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CADTH DRUG REIMBURSEMENT REVIEW

Pharmacoeconomic Report

APALUTAMIDE (ERLEADA)

(Janssen Inc.)

Indication: For the treatment of patients with metastatic castration-sensitive prostate cancer.

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Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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Abbreviations

AAP + ADT	abiraterone acetate plus prednisone in combination with androgen deprivation therapy
ADT	androgen deprivation therapy
AE	adverse event
APA + ADT	apalutamide in combination with androgen deprivation therapy
AUC	area under the curve
BIA	budget impact analysis
CAD	Canadian Dollars
CGP	clinical guidance panel
DOC + ADT	docetaxel in combination with androgen deprivation therapy
ECOG	Eastern Cooperative Oncology Group
FACT-P	Functional Assessment of Cancer Therapy-Prostate
ICER	incremental cost-effectiveness ratio
HR	hazard ratio
ITC	indirect treatment comparison
IV	intravenous
LHRH	luteinizing hormone-releasing hormone
mCRPC	metastatic castration-resistant prostate cancer
mCSPC	metastatic castration-sensitive prostate cancer
NICE	National Institute for Health and Care Excellence
OS	overall survival
PAG	Provincial Advisory Group
PPS	post-progression survival
QALY	quality-adjusted life year
QoL	quality of life
rPFS	radiographic progression-free survival
SMC	Scottish Medicines Consortium
USD	United States Dollar
WTP	willingness-to-pay

Executive Summary

The executive summary is comprised of two tables (Table 1: Background and Table 2: Economic) and a conclusion.

Table 1: Submitted for Review

Item	Description
Drug Product	Apalutamide (Erleada), 60 mg tablet
Submitted Price	Apalutamide, 60 mg tablet: $28.35
Indication	For the treatment of patients with metastatic castration-sensitive prostate cancer (mCSPC)
Health Canada Approval Status	NOC
Health Canada review pathway	Standard review
NOC Date	Dec 12, 2019
Reimbursement Request	As per indication
Sponsor	Janssen Inc
Submission History	Previously Reviewed: Yes Indication: For the treatment of patients with castration-resistant prostate cancer (CRPC) who have no detectable distant metastases be either computed tomography scan, magnetic resonance imaging, or technetium-99m bone scan. Recommendation date: Nov 1, 2018 Recommendation: Recommended with the condition of cost-effectiveness being improved to an acceptable level.[1]

CRPC = castration-resistant prostate cancer; NOC = Health Canada Notice of Compliance; mCSPC = metastatic castration-sensitive prostate cancer.

Table 2: Summary of Economic Evaluation

Component	Description
Type of Economic Evaluation	Cost-utility analysis Partitioned survival model
Target Population	Adult male patients with metastatic castration-sensitive prostate cancer (aligned with reimbursement request)
Treatment	Apalutamide in combination with androgen deprivation therapy (APA + ADT)
Comparators	Androgen deprivation therapy (ADT) alone Docetaxel in combination with ADT (DOC + ADT) Abiraterone acetate plus prednisone in combination with ADT (AAP + ADT)
Perspective	Canadian publicly-funded health care payer
Outcomes	QALYs, LYs
Time Horizon	20 years
Key Data Source	TITAN trial and sponsor submitted indirect treatment comparison (ITC) reporting overall survival and radiographic progression-free survival (rPFS)
Submitted Results for Base Case	• APA+ ADT pairwise ICERs are as follows: ○ APA + ADT vs. ADT: $103,998 per QALY (1.45 inc. QALYs; $150,548 inc. costs) ○ APA + ADT vs. DOC + ADT: $286,998 per QALY (0.51 inc. QALYs; $145,413 inc. costs) • Based on the sequential analyses, APA + ADT was less costly and less effective than AAP + ADT. Further, APA + ADT was extendedly dominated by DOC + ADT and AAP + ADT (i.e., not on the efficiency frontier) • The sequential ICERs are as follows: ○ DOC + ADT vs. ADT: $5,457 per QALY (0.94 inc. QALYs; $5,134 inc. costs) ○ AAP + ADT vs. DOC + ADT: $276,173 per QALY (0.62 inc. QALYs; $170,478 inc. costs)
Key Limitations	• Uncertainty exists regarding the duration of treatment effect and the long-term extrapolation of OS. The approach taken by the sponsor appeared to overestimate patient survival in the model. • The sponsor inappropriately applied treatment-dependent utilities, which should be captured by the model structure, independent of assigned treatment. • A short time horizon was utilized, however with interventions that have differential effects on mortality a lifetime time horizon is more appropriate. • Adjustment of drug costs according to dose intensity underestimated treatment costs. • Subsequent treatment sequencing was not fully captured in the model, limiting generalizability to clinical practice. • Docetaxel drug costs were overestimated as only the highest available strength was included.
CADTH Reanalysis Results	• CADTH reanalyses included: using health state utilities independent of treatment-assignment and including AE utility decrements, corrected docetaxel cost calculations, revised dose intensity, adjusting mortality to include non-cancer death, and extending the time horizon. CADTH was unable to address the application of subsequent treatment, uncertainty associated with the sponsor ITC, limitations with the TITAN trial, and the duration of treatment effect. • Based on CADTH reanalyses, APA + ADT is extendedly dominated. • Based on sequential analyses: ○ ADT is the preferred option if a decision maker's WTP is less than $939 per QALY ○ DOC + ADT is the preferred option if the WTP is between $939 and $282,082 per QALY ○ AAP + ADT is the preferred option if the WTP is more than $282,082 per QALY. • At WTP thresholds of $100,000 and $50,000 per QALY, approximate price reductions between 60% to 70% and 80%, respectively, would be required.

AAP + ADT = abiraterone acetate plus prednisone in combination with androgen deprivation therapy; ADT = androgen deprivation therapy; DOC + ADT = docetaxel in combination with androgen deprivation therapy; ICER = incremental cost-effectiveness ratio; inc. = incremental; ITC = indirect treatment comparison; LY = life year; LYG = life year gained; OS = overall survival; QALY= quality-adjusted life-year; rPFS = radiographic progression-free survival; WTP = willingness-to-pay.

Note: Extendedly dominated refers to a treatment having a higher ICER when compared to both the previous and next most effective treatment.

Conclusions

CADTH undertook reanalyses to address limitations that included removing treatment specific utilities and including AE-related utility decrements, correcting docetaxel cost calculations, revising dose intensity, adjusting mortality to account for non-cancer death, and extending the time horizon (30 years) to reflect a patient's lifetime (i.e., 100 years).

CADTH's findings were aligned with the sponsor's results. According to CADTH reanalyses, APA + ADT is extendedly dominated and did not comprise the cost effectiveness frontier. Based on the CADTH base case, ADT is the preferred treatment option if a decision maker's WTP is less than $939 per QALY; DOC + ADT is the preferred option if the WTP is between $939 to $282,082 per QALY; and, AAP + ADT is the preferred option if the WTP is more than $282,082 per QALY. Price reductions can improve the cost-effectiveness of APA + ADT in patients with mCSPC, if a decision maker's WTP is $100,000 and $50,000 per QALY, approximate price reductions between 60% to 70% and 80%, respectively, are required.

While the submitted model was reflective of the current treatment landscape for mCSPC, the model structure precluded CADTH from exploring the downstream impact of subsequent treatment and the impact of treatment effect waning.

Based on the sponsor's submitted budget impact analysis, the total incremental cost is estimated to be $[redacted] over the first 3 years. *Non-Disclosable information was used in this pCODR Guidance Report and the sponsor requested this economic information not be disclosed pursuant to the pCODR Disclosure of Information Guidelines. This information will remain redacted until notification by the sponsor that it can be publicly disclosed.* CADTH reanalyses suggest that the budget impact of introducing apalutamide to the market was underestimated in the sponsor's results and estimated to be $28,574,855 over the first 3 years in CADTH reanalyses.

Stakeholder Input Relevant to the Economic Review

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Economic Review

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 1: Cost Comparison Table

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 2: Submission Quality

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 3: Additional Information on the Submitted Economic Evaluation

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 4: Additional Details on the CADTH Reanalyses and Sensitivity Analyses of the Economic Evaluation

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 5: Submitted Budget Impact Analysis and CADTH Appraisal

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

References

1. pan-Canadian Oncology Drug Review. pCODR Expert Review Committee (pERC) Final Recommendation: Apalutamide (Erleada) for Castration-Resistant Prostate Cancer. Toronto (ON): CADTH; 2018: https://www.cadth.ca/sites/default/files/pcodr/pcodr_apalutamide_erleada_crpc_fn_rec.pdf. Accessed 2019 Nov 07.
2. pan-Canadian Oncology Drug Review sponsor submission: Erleada® (apalutamide) for metastatic castration-sensitive prostate cancer, 60mg tablets. Toronto (ON): Janssen Inc.; 2019 Oct 15.
3. Chi KN, Agarwal N, Bjartell A, et al. Apalutamide for metastatic, castration-sensitive prostate cancer. *N Engl J Med.* 2019;381(1):13-24.
4. Erleada® (apalutamide): 60 mg tablets, oral [product monograph]. Toronto (ON): Janssen Inc.; 2019 Jun 12.
5. Docetaxel ([PR]Docetaxel Injection): 20 mg/mL, 80 mg/4 mL, 160 mg/8 mL one-vial formulation, for intravenous infusion [Product Monograph]. St. Catharines (ON): Biolyse Pharma Corporation; 2016: https://pdf.hres.ca/dpd_pm/00036571.PDF. Accessed 2019 Nov 07.
6. Abirateron Acetate (Zytiga): 250 mg and 500 mg tablets, for oral use [Product Monograph]. Toronto (ON): Janssen Inc; 2019: https://www.janssen.com/canada/sites/www_janssen_com_canada/files/prod_files/live/zytiga_cpm.pdf. Accessed 2019 Nov 07.
7. Apalutamide in the Treatment of Metastatic Hormone-sensitive Prostate Cancer Network Meta-analysis (Technical Report). London (UK): Janssen Inc; 2019. Accessed 2019-10-30.
8. Gravis G, Boher JM, Joly F, et al. Androgen Deprivation Therapy (ADT) Plus Docetaxel Versus ADT Alone in Metastatic Non castrate Prostate Cancer: Impact of Metastatic Burden and Long-term Survival Analysis of the Randomized Phase 3 GETUG-AFU15 Trial. *Eur Urol.* 2016;70(2):256-262.
9. James ND, de Bono JS, Spears MR, et al. Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy. *N Engl J Med.* 2017;377(4):338-351.
10. James ND, Sydes MR, Clarke NW, et al. Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial. *Lancet.* 2016;387(10024):1163-1177.
11. Kamba T, Kamoto T, Maruo S, et al. A phase III multicenter, randomized, controlled study of combined androgen blockade with versus without zoledronic acid in prostate cancer patients with metastatic bone disease: results of the ZAPCA trial. *Int J Clin Oncol.* 2017;22(1):166-173.
12. Kyriakopoulos CE, Chen Y-H, Carducci MA, et al. Chemohormonal therapy in metastatic hormone-sensitive prostate cancer: long-term survival analysis of the randomized phase III E3805 CHAARTED trial. *J Clin Oncol.* 2018;36(11):1080-1087.
13. Mason MD, Clarke NW, James ND, et al. Adding Celecoxib With or Without Zoledronic Acid for Hormone-Naive Prostate Cancer: Long-Term Survival Results From an Adaptive, Multiarm, Multistage, Platform, Randomized Controlled Trial. *J Clin Oncol.* 2017;35(14):1530-1541.
14. Parker CC, James ND, Brawley CD, et al. Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial. *The Lancet.* 2018;392(10162):2353-2366.
15. Smith MR, Halabi S, Ryan CJ, et al. Randomized controlled trial of early zoledronic acid in men with castration-sensitive prostate cancer and bone metastases: results of CALGB 90202 (alliance). *J Clin Oncol.* 2014;32(11):1143-1150.
16. Ontario Ministry of Health and Long-Term Care. Exceptional Access Program. 2019; http://www.health.gov.on.ca/en/pro/programs/drugs/odbf/odbf_except_access.aspx. Accessed 2019 Nov 1.
17. Ontario Ministry of Health and Long-Term Care. Drug Benefit Formulary/Comparative Drug Index. 2019; https://www.formulary.health.gov.on.ca/formulary/. Accessed 2019 Nov 1.
18. pan-Canadian Oncology Drug Review. pCODR Final Economic Guidance Report: Enzalutamide for First-Line Metastatic Castration-Resistant Prostate Cancer. Toronto (ON): CADTH; 2015: https://www.cadth.ca/sites/default/files/pcodr/pcodr_enzalutamide_xtandi_1stln_mcrpc_fn_egr.pdf. Accessed 2019 Nov 08.
19. pan-Canadian Oncology Drug Review. pCODR Final Economic Guidance Report - Nivolumab (Opdivo) for Non-Small Cell Lung Cancer. Ottawa (ON): CADTH; 2016: https://www.cadth.ca/sites/default/files/pcodr/nivolumab_opdivo_nsclc_fn_egr.pdf. Accessed 2019-10-30.
20. Pollard ME, Moskowitz AJ, Diefenbach MA, Hall SJ. Cost-effectiveness analysis of treatments for metastatic castration resistant prostate cancer. *Asian J Urol.* 2017;4(1):37-43.
21. Ontario Ministry of Health and Long-Term Care. Schedule of benefits for physician services under the Health Insurance Act: effective October 1, 2019. Toronto (ON): The Ministry of Health and Long-Term Care; 2016: http://www.health.gov.on.ca/en/pro/programs/ohip/sob/. Accessed 2019 Nov 12.
22. Ontario Ministry of Health and Long-Term Care. Schedule of Benefits for Laboratory Services: Effective July 1, 2019. Toronto (ON): The Ministry of Health and Long-Term Care; 2019: http://www.health.gov.on.ca/en/pro/programs/ohip/sob/lab/lab_mn2019.pdf. Accessed 2019 Nov 12.
23. Tam VC, Ko YJ, Mittmann N, et al. Cost-effectiveness of systemic therapies for metastatic pancreatic cancer. *Curr Oncol.* 2013;20(2):e90-e106.
24. Clarke NW, Ali A, Ingleby FC, et al. Addition of docetaxel to hormonal therapy in low- and high-burden metastatic hormone sensitive prostate cancer: long-term survival results from the STAMPEDE trial. *Ann Oncol.* 2019;30(12):1992-2003.
25. Baade PD, Fritschi L, Eakin EG. Non-cancer mortality among people diagnosed with cancer (Australia). *Cancer Causes Control.* 2006;17(3):287-297.
26. Marchioni M, Di Nicola M, Primiceri G, et al. New anti-androgen compounds compared to docetaxel in metastatic hormone sensitive prostate cancer: results from a network meta-analysis. *J Urol.* 2019.
27. Sathianathen NJ, Koschel S, Thangasamy IA, et al. Indirect comparisons of efficacy between combination approaches in metastatic hormone-sensitive prostate cancer: a systematic review and network meta-analysis. *Eur Urol.* 2019.
28. Patrick-Miller LJ, Chen Y-H, Carducci MA, et al. Quality of life (QOL) analysis from CHAARTED: Chemohormonal androgen ablation randomized trial in prostate cancer (E3805). *J Clin Oncol.* 2016;34(15_suppl):5004-5004.

29. Guidelines for the Economic Evaluation of Health Technologies: Canada 4th Edition. Ottawa (ON): CADTH; 2017: https://www.cadth.ca/sites/default/files/pdf/guidelines_for_the_economic_evaluation_of_health_technologies_canada_4th_ed.pdf. Accessed 2019 Nov 22.
30. Xtandi (Enzalutamide): 40 mg capsules, for oral use [Product Monograph]. Markham (ON): Astellas Pharma Canada Inc; 2019: https://pdf.hres.ca/dpd_pm/00049227.PDF. Accessed 2019 Nov 07.
31. Sweeney CJ, Chen Y-H, Carducci M, et al. Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer. *N Engl J Med.* 2015;373(8):737-746.
32. Saad F, Aprikian A, Finelli A, et al. 2019 Canadian Urological Association (CUA)-Canadian Uro Oncology Group (CUOG) guidelines for the management of castration-resistant prostate cancer (CRPC). *Canadian Urological Association journal = Journal de l'Association des urologues du Canada.* 2019.
33. Alberta Health Services. Advanced/Metastatic Prostate Cancer Clinical Practice Guideline GU-010. Alberta Health Services; 2018: https://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-gu010-met-prostate.pdf. Accessed 2019 Nov 08.
34. Hatswell AJ, Porter J, Lee D, Hertel N, Latimer NR. The Cost of Costing Treatments Incorrectly: Errors in the Application of Drug Prices in Economic Evaluation Due to Failing to Account for the Distribution of Patient Weight. *Value Health.* 2016;19(8):1055-1058.
35. National Institute for Health and Care Excellence. Radium-223 dichloride for treating hormone-relapsed prostate cancer with bone metastases. London (UK): NICE; 2016: https://www.nice.org.uk/guidance/ta412/resources/radium223-dichloride-for-treating-hormonerelapsed-prostate-cancer-with-bone-metastases-pdf-82604599866565. Accessed 2019 Nov 13.
36. Scottish Medicines Consortium. Radium-223 dichloride 1000kBq/mL solution for injection (Xofigo®) - SMC No. (1077/15) Glasgow (UK): SMC; 2015: https://www.scottishmedicines.org.uk/media/2205/radium_223__xofigo__final_sept_2015_160915_for_website.pdf. Accessed 2019 Nov 13.
37. Organization for Economic Co-Operation and Development. Purchasing power parities (PPP). OECD; 2018: https://data.oecd.org/conversion/purchasing-power-parities-ppp.htm. Accessed 2019 Nov 22.
38. Phase 3 Randomized, Placebo-controlled, Double-blind Study of Apalutamide Plus Androgen Deprivation Therapy (ADT) Versus ADT in Subjects with Metastatic Hormone sensitive Prostate Cancer (mHSPC). *CSR 56021927PCR3002*: Janssen Inc. Accessed 2019 Oct 30.
39. Davis ID, Martin AJ, Stockler MR, et al. Enzalutamide with standard first-line therapy in metastatic prostate cancer. *N Engl J Med.* 2019;381(2):121-131.
40. Beca J, Majeed H, Chan KKW, Hotte SJ, Loblaw A, Hoch JS. Cost-effectiveness of docetaxel in high-volume hormone-sensitive metastatic prostate cancer. *Canadian Urological Association journal = Journal de l'Association des urologues du Canada.* 2019;13(12):396-403.
41. DeltaPA [Database on Internet]. Ottawa (ON): IQVIA; 2019: https://www.iqvia.com/. Accessed 2019 Nov 1
42. Tannock IF, de Wit R, Berry WR, et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. *N Engl J Med.* 2004;351(15):1502-1512.
43. Bahl A, Oudard S, Tombal B, et al. Impact of cabazitaxel on 2-year survival and palliation of tumour-related pain in men with metastatic castration-resistant prostate cancer treated in the TROPIC trial. *Annals of oncology : official journal of the European Society for Medical Oncology.* 2013;24(9):2402-2408.
44. Fizazi K, Tran N, Fein L, et al. Abiraterone plus prednisone in metastatic, castration-sensitive prostate cancer. *N Engl J Med.* 2017;377(4):352-360.
45. Ontario Case Costing Initiative (OCCI). Toronto (ON): Health and Long-Term Care; 2019: https://www.ontario.ca/data/ontario-case-costing-initiative-occi. Accessed 2019-11-12.
46. Yong JH, Beca J, McGowan T, Bremner KE, Warde P, Hoch JS. Cost-effectiveness of intensity-modulated radiotherapy in prostate cancer. *Clin Oncol (R Coll Radiol).* 2012;24(7):521-531.
47. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2017. Toronto (ON): Canadian Cancer Society; 2017: http://www.cancer.ca/~/media/cancer.ca/CW/cancer%20information/cancer%20101/Canadian%20cancer%20statistics/Canadian-Cancer-Statistics-2017-EN.pdf. Accessed 2019 Oct 30.
48. Mosillo C, Iacovelli R, Ciccarese C, et al. De novo metastatic castration sensitive prostate cancer: State of art and future perspectives. *Cancer Treat Rev.* 2018;70:67-74.
49. Buzzoni C, Auvinen A, Roobol MJ, et al. Metastatic Prostate Cancer Incidence and Prostate-specific Antigen Testing: New Insights from the European Randomized Study of Screening for Prostate Cancer. *Eur Urol.* 2015;68(5):885-890.
50. Weiner AB, Matulewicz RS, Eggener SE, Schaeffer EM. Increasing incidence of metastatic prostate cancer in the United States (2004-2013). *Prostate Cancer Prostatic Dis.* 2016;19(4):395-397.
51. Liede A, Arellano J, Hechmati G, Bennett B, Wong S. International prevalence of nonmetastatic (M0) castration-resistant prostate cancer (CRPC). *J Clin Oncol.* 2013;31(15_suppl):e16052-e16052.
52. Pascale M, Azinwi CN, Marongiu B, Pesce G, Stoffel F, Roggero E. The outcome of prostate cancer patients treated with curative intent strongly depends on survival after metastatic progression. *BMC Cancer.* 2017;17(1):651.
53. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics: A 2018 Special Report on Cancer Incidence by Stage. Toronto (ON): Canadian Cancer Society; 2018: http://www.cancer.ca/~/media/cancer.ca/CW/cancer%20information/cancer%20101/Canadian%20cancer%20statistics/Canadian-Cancer-Statistics-2018-EN.pdf?la=en. Accessed 2019 Nov 22.
54. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2019. Toronto (ON): Canadian Cancer Society; 2019: https://www.cancer.ca/~/media/cancer.ca/CW/publications/Canadian%20Cancer%20Statistics/Canadian-Cancer-Statistics-2019-EN.pdf. Accessed 2019 Nov 12.