big4 price
Intravenous (IV) administration cost	$302.82	N/A	N/A	N/A	Kruse et al. 2008
Cost after disease progression (per cycle)	$16,398.22	$13,184.17	$19,612.27	Gamma	Chastek et al. 2012
LVEF exam cost (per visit)	$250.00	N/A	N/A	N/A	CMS Addendum B 2022
Adverse event costs (Grades 3 & 4)					
Nausea/Vomiting	$12,045.23	N/A	N/A	Gamma	Burke et al. 2011
Decreased neutrophil count (neutropenia)	$15,620.81	N/A	N/A	Gamma	Benett et al. 2007
Anemia	$14,068.25	N/A	N/A	Gamma	Elting et al. 2004
Diarrhea	$9,668.11	N/A	N/A	Gamma	Dranitsaris et al. 2005
Decreased white-cell count (leukopenia)	$15,620.81	N/A	N/A	Gamma	Benett et al. 2007
Decreased platelet count (Thrombocytopenia)	$29,055.88	N/A	N/A	Gamma	Wong et al. 2018
Interstitial lung disease	$25,293.25	N/A	N/A	Gamma	Olson et al. 2020
Treatment Effects					
Health state utilities (QALYs)					
Progression-free state	0.731	0.577	0.861	Beta	Sunitinib NICE Submission
Post-progression state	0.577	0.463	0.687	Beta	Sunitinib NICE Submission
Treatment response	0.075	0.061	0.09	Beta	Lloyd et al. 2006

Table 1. Model parameters: base case values, lower bound values, upper bound values, and distributions for probabilistic sensitivity analysis

RESULTS

Strategy	Total Costs	Total QALYs	Δ Costs	Δ QALYs	ICER	Cost-effectiveness probability at $150,000 WTP
Base case (Waning Treatment Effect): Time-dependent HR + 5-year Time Horizon + Drug Wastage						
Chemotherapy	$80,261	0.558				
T-DXd	$363,944	0.905	$283,734	0.346	$819,477 / QALY	0%
Scenario 2 (Full Treatment Benefit): Constant HR + 5-year Time Horizon + Drug Wastage						
Chemotherapy	$80,261	0.558				
T-DXd	$451,180	1.123	$370,919	0.565	$656,522 / QALY	0%
Scenario 3 (No Treatment Benefit Beyond Trial): HRs at 1 Post-24 months + 5-year Time Horizon						
Chemotherapy	$80,261	0.558				
T-DXd	$399,125	0.995	$318,865	0.437	$729,884 / QALY	0%
Scenario 4 (Waning Treatment Effect): Time-dependent HR + 5-year Time Horizon WITHOUT DRUG WASTAGE						
Chemotherapy	$80,215	0.558				
T-DXd	$352,763	0.995	$272,548	0.437	$623,865 / QALY	0%

Table 2. Abbreviation: *T-DXd* trastuzumab deruxtecan, *ICER* incremental cost-effectiveness ratio, *QALY* quality-adjusted life year, *WTP* willingness-to-pay

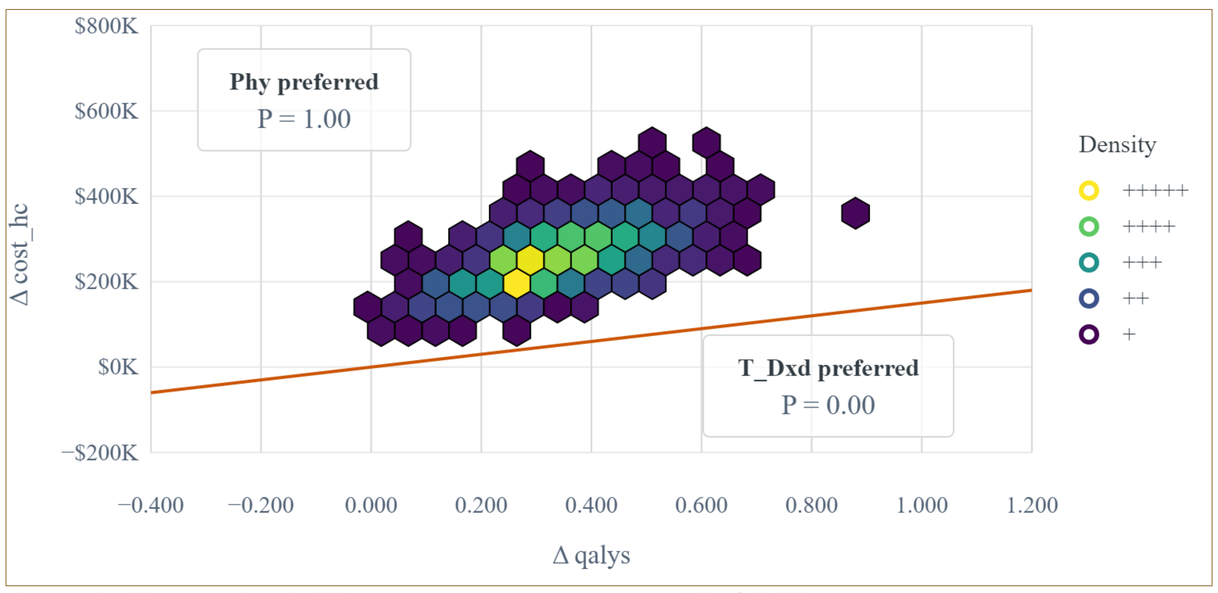

Figure 4. Cost-Effectiveness Plane for T-DXd vs. physician's choice of chemotherapy (WTP = $150,000)

MODEL OVERVIEW

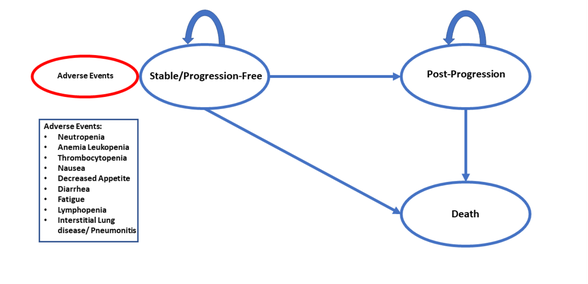

Figure 1. Partitioned survival model health states

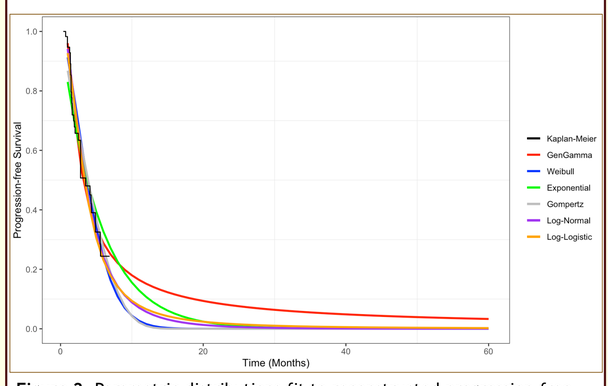

Figure 2. Parametric distributions fit to reconstructed progression-free survival curve in the chemotherapy arm; generalized gamma distribution selected

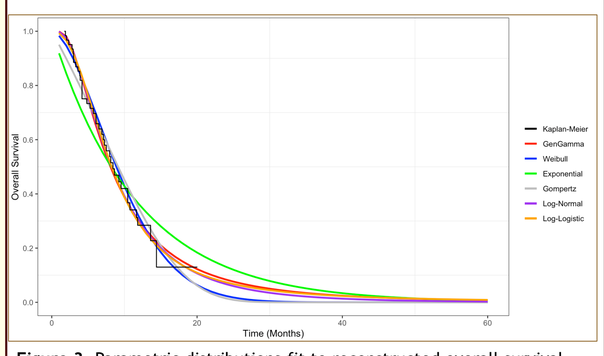

Figure 3. Parametric distributions fit to reconstructed overall survival curve in the chemotherapy arm; lognormal distribution selected

RESULTS

Base-case results: In our base case analysis, total costs for trastuzumab deruxtecan were $363,944, compared to $80,261 for physician's choice of chemotherapy. Total QALYs for trastuzumab deruxtecan were 0.56, compared to 1.84 for chemotherapy. The base-case ICER was $819,477/QALY.

Sensitivity Analysis: Probabilistic sensitivity analysis indicated that trastuzumab deruxtecan had a 0% probability of being cost-effective at a $150,000 per QALY willingness-to-pay (WTP) threshold.

Using this WTP threshold, the value-based price of trastuzumab deruxtecan per 100-mg vial to be cost-effective was $615, compared to the current drug cost (ASP + 6%) of $2,717.

Scenario Analysis: Our scenario analyses examining full treatment benefit, no additional benefit beyond trial, and no drug wastage yielded ICERs of $656,522, $729,884 and $729,884 per QALY respectively, showing high incremental cost-effectiveness ratios across various assumptions.

CONCLUSION

Despite the higher efficacy of trastuzumab deruxtecan in patients with HER2+ advanced gastric cancer, our model highlights serious concerns regarding its cost-effectiveness.

REFERENCES

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CONTACT

Rahul Mudumba: mudumba@usc.edu
PhD Student
Department of Pharmaceutical and Health Economics, Alfred E. Mann School of Pharmacy, University of Southern California
Los Angeles, CA, USA