COST-BENEFIT ANALYSIS OF TRILACICLIB FOR THE PREVENTION OF CHEMOTHERAPY-INDUCED MYELOSUPPRESSION IN EXTENSIVE-STAGE SMALL CELL LUNG CANCER

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INTRODUCTION

- Chemotherapy-induced myelosuppression, which may manifest as neutropenia, anemia, and/or thrombocytopenia, is a frequent complication of chemotherapy that places a burden on health care systems and is associated with reduced quality of life among patients[1]
- Small cell lung cancer (SCLC) accounts for ~13–17% of lung cancer cases diagnosed annually in the United States; of these, ~60–70% of patients have extensive-stage (ES) disease at diagnosis[2,3]
  - Patients with ES-SCLC are often older and have comorbid conditions, which may impact their tolerance of cancer treatments[4,5]
  - Chemotherapy remains a cornerstone of treatment for ES-SCLC
- Data from 3 clinical trials (G1T28-05, -02, and -03) in adult patients with ES-SCLC showed that administering trilaciclib, an intravenous myeloprotective kinase inhibitor, prior to chemotherapy reduced the incidence of multilineage myelosuppression, and reduced the need for supportive care interventions and chemotherapy dose reductions/delays[6–8]
- In February 2021, trilaciclib was approved to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide- or topotecan-containing regimen for ES-SCLC[9]
  - Trilaciclib is listed as a prophylactic option to decrease the incidence of chemotherapy-induced myelosuppression in the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hematopoietic Growth Factors and SCLC[10,11]

OBJECTIVE

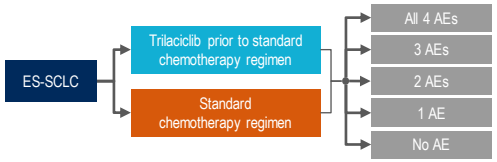
- To estimate the cost and benefit of prophylactic use of trilaciclib prior to standard chemotherapy in patients with ES-SCLC

METHODS

Model Overview

- A decision analytical model was developed to estimate the cost and benefit associated with trilaciclib from a US commercial payer perspective
- Health outcomes and related economic consequences were estimated and compared for adult patients receiving trilaciclib or placebo prior to treatment with first-line (etoposide, carboplatin, and atezolizumab) chemotherapy regimens (**Figure 1**)
- The time horizon was 12 weeks, consistent with clinical trial duration[6]
- Patients may have had 1 of 4 myelosuppressive adverse events (AEs): neutropenia, febrile neutropenia, anemia, or thrombocytopenia
  - Patients may have had ≥1 AE and/or multiple episodes of the same AE
  - AE management costs were applied to each episode and added cumulatively
- Quality-adjusted life years (QALYs) were rescaled to a monetary value at a $50,000 willingness-to-pay (WTP) threshold
- Net monetary benefit (NMB) was calculated using the following formula: NMB = (QALY improvement * WTP) – incremental cost
- Costs were expressed in 2019 $US

Figure 1. Model Schematic



AE, adverse event; ES-SCLC, extensive-stage small cell lung cancer.

Model Inputs

- Incidence rates (% of patients) and frequency (average number of AEs in patients with ≥1 AE) of grade 3/4 myelosuppressive AEs were calculated from clinical studies of trilaciclib (**Table 1**)

Table 1. Clinical Inputs Related to AEs

AE	Trilaciclib Prior to E/P/A		E/P/A	
	Patients With an Event, %[a]	Average No. of Events per Patient[b]	Patients With an Event, %[a]	Average No. of Events per Patient[b]
Neutropenia	21	1.3	60	2.5
Febrile neutropenia	2	1.0	6	1.3
Anemia	17	1.5	30	1.6
Thrombocytopenia	2	1.5	38	1.7

[a] Data on file (G1T28-05).
[b] Data on file (G1T28-05 and G1T28-02).
AE, adverse event; E/P/A, etoposide, carboplatin, atezolizumab.

- Inputs related to the use of granulocyte colony–stimulating factors (G-CSFs) and AE management costs were obtained from published literature, and drug expenses calculated from published wholesale acquisition costs (**Table 2**)[12–17]
- The wholesale acquisition cost for trilaciclib was $1,417 per 300-mg vial, or $2,834 per dose
  - The total cost of trilaciclib per course of chemotherapy was calculated by multiplying the cost per dose of trilaciclib by the number of cycles in each chemotherapy regimen, then multiplying by the number of doses required per cycle
- Utility weights for each treatment arm were estimated based on the Functional Assessment of Cancer Therapy—General (FACT-G) survey conducted in the G1T28-05 study of trilaciclib[6]
  - FACT-G scores were converted to EuroQol 5-dimension utility weights[18]

Scenario and Sensitivity Analysis

- Deterministic 1-way sensitivity analysis
  - For AE-related parameters, 2 approaches were analyzed:
    - Varying the underlying baseline AE rates or frequencies, while keeping the risk reduction associated with trilaciclib constant
    - Varying the relative risk reduction ratio associated with trilaciclib, while keeping the baseline AE rates and frequencies constant
  - Utility weights and AE management costs were analyzed by applying a 10% change to base case estimates

Table 2. Economic and Utility Inputs

Model Input	Base Case Estimate
Inputs related to G-CSF use[12–14]	
Prophylactic G-CSF use without trilaciclib, %	26[a]
Reduction in prophylactic G-CSF use with trilaciclib, %	50
Average G-CSF cost (including administration) per cycle, $US	5,455
Average no. of prophylactic G-CSF cycles, n	3.41
AE management cost, $US[15,16]	
Neutropenia	19,519
Febrile neutropenia	21,474
Anemia	23,017
Thrombocytopenia	25,786
Treatment cost, $US	
E/P/A (cost per regimen)	44,907
Trilaciclib (cost per dose)[17]	2,834
Utility inputs[6,18]	
E/P/A	0.58
Trilaciclib prior to E/P/A	0.59

[a] Based on market research, the model estimates that 26% of patients in the placebo group receive prophylactic G-CSFs.
AE, adverse event; E/P/A, etoposide, carboplatin, atezolizumab; G-CSF, granulocyte colony–stimulating factor.

- Probabilistic sensitivity analysis (PSA)
  - PSA with 1,000 simulations was performed to address multivariate uncertainty in the model
  - Normal distributions were used for AE parameters, beta distributions for utilities, and gamma distributions for costs
  - Cholesky decomposition was applied to correlated parameters[19]
- A scenario analysis was conducted to estimate the NMB for trilaciclib prior to second-line chemotherapy treatment

Model Assumptions

- Because grade 1 and 2 AEs were assumed to be of negligible impact on health and economic outcomes from the payer perspective, only grade ≥3 AEs were included in the analysis
- Given the short duration of treatment and the time horizon, the model did not discount future costs or clinical benefit
- All patients were assumed to be treated over 4 cycles, without treatment interruptions, dose adjustments, or discontinuations
- In the base case, the model assumed a 50% reduction in prophylactic G-CSF use in the trilaciclib arm[12]
- The model did not account for the use of concomitant therapies or the use of study therapies as maintenance
- The model assumed that trilaciclib therapy had no effect on the treatment response or survival of the patient

RESULTS

Base Case Results

- In the first-line setting, the prophylactic use of trilaciclib prior to chemotherapy was associated with fewer myelosuppressive AEs (0.6 vs 2.7 events per patient)
  - Among the myelosuppressive AEs considered, the largest decreases in frequency were seen with neutropenia
- Overall, the model estimated total cost savings of $15,006 per patient (**Table 3**)
- Owing to the short time horizon of the model, QALY differences were small; the model estimated an incremental QALY improvement of 0.002 in the trilaciclib arm, translating to $115 at a WTP threshold of $50,000/QALY
- With a positive NMB of $15,121, our analysis suggests that use of trilaciclib is a favorable economic strategy in the first line of therapy compared with standard care

Table 3. Base Case Results

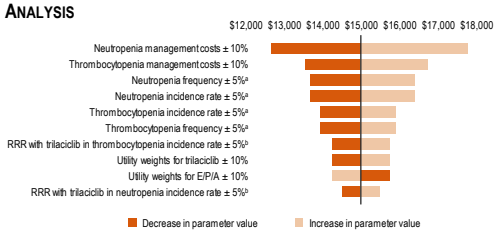
Parameter	Trilaciclib Prior to E/P/A	E/P/A	Difference
Economic outcomes, $US			
Total costs	**94,147**	**109,153**	**–15,006**
Treatment cost			
E/P/A	44,907	44,907	0
Trilaciclib	34,008	0	34,008
Prophylactic G-CSF	2,418	4,837	–2,418
AE management	12,814	59,409	–46,595
Neutropenia	5,517	29,990	–24,473
Febrile neutropenia	408	1,632	–1,224
Anemia	6,154	10,880	–4,726
Thrombocytopenia	735	16,907	–16,172
Clinical outcomes and QoL			
Total AEs, n	**0.6**	**2.7**	**–2.1**
Neutropenia	0.3	1.5	–1.3
Febrile neutropenia	0.0	0.1	–0.1
Anemia	0.3	0.5	–0.2
Thrombocytopenia	0.0	0.7	–0.6
QALYs	0.136	0.133	0.002
NMB, $US	**15,121**		

Red, cost adding; orange, cost neutral; green, cost saving.
AE, adverse event; E/P/A, etoposide, carboplatin, atezolizumab; G-CSF, granulocyte colony–stimulating factor; NMB, net monetary benefit; QALYs, quality-adjusted life years; QoL, quality of life.

Scenario and Sensitivity Analysis

- Trilaciclib led to economic benefit in all deterministic sensitivity analysis scenarios
  - NMB ranged from $12,673 to $17,568 at the $50,000 WTP threshold (**Figure 2**)

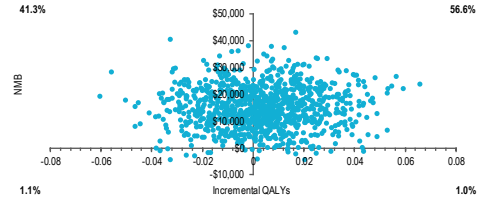
Figure 2. Tornado Diagram of Deterministic Sensitivity Analysis



[a] Varying underlying baseline AE event rate (incidence rate: patients with an AE, %; frequency: average AEs per patient, n).
[b] Varying the RRR of trilaciclib versus placebo.
AE, adverse event; E/P/A, etoposide, carboplatin, atezolizumab; RRR, relative risk reduction.

- On average, PSA results showed a positive NMB of $15,169 and a standard deviation of $7,774 when trilaciclib was used prior to first-line therapy (**Figure 3**)
  - NMB was positive for 98% of the sensitivity analysis iterations

Figure 3. PSA Results: NMB Scatter Plot



NMB, net monetary benefit; PSA, probabilistic sensitivity analysis; QALYs, quality-adjusted life years.

- Results were consistent (NMB ranged from $12,702 to $17,539) when the reduction in prophylactic G-CSF use related to trilaciclib ranged from 0 to 100%
- Trilaciclib use in second line yielded an uncertain mean NMB of –$8,159 (± $19,763 standard deviation); NMB was positive for 32% of the sensitivity analysis iterations
  - This may reflect the extrapolation of clinical outcomes from a combined phase 2a and 2b study of patients assigned to 2 different doses of topotecan[8]

CONCLUSIONS

- The prophylactic use of trilaciclib prior to first-line chemotherapy was cost-beneficial, owing to fewer myelosuppressive AEs, lower costs, and improved QALYs
- Economically, trilaciclib is a favorably valued innovation for reducing the incidence of myelosuppression in patients with ES-SCLC receiving a platinum/etoposide-containing chemotherapy regimen

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