CADTH | pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review
Final Economic Guidance Report

Dabrafenib (Tafinlar) Trametinib (Mekinist) for Non-Small Cell Lung Cancer

November 2, 2017

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INQUIRIES

Inquiries and correspondence about the pan-Canadian Oncology Drug Review (pCODR) should be directed to:

pan-Canadian Oncology Drug Review
154 University Avenue, Suite 300
Toronto, ON
M5H 3Y9

Telephone: 613-226-2553
Toll Free: 1-866-988-1444
Fax: 1-866-662-1778
Email: info@pcodr.ca
Website: www.cadth.ca/pcodr

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1 ECONOMIC GUIDANCE IN BRIEF

1.1 Submitted Economic Evaluation

The economic analysis **submitted to pCODR by Novartis Pharmaceuticals** compared dabrafenib (Tafinlar) plus trametinib (Mekinist), to each of the following treatment regimens – docetaxel, erlotinib, pemetrexed, nivolumab, pembrolizumab or best supportive care -- for patients with BRAF V600 mutant positive non-small cell lung cancer (NSCLC) who have been previously treated with chemotherapy. Patients were confirmed to be BRAF V600 mutant positive prior to initiation of treatment.

Table 1. Submitted Economic Model

Funding Request/Patient Population Modelled	*The funding request is the treatment of adult patients with advanced BRAF V600E mutation positive NSCLC who have been previously treated with chemotherapy.*
Type of Analysis	*CUA & CEA*
Type of Model	*Partitioned-survival*
Comparator[&]	*Docetaxel* *Erlotinib* *Pemetrexed* *Best supportive* *Nivolumab* *Pembrolizumab*
Year of costs	*2016*
Time Horizon	*5 years, cycle length of 1 month*
Perspective	*Government*
Dabrafenib	*Dabrafenib costs $65.23 per 75mg capsule.* • *At the recommended dose on 150mg twice daily, dabrafenib costs:* o *$260.93 per day* o *$7306.10 per 28 day course*
Trametinib	*Trametinib costs $298.70 per 2mg tablet.* • *At the recommended dose on 2mg once daily, trametinib costs:* o *$298.70 per day* o *$8363.60 per 28 day course*
Cost of nivolumab	*Nivolumab costs $782.22 per 40mg vial or $1,955.56 per 100mg vial.* • *At the recommended dose of 3 mg/kg of body weight every 2 weeks, nivolumab costs* o *$335.24 per day* o *$9386.68 per 28-day course*
Cost of pembrolizumab	Pembrolizumab costs $44.00 per mg. • At the recommended dose of 2 mg/kg every three weeks, pembrolizumab costs o $294.18 per day o $8,237 per 28-day
Cost of docetaxel*	*Docetaxel costs $11.42 per mg. (Cost is for both generic and brand name docetaxel)* • *At the recommended dose 75 mg/per m^2 every 3 weeks, docetaxel costs* o *$69.36 per day* o *$1,942.00 per 28-day cycle*

Cost of pemetrexed*	*Brand Name pemetrexed costs $5.50 per mg.* • *At the recommended dose 500mg/m^2 every 3 weeks, pemetrexed costs* o *$222.62 per day* o *$6,233.33 per 28-day cycle* *Generic pemetrexed costs $0.83 per mg.* • *At the recommended dose 500mg/m^2 every 3 weeks, pemetrexed costs* o *$33.67 per day* o *$942.66 per 28-day cycle*
Model Structure	*A partitioned survival model was developed with three mutually exclusive health states: i) stable disease (SD); ii) progressive disease (PD); and iii) death. All patients start in stable disease despite having progressed on prior treatment. Proportion of patients in the PD state calculated as the difference between proportion of patients who were alive and the proportion of patients who remained in SD.*
Key Data Sources	*Dabrafenib + trametinib: Single-arm trial data, BRF113928* *Docetaxel: JMEI trial* *Erlotinib: BR.21 trial* *Pemetrexed: JMEI trial* *Nivolumab: Checkmate 057* *Pembrolizumab: KEYNOTE 010* *Best supportive care: TAX 317 trial*

[&]The Clinical Guidance Panel (CGP) confirmed that BSC and erlotinib are not relevant comparators and are therefore not presented in the results.

** Drug costs for all comparators in this table are based on costing information under license from IMS Health Canada Inc. concerning the following information service(s): DeltaPA. and may be different from those used by the submitter in the economic model. The analyses, conclusions, opinions and statements expressed are those of the Canadian Agency for Drugs and Technologies in Health and not those of IMS Health Canada Inc. Quintile IMS DeltaPA– accessed on June 7, 2017*

All calculations are based on = 70kg and BSA = 1.7m^2

1.2 Clinical Considerations

According to the pCODR Clinical Guidance Panel (CGP), the comparisons to docetaxel, pemetrexed, nivolumab and pembrolizumab are appropriate. The CGP did not consider the comparison to erlotinib and best supportive care appropriate for this patient population.

- Relevant issues identified included:
  - Although the CGP agree there is a net overall benefit with the use of dabrafenib plus trametinib in patients with advanced non-small cell lung cancer (NSCLC) with a BRAF V600E mutation who have been previously treated with chemotherapy, the lack of data from randomized trials, or an appropriate control group of *BRAF* positive NSCLC patients, make it unclear what the magnitude of benefit is on overall survival and other clinically relevant outcomes for the combination treatment.
  - Indirect comparison of matched data from other trials of second-line therapy are inherently subject to bias, to make these comparisons difficult to interpret. They compare data from a highly select group of patients with a population of patients unselected for molecular characteristics. Neither old data from trials of docetaxel, or more recent data from trials of immune checkpoint inhibitors have information on BRAF mutation status to understand the expected ORR, PFS, or OS for BRAF mutated NSCLC treated with existing standard second-line therapies.
  - There are no randomized trials ongoing, or planned to compare dabrafenib and trametinib with current second-line therapies in *BRAF* mutated NSCLC.

- Based on the estimated gains in QALY's for dabrafenib plus trametinib when compared to all relevant comparators, the submitter assumes a 4 to 5 month advantage in survival compared to immunotherapies and nearly 9 months advantage compared to chemotherapies. The CGP agreed there is uncertainty in these estimates.
- Dabrafenib and trametinib would insert into the existing NSCLC treatment algorithm following first-line chemotherapy and before immune checkpoint inhibitors such as nivolumab or pembrolizumab. In most patients that would be following platinum-based chemotherapy.
- The CGP does not support generalizing the available the evidence to include patients with the BRAF V600K mutation.
- As BRAF is a relatively simple and established test it is available throughout Canada. Molecular analysis is already routinely performed on lung samples for EGFR testing therefore BRAF analysis would need to be added. With funding for the test this should not be an obstacle (as stated in the document).

Summary of registered clinician input relevant to the economic analysis

Registered clinicians considered

- There is a very small number of patients with BRAF V600E mutation positive NSCLC who could benefit from treatment with dabrafenib/trametinib. Patients who do not have the BRAF V600E mutation would be out of scope and would not be eligible for treatment with dabrafenib/trametinib.
- The current treatment for metastatic NSCLC is immunotherapy or chemotherapy (e.g. pemetrexed or docetaxel).
- Dabrafenib and trametinib are both oral agents and can be taken at home
- It is unclear whether dabrafenib/trametinib combination is superior to immunotherapy in the second-line setting in this population.
- While there is no data on the optimal sequencing of treatments, one group of clinicians would sequence the use of BRAF inhibitors after failure of platinum doublet while another group of clinicians felt that dabrafenib/trametinib would shift current treatments downstream using it as third-line or last line of therapy after platinum doublet and immunotherapy.
- BRAF mutation testing is already currently accredited in many labs across the country for use in melanoma and in Alberta for colorectal cancer. The same test can be validated and expanded for use in lung cancer as patients will need to be BRAF V600E positive to derive benefit from this combination.

The economic model considered all relevant comparators however it only allowed for the assessment of dabrafenib plus trametinib as a second line option. BRAF testing was incorporated into the model as a scenario analysis based on the cost of identifying one positive patient.

Summary of patient input relevant to the economic analysis

Patients considered quality of life impact and high symptom burden of lung cancer. The patients input reported that for the vast majority of this patient population, the current standard of care will be chemotherapy. Chemotherapy is viewed as a necessary, but feared treatment. Key treatment outcomes that respondents would most like to address are to stop or slow the progression of the disease, to reduce or eliminate side effects (e.g., reduce pain, fatigue, cough and shortness of breath, inability to fight infection, burning of skin and impact to mood), and to improve appetite and energy. Ability to have treatments at home, so it would remove the need for the patient or the caregiver to take time off of work.

The economic model considered various clinical inputs (PFS, OS, ORR). Although uncertainty remained on the robustness of the inputs. The economic model also considered health utilities

and disutilities associated with treatment related side effects. Notably these were not measured directly from the trial but used literature values that included Canadian NSCLC patients. Although the patient input indicated that chemotherapy was the treatment option for the vast majority of patients, the economic model also considered immunotherapies (nivolumab and pembrolizumab).

Summary of Provincial Advisory Group (PAG) input relevant to the economic analysis
PAG considered the following factors (enablers or barriers) important to consider if implementing a funding recommendation for dabrafenib plus trametinib which are relevant to the economic analysis:

Clinical factors:

- Place in therapy of dabrafenib/trametinib and sequencing with currently available publicly funded treatments for NSCLC
- Comparison with other treatments, both chemotherapies and immunotherapies
- BRAF testing not currently routinely done for NSCLC.

Economic factors:

- High cost of combination therapy.
- Cost of BRAF testing for all patients with NSCLC who have failed first-line platinum therapy to identify the 1-2% with BRAF mutation (the number of patients to be tested and the number of patients with BRAF mutation).

1.3 Submitted and EGP Reanalysis Estimates

Table 2. Submitted and EGP Estimates

Dabrafenib plus Trametinib versus Nivolumab			
Estimates (range/point)	**Submitted**	**EGP Reanalysis Lower bound**	**EGP Reanalysis Upper bound**
ΔE (LY)	0.51	0.54	N/C
Stable	0.61	0.63	
Progressive	-0.10	-0.10	
ΔE (QALY)	0.40	0.43	N/C
Stable	0.47	0.48	
Progressive	-0.06	-0.06	
ΔC ($)	$131,285	$175,267	
ICER estimate ($/QALY)	$324,269	$411,604	
Dabrafenib plus Trametinib versus Pembrolizumab			
ΔE (LY)	0.42	0.45	N/C
Stable	0.69	0.73	
Progressive	-0.27	-0.27	
ΔE (QALY)	0.37	0.39	N/C
Stable	0.53	0.56	
Progressive	-0.16	-0.16	
ΔC ($)	$140,654	$187,620	N/C
ICER estimate ($/QALY)	$379,402	$476,951	
Dabrafenib plus Trametinib versus Pemetrexed			
ΔE (LY)	0.99	1.07	N/C
Stable	0.77	0.81	
Progressive	0.22	0.26	

Dabrafenib plus Trametinib versus Nivolumab			
Estimates (range/point)	**Submitted**	**EGP Reanalysis Lower bound**	**EGP Reanalysis Upper bound**
ΔE (QALY)	0.72	0.77	N/C
Stable	0.59	0.62	
Progressive	0.13	0.16	
ΔC ($)	$160,496	$235,640	N/C
ICER estimate ($/QALY)	$222,716	$304,214	
Dabrafenib plus Trametinib versus Docetaxel			
ΔE (LY)	0.99	1.06	N/C
Stable	0.76	0.80	
Progressive	0.23	0.27	
ΔE (QALY)	0.71	0.77	N/C
Stable	0.58	0.61	
Progressive	0.13	0.16	
ΔC ($)	$181,249	$231,929	N/C
ICER estimate ($/QALY)	$253,767	$302,153	

The main assumptions and limitations with the submitted economic evaluation were:

- There is no direct comparative effectiveness data. The submitter generated comparative effectiveness data through a matched-adjusted indirect comparison fractional polynomial network meta-analysis using trials in previously treated NSCLC patients and linking the dabrafenib plus trametinib trial to the CheckMate 057 trial via docetaxel (Please see Section 7 of the Clinical Guidance Report for further details on this methodology). Several limitations were identified with the indirect comparison, most notably related to the comparison of selected (BRAF V600E in BRF113928) and unselected patients in the all other data for comparators. The CGP has identified that not matching on BRAF mutation status is a significant limitation and introduces severe bias in the results. In the absence of more robust alternative sources of data, the EGP used the results of this analysis.
- In the absence of robust direct or indirect evidence, the CGP and EGP were unable to explore uncertainty in the magnitude of benefit with dabrafenib plus trametinib. Based on the estimates of effectiveness reported in the submitter base case, dabrafenib plus trametinib indicates a 4 to 8 month advantage compared to immunotherapies and chemotherapies, respectively (see submitted results tables). The CGP agree these estimates are uncertain. The EGP was unable to account for this uncertainty as there were no alternative sources of data to use.
- Given the absence of quality of life data from within the trial, literature values were used and were then adjusted for response rate. Based on input from the CGP, in general, immunotherapies would have much less serious toxicity than docetaxel and most likely, less toxicity than dabrafenib plus trametinib. Though this toxicity was not captured through quality of life estimates used in the model, disutilities were incorporated into the model. The disutilities captured the CGP input that dabrafenib plus trametinib has higher toxicity than other agents. One way sensitivity analysis using unadjusted utility values did not have a big impact on the ICER for the comparisons being made to chemotherapy. There was however more of an impact on the comparisons to nivolumab and pembrolizumab.
- The economic model did not include subsequent treatments for the comparison to chemotherapies (docetaxel and pemetrexed) as the submitter explained that subsequent therapies were modeled only where data was available. The exclusion of subsequent therapies for docetaxel and pemetrexed is a conservative estimate, as including these costs for the comparator would decrease the incremental cost, lowering the incremental cost with dabrafenib plus trametinib.

- The submitter used the cost of brand name pemetrexed in the analysis with this agent. Given that generic pemetrexed is available, the EGP used this cost in their re-analysis.

1.4 Detailed Highlights of the EGP Reanalysis

The EGP made the following changes to the submitted economic model:

A. Dabrafenib in combination with trametinib vs nivolumab

Overall the ICER is difficult to estimate because: of uncertainty in survival benefit. Therefore, the EGP has a lower bound of $411,604 and no upper bound.

The EGP made the following changes to the economic model:

- Discount rate of 1.5%: In order to align with the recent CADTH guidelines, a 1.5% discount rate was applied to both costs and effects.
- Treatment until discontinuation: Though the Health Canada product monograph of dabrafenib in combination with trametinib indicates treating until progression, the CGP and the data from the BRF113928 trial indicate that patients may be treated with dabrafenib+trametinib beyond disease progression. The CGP confirmed that treatment beyond progression given this is a common, widely accepted practice for molecularly driven NSCLC.
- Inclusion of BRAF testing: There remains uncertainty how BRAF testing will be included or considered for patients with NSCLC. In order to explore the most conservative scenario, costs for testing was included.
- Based on input from the CGP, the incremental benefit modeled in the base case and used as part of the EGP's re-analysis estimates (nearly a 5 month advantage compared to nivolumab as calculated in the indirect comparison), is uncertain given the limitations in the evidence used to determine these estimates. Therefore, the ICER may be higher than what is presented in the EGP's re-analysis. Note that given the lack of certainty in the magnitude of benefit of dabrafenib plus trametinib, the EGP could not place an upper bound on its best case reanalysis.

Table 3. EGP Reanalysis Estimates for dabrafenib + trametinib vs nivolumab

Description of Reanalysis	ΔC	ΔE QALYs	ICUR (QALY)	Δ from baseline submitted ICER
Submitted base case	$131,285	0.40	$324,269	-----
EGP's Reanalysis for the Best Case Estimate				
LOWER BOUND				
Discount rate 1.5% - both costs and effects	$136,259	0.43	$319,994	-$4,275
Treatment until discontinuation	$176,561	0.40	$436,097	$111,828
Inclusion of BRAF testing	$146,769	0.40	$362,513	$38,244
Best case estimate of above parameters	$175,267	0.43	$411,604	$87,335
UPPER BOUND				
Best case estimate of all above parameters			Uncertain	

B. Dabrafenib in combination with trametinib vs pembrolizumab

Overall the ICER is difficult to estimate because: of uncertainty in survival benefit. Therefore, the EGP has a lower bound of $476,951 and no upper bound.

The EGP made the following changes to the economic model:

- Discount rate of 1.5%: In order to align with the recent CADTH guidelines, a 1.5% discount rate was applied to both costs and effects.
- Treatment until discontinuation: Though the Health Canada product monograph of dabrafenib in combination with trametinib indicates treating until progression, the CGP and the data from the BRF113928 trial indicate that patients may be treated with dabrafenib+trametinib beyond disease progression. The CGP confirmed that treatment beyond progression given this is a common, widely accepted practice for molecularly driven NSCLC
- Inclusion of BRAF testing: There remains uncertainty how BRAF testing will be included or considered for patients with NSCLC. In order to explore the most conservative scenario, costs for testing was included.
- Inclusion of PD-L1 testing: Given that pembrolizumab is conditional to a test, the cost of this test was included as a conservative scenario, in line with the inclusion of BRAF testing.
- Based on input from the CGP, the incremental benefit modeled in the base case and used as part of the EGP's re-analysis estimates (nearly a 5 month advantage compared to nivolumab as calculated in the indirect comparison), is uncertain given the limitations in the evidence used to determine these estimates. Therefore, the ICER may be higher than what is presented in the EGP's re-analysis. Note that given the lack of certainty in the magnitude of benefit of dabrafenib plus trametinib compared with pembrolizumab, the EGP could not place an upper bound on its best case reanalysis.

Table 4. EGP Reanalysis Estimates for dabrafenib + trametinib vs pembrolizumab

Description of Reanalysis	ΔC	ΔE QALYs	ICUR (QALY)	Δ from baseline submitted ICER
Submitted base case	$140,654	0.37	$379,402	-----
EGP's Reanalysis for the Best Case Estimate				
LOWER BOUND				
Discount rate 1.5% - both costs and effects	$146,673	0.39	$372,858	-$6,544
Treatment until discontinuation	$166,340	0.37	$448,689	$69,287
Inclusion of BRAF testing	$156,137	0.37	$421,167	$41,765
Inclusion of PD-L1 testing	$138,542	0.37	$373,705	-$5,697
Best case estimate of above parameters	$187,620	0.39	$476,951	$97,549
UPPER BOUND				
Best case estimate of all above parameters			Uncertain	

C. Dabrafenib in combination with trametinib vs pemetrexed

Overall the ICER is difficult to estimate because: of uncertainty in the survival benefit. Therefore the EGP has a lower bound of $273,138 and no upper bound.

The EGP made the following changes to the economic model:

- Discount rate of 1.5%: In order to align with the recent CADTH guidelines, a 1.5% discount rate was applied to both costs and effects.
- Treatment until discontinuation: Though the Health Canada product monograph of dabrafenib in combination with trametinib indicates treating until progression, the CGP and the data from the BRF113928 trial indicate that patients may be treated with dabrafenib+trametinib beyond disease progression. The CGP confirmed that treatment beyond progression given this is a common, widely accepted practice for molecularly driven NSCLC
- Inclusion of BRAF testing: There remains uncertainty how BRAF testing will be included or considered for patients with NSCLC. In order to explore the most conservative scenario, costs for testing was included.
- Generic pricing of pemetrexed as this is what is available and used across Canada.
- Based on input from the CGP, the incremental benefit modeled in the base case and used as part of the EGP's re-analysis estimates (nearly a 5 month advantage compared to nivolumab as calculated in the indirect comparison), is uncertain given the limitations in the evidence used to determine these estimates. Therefore, the ICER may be higher than what is presented in the EGP's re-analysis. Note that given the lack of certainty in the magnitude of benefit of dabrafenib plus trametinib compared with pemetrexed, the EGP could not place an upper bound on its best case reanalysis.

Table 5. EGP Reanalysis Estimates for dabrafenib + trametinib vs pemetrexed

Description of Reanalysis	ΔC	ΔE QALYs	ICUR (QALY)	Δ from baseline submitted ICER
Submitted base case	$160,496	0.72	$222,716	-----
EGP's Reanalysis for the Best Case Estimate				
LOWER BOUND				
Discount rate 1.5% - both costs and effects	$167,243	0.77	$215,913	-$6,803
Treatment until discontinuation	$187,549	0.72	$260,256	$37,540
Inclusion of BRAF testing	$175,979	0.72	$244,202	$21,486
Generic pricing of pemetrexed	$185,693	0.72	$258,950	$36,234
Best case estimate of above parameters	$235,640	0.77	$304,214	$81,498
UPPER BOUND				
Best case estimate of all above parameters			Uncertain	

D. Dabrafenib in combination with trametinib vs docetaxel

Overall the ICER is difficult to estimate because: of uncertainty in survival benefit. Therefore, the EGP has a lower bound of $302,151 and no upper bound.

The EGP made the following changes to the economic model:

- Discount rate of 1.5%: In order to align with the recent CADTH guidelines, a 1.5% discount rate was applied to both costs and effects.
- Treatment until discontinuation: Though the Health Canada product monograph of dabrafenib in combination with trametinib indicates treating until progression, the CGP and the data from the BRF113928 trial indicate that patients may be treated with dabrafenib+trametinib beyond disease progression. The CGP confirmed that treatment beyond progression given this is a common, widely accepted practice for molecularly driven NSCLC
- Inclusion of BRAF testing: There remains uncertainty how BRAF testing will be included or considered for patients with NSCLC. In order to explore the most conservative scenario, costs for testing was included.
- Based on input from the CGP, the incremental benefit modeled in the base case and used as part of the EGP's re-analysis estimates (nearly a 5 month advantage compared to nivolumab as calculated in the indirect comparison), is uncertain given the limitations in the evidence used to determine these estimates. Therefore, the ICER may be higher than what is presented in the EGP's re-analysis. Note that given the lack of certainty in the magnitude of benefit of dabrafenib plus trametinib compared with docetaxel, the EGP could not place an upper bound on its best case reanalysis.

Table 6. EGP Reanalysis Estimates for dabrafenib + trametinib vs docetaxel

Description of Reanalysis	ΔC	ΔE QALYs	ICUR (QALY)	Δ from baseline submitted ICER
Submitted base case	$181,249	0.71	$253,767	-----
EGP's Reanalysis for the Best Case Estimate				
LOWER BOUND				
Discount rate 1.5% - both costs and effects	$188,221	0.77	$245,211	-$8,556
Treatment until discontinuation	$207,687	0.71	$290,783	$37,016
Inclusion of BRAF testing	$196,732	0.71	$275,445	$21,678
Best case estimate of above parameters	$231,929	0.77	$302,153	$48,386
UPPER BOUND				
Best case estimate of all above parameters			Uncertain	

1.5 Evaluation of Submitted Budget Impact Analysis

Key limitations of the BIA model include not include the administration costs of the included drugs. These parameters were not able to be modified and explored by the EGP. Although dabrafenib plus trametinib is a fully oral therapy, administration costs would factor in for the comparators which are administered IV. Given that the BIA included all patients with BRAF V600, while the CGP concluded that this treatment should only be used in patients with BRAF V600E mutation, the results provided are overestimated.

Though not a limitation, the assumption of market share for docetaxel was found to be high by the CGP. This however leads to a conservative estimate in the BIA.

1.6 Conclusions

The EGP's best estimate of ΔC and ΔE for dabrafenib in combination with trametinib when compared to a selection of comparators is summarized in the below table. The EGP cautions that there is considerable uncertainty in the clinical effect estimates used to derive the ICER's. Although the CGP agreed there is a net clinical benefit with dabrafenib plus trametinib compared to all relevant comparators, there was no robust direct or indirect data available to guide the EGP on what the magnitude of this benefit may be. In the absence of alternative data, the EGP was unable to fully explore the uncertainty in the clinical effect estimates.

Comparator	ΔC	ΔE QALYs	Lower Estimate ICUR (QALY)	Upper ICUR (QALY) Estimate
Nivolumab	$175,267	0.43	$411,604	Not calculable
Pembrolizumab	$187,620	0.39	$476,951	
Pemetrexed	$235,640	0.77	$304,214	
Docetaxel	$231,929	0.77	$302,153	

- It is difficult to estimate the ICER due to uncertainty in the clinical effect estimates from available trials. The main trial used to inform the data inputs was a non-randomised trial with immature survival data. Mature survival results were available during the review, however an updated model using this data was not provided to the pCODR reviewers. Comparative effectiveness evidence generated through a NMA and MAIC was prone to bias given the limitation in the comparability of patients in the BRF113928 trial and corresponding trials used to generate evidence for the appropriate comparators. Without robust direct or indirect comparative effectiveness data, the magnitude and direction of the impact of key factors of economic models, such as survival, utilities or treatment duration, are unknown.

Overall conclusions of the submitted model:

- *The submitted model is very sound and well designed. However, a well-designed model is dependent on the quality and source of the inputs.*
- *The EGP's ICERs are presented as best case scenarios with the caveat that limited evidence was available to further explore uncertainty in the magnitude of survival benefit gained with the use of dabrafenib plus trametinib.*

2 DETAILED TECHNICAL REPORT

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in Section 1. Pursuant to the *pCODR Disclosure of Information Guidelines*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations.

3 ABOUT THIS DOCUMENT

This Economic Guidance Report was prepared by the pCODR Economic Guidance Panel and supported by the pCODR Lung Clinical Guidance Panel and the pCODR Methods Team. This document is intended to advise the pCODR Expert Review Committee (pERC) regarding resource implications and the cost-effectiveness off dabrafenib plus trametinib for BRAF V600 mutation positive NSCLC.A full assessment of the clinical evidence of [drug name and indication] is beyond the scope of this report and is addressed by the relevant pCODR Clinical Guidance Report. Details of the pCODR review process can be found on the pCODR website (www.cadth.ca/pcodr).

pCODR considers it essential that pERC recommendations be based on information that can be publicly disclosed. Information included in the Economic Guidance Report was handled in accordance with the *pCODR Disclosure of Information Guidelines*. There was no non-disclosable information in the Economic Guidance Report provided to pERC for their deliberations.

This Final Economic Guidance Report is publicly posted at the same time that a pERC Final Recommendation is issued. The Final Economic Guidance Report supersedes the Initial Economic Guidance Report. Note that no revisions were made in between posting of the Initial and Final Guidance Reports.

The Economic Guidance Panel is comprised of economists selected from a pool of panel members established by the pCODR Secretariat. The panel members were selected by the pCODR secretariat, as outlined in the pCODR Nomination/Application Information Package and the Economic Guidance Panel Terms of Reference, which are available on the pCODR website (www.cadth.ca/pcodr). Final selection of the pool of Economic Guidance Panel members was made by the pERC Chair in consultation with the pCODR Executive Director. The Economic Guidance Panel is editorially independent of the provincial and territorial Ministries of Health and the provincial cancer agencies.

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