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pan-Canadian Oncology Drug Review
Final Economic Guidance Report

Brigatinib (Alunbrig) for Non-Small Cell Lung Cancer

August 1, 2019

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1 ECONOMIC GUIDANCE IN BRIEF

1.1 Submitted Economic Evaluation

The economic analysis **submitted to pCODR by Takeda Canada Inc**. compares brigatinib with alectinib or ceritinib in adult patients with previously treated anaplastic lymphoma kinase (ALK) positive metastatic non-small cell lung cancer (NSCLC), who have progressed on or who were intolerant to an ALK inhibitor (crizotinib). In addition, a comparison was made to chemotherapy, a rarely used option.

Table 1. Submitted Economic Model

Funding Request/Patient Population Modelled	Adult patients with previously treated anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC), who have progressed on or who were intolerant to an ALK inhibitor (crizotinib). The funding request aligns with the patient population of the economic model.
Type of Analysis	Cost Utility Analysis (cost per quality adjusted life year) Cost Effectiveness Analysis (cost per life year gained)
Type of Model	Partitioned-survival model
Comparators	Brigatinib (Alunbrig) Alectinib (Alecensaro) Ceritinib (Zykadia) Pemetrexed (single-agent chemotherapy)
Year of costs	2018
Time Horizon	Lifetime (20 years)
Perspective	Government health-care payer perspective
Cost of brigatinib	180 mg tablet once daily with a 7-day lead-in at 90 mg tablet. 1 cap cost per day=$336.96 Cost per 28-day course=$9,435.00
Cost of alectinib	4-150mg capsules twice daily Cost per day=$42.17*4*2=$337.33 Cost per 28-day course=$9,445.32
Cost of ceritinib	150 mg capsule 5 times daily Cost per day=$67.47*5=337.35 Cost per 28-day course=$9,445.80
Cost of chemotherapy (drug) Additional average weekly administration cost=$30.56.	Pemetrexed: 500mg/m2 every three weeks=$165.89. Cost per day=$23.70 Cost per 28 days=$663.56
Model Structure	Model was built on the costs and QALYs for 3 health states: progression free, progressed disease, and death
Key Data Sources	*Efficacy data from different trials:*

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	Brigatinib data from non-comparative phase 2ALTA and Study 101 trial (primary endpoint was ORR, with secondary endpoints PFS and OS). *Alectinib data from phase 3 ALUR/NP28673 (primary endpoint was PFS).* *Ceritinib data from phase 1 ASCEND-1/phase 2 ASCEND-2/ phase 4 ASCEND-5 (primary endpoint was PFS).*

1.2 Clinical Considerations

Clinical Guidance Panel:

- The CGP concluded that there is a net clinical benefit to brigatinib compared with chemotherapy in the treatment of adult patients with ALK-positive locally advanced or metastatic non–small cell lung cancer (NSCLC) who have progressed on or who were intolerant to an ALK inhibitor (crizotinib).

- The CGP concluded that there may be a net clinical benefit of brigatinib compared with alectinib and ceritinib.

- The data supporting the CGP conclusions are from a non-randomized study. Hence there is no reliable estimate of the comparative efficacy or effectiveness of brigatinib to alectinib, ceritinib or chemotherapy. The CGP agreed with the Methods Team and cautioned against drawing conclusions from the ITCs on the magnitude of effect of brigatinib compared with brigatinib, ceritinib, or chemotherapy, given its substantial limitations and the absence of more robust direct evidence from a randomized trial and lack of long term outcomes such as survival and safety. However, the CGP noted that it seemed likely that in clinical practice brigatinib would compare favorable to standard chemotherapy regimens in terms of ORR, duration of PFS and toxicity.

- The comparisons in the economic model to alectinib, ceritinib and single-arm chemotherapy (pemetrexed) are appropriate. The CGP suggested that currently clinicians would prefer to give alectinib (unless there are contraindications to alectinib) due to ceritinib's substantial toxicity profile. Further, the CGP suggested that clinicians' preference is to treat with targeted options (such as ALK-inhibitors: alectinib or ceritinib) prior to considering chemotherapy. Chemotherapy is a relevant comparator in situations where ALK-inhibitors are not available (e.g., currently in the Atlantic Provinces ALK-inhibitors are not funded). Chemotherapy options may include docetaxel, platinum doublet or pemetrexed.

- The CGP noted that the submitter-provided indirect treatment comparisons (ITCs) included 're-treatment with crizotinib' as a comparator. This comparator was not included in the economic model and the CGP did not consider 're-treatment with crizotinib' an appropriate comparator as is not funded for patients with ALK-positive NSCLC who have progressed on or are intolerant to crizotinib. The CGP noted that clinicians would not retreat with crizotinib in the present setting.

- The CGP noted that the majority of patients included in the brigatinib trial (ALTA) had received platinum-based chemotherapy in addition to crizotinib. The CGP agreed, that the results of the ALTA trial are generalizable to patients without prior chemotherapy as the

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presence of the target (the ALK tyrosine kinase receptor enzyme) rather than prior treatments is most responsible for the efficacy of the therapy.

- The CGP agreed that brigatinib has a favourable toxicity profile compared to chemotherapy and ceritinib.

- The presence of pulmonary adverse events with early onset does set brigatinib apart from its comparators, however, the incidence is low and not out of keeping with pneumonitis rates seen through the course of treatment with crizotinib, ceritinib and alectinib.

- There was no evidence presented for the efficacy of brigatinib in patients who are intolerant to crizotinib. CGP acknowledged that crizotinib intolerance occurs in few cases and agreed that it would be reasonable to use brigatinib in patients who experience intolerance to crizotinib.

- The landscape of ALK inhibition is constantly evolving and the optimum sequencing of agents is currently unknown. Current front-line therapies include crizotinib and alectinib. Crizotinib is funded across Canada and provincial funding for alectinib is anticipated in the second quarter of 2019 with Alberta, Saskatchewan, and British Columbia being the first provinces to have already started funding it in the first-line. Based on the impressive PFS compared to crizotinib, alectinib is now the ALK inhibitor of choice in the first-line setting for newly diagnosed patients. Once alectinib is adopted in clinical practice in first-line across Canada, it would not be given as second-line therapy and the sequencing would not be as reflected in this economic model.

- At the discretion of the treating oncologist, brigatinib would be continued beyond radiologic progression until loss of clinical benefit. This has become the standard practice for patients with molecular drivers treated with TKIs (as for example with comparators alectinib and ceritinib). This is in line with the ALTA and Study 101 trials, where at the investigators' discretion, brigatinib could be continued beyond radiologic progression until loss of clinical benefit. Patients in the ALTA trial were treated for a median of 17.15 months, compared to a median PFS (investigator assessed) of 15.61 months. This suggests that patients are treated 1.54 months after progression. Many of these patients progress in one or a few sites that can be managed with local therapy such as radiation, or have asymptomatic progression not requiring intervention.

Registered clinician input:

- The clinicians providing input noted that for the present indication, the most relevant comparators to brigatinib would be ceritinib or alectinib (the latter depending on availability). It was also noted by clinicians from the LCC that in provinces where ceritinib is not funded, the current standard of care is platinum-based doublet therapy.

    - *The economic model included the comparators ceritinib, alectinib and single-agent chemotherapy, but not platinum doublet chemotherapy. Comparative effectiveness estimates were based on indirect comparisons methods.*

- The clinicians from both groups agreed that the eligible patient population in clinical practice aligns with the patient population in the ALTA trial. Clinicians from LCC further suggested that brigatinib would be an excellent alternative in patients who are intolerant to crizotinib.

    - *The patient population in the model aligns with the indication, which is failed or intolerant to crizotinib.*

- The clinicians felt that PFS is an appropriate surrogate outcome for overall survival (OS) in this setting, as the availability of multiple ALK TKIs after progression may confound comparative OS estimates. It was estimated that patients who would receive brigatinib in

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second-line would have a median OS of over 27 months from the time of the start of brigatinib (with a median PFS of 11 months while on prior crizotinib, based on multiple PROFILE trial data). Clinicians felt that these long median OS estimates further provide support for PFS surrogacy.

    - The *economic model was built on PFS and OS.*

- The clinicians from CCO noted that the present unmet need will be addressed once alectinib is available. This group indicated that once alectinib is available, most clinicians will chose alectinib as 1st line therapy or post progression on crizotinib.

    - *Once alectinib is adopted in clinical practice in first-line across Canada, it would not be given as second-line therapy and the sequencing would not be as reflected in his economic model.*

- The clinicians from LCC noted that patients with high levels of oxygen supplementation should consider brigatinib only after the failure of alternative treatments, and those on an ALK TKI should stop 7 days prior to initiation of brigatinib because of the greater risk of developing early onset pulmonary events. As these events typically occur within two to three days of drug initiation, starting patients at the beginning of the week is recommended, so that the greater risk period of developing an early onset pulmonary event occurs during the work week.

    - *Pulmonary events were captured as adverse events (dyspnoea, hypoxia, malignant pleural effusion, pulmonary embolism and pneumonia), which were costed as one-time events for each cycle (month) in which they occurred.*

- Need for testing: ALK testing already routinely performed on all patients.

    - *Costs for testing have not been included in the economic model.*

Patient advocacy group input:

- The symptoms and problems that patients experience as a result of lung cancer are: pain (very intense at times), shortness of breath, cough, weakness and extreme fatigue/ exhaustion. Many patients stressed that the extreme fatigue was difficult to handle and they had to plan their day around managing their exhaustion. Symptoms change frequently, which impacts daily activities, day-to-day planning, and can be challenging to manage.

    - 67 different Grade 3 adverse events were captured and the costs and quality of life impact where included in the economic model, including pain and fatigue.

- In terms of expectations for alternative treatment options it was noted that focus was placed on manageable side effects and extension of life and quality of life. The importance of new and better treatments that provide the opportunity to extend survival, give patients hope for the future, and provide time to wait for new treatment options was also highlighted.

    - *Progression-free survival, overall-survival, adverse events and quality of live were incorporated into the model.*

Provincial Advisory Group input:

PAG identified the following as factors that could impact implementation of brigatinib in the treatment of non-small cell lung cancer (NSCLC):
Clinical factors:

- Indication creep into first-line treatment.

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        - *The economic model and budget impact analyses do not include a scenario in which brigatinib is administered in first-line. This was out of scope of the present review.*

    - Comparative data to ceritinib as well as alectinib.
        - *Comparative data was generated with indirect comparison analysis methods.*

Economic factors:

- Additional costs to manage and treat adverse events.
    - *67 different Grade 3 adverse events were captured and the costs and quality of life impact where included in the economic model, including pain and fatigue.*

PAG noted that alectinib will likely become the standard first-line treatment option and is seeking guidance on the use of brigatinib following first-line treatment with alectinib.

- *The budget impact analysis included a scenario where alectinib became first-line therapy.*

As brigatinib is administered orally, PAG noted that chemotherapy units and chair time would not be required. This is an enabler to implementation. Additional pharmacy resources will be required for drug preparation, administration time, and monitoring for multiple severe adverse effects including pulmonary toxicity (i.e., interstitial lung disease) and drug-drug interactions. PAG also noted some patients may require emergency treatment for interstitial lung disease.

- *These costs are included in the economic model but the budget impact analysis only includes drug costs. The CGP noted that the development of pulmonary adverse events with early onset with brigatinib occurred in 6% of all grades and 3% of grade ≥3 in ALTA and 4% of all grades and 3% of grade 3 or 4 in the ALTA-1L trial. Predictors for this toxicity included older age and shorter interval (<7 days) between the last dose of crizotinib and first dose of brigatinib. Management included steroids but a small subset of patients who experience this toxicity required oxygen supplementation. The pulmonary toxicity was a self-limited pneumonitis like event. There is a heightened awareness of this toxicity in the lung oncology community with the recommendation to start treatment early in the week as the median time to onset was 2 days. Patients should be monitored for new or worsening respiratory symptoms particularly in the first week of treatment. Evidence of pneumonitis in any patient with worsening respiratory symptoms should be promptly investigated. If pneumonitis is suspected, brigatinib should be held and the patient evaluated for other causes of symptoms.*
    - *Pulmonary events were captured in the model as adverse events (dyspnoea, hypoxia, malignant pleural effusion, pulmonary embolism and pneumonia), which were costed as one-time events for each cycle (week) in which they occurred*

Brigatinib is an oral tablet with multiple strengths, dose adjustment is accomplished by adjusting the number of tablets to take. This is an enabler to implementation. However, PAG noted there may be a potential for drug wastage for dose adjustments from 180mg back to 90mg daily.

- *The submitted base case excluded wastage by using the drug intensity of the trials. The model allows including wastage by setting the drug intensity to 100%. 100% dose intensity is a scenario analysis in the budget impact analysis. As well, it was a sensitivity analysis (SA) around the ICURs, but it did not make the top 20 reported One-Way SA for ICURs.*

  The CGP noted that in the ALTA study the rate of dose reduction on the 180 mg arm was 20%. In the ALTA-1L study in which all patients received 180 mg dosing, the dose reduction rate was 29%. While both studies permitted inclusion of ECOG 2 patients, they comprised only 7% and 4% of the study populations, respectively. In clinical practice dose reductions are much more common given than in the real world patients often have other comorbidities and functional limitations than trial patients. The CGP felt that dose reduction may be as high as 40% when implemented in practice.

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PAG is seeking clarity on treatment until "disease progression", treatment duration and treatment discontinuation.

- *The economic analysis does address these issues in terms of their impact on the cost of brigatinib treatment. Patients in the ALTA trial were treated for a median of 17.15 months, compared to a median PFS (investigator assessed) of 15.61 months. This suggests that patients are treated 1.54 months after progression. Base case analysis included time to treatment to be until PFS. In the EGP reanalyses treatment beyond progression until clinical benefit was incorporated.*

1.3 Submitted and EGP Reanalysis Estimates

The main cost driver is the cost of the drugs, which was estimated based on a daily price and duration of treatment. Duration of treatment is based on time until disease progression in the base case. Given that brigatinib has a longer time until disease progression based on mean progression free survival (PFS) time, the cost of drugs for brigatinib is higher despite the comparators brigatinib, alectinib and ceritinib having nearly identical daily costs. Differences in costs between comparators based on health states and adverse events have much less impact.

Differences between the comparators for effectiveness (QALYs) was based on longer time before disease progression and a longer overall survival after disease progression for brigatinib. The duration of time in the progressed health state was sensitive to long term regression modelling of overall survival (OS), and choice of indirect analysis method which estimated relative OS from abstracting single-arm summary data from studies evaluating comparator therapies. After updating OS for alectinib with a recent publication, choosing a less optimistic long term regression model for OS for brigatinib, and using a different indirect analysis method lead to reduced time in disease progressive heath state for brigatinib, decreased incremental QALYs and this reduced the ICUR.

Table 2a. **Submitted and EGP Reanalysis Estimates, Brigatinib vs alectinib** (deterministic)

Estimates (range/point)	Submitted	EGP Reanalysis Lower bound
ΔE (QALY)	2.753	0.730
Progression-free	0.602	0.631
Post-progression	2.157	0.105
Adverse event disutility	-0.006	-0.006
ΔC ($)	$103,885	$89,280
ICER estimate ($/QALY)	$37,733	$122,344

Table 2b. Submitted and EGP Reanalysis Estimates, Brigatinib versus ceritinib (deterministic)

Estimates (range/point)	Submitted	EGP Reanalysis Lower bound
ΔE (QALY)	2.688	1.437
Progression-free	0.968	1.009
Post-progression	1.726	0.434
Adverse event disutility	-0.006	-0.006
ΔC ($)	$172,769	$170,025
ICER estimate ($/QALY)	$64,285	$118,280

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Table 2c. Submitted and EGP Reanalysis Estimates, Brigatinib versus single-arm chemotherapy- **(deterministic)**

Estimates (range/point)	Submitted	EGP Reanalysis Lower bound
ΔE (QALY)	2.443	1.413
Progression-free	1.063	1.105
Post-progression	1.389	0.316
Adverse event disutility	-0.008	-0.008
ΔC ($)	$196,022	$209,833
ICER estimate ($/QALY)	$80,224	$148,460

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

No evidence from direct randomized trial data between comparators was available. Indirect analysis including short term single arm Phase II studies was used but assessed exhaustively. Substantial uncertainty exists because the cost-effectiveness analysis is built on indirect treatment comparisons that have serious limitations and thus lead to uncertainty in the comparative effect estimates.

No long term data was available. Long term outcomes for brigatinib relied on extrapolation using long-term survival modeling techniques. OS, PFS and time on treatment (ToT) for the comparators were estimated by digitally extracted survival curves from published journal articles.

The trials did not use generic health related quality of life scales such as EQ5D which are required to generate QALY estimates. Instead a disease specific cancer scale was mapped onto EQ5D. In addition, the effect of different adverse events was not estimated. Further, Canadian specific preferences for health states were not included.

1.4 Detailed Highlights of the EGP Reanalysis

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

[Issue 1]. The base case of the submitted economic model used the HR-OS for brigatinib versus alectinib which was based on 24 months of follow-up for brigatinib and 6.9 months of average follow-up for alectinib. A recent publication provided an update of OS for alectinib with 24 months of follow-up. This changed the mean OS for alectinib from 18.8 months to 29.1 months, which in turn changed the HR-OS brigatinib versus alectinib from 1.62 to 1.35.

[Issue 2]. There were 20 different options for the choice of indirect analysis method for OS comparing brigatinib to alectinib, with the base case using the NMA full MAIC fixed effects estimates, with all available studies for each comparator included versus the pooled brigatinib data. For the EGP reanalyses the EGP elected to use the following option for MAIC: pooled brigatinib data (ALTA plus study 101) versus ALUR (alectinib) and ASCEND-5 (ceritinib and chemotherapy) data with a MAIC full analysis. While the unanchored MAIC had its own limitation, the EGP felt that using the NMA would add additional limitations due to (1) double-counting of patients on brigatinib and (2) the fact that important covariates were not captured in all of the included studies in the MAIC comparisons. There were no statistical techniques to adjust for these limitations.

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[Issue 3]. The optimistic choice for OS survival model for brigatinib resulted in a predicted mean OS of 73 months (submitted base-case: log-logistic model), while all other OS models resulted in a mean OS of 50 months. Thus, in the EGP's reanalysis the gamma model was selected for the OS survival model for brigatinib, based on using a conservative approach to long term modelling.

[Issue 4]. The submitted model assumed in the base case that all grade 3+ adverse events with brigatinib resulted in a hospital admission, the costs of which were based on the in-patient CIHI patient cost calculator. Meanwhile, the European Medicines Agency reported that for patients in the trials treated with brigatinib, 49.7% of Grade 3+ adverse events resulted in a hospital admission[8]. Thus, the EGP's reanalysis estimated the average cost for non-major grade 3+ adverse events which were short in duration to involve a specialist consultation and follow-up visit.

[Issue 5]. The submitted excel model allowed the user to adjust the time on treatment model for brigatinib or the comparator treatments, by selecting the time on treatment regression model, which is limited by PFS or OS. While extending time on treatment until death or disease progression were available options, in the base case time on treatment was limited to PFS. The EGP selected the time on treatment to continue for 1.54 months after radiological disease progression, based on CGP opinion.

Table 3: Detailed Description of EGP Reanalysis - (probabilistic)

	ΔC	ΔE (QALYs)	ΔE (LYs)	ICUR ($/QALY)	Δ from baseline submitted ICUR
Brigatinib versus alectinib					
Base case	$101,268	2.61	3.78	$38,745	
[1] Updated alectinib OS	$91,650	1.06	1.44	$86,655	$47,910
[2] MAIC - pooled brigatinib data	$101,318	2.14	3.14	$47,280	$8,536
[3] Brigatinib OS model - gamma	$99,314	1.83	2.57	$54,406	$15,661
[4] Cost adverse events	$97,325	2.59	3.78	$37,549	-$1,196
[5] Time on Treatment	$98,331	2.59	3.78	$37,969	-$776
Best case estimate of above [1,2,3,4,5] parameters					
EGP estimate	$86,040	0.73	0.96	$117,763	$79,018
Brigatinib versus ceritinib					
Base case	$168,749	2.56	3.66	$66,010	
[1] Updated alectinib OS	No change				
[2] MAIC - pooled brigatinib data	$171,893	2.04	2.87	$84,167	$18,158
[3] Brigatinib OS model-gamma	$166,540	1.80	2.48	$92,361	$26,352
[4] Cost adverse events	$165,582	2.55	3.66	$64,951	-$1,059
[5] Time on Treatment	$169,356	2.56	3.66	$66,108	$99
Best case estimate of above [1,2,3,4,5] parameters					
EGP estimate	$169,456	1.41	1.89	$120,597	$54,588

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	ΔC	ΔE (QALYs)	ΔE (LYs)	ICUR ($/QALY)	Δ from baseline submitted ICUR
Brigatinib versus single-agent chemotherapy					
Base case	$192,820	2.20	3.31	$87,530	
[1] Updated alectinib OS	No change				
[2] MAIC - pooled brigatinib data	$196,839	1.84	2.81	$106,789	$19,260
[3] Brigatinib OS model-gamma	$190,813	1.53	2.23	$124,408	$36,878
[4] Cost adverse events	$188,095	2.17	3.31	$86,606	-$923
[5] Time on Treatment	$211,399	2.19	3.31	$96,447	$8,918
Best case estimate of above [1,2,3,4,5] parameters					
EGP estimate	$210,210	1.28	1.85	$163,603	$76,073

Note: the EGP reanalysis with [1] updated alectinib OS, [2] pooling brigatinib data, and [3] brigatinib OS model-gamma together have interaction and does not equal the sum of the individual effects.

1.5 Evaluation of Submitted Budget Impact Analysis

The factors that most influence the budget impact analysis leading to an increased budget impact are an increase in the estimated percentage of patients that are ALK+, and alectinib being available in the first-line setting, which assumes that brigatinib will replace alectinib in the second-line setting. Decrease in budget impact would occur to a lesser extent if time on treatment is decreased.

The key limitations of the budget impact analysis are the unknown parameters of the size of patient population, and overall impact on second-line treatment patterns if alectinib is used in the first-line setting.

1.6 Conclusions

The EGP's best estimate of ΔC and ΔE for brigatinib when compared to alectinib is:

- The EGP best estimate would likely be: $117,763/QALY. This estimate is the best estimate because it includes the updated 24 month follow-up estimate of overall survival for alectinib, to be similar to brigatinib follow-up duration. *The cost-effectiveness analysis is built on indirect treatment comparisons with serious limitations which lead to substantial uncertainty in the comparative effect estimates.*
- The extra cost best case estimate was $86,040. The lower relative estimate in the reanalysis was due to shorter projected relative time of survival and time on treatment.
- The extra clinical effect best case estimate was 0.73 QALYs. Similar to costs, the lower relative estimate in reanalysis was due to shorter projected relative time survival and time on treatment.

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The EGP's best estimate of ΔC and ΔE for brigatinib when compared to ceritinib is:

- The best estimate would likely be: $120,957/QALY. This estimate is the best case estimate because it includes the conservative modelling for overall survival, which decrease the projected quality of life benefit. The choice of indirect analysis method does not affect the comparison between brigatinib and ceritinib.
- The extra cost best case estimate was $169,456. The lower relative estimate in reanalysis was because it includes the conservative modelling for overall survival.
- The extra clinical effect best case estimate was 1.41 QALYs. Similar to costs, the lower relative estimate in reanalysis is due to conservative modelling for overall survival.

The EGP's best estimate of ΔC and ΔE for brigatinib when compared to single-agent chemotherapy is:

- The EGP best estimate would likely be: $163,603/QALY.
- The incremental cost best case estimate was $210,210. The increased relative estimate in the reanalysis was due to increased time on treatment.
- The extra clinical effect best case estimate was 1.28 QALYs. The lower relative estimate in reanalysis was due to shorter projected relative survival time.

Overall conclusions of the submitted model:

The submitted economic model is built on an observed increased PFS benefit for brigatinib, and this is projected to increased relative long term overall survival. *However, there are no comparative randomized control trials to compare brigatinib versus the appropriate comparators of alectinib and ceritinib, and relative efficacy is based on indirect analysis between the drugs. The submitter-provided indirect treatment comparisons have limitations which lead to substantial uncertainty in the comparative efficacy estimates.* While, varying the choice of the parametric model for PFS and time on treatment did not impact the economic results, the projection of OS varied with the choice of regression model. Thus, the best case EGP reanalysis is a conservative approach for cost-effectiveness analysis, using conservative long term survival modelling.

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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.

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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 of brigatinib (Alunbrig) for non-small cell lung cancer (NSCLC). A full assessment of the clinical evidence of brigatinib (Alunbrig) for NSCLC 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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