CADTH | pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review
Final Economic Guidance Report

Osimertinib (Tagrisso) for Non-Small Cell Lung Cancer

May 4, 2017

DISCLAIMER

Not a Substitute for Professional Advice

This report is primarily intended to help Canadian health systems leaders and policymakers make well-informed decisions and thereby improve the quality of health care services. While patients and others may use this report, they are made available for informational and educational purposes only. This report should not be used as a substitute for the application of clinical judgment in respect of the care of a particular patient or other professional judgment in any decision making process, or as a substitute for professional medical advice.

Liability

pCODR does not assume any legal liability or responsibility for the accuracy, completeness or usefulness of any information, drugs, therapies, treatments, products, processes, or services disclosed. The information is provided "as is" and you are urged to verify it for yourself and consult with medical experts before you rely on it. You shall not hold pCODR responsible for how you use any information provided in this report.

Reports generated by pCODR are composed of interpretation, analysis, and opinion on the basis of information provided by pharmaceutical manufacturers, tumour groups, and other sources. pCODR is not responsible for the use of such interpretation, analysis, and opinion. Pursuant to the foundational documents of pCODR, any findings provided by pCODR are not binding on any organizations, including funding bodies. pCODR hereby disclaims any and all liability for the use of any reports generated by pCODR (for greater certainty, "use" includes but is not limited to a decision by a funding body or other organization to follow or ignore any interpretation, analysis, or opinion provided in a pCODR report).

FUNDING

The pan-Canadian Oncology Drug Review is funded collectively by the provinces and territories, with the exception of Quebec, which does not participate in pCODR at this time.

© 2017 pCODR | PAN-CANADIAN ONCOLOGY DRUG REVIEW

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

© 2017 pCODR | PAN-CANADIAN ONCOLOGY DRUG REVIEW

TABLE OF CONTENTS

DISCLAIMER ii
FUNDING ii
INQUIRIES iii
TABLE OF CONTENTS iv
1 ECONOMIC GUIDANCE IN BRIEF 1
1.1 Submitted Economic Evaluation 1
1.2 Clinical Considerations 2
1.3 Submitted and EGP Reanalysis Estimates 4
1.4 Detailed Highlights of the EGP Reanalysis 5
1.5 Evaluation of Submitted Budget Impact Analysis 6
1.6 Conclusions 6
2 DETAILED TECHNICAL REPORT 7
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 8
REFERENCES 9

© 2017 pCODR | PAN-CANADIAN ONCOLOGY DRUG REVIEW

1 ECONOMIC GUIDANCE IN BRIEF

1.1 Submitted Economic Evaluation

The economic analysis **submitted to pCODR by Astra Zeneca Canada** compared osimertinib (Tagrisso) to doublet chemotherapy incorporating platinum for patients with locally advanced or metastatic EGFR T790M mutation-positive NCSLC.

Table 1. Submitted Economic Model

Funding Request/Patient Population Modelled	*Patients with locally advanced or metastatic EGFR T790M mutation-positive NCSLC*
Type of Analysis	*CUA*
Type of Model	*Partitioned survival*
Comparator	*Platinum doublet chemotherapy comprising pemetrexed plus cisplatin*
Year of costs	*2016*
Time Horizon	*10 years*
Perspective	*Government*
Cost of osimertinib	Osimeritinib costs $294.6764 for the 40mg or 80 mg tablet At the recommended dose of 80mg once daily, osimeritinib costs • $294.6764 per day • $8,250.94 per 28-day course
Cost of cisplatin ** Price Source: QuintilesIMS accessed [November 7, 2016]*	Cisplatin costs $2.70 per mg. At the recommended dose of 75 mg/m^2 every 21 days, cisplatin costs • $16.39 per day • $459.00 per 28-day course
Cost of pemetrexed ** Price Source: QuintilesIMS accessed [November 7, 2016]*	At the list generic price pemetrexed costs $0.8318 per mg. At the recommended dose of 500 mg/m^2 every 21 days, pemetrexed costs • $33.67 per day • $942.66 per 28-day course
Model Structure	*The model is a partitioned survival model whereby OS and PFS are extrapolated independently. Data for overall survival for osimertinib comes from a combination of Phase 1 and 2 trial data (AURAext/AURA2) and for platinum doublet chemotherapy comes from the control arm of a recent trial (IMPRESS). Data on progression free survival comes from the AURA3 randomised controlled clinical trial. The use of the partitioned survival approach requires the assumption that the probability of death for a patient is a function of time and not a function of whether they are in progression free or progression state. The model was comprised of 3 health states: pre-progression, post progression and death.*
Key Data Sources	*AURA pooled data[1,2] , IMPRESS clinical trial[3], AURA 3 clinical trial[4,5]*
**Drug costs for all comparators in this table are based on costing information under license from QuintilesIMS concerning the following information service(s): DeItaPA. 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 QuintilesIMS.*	

© 2017 pCODR | PAN-CANADIAN ONCOLOGY DRUG REVIEW

1.2 Clinical Considerations

According to the pCODR Clinical Guidance Panel (CGP), this comparison between osimeritinib and platinum doublet is appropriate

Relevant issues identified included:

- *The Clinical Guidance Panel concluded that there is a net overall clinical benefit to osimertinib in the treatment of advanced EGFR mutant lung cancer patients with acquired resistance to initial EGFR kinase inhibitor therapy and demonstration of a tumour T790M resistance mutation. This is based on prospective data from the AURA 3 study and retrospective data from the AURA dose escalation study demonstrating that patients with plasma T790M mutations do derive significant benefit from osimertinib, similar to the overall population with mutations detected by repeat tumour biopsy [5,6].*
- Overall survival data are immature and an estimated 60% of patients on the chemotherapy arm crossed over to the osimeritinib, thus making it unlikely that a survival benefit will be detected.

  Following the receipt of feedback from the submitter on the Initial Economic Guidance Report, the CGP noted the following for long term survival estimates:
  - As related to the feedback referencing a survey of clinicians who provided estimates of the anticipated long term OS with osimertinib, the CGP agreed that some patients in clinical practice have been on osimertinib for several years. The CGP considered that this is likely linked to the PFS gain as most patients in their clinical practice progress and die quickly when they come off treatment with osimertinib. The CGP further commented that updated OS data from the AURA3 trial should be provided to substantiate these estimates of post-progression survival.
  - In considering feedback received on the impact subsequent therapies are expected to have on patients' long term survival, the CGP agreed that patients gain substantial benefit from osimertinib while on treatment. Once progression occurs, clinical experience (in the absence of OS data from AURA 3) suggests that these patients do not have prolonged survival after stopping osimertinib. In particular, these patients do not benefit from immune checkpoint inhibitors based on subgroup analyses of randomized trials and a limited number go on to platinum doublet therapy in the 3rd line setting.
  - The CGP considered the submitter's assumptions related to the use of evidence from first line EGFR TKI treatment to estimate long term treatment effect in second line treatment with osimertinib. The CGP agreed that such an assumption is unsubstantiated and it is not likely that patients will have longer survival in second line treatment compared to the first. While it may be possible for patients to have 23 months survival from start of treatment, 33 months (nearly 2 years post progression), seems very optimistic.
  - The CGP agreed that the introduction of crossover in trials is a significant source of confounding. While taking this into consideration, the CGP noted that the cited 13 month benefit reported in the retrospective study using gefitinib is not fully attributable to the use of gefitinib and is overestimating the treatment related benefit. The CGP consider that other factors such as early detection of lung cancer, stage migration via PET and other technological advances have contributed to the prolonged survival seen in patients following the introduction of targeted therapies. The CGP consider that the median survival advantage with gefitinib would be somewhere between 3 and 13 months. Therefore, based on clinical experience with this population and submitted data, the CGP do not concur with the submitter's projected survival gain in the AURA 3 trial and the submitter's assumptions including the proposed "gearing" effect. The CGP believe, based on clinical experience, that 16.85 months is an overestimate of the projected survival gain, and that the true survival gain without crossover would be closer to the duration of PFS gain.

© 2017 pCODR | PAN-CANADIAN ONCOLOGY DRUG REVIEW

- *The CGP concluded the correct comparator was platinum doublet chemotherapy.*
- *Both the submitted economic model and EGP reanalysis incorporated these issues.*

Summary of registered clinician input relevant to the economic analysis
Registered clinicians considered

- Upon progression from first line EGFR TKI, about 50-60% of patients will have the emergent T790M mutation. The majority of these patients would be eligible for osimertinib.
- Osimertinib is clinically vastly superior to the current standard treatment (platinum based chemotherapy or best supportive care).
- Observed toxicity rates (diarrhea, rash) are lower than with first generation EGFR TKIs.
- Osimertinib would be sequenced as second-line therapy in patients with EGFRm+ NSCLC, after failure of first line EGFR TKI, and where a new biopsy upon first line progression has identified the T790M mutation. Platinum-doublet chemotherapy, would then become the standard third line option.
- Companion diagnostic test is required and upon progression on first line EGFR TKI, a new biopsy is required with repeat analysis for EGFR mutations, specifically the T790M mutation.
- T790M mutation testing infrastructure is already in place so repeat testing is both reasonable and realistic. Additional resources for the performance of tumour biopsy in the progression lesion(s) will also be required due to the volume of repeat EGFR mutation

Summary of patient input relevant to the economic analysis
Patients considered the following factors as important. The economic analysis incorporated patient values as survival, adverse events and quality of life.

- Reduction or elimination of disease related side effects.
- Desired treatment outcomes:
    - Stop or slow the progression of the disease, to reduce pain, fatigue, cough and shortness of breath, and to improve appetite and energy.
    - Improved independence and require less assistance from others
    - Fewer medical appointments, and lower financial cost burden (i.e. secondary costs of lung cancer and treatments).

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 osimeritinib which are relevant to the economic analysis. The EGP noted that costs for testing the T790M mutation were included in the economic analysis.

Enablers:

- Continuous once daily dosing schedule, the flat dose of 80mg or 40mg, and one tablet per dose would be enablers to implementation

Barriers:

- Lack of long-term data from phase 3 trial
- Additional biopsy would require resources and is a barrier to implementation.
- The flat pricing structure of both doses
- Potential limited accessibility of drug due to drug funding structure of oral therapies

© 2017 pCODR | PAN-CANADIAN ONCOLOGY DRUG REVIEW

Submitted and EGP Reanalysis Estimates

Table 2. Submitted and EGP Estimates

Estimates (range/point)	Submitted	EGP Reanalysis
ΔE (LY)	1.525	0.404
Progression-free	0.473	0.473
Post-progression	1.052	-0.069
ΔE (QALY)	1.171	0.356
Progression-free	0.406	0.406
Post-progression	0.765	-0.050
ΔC ($)	$91,599	$94,964
ICER estimate ($/QALY)	$78,178	$266,492

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

- At the April 15, 2016 data cut, overall survival (OS) analysis had not been conducted for the AURA3 trial as a sufficient number of events had not occurred. Additionally, 82/140 patients who had disease progression had crossed from the chemotherapy group to receive osimeritinib further confounding OS results. Therefore the model inputs used for OS were derived from pooled data of second line patients from the AURA2 and AURAext studies and the chemotherapy arm was from the IMPRESS trial. A naïve comparison was conducted to determine overall survival with the two treatments. Based on this data, the submitter assumed that osimeritinib provided a survival benefit more than three times greater than the gain in progression free survival.
- Based on the results of the naïve comparison, the base case analysis assumed that there would be continued survival benefit after treatment was stopped (i.e. survival benefit with osimeritinib). More than two thirds of the improvement in life expectancy was estimated to occur after treatment curtailment. Given the lack of evidence to support a survival benefit with osimeritinib, the CGP, agreed that such an assumption is not clinically valid. To address this the EGP, based on CGP input, assumed that the mortality rate post progression was the same for **both** treatments. This leads to slightly less life years and QALYs post progression for osimertinib due to two factors: a higher proportion (8%) of patients with osimertinib compared to platinum doublet (5%) died rather than progressed; and given the longer survival in the pre progression state with osimertinib, the time in the post progression state would be subject to a slightly greater effect of discounting.
- The CGP noted a number of concerns with assumptions and data inputs within the manufacturer's analysis. Two of these impacted the results: the choice of time horizon (use 5 years); and the cost of pemetrexed (use of generic list price). These are considered in the EGP's scenario analysis.

  Following the receipt of feedback from the submitter on the Initial Economic Guidance Report, the EGP noted the following:
  - The EGP considered feedback describing the EGP's reanalysis estimates to be clinically implausible, deviating from established statistical methods and underestimating the benefits derived from osimertinib. The EGP strongly disagrees with the manufacturer's assessment. The reanalysis was based on input from the CGP and was justified based on inappropriate assumption made by the manufacturer, mainly that survival was independent of whether the patients were progression free or not. Given that overall survival was not mature in the relevant clinical trial the approach adopted by the EGP was reasonable. Should longer term overall survival data be available, a reanalysis based on the updated data would be reasonable.
  - In considering feedback received related to the methodology used to remove post progression benefit, the EGP assumed equal probability of death post progression not equal mortality post progression. The EGP did not use the OS curve provided given that it was

© 2017 pCODR | PAN-CANADIAN ONCOLOGY DRUG REVIEW

not obtained from a RCT. Rather to replicate the median overall survival for the comparator the EGP identified the required monthly probability of death in the post progression state. Based on the PFS survival curve for osimertinib the proportion of patients at the start of the month who were in the pre progression state, the post progression state or death were modelled. For those in the post progression state the EGP then applied the probability of mortality identified above. This assumes that the probability of dying once in the post progression state was the same for both treatments i.e. independent of treatment as recommend by the CGP.

1.3 Detailed Highlights of the EGP Reanalysis

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

- To address the issue relating to the manufacturer's assumption of long term survival being unrelated to the proportion of patients who are progression free, the EGP assumed the same rate of mortality in the post progression state for both regimens based on the assumption that survival post progression would not be influenced by treatment prior to progression. Based on CGP input, the EGP were advised that this was a reasonable assumption to make.
- Naïve comparison to determine OS curves: The EGP was not able to fully address the issue related to differences in the study populations within the naïve comparison. The submitter had conducted an adjusted analysis using propensity scores. This is however based on the premise that the factors used to generate propensity scores (for the adjusted analysis) and the subsequent parametric model used to extrapolate the data were all appropriate. The reanalysis above, assuming equal post progression survival, partially addresses concerns related to possible differences within the patients populations used for the naïve comparison with respect to differences in post progressions survival.
- Time Horizon: Based on input from the CGP, it is unlikely that previously treated patients with advanced or metastatic NSCLC would have survival lasting 10 years. The CGP suggested that 5 years would be a more appropriate time horizon in this population, thus, the EGP explored the impact of this in a scenario analysis combined with equal post progression survival.
- Cost of pemetrexed. Scenario analysis used the generic list price of pemetrexed combined with equal post progression survival.
- **EGP's best case estimate:** EGP's best case estimate combined the 5 year time horizon , the generic price of pemetrexed and equal post progression survival
- Further analyses were conducted to demonstrate the sensitivity of the ICER to the cost of osimertinib. To explore this, a 25%, 50% and 75% price reduction for osimertinib were explored using the EGP reanalysis estimate.

Table 3: Detailed Description of EGP Reanalysis

	ΔC	ΔE QALYs	ΔE LYs	ICUR (QALY)	Δ from baseline submitted ICER
Baseline (Submitter's best case)	$91,559	1.171	1.525	$78,178	--
Analysis based on extrapolation beyond censoring with equal mortality post progression	$85,881	0.368	0.419	$233,616	$155,438
Equal mortality post progression + generic price of pemetrexed	$95,403	0.368	0.419	$259,518	$181,340
Equal mortality post progression + five year time horizon	$85,442	0.356	0.404	$239,771	$161,593
EGP Best case estimate:	$94,964	0.356	0.404	$266,402	$188,314

© 2017 pCODR | PAN-CANADIAN ONCOLOGY DRUG REVIEW

Equal mortality post progression + generic price of pemetrexed + five year time horizon					
EGP best case estimate + 25% reduction in cost of osimertinib	$69,970	0.356	0.404	$196,351	$118,174
EGP best case estimate + 50% reduction in cost of osimertinib	$44,975	0.356	0.404	$126,211	$48,033
EGP best case estimate + 75% reduction in cost of osimertinib	$19,981	0.356	0.404	$56,071	-$22,107

1.4 Evaluation of Submitted Budget Impact Analysis

There were three major limitations with the submitted BIA model. First, analysis included an assumption of longer duration on therapy with comparators and shorter duration on therapy with osimertinib than was assumed by the manufacturer within the economic model. Secondly, analysis did not allow for the increase in number of patients receiving treatment given that there will be some patients for which clinicians may recommend treatment with osimertinib but would not have recommended platinum doublet treatment. Finally, treatment with osimertinib does not preclude patients who progress with osimertinib subsequently receiving platinum doublet treatment - the manufacturer's budget impact analysis did not consider such a possibility. These parameters were able to be modified based on input from the CGP and their impact explored by the EGP. Based on this reanalysis the forecasted incremental cost per annum of funding osimertinib was double compared to what the manufacturer estimated.

1.5 Conclusions

The EGP's best estimate of ΔC and ΔE for osimertinib when compared to platinum doublet chemotherapy is:

- Between $233,616/QALY and $266,402/QALY
- Within this range, the best estimate would likely be the upper of the range: $266,402/QALY. However, it is unlikely that the ICER will be lower.
- The extra cost of osimertinib is $94,964. The main factors relating to the size of the cost difference is the incremental cost of osimertinib, the forecasted increase in progression free survival and the availability of generic pemetrexed at a significantly lower cost.
- The extra clinical effect of osimertinib is 0.356 QALYs. The biggest influence over this is the methods of extrapolation, the forecasted increase in post progression survival and the time horizon.

Overall conclusions of the submitted model:

- The manufacturer submitted an analysis whereby two thirds of the survival gain from osimertinib was due to an assumption of improved survival after treatment curtailment which, in the absence of evidence, was not thought to be valid. When appropriate assumptions were made the incremental cost per QALY gained increased dramatically.
- Based on revised analysis, the EGPs concluded that the best case estimate of the incremental cost per QALY gained was $266,402.

© 2017 pCODR | PAN-CANADIAN ONCOLOGY DRUG REVIEW

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.

© 2017 pCODR | PAN-CANADIAN ONCOLOGY DRUG REVIEW

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 Osimertinib (Tagrisso) for Non-small Cell Lung Cancer. A full assessment of the clinical evidence of Osimertinib (Tagrisso) for Non-small Cell Lung Cancer 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.

© 2017 pCODR | PAN-CANADIAN ONCOLOGY DRUG REVIEW

REFERENCES

1. Goss GD et al, AZD9291 in pre-treated patients with T790M positive advanced non-small cell lung cancer (NSCLC): pooled analysis from two Phase II studies. Presented at the European Cancer Congress, 25-29 September 2015. Abstract number 3113.

2. National Institutes of Health. Phase II AZD9291 Open Label Study in NSCLC After Previous EGFR TKI Therapy in EGFR and T790M Mutation Positive Tumours (AURA2). Available at: https://clinicaltrials.gov/ct2/show/NCT02094261?term=AURA2&rank=1.

3. Soria JC, Wu YL, Nakagawa K, et al. Gefitinib plus chemotherapy versus placebo plus chemotherapy in EGFR-mutation-positive non-small-cell lung cancer after progression on firstline gefitinib (IMPRESS): a phase 3 randomised trial. Lancet Oncol. Aug 2015;16(8):990-998.

4. AstraZeneca [data on file]. (2016a) AURA3 CSR (D5160C00003).

5. Mok TS, Wu YL, Ahn MJ, Garassino MC, Kim HR, Ramalingam SS, Shepherd FA et al. Osimertinib or platinum-pemetrexed in EGFR T790M-positive lung cancer. N Engl J Med. 2016 Dec 6. [Epub ahead of print]

6. Oxnard GR, Thress KS, Alden RS, Lawrance R, Paweletz CP, Cantarini M et al. Association between plasma genotyping and outcomes of treatment with osimertinib (AZD9291) in advanced non-small-cell lung cancer. J Clin Oncol. 2016 Oct 1;34(28):3375-82.

7. Nafees B, Stafford M, Gavriel S, Bhalla S, Watkins J. Health state utilities for non small cell lung cancer. Health Qual Life Outcomes. 2008 Oct 21;6:84.

8. van Hout B, Janssen MF, Feng YS, Et al. Interim scoring for the EQ-5D-5L: mapping the EQ-5D-5L to EQ-5D-3L value sets. Value Health. 2012;15(5):708-715.

9. National Institute for Health and Clinical Excellence. Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer. Technology appraisal guidance [TA347] Published date: 22 July 2015

10. National Institute for Health and Clinical Excellence. Lung cancer (non-small-cell, squamous, metastatic) - nivolumab (after chemotherapy) [ID811] In development

11. Tam VC, Ko YJ, Mittmann N, et al. Cost-effectiveness of systemic therapies for metastatic pancreatic cancer. Curr Oncol. 2013;20(2):e90-e106.

12. Walker H, Anderson M, Farahati F, al. E. Resource use and costs of end-of-Life/palliative care: Ontario adult cancer patients dying during 2002 and 2003. J Palliat Care. 2011;27(2):79-88.

13. pan-Canadian Oncology Drug Review Final Economic Guidance Report. Ceritinib (Zykadia) for Metastatic Non-Small Cell Lung Cancer. December 3, 2015. Available at: https://www.cadth.ca/sites/default/files/pcodr/pcodr_ceritinib_zykadia_nsclc_fn_egr.pdf.

14. Djalalov S, Beca J, Hoch J, et al. Cost effectiveness of EML4-ALK fusion testing and first-line crizotinib treatment for patients with advanced ALK-positive non–small-cell lung cancer. Journal of Clin Onc. 2014;32(10):1012-1019.

15. Chen W. Cost-effectiveness of epidermal growth factor receptor gene mutation testing for patients with advanced non-small cell lung cancer living in Ontario. THETA Collaborative 2010.

16. Cromwell I, van der Hoek K, Melosky B, Peacock S. Erlotinib or docetaxel for second-line treatment of non-small cell lung cancer a real-world cost-effectiveness analysis. Thorac Oncol. 2011;2097–2103:2097-2103.

© 2017 pCODR | PAN-CANADIAN ONCOLOGY DRUG REVIEW