Cost-Effectiveness Analysis of Valbenazine and Deutetrabenazine Use in Tardive Dyskinesia

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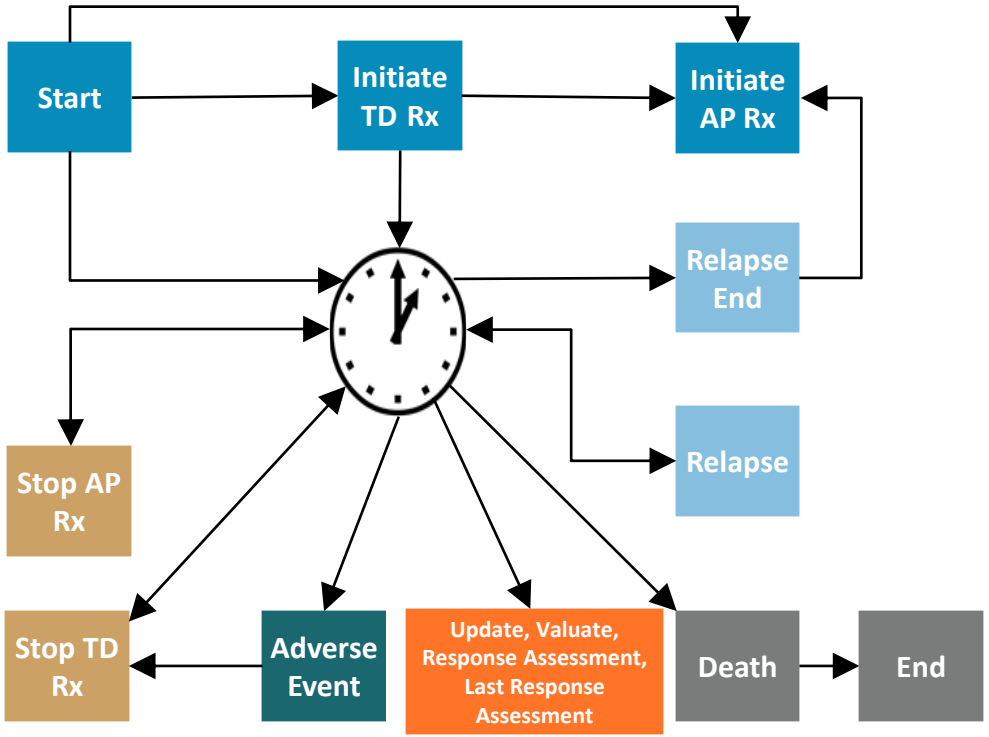
Cost-Effectiveness Analysis: Model Overview

- A discretely integrated condition event (DICE) model[1] was used to evaluate clinical and economic outcomes associated with valbenazine (VBZ) and deutetrabenazine (DTBZ) treatment of tardive dyskinesia (TD)
- The model conceptualizes "conditions" that reflect aspects of the model or patient attributes that persist, and "events" that reflect points in time when conditions may change



Times to events are initially determined at the start of the model. These times are periodically revised during Update, Valuate, Response Assessment, and Last Response Assessment events, which are part of the scheduling process represented by the clock, and when other events occur, as indicated by arrowheads.
The Update, Valuate, Response Assessment, and Last Response Assessment events are part of the scheduler.
AP, antipsychotic; Rx, prescription; TD, tardive dyskinesia

1. Caro JJ. Pharmacoeconomics.2016;34:665-72

Ganz ML, et al. AMCP 2019. San Diego, CA.

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Cost-Effectiveness Analysis: Patient Population and Perspective

- A synthetic population of 1,000 simulated patients with demographic and clinical characteristics derived from population statistics in the KINECT 3 trial of VBZ was created and used in the model
- Simulated patients could have only one underlying psychiatric condition: schizophrenia, bipolar disorder, or major depressive disorder (MDD)
- The model was analyzed from a U.S. third-party payer perspective over a lifetime horizon
  - Only direct costs (drug acquisition costs, disease management costs, and relapse treatment costs) were included in the analysis
- The primary health outcomes assessed were Quality Adjusted Life Years (QALYs), life years, response to TD treatment at 1 year, and number of relapses
  - A QALY is a generic measure of disease burden, including both the quality and the quantity of life lived. Where one QALY equates to one year in perfect health.

MDD, Major Depressive Disorder QALY, quality-adjusted life-year

Ganz ML, et al. AMCP 2019. San Diego, CA.

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Cost-Effectiveness Analysis: Model Assumptions

- All simulated patients began with moderate to severe TD, having attempted titration/optimization of their antipsychotic medications
- During the first 24 weeks of treatment with VBZ, DTBZ, or no treatment, simulated patients were assessed every 8 weeks for response, defined as ≥50% improvement in AIMS total score or a Clinical Global Impression of Change (CGIC) score ≤2
  - Simulated patients who responded at a given assessment suffered no disutility due to TD until at least the next assessment
- A final assessment of response was conducted at Week 48, at which time responders continued TD treatment until death, and non-responders discontinued TD treatment
- Simulated patients who discontinued one TD treatment did not attempt another
- All simulated patients with a psychiatric diagnosis were at risk of discontinuing their antipsychotic medications, putting them at increased risk of relapse
  - Simulated patients who respond to treatment were assumed to have reduced symptoms of TD, which improves adherence to antipsychotic treatment and lowers the risk of relapse
  - Simulated patients receiving antipsychotic medication were assumed to discontinue upon relapse
  - Antipsychotic medication was restarted at the end of the relapse

Ganz ML, et al. AMCP 2019. San Diego, CA.

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Cost-Effectiveness Analysis: Model Inputs (Clinical 1/2)

Average Daily TD Medication Doses[a]		
Drug/Dose	**Proportion of Patients**	**Source**
VBZ 40 mg	0.200	Factor et al. *J Clin Psychiatry*; 2017 Marder et al. *Neuropsychopharmacol*; 2017 (Suppl) Anderson et al. *Lancet Psychiatry*; 2017 Fernandez et al. *Neurology*; 2017 Hauser et al. *Neurology*; 2018 (15 Suppl)
VBZ 80 mg	0.800	
DTBZ 24 mg	0.270	
DTBZ 36 mg	0.270	
DTBZ 48 mg	0.460	

Probability of Response Measured by ≥50% Improvement in AIMS Total Score (sum of items 1-7) or CGIC Score ≤2				
Week	**VBZ 40 mg**	**VBZ 80 mg**	**DTBZ**	**Source**
Week 8	0.291, 0.425	0.361, 0.473	0.247, 0.410	Factor et al. *J Clin Psychiatry*; 2017 Marder et al. *Neuropsychopharmacol*; 2017 (Suppl) Anderson et al. *Lancet Psychiatry*; 2017 Fernandez et al. *Neurology*; 2017 Hauser et al. *Neurology*; 2018 (15 Suppl)
Week 16	0.288, 0.559	0.429, 0.595	0.279, 0.440	
Week 24	0.374, 0.648	0.494, 0.821	0.374, 0.620	
Week 48	0.350, 0.667	0.547, 0.869	0.418, 0.680	

Parameters for Antipsychotic Treatment Discontinuation				
Patient population	**Schizophrenia**	**Bipolar Disorder**	**MDD**	**Source**
Weibull parameters (γ, λ), Patients with TD	0.783, 0.952	0.914, 1.268	0.914, 1.268	Greene et al. *J Med Econ*; 2018 Institute for Clinical and Economic Review; 2017
Hazard ratio, TD responder	0.593	0.593	0.593	

[a]Average cohort dose: 72.0 mg/day for VBZ, 38.3 mg/day for DTBZ.

AIMS, Abnormal Involuntary Movement Scale; CGIC, Clinical Global Impression of Change; DTBZ, deutetrabenazine; MDD, major depressive disorder; TD, tardive dyskinesia; VBZ, valbenazine.

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Cost-Effectiveness Analysis: Model Inputs (Clinical 2/2)

Annual Risk for Psychiatric Relapse by Antipsychotic Medication Status				
Medication Status	**Schizophrenia**	**Bipolar Disorder**	**MDD**	**Source**
On medication	0.315	0.528	0.528	Leucht et al. *Lancet*; 2012 Derry et al. *BMC Psychiatry*; 2007 Di Capite et al. *Early Interv Psychiatry*; 2018
Off medication	1.022	1.050	1.050	
Psychiatric Relapse Sequelae				
Parameter	**Schizophrenia**	**Bipolar Disorder**	**MDD**	**Source**
Proportion hospitalized	0.564	0.564	0.564	Panish et al. *J Pharm Health Serv Res*; 2013 Park et al. *Value Health*; 2014 Rajagopalan et al. *J Med Econ*; 2013 Ascher-Svanum et al. *BMC Psychiatry*; 2010
Duration of hospitalization, days	10.7	6.9	6.5	
Duration of outpatient treatment, days	9.0	9.0	9.0	
Hazard Ratio for Mortality by Psychiatric Condition				
Gender	**Schizophrenia**	**Bipolar Disorder**	**MDD**	**Source**
Male	2.210	1.750	0.880	Crump et al. *JAMA Psychiatry*; 2013 Chiu et al. *J Affect Discord*; 2018
Female	2.660	2.090	2.140	

MDD, major depressive disorder.

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Cost-Effectiveness Analysis: Model Inputs (TD Treatment Costs)

Daily Medication Costs			
Drug	**Daily Dose (mg)[a]**	**Daily Cost (2017 US $)**	**Source**
VBZ	40	139.92	For VBZ and DTBZ, based on 27% discount to Wholesale Acquisition Cost For Antipsychotic, Gilmer et al. *Am J Psychiatry*; 2004
VBZ	80	151.48	
DTBZ	12	83.94	
DTBZ	18	94.42	
DTBZ	24	125.90	
DTBZ	30	178.35	
DTBZ	36	188.84	
DTBZ	42	220.31	
DTBZ	48	251.79	
Antipsychotic	—	17.35	
Annual Disease Management Costs			
Disorder	**Cost with TD (2017 US $)**	**Cost without TD (2017 US $)**	**Source**
Schizophrenia	7,909.94	5,361.92	Gilmer et al. *Am J Psychiatry*; 2004 Guo et al. *Value Health*, 2008
Bipolar disorder	3,983.06	1,435.04	
MDD	3,983.06	1,435.04	
No psychiatric disorder	2,548.02	—	
Psychiatric Disorder Relapse Costs			
Disorder	**Hospital Costs (2017 US $)**	**Outpatient Costs (2017 US $)**	**Source**
Schizophrenia	853.72	84.13	Park et al. *Value Health*; 2014
Bipolar disorder	839.05	84.13	
MDD	546.08	84.13	

[a]Average cohort dose: 72.0 mg/day for valbenazine, 38.3 mg/day for deutetrabenazine; DTBZ, deutetrabenazine; MDD, major depressive disorder; TD, tardive dyskinesia; VBZ, valbenazine.

Ganz ML, et al. AMCP 2019. San Diego, CA.

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Cost-Effectiveness Analysis: Utility and Mortality Inputs

- The mean utilities for baseline psychiatric conditions of schizophrenia, bipolar disorder, and MDD were 0.83, 0.80, and 0.80, respectively
- A utility decrement of 0.143 was applied to reflect moderate to severe TD
- Utility decrements of 0.081, 0.118, and 0.118 were applied to reflect relapses in schizophrenia, bipolar disorder, and MDD, respectively
- Mortality was modeled using estimates from the general population adjusted to reflect condition-specific hazard ratios of the underlying psychiatric disorders
- The hazard ratio for mortality used for patients with TD was 1.900
- Costs, quality-adjusted life years (QALYs), and life years were discounted at an annual rate of 3%

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Cost-Effectiveness Analysis: Sensitivity Analysis

- Deterministic sensitivity analyses assessed the impact of varying drug acquisition costs, probabilities of response, risk of relapse, and hazard ratio for TD mortality by ±20%
- Probabilistic sensitivity analyses that drew random values from the distributions of all the model parameters assessed the likelihood of cost-effectiveness of each intervention relative to a range of willingness-to-pay thresholds

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Cost-Effectiveness Analysis: Base Case Results

Outcome	VBZ	DTBZ	No Treatment	VBZ vs. No Treatment	VBZ vs. DTBZ
Response Criterion: ≥50% Improvement in AIMS Total Score					
QALYs (discounted)	9.094	8.734	7.163	1.931	0.360
LYs (discounted)	11.993	11.731	10.588	1.405	0.262
Responders at year 1, %	49.0	39.9	0	—	—
Relapses, n	10.3	10.2	9.3	—	—
Total costs (2017 US $)	543,692	591,658	139,578	404,114	(47,966)
ICER/QALY	—	—	—	209,281	Dominant
Response Criterion: CGIC Score ≤2					
QALYs (discounted)	10.232	9.704	7.163	3.069	0.528
LYs (discounted)	12.843	12.453	10.588	2.255	0.390
Responders at year 1, %	79.1	65.5	0	—	—
Relapses, n	10.8	10.6	9.3	—	—
Total costs (2017 US $)	748,053	828,298	139,578	608,475	(80,244)
ICER/QALY	—	—	—	198,243	Dominant

AIMS, Abnormal Involuntary Movement Scale; CGIC, Clinical Global Impression of Change; DTBZ, deutetrabenazine; ICER, incremental cost-effectiveness ratio; LY, life year; QALY, quality-adjusted life year; VBZ, valbenazine.
Red font color signifies a negative number

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Cost-Effectiveness Analysis: Lifetime Treatment Costs

Cost Component	VBZ (2017 US $)	DTBZ (2017 US $)	No Treatment (2017 US $)
Response Criterion: ≥50% Improvement in AIMS Total Score			
TD medication	399,975	448,667	—
AP medication	45,024	43,087	34,561
Disease management	63,481	64,901	71,349
Disease relapse	35,212	35,003	33,668
Total	543,692	591,658	139,578
Response Criterion: CGIC Score ≤2			
TD medication	601,360	682,969	—
AP medication	51,008	48,203	34,561
Disease management	59,237	61,277	71,349
Disease relapse	36,448	35,849	33,668
Total	748,053	828,298	139,578

AIMS, Abnormal Involuntary Movement Scale; AP, antipsychotic; CGIC, Clinical Global Impression of Change; DTBZ, deutetrabenazine; TD, tardive dyskinesia; VBZ, valbenazine.

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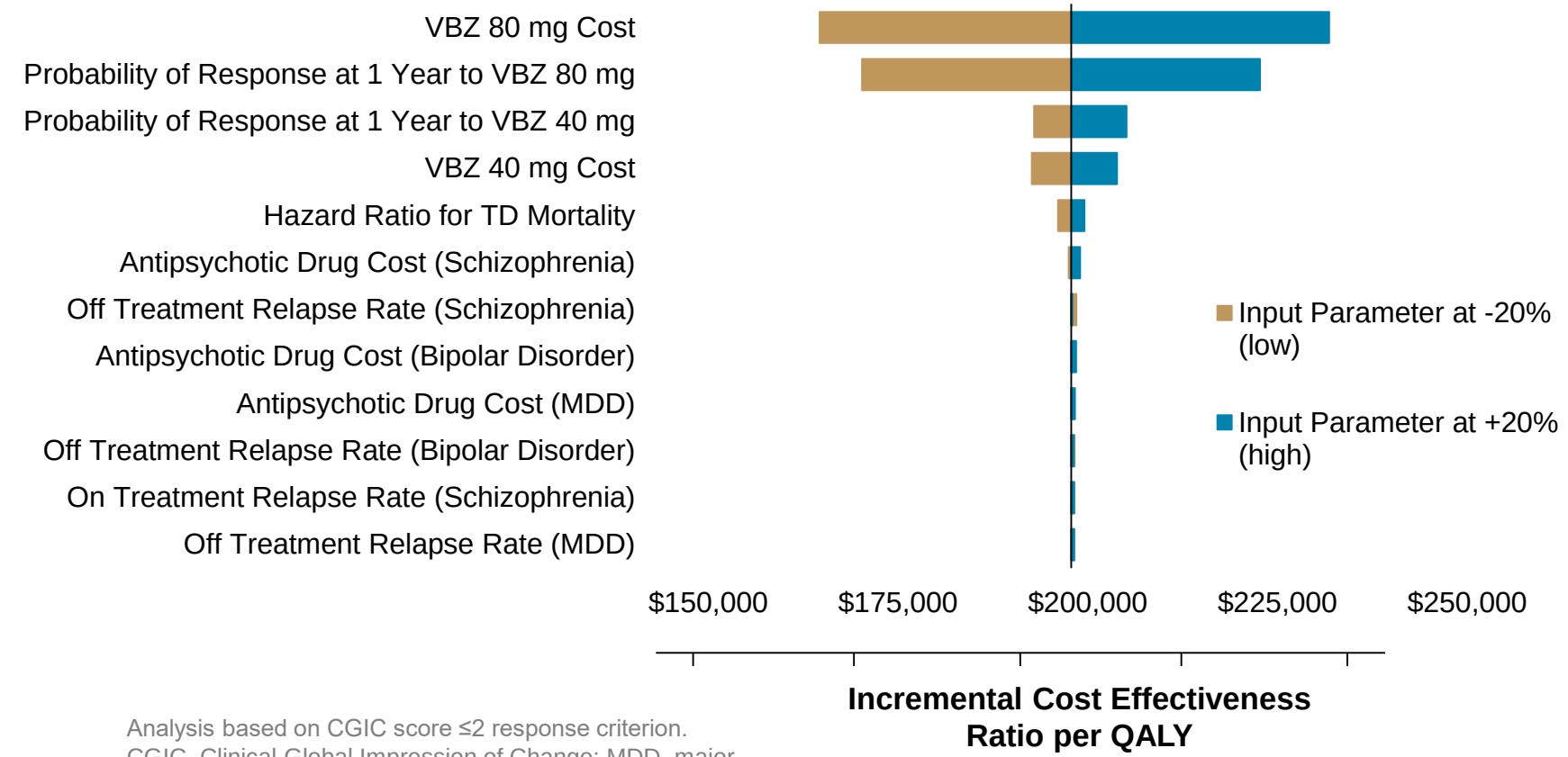
Cost-Effectiveness Analysis: VBZ vs. No Treatment

Tornado Plot for Deterministic Sensitivity Analysis of Cost-Effectiveness of Valbenazine Compared with No Treatment



Analysis based on CGIC score ≤2 response criterion.
CGIC, Clinical Global Impression of Change; MDD, major depressive disorder; QALY, quality-adjusted life year; TD, tardive dyskinesia; VBZ, valbenazine.

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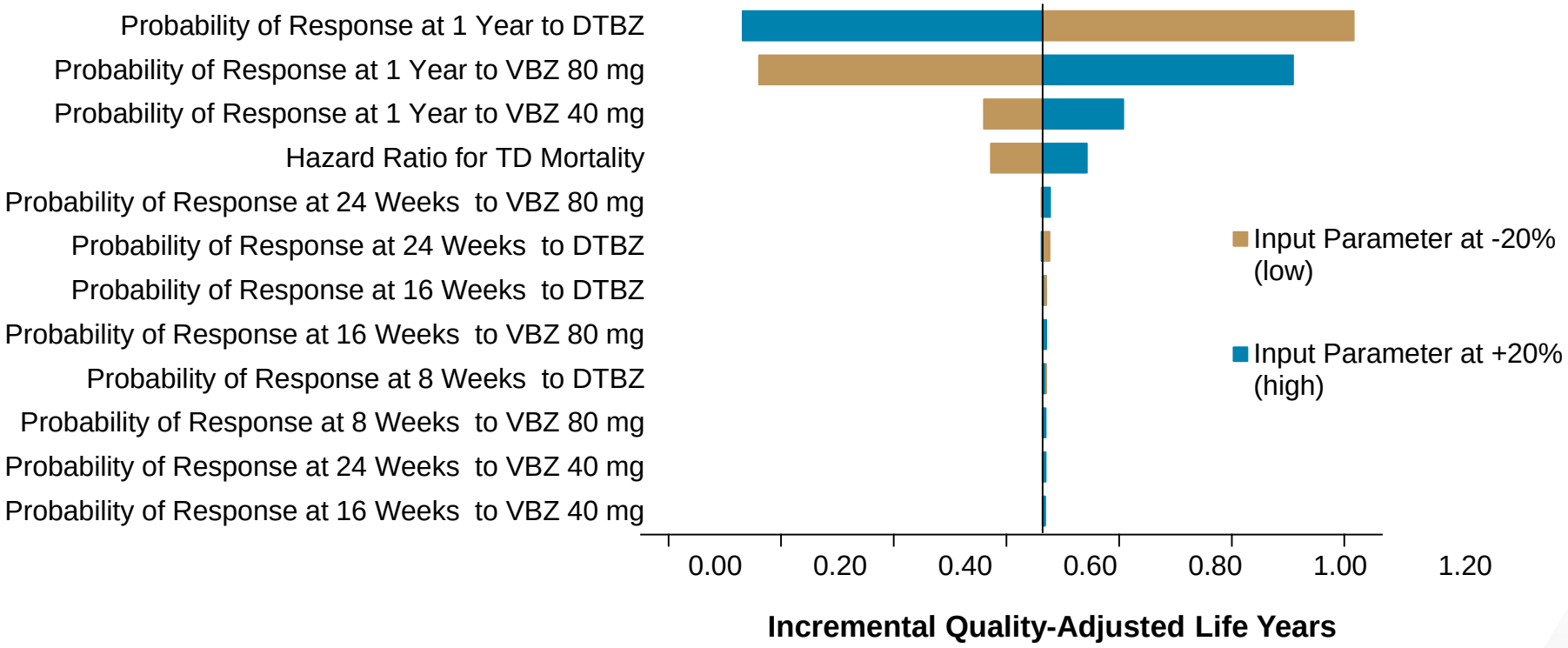
Cost-Effectiveness Analysis: VBZ vs. DTBZ (QALYs)

Tornado Plots for Deterministic Sensitivity Analysis of Valbenazine Compared with Deutetrabenazine



Analysis based on CGIC score ≤2 response criterion.
CGIC, Clinical Global Impression of Change; DTBZ, deutetrabenazine; MDD, major depressive disorder; QALY, quality-adjusted life year; TD, tardive dyskinesia; VBZ, valbenazine.

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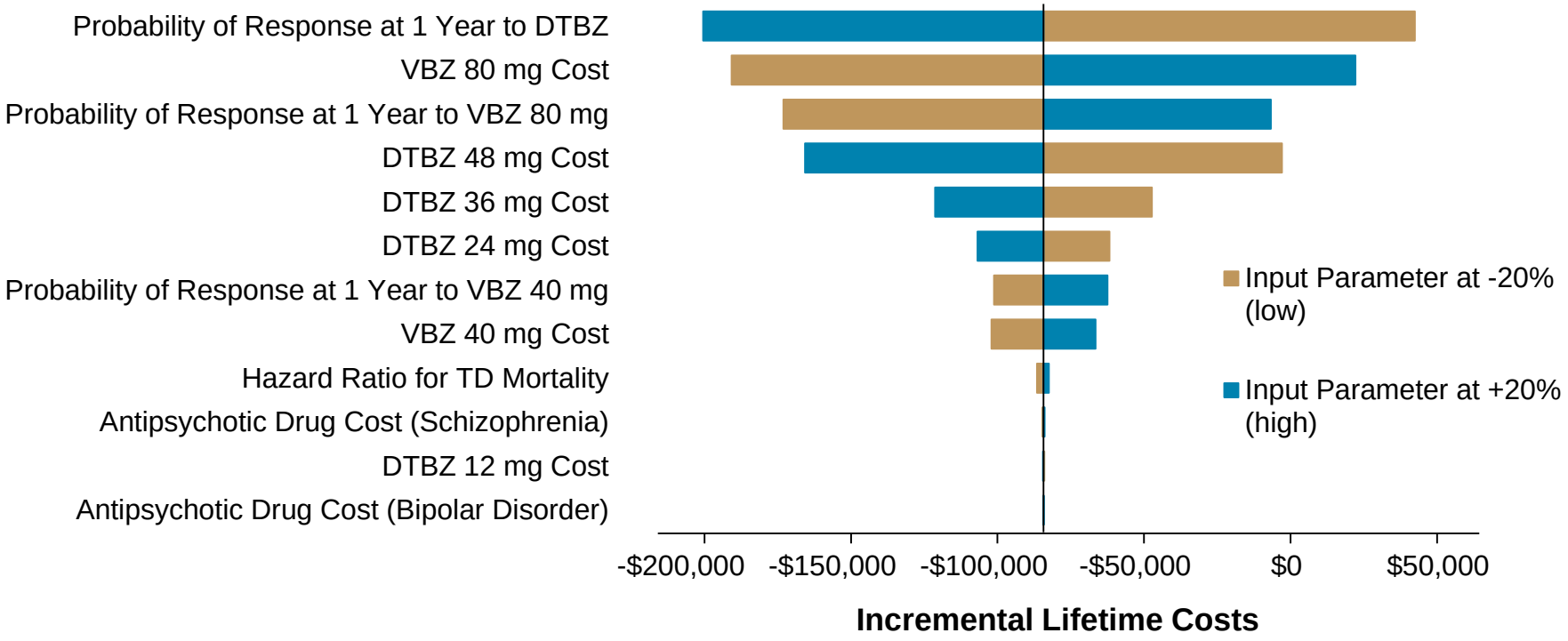
Cost-Effectiveness Analysis: VBZ vs. DTBZ (Costs)

Tornado Plots for Deterministic Sensitivity Analysis of Valbenazine Compared with Deutetrabenazine



Analysis based on CGIC score ≤2 response criterion.
CGIC, Clinical Global Impression of Change; DTBZ, deutetrabenazine; MDD, major depressive disorder; QALY, quality-adjusted life year; TD, tardive dyskinesia; VBZ, valbenazine.

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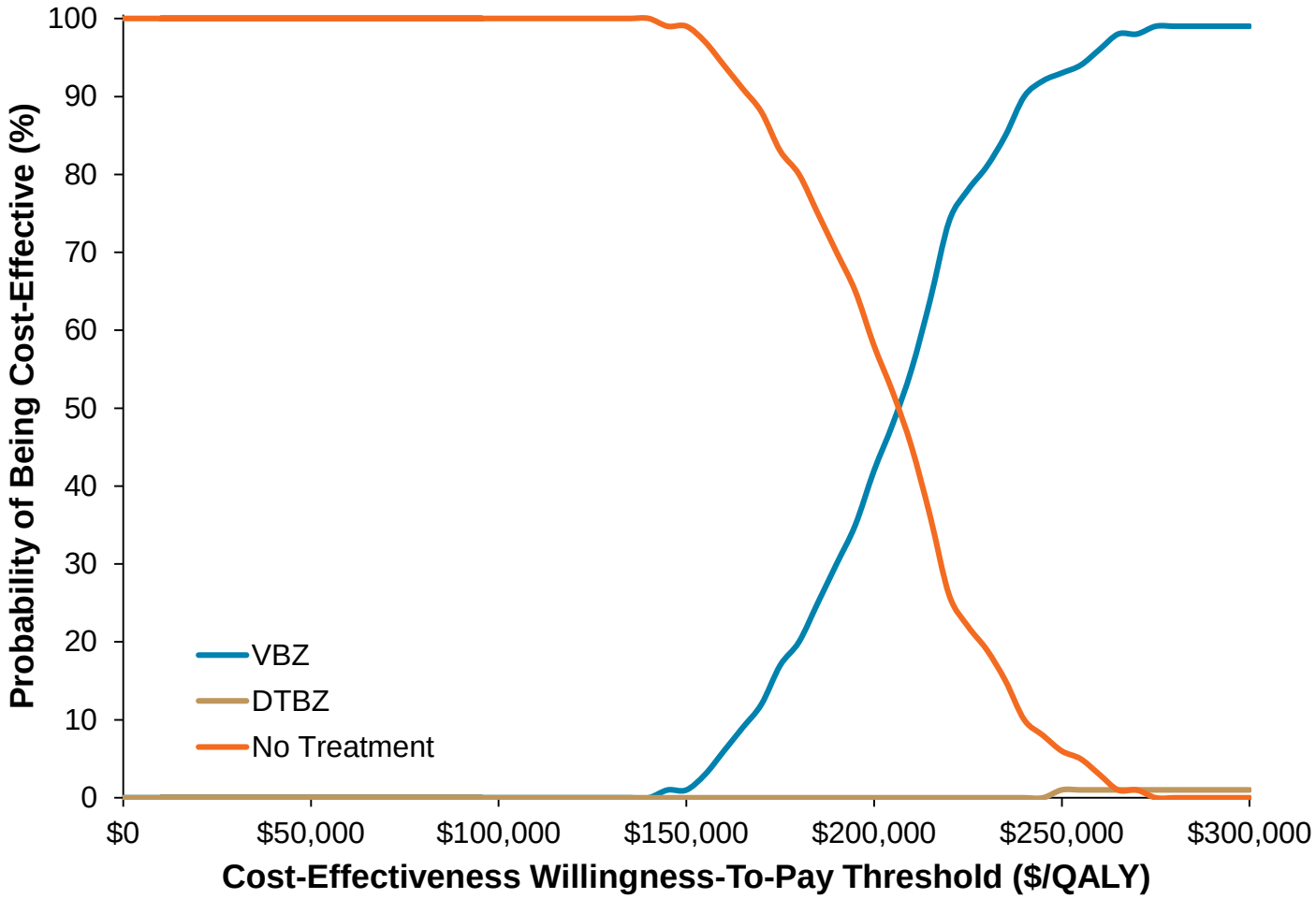
Cost-Effectiveness Analysis: Cost-Effectiveness Acceptability Curve



Analysis based on CGIC score ≤2 response criterion.
CGIC, Clinical Global Impression of Change; DTBZ, deutetrabenazine; QALY, quality-adjusted life year; VBZ, valbenazine.

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Cost-Effectiveness Analysis: Summary of Figures

- Base Case Results
  - Simulated patients treated with VBZ or DTBZ showed reduced TD symptoms, increased survival and QALYs, and decreased disease management costs compared with no treatment
  - Probability of response to VBZ and DTBZ at 1 year was approximately 50% greater for the CGIC measure compared with the AIMS criterion
  - Regardless of the response criterion, VBZ had higher probability of response at 1 year, more QALYs, and lower lifetime costs per the model than DTBZ
- Sensitivity Analysis
  - The results were most sensitive to the acquisition cost of VBZ 80 mg
  - VBZ continued to have higher QALYs gained and lower lifetime costs compared to DTBZ when varying most model inputs by ±20%
  - At a cost threshold of just over $200,000 per QALY, VBZ is more likely than not to be cost effective compared with no treatment
  - DBTZ is not a cost-effective option at any willingness-to-pay threshold ≤$300,000 per QALY

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Cost-Effectiveness Analysis: Summary

- In simulated patients with moderate or severe TD, treatment with VBZ and DTBZ is associated with improved clinical outcomes, increased survival, and better quality of life compared with no treatment
- Measures of global improvement may be more sensitive to improvements in quality of life than improvement in AIMS score
- Simulated patients using VBZ accrued more lifetime QALYs (+0.5 QALYs) and incurred lower lifetime costs (-$80,000) than simulated patients using DTBZ

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