Expected impact of new therapies for advanced NSCLC on patient survival and costs in Canada over the next 5 years: an iTEN model assessment

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Disclosures

I have received honorarium from AstraZeneca, Boehringer-Ingelheim, Bristol Myers-Squibb, Roche, Pfizer, Novartis, Takeda, Merck and Genomic health.

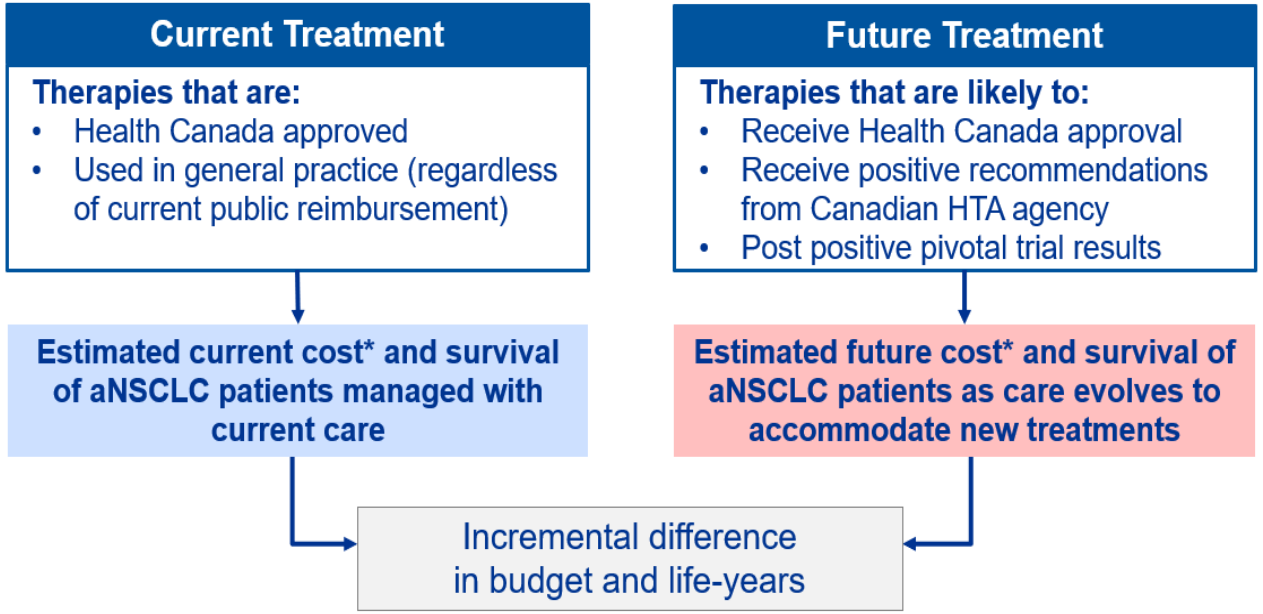
Other disclosures:

- DM, DT and DG are employees of Cornerstone Research Group.
- MH is an employee of AstraZeneca Canada.
- Cornerstone Research Group was funded by AZ Canada to develop the iTEN model.

INTRODUCTION

Background:

- The iTEN (*impact of treatment evolution in NSCLC*) model was developed to estimate the impact of a changing treatment environment for advanced non-small cell lung cancer (aNSCLC) in Canada on long-term survival and costs.



Objectives for the CADTH Conference

1. Illustrate the unique approach and abilities of the iTEN model
2. Demonstrate the ability of the iTEN model to assess the potential impact of the expansion of treatment options for Canadian patients with NSCLC
3. Provide results for a treatment scenario that may emerge in late 2019 compared to current treatment

iTEN Model Overview

Key model design elements:

- Discrete event, individual patient simulation model that has undergone extensive validation
- Simulated time until progression & death based upon PFS and OS KM data for each treatment.
- Lifetime horizon and Canadian health care system perspective

Population:

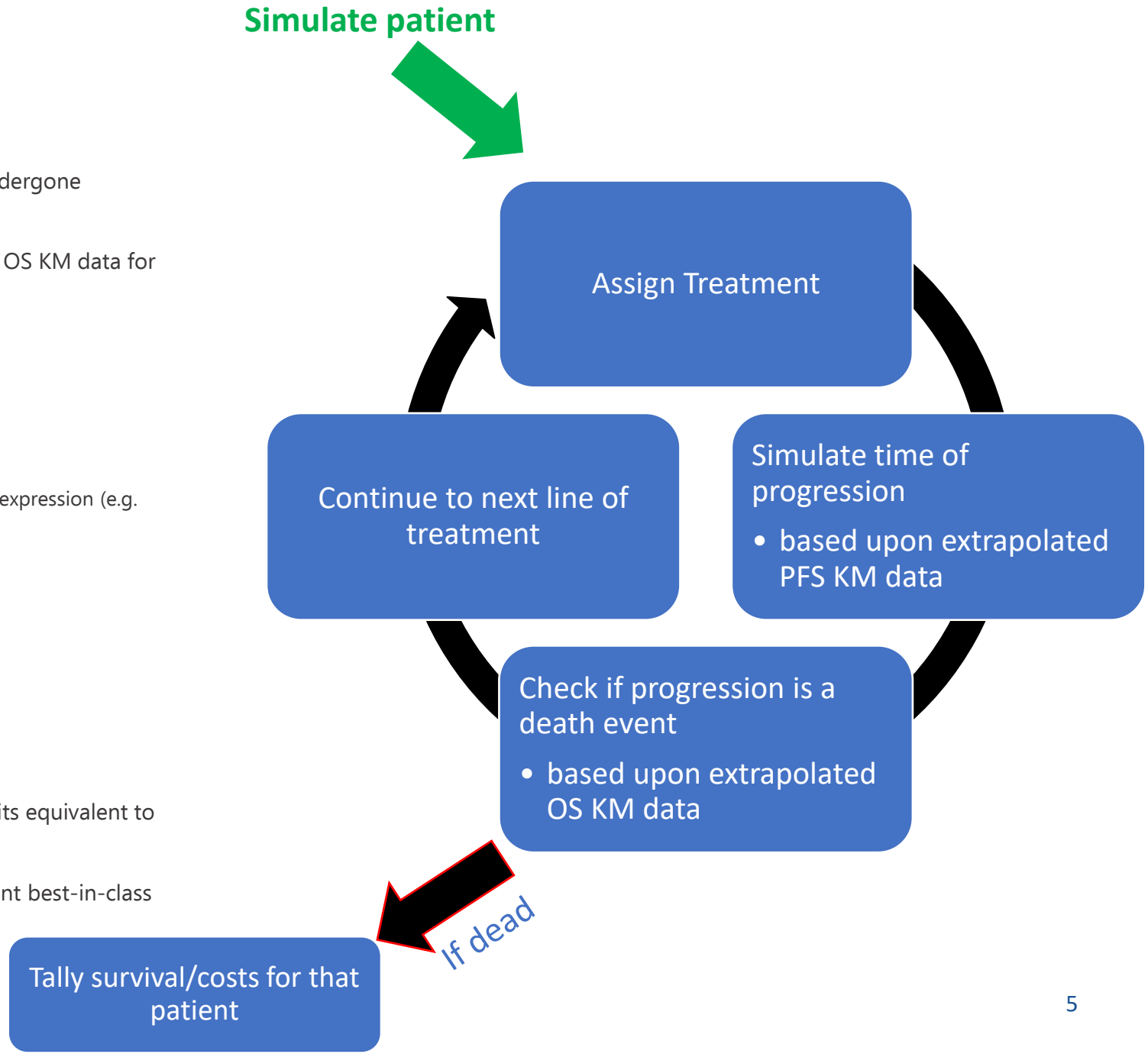
- Advanced non-squamous and squamous NSCLC.
- Considers mutation status (EGFR, ALK, ROS, BRAF, NTRK, etc.), PD-L1 expression (e.g. <1%, 1-49%, >49%), smoking status and performance status.

Data sources:

- PFS and OS KM data from pivotal trials
- List prices from Ontario formularies.

Key Assumptions for the future

- New therapies without OS data are assumed to offer OS benefits equivalent to the current best-in-class treatment.
- The cost of new therapies was assumed equivalent to the current best-in-class option.



TREATMENT of aNSCLC Patients in 2017/2018

A 2017-2018 treatment algorithm was created via a modified Delphi approach with 5 Canadian clinicians and 3 provincial payers.

'Current' Treatment

	EGFR	T790m+	ALK	BRAF	PD-L1 ≥ 50%	Non-squamous & squamous (PD-L1 < 50%)
1L	TKI (Gefitinib)		Crizotinib	Treated by PD-L1 status	Pembrolizumab monotherapy	Chemo (PD)
2L	Chemo (PD)	Osimertinib	Alectinib		Chemo (PD)	I-O (nivolumab or pembrolizumab)
3L	I-O	Chemo	Chemo (PD) with maintenance pemetrexed		BSC or docetaxel	BSC or docetaxel
4L	Docetaxel or BSC	BSC or Docetaxel	BSC		BSC or erlotinib	BSC or erlotinib

**Note, that these algorithms are representative of a plausible 2019 Canadian treatment algorithm, and not treatment in clinical trials*

Therapies Expected to Make an IMPACT in 2019

Background:

- Treatment of aNSCLC in Canada has been rapidly evolving throughout 2018, and many new treatments could reach patients by the end of 2019.

Treatment	pCODR Status
2L Atezolizumab for non-squamous and squamous	Positive recommendation with criteria
1L Osimertinib for EGFR	Positive recommendation with criteria
1L Alectinib for ALK	Positive recommendation with criteria
1L Pembrolizumab, carboplatin & paclitaxel for squamous	Under review
1L Pembrolizumab, pemetrexed and platinum chemotherapy for non-squamous	Under review
Larotrectinib for NTRK1, 2 or 3 positive tumours	Under review
2L Brigatinib for ALK	Under review
1L Dacomitinib for EGFR	Under review
1L Crizotinib for ROS	Under review
1L Atezolizumab + Chemo non-squamous and squamous	Potential 2019 submission
2L Lorlatinib (ALK)	Potential 2019 submission
2L Lorlatinib (ROS)	Potential 2019 submission
1L Brigatinib (ALK)	Potential 2019 submission
1L Dabrafenib + Trametinib (BRAF)	Potential 2019 submission
2L Entrectinib (ROS)	Potential 2019 submission
Bolded treatments are examined in this presentation	

Evolving TREATMENT of aNSCLC Patients in 2019

To illustrate the capabilities of the iTEN model, a treatment algorithm representing what care may look like at the end of 2019 was simulated.

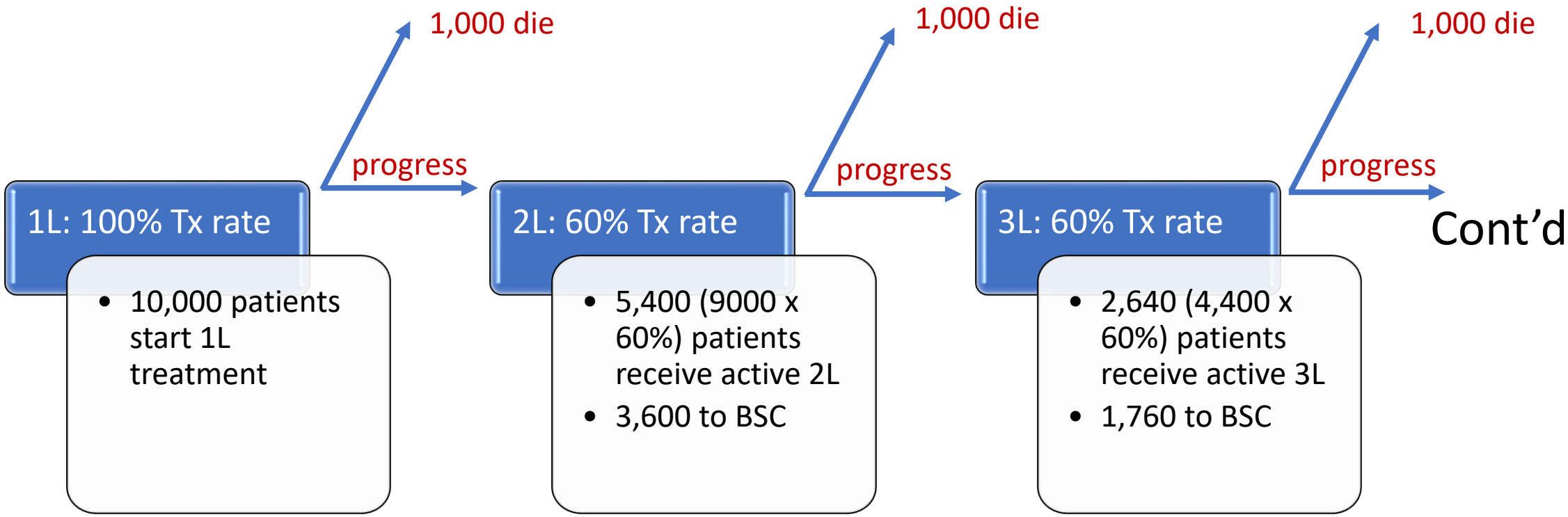
- Treatments highlighted in **green** are new additions to common Canadian aNSCLC treatment patterns.
- Treatments highlighted in ~~**red**~~ represent therapies displaced/replaced from current Canadian aNSCLC treatment patterns.

	EGFR	ALK	BRAF	PD-L1 ≥ 50%	Non-squamous & squamous (PD-L1 <50%)
1L	**Osimertinib** ~~TKI (Gefitinib)~~	**Alectinib** ~~Crizotinib~~	**Dabrafenib plus trametinib** ~~Treated by PD-L1 status~~	Pembrolizumab monotherapy	**Pembrolizumab plus chemotherapy** ~~Chemo (PD)~~
2L	Chemo (PD)	**Brigatinib** ~~Alectinib~~	• IO for those PD-L1 > 50% • PD Chx for remainder	Chemo (PD)	Docetaxel ~~I-O (nivolumab or pembrolizumab)~~
3L	I-O	Chemo (PD) with maintenance pemetrexed	Switch • Chx for those that received IO, IO for those that received Chx	Docetaxel	Erlotinib ~~Docetaxel~~
4L	Docetaxel or BSC	I-O	Docetaxel	Erlotinib/BSC	BSC ~~Erlotinib~~

**Note, that these algorithms are representative of a plausible 2019 Canadian treatment algorithm, and not treatment in clinical trials*

RESULTS

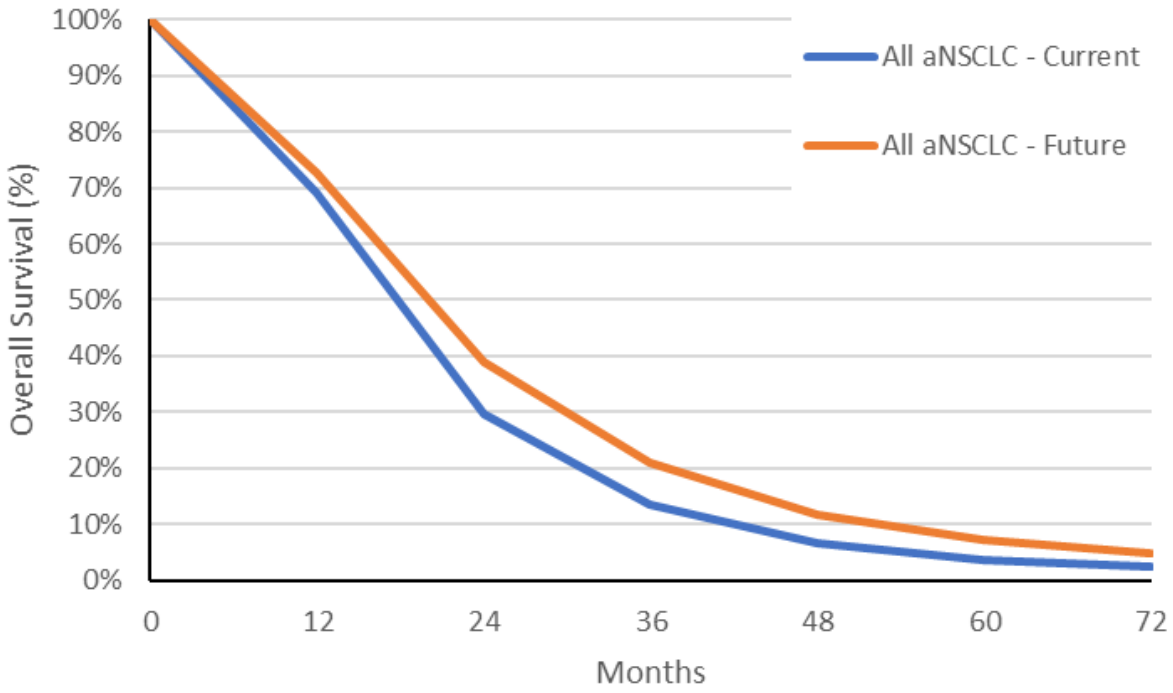
To demonstrate the capabilities of the model, the **current** and **future** algorithms were tested assuming 100% treatment rate in first-line therapy, followed by 60% active treatment rate in all subsequent lines.



Impact of CURRENT versus FUTURE Treatment on OS

- Estimated survival of the entire population (weighted average of EGFR, ALK, BRAF, and PD-L1)

100% Treatment Rate in 1L, 60% in subsequent



	3-yr OS (%, n)	5-yr OS (%, n)
Current	14%, 1,661	4%, 446
Future	36%, 2,552	7.2%, 885

n represents estimated patients alive at each time point, derived from Canadian incidence estimates.

80% increase in 5-year survival

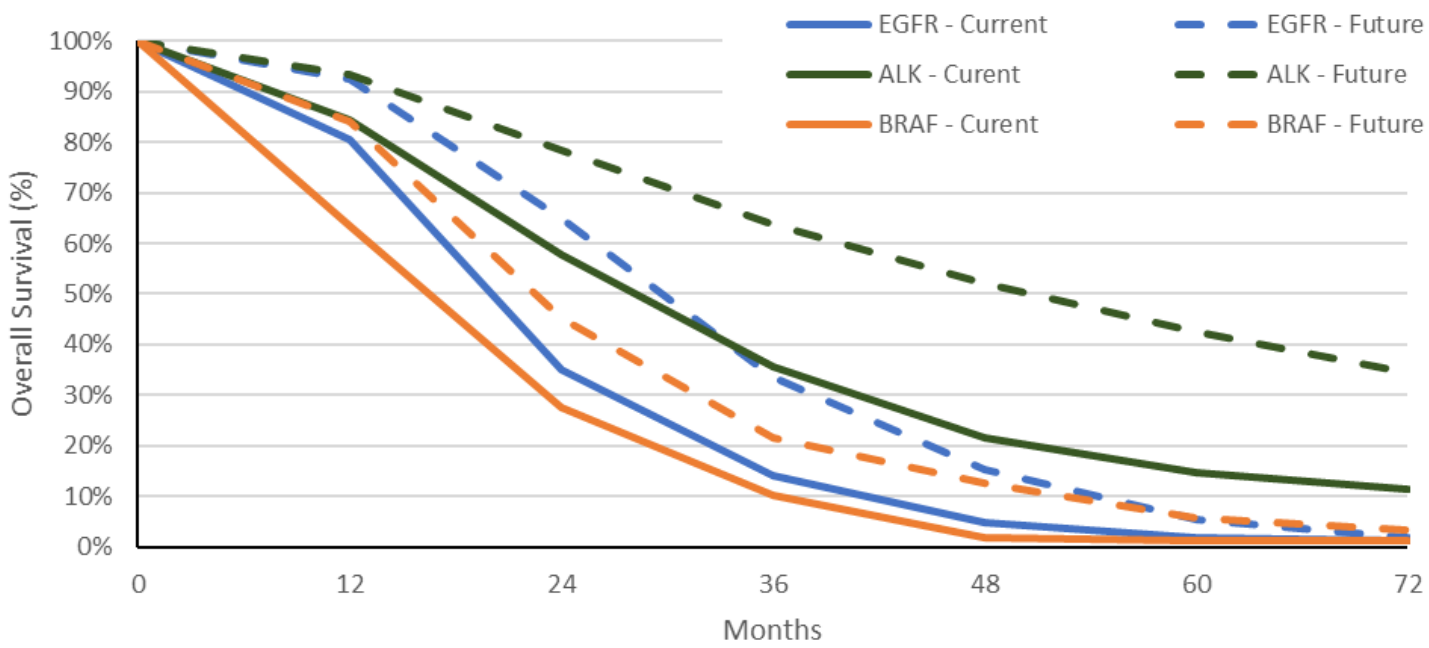
69% increase in lifetime cost per treated patient from $160K to $269K, excluding any formulary discounts.

Notes, 1) **Current** survival estimates are derived from simulating a treatment algorithm generated with a modified Delphi process that included 5 Canadian oncologists and 3 Canadian payers. 2) To derive n, both algorithms were applied to the calculated number of incident stage IV NSCLC patients in Canada (12,247), which was derived from published incidence estimates.

Impact of CURRENT versus FUTURE Treatment on OS

- Current and future overall survival estimates for *EGFR, ALK and BRAF* aNSCLC patients.

100% Treatment Rate in 1L, 60% in subsequent



	Current OS (%, n)	Future OS (%, n)	5-yr OS Benefit
EGFR	3-yr: 14%, 249 5-yr: 2%, 33	3-yr: 34%, 596 5-yr: 5%, 97	193%
ALK	3-yr: 35%, 249 5-yr: 15%, 103	3-yr: 64%, 446 5-yr: 42%, 298	189%
BRAF	3-yr: 10%, 22 5-yr: 1%, 2	3-yr: 20%, 43 5-yr: 5%, 11	400%

n represents estimated patients alive at each time point, derived from Canadian incidence estimates.

ALK

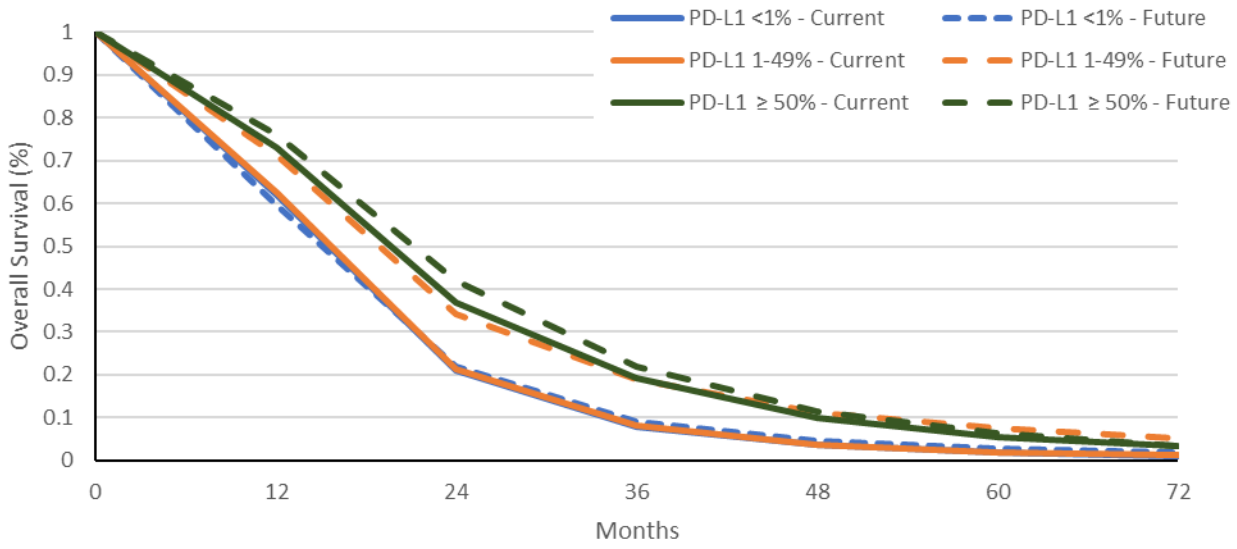
- Two new therapies nearly tripled 5-yr OS.
- Lifetime costs per treated ALK patient increased by 137% from 315K to 748K, excluding any formulary discounts.

Notes, 1) **Current** survival estimates are derived from simulating a treatment algorithm generated with a modified Delphi process that included 5 Canadian oncologists and 3 Canadian payers. 2) To derive n, both algorithms were applied to the calculated number of incident stage IV NSCLC patients in Canada (12,247), which was derived from published incidence estimates. There were an estimated **1,779** EGFR patients, **701** ALK patients and **214** BRAF patients that started treatment.

Impact of CURRENT versus FUTURE Treatment on OS

- Results present the current and future overall survival estimates for *PD-L1 >1%, 1-49% and ≥ 50%*

100% Treatment Rate in 1L, 60% in subsequent



PD-L1 expression	Current OS (%, n)	Future OS (%, n)	5-yr OS Benefit
<1%	3-yr: 8%, 356 5-yr: 2%, 83	3-yr: 9%, 413 5-yr: 3%, 131	57%
1-49%	3-yr: 8%, 153 5-yr: 2%, 36	3-yr: 19%, 356 5-yr: 7%, 141	296%
≥50%	3-yr: 19%, 573 5-yr: 6%, 167	3-yr: 22%, 650 5-yr: 6%, 190	14%

n represents estimated patients alive at each time point, derived from Canadian incidence estimates.

PD-L1 1-49%

- Introduction of Pembro+Chx increases 5-yr OS and lifetime costs per treated patient (187K to 392K, excluding any formulary discounts).

Notes, 1) **Current** survival estimates are derived from simulating a treatment algorithm generated with a modified Delphi process that included 5 Canadian oncologists and 3 Canadian payers. 2) To derive n, both algorithms were applied to the calculated number of incident stage IV NSCLC patients in Canada (12,247), which was derived from published incidence estimates. There were an estimated **4,551**, **1,882** and **2,983** patients that started treatment by their PD-L1 expression of <1%, 1-49% and ≥50%, respectively.

Why is this Model Novel?

- The discrete event structure is more flexible than traditional patient simulations or cohort models.
  - Allows examination of treatment sequencing and inclusion of patients receiving no active treatment (ie, those on best supportive care alone).
- Model can easily adjust to dramatic changes in treatment patterns.
- Model results are driven by PFS data, which are the most complete data available at therapy launch.
  - For treatments that lead to OS benefits after progression, the DES structure may underestimate long-term survival.
- Other considerations:
  - The model highlights potential treatment in Canada, and is not meant to represent subsequent care patients received in trials (ie, model estimated long-term OS may not align with reported trial OS extrapolations)
  - The model does not consider treatment beyond progression (ie, all patients switch to next-line treatment) or benefits to patients after progression.

CONCLUSIONS & LIMITATIONS

- Evolving care that could be available to Canadians by the end of 2019 is expected to increase both the survival and average per-patient treatment costs.

- The unique structure of the iTEN model allows rapid and flexible assessment of new treatments for aNSCLC patients.

- Limitation
  - Assumed that all requirements for treatment (funding, access, molecular testing) were in place at the start of simulation.

Next Steps

- Examine alternative patient sub populations
- Examine impact of treatment rates
- Examine sequential TKI therapy

Thank You

For follow-up questions on the model, please contact either:

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