Assessing the cost and survival impact of treatment evolution in advanced NSCLC: application of the iTEN model

Presenter: Daniel Moldaver, Cornerstone Research Group
Moderator: Manjusha Hurry, AstraZeneca Canada
Q&A Session to follow with: Dr. Paul Wheatley-Price & Jaya Venkatesh

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Disclosures

This project was funded by AstraZeneca Canada. Cornerstone Research Group was contracted to develop the model and complete all associated analyses/reporting.

- Daniel Moldaver is an employee of Cornerstone Research Group
- Manjusha Hurry is an employee of AstraZeneca Canada
- Jaya Venkatesh is an independent financial healthcare consultant to the Saskatchewan Cancer Agency
- Dr. Paul Wheatley-Price declares personal fees from Novartis, BMS, Merck, AZ, Takeda, Roche and Abbvie

Model description, validation and results have previously been presented at:

- SMDM, ISPOR EU, ISPOR US, CADTH, WCLC, AHESG.
- The model description and validation manuscript is currently under review for publication

Disclaimer The views and opinions expressed within this presentation are those of the authors and do not necessarily reflect the official policy or position of AstraZeneca, Cornerstone Research Group or the Saskatchewan Cancer Agency.

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  - Clinical Assistant Professor, UBC

Alberta

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  - Medical Oncologist at William Osler Health Systems
- **Dr. Bill Evans**
  - Medical Oncologist & Professor Emeritus, McMaster.
- **Dr. Paul Wheatley-Price**
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  - President of Lung Cancer Canada

Joining Us Today

Payer KEEs

British Columbia

- **Susan Walisser**
  - Retired Provincial Pharmacy Professional Practice Leader

Saskatchewan

- **Jaya Venkatesh**
  - Independent financial healthcare consultant to the Saskatchewan Cancer Agency

Joining Us Today

- **Darryl Boehm**
  - Director, Oncology Pharmacy Services, Saskatchewan Cancer Agency

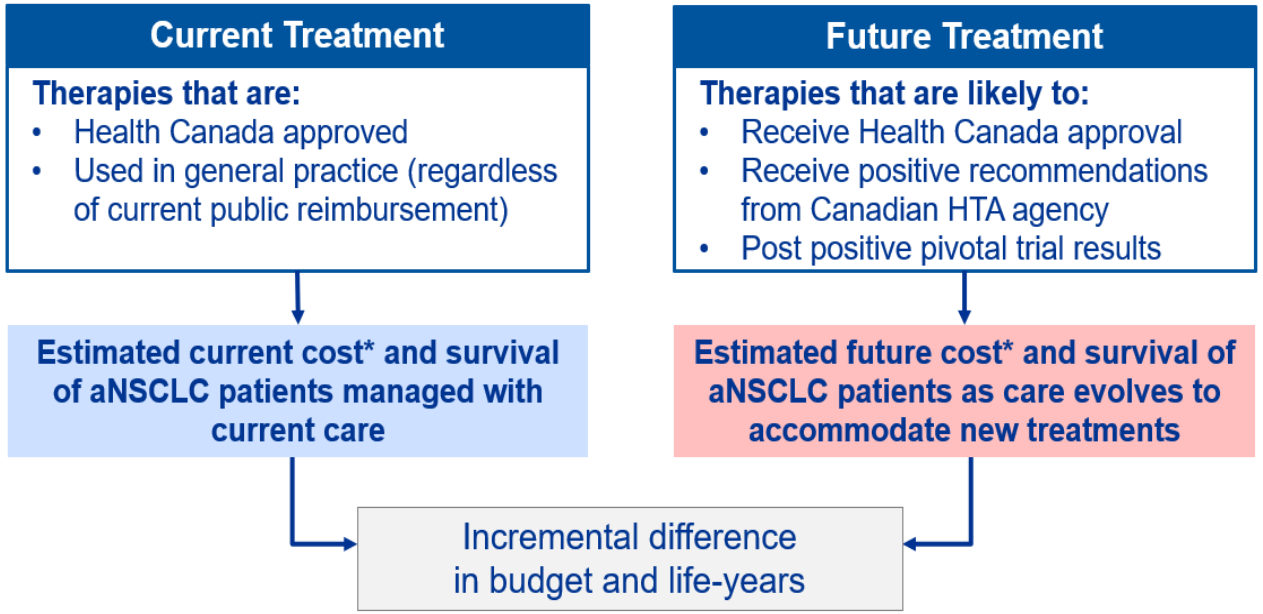
Ontario

- **Dr. Bill Evans**
  - Medical Oncologist & Professor Emeritus, McMaster.

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 & Agenda

1. Illustrate the unique approach and abilities of the iTEN model

2. Demonstrate the adaptability of the model to new treatment sequences in aNSCLC

3. Estimate the impact of upcoming treatment sequencing changes to a hypothetical province.

Agenda

Focus	Allocated Time	Presenter
Model overview and objectives	10 minutes	Dan Moldaver & Manjusha Hurry
Hypothetical province BIA	15 minutes	Dan Moldaver
Model demonstration	10 minutes	Dan Moldaver
Discussion with panel members	25 minutes	• Dr. Paul Wheatley-Price • Jaya Venkatesh

iTEN Model Overview

Agenda	Focus	Time	Presenter
	Model overview	10 minutes	Dan Moldaver & Manjusha Hurry
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Model Type

Patient Level Discrete Event Simulation

Time Horizon

Lifetime

Perspective

Canadian Healthcare System

Target Population

Advanced non-small cell lung cancer (NSCLC) patients

iTEN Model Overview

Key model design elements:

- Lifetime horizon and Canadian health care system perspective

Population:

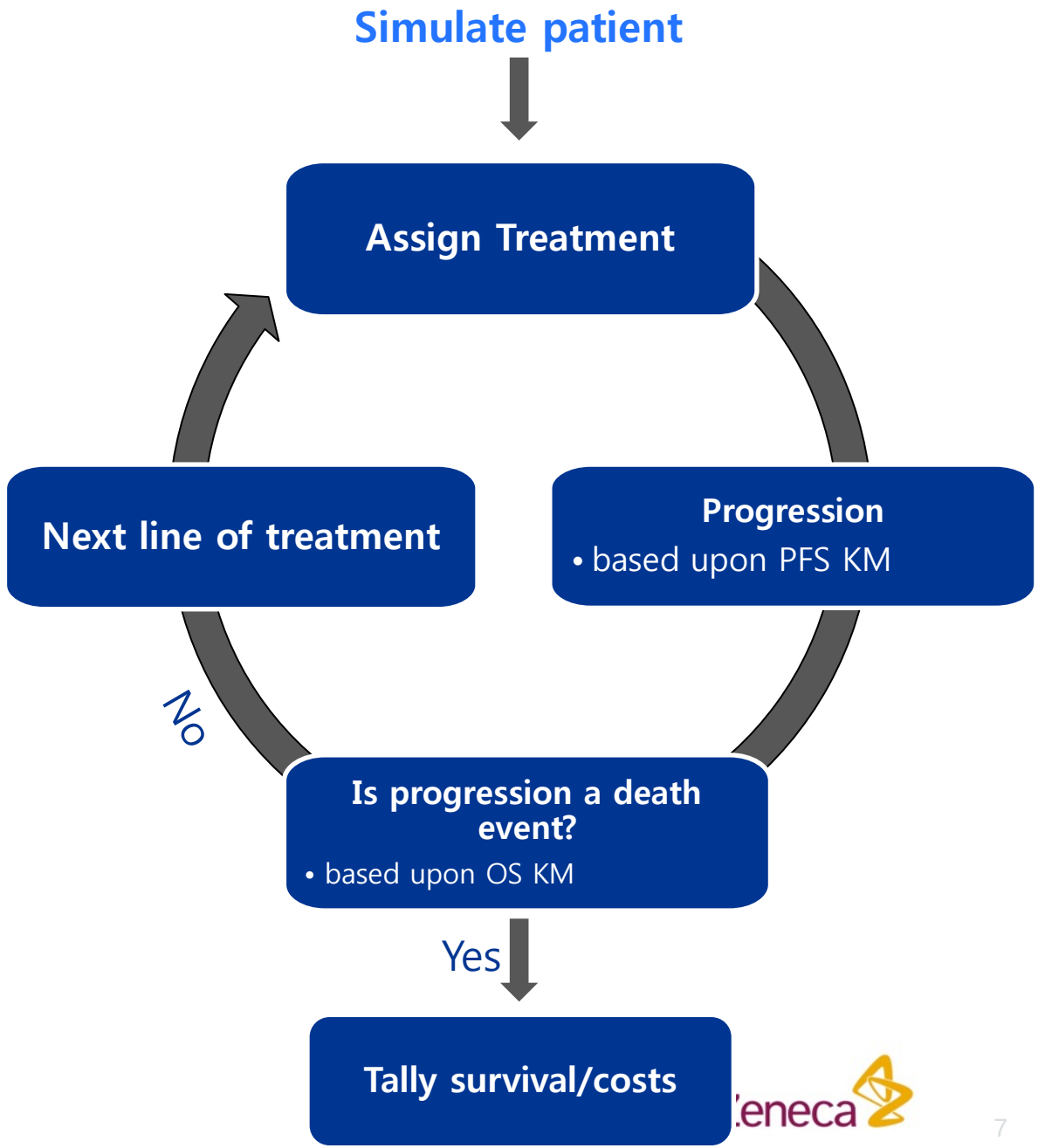
- Advanced non-squamous and squamous NSCLC.
- Considers mutation status (EGFR, ALK, ROS, BRAF, NTRK, etc.), PD-L1 expression (e.g. <1%, 1-49%, >49%), smoking status and performance status.

Data sources:

- PFS and OS KM data extrapolated from pivotal trials using 5 common parametric functions. The best fit curve was selected by AIC, BIC and clinical plausibility.
- List prices from Ontario formularies.

Key Assumptions for the 2019

- 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.



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Why is this Model Novel?

- **The discrete event structure is more flexible than traditional partition survival or cohort models, which allows quick and easy modeling of dramatic shifts in treatment patterns**
  - Allows consideration of patients receiving no active treatment
  - Allows comparison of the benefits/costs of, for example: a new 3L BRAF tx vs a new treatment for KRAS

- **The model is intended to allow rapid assessment of numerous scenarios that together can establish a plausible range of outcomes.**

- **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.

iTEN VALIDATION

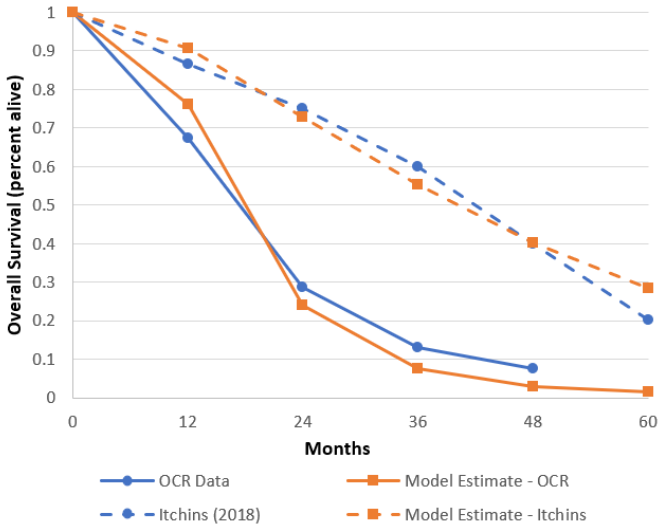
- The model was extensively **validated to five real-world data sets**, from Canada, Austria, the USA and Australia.

Validation Methods:

- Visual inspection
- Statistical methods
  - Mean Absolute Percent Error (MAPE)
  - Coefficient of Determination (ie, R^2)

iTEN VALIDATION

Visual inspection



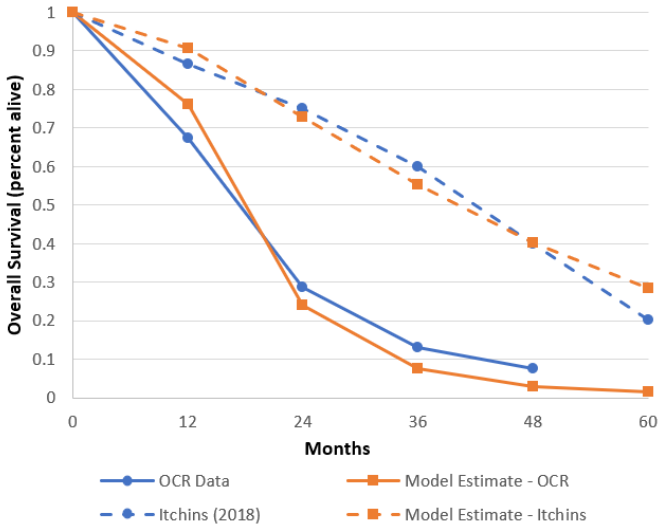
Interpretation:
1) Modeled estimates (**orange lines**) matched well to RWE/Registry data (**blue lines**) and show a clear difference due to treatment distribution

Mean Absolute Percent Error

Coefficient of Determination

iTEN VALIDATION

Visual inspection



Interpretation:
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Mean Absolute Percent Error

Source	Treatment Distribution	MAPE
Sacher 2015	Chx	**33%**
Kocher 2015	Chx + EGFR TKI	**35.4%**
Nadler 2018	Chx + IO	**49.3%**
Nadler 2018	EGFR + ALK TKI	**23.6%**
Itchins 2018	ALK TKI + Chx + IO	**11.6%**

KEY: Chx, chemotherapy; IO, immuno-oncology therapy; MAPE, mean absolute percent error; TKI, tyrosine kinase inhibitor

Interpretation:
1) Smaller MAPE vales represent better forecast accuracy
2) MAPE between 23-90% was considered very good for a leading T2D model (Cardiff)

Coefficient of Determination

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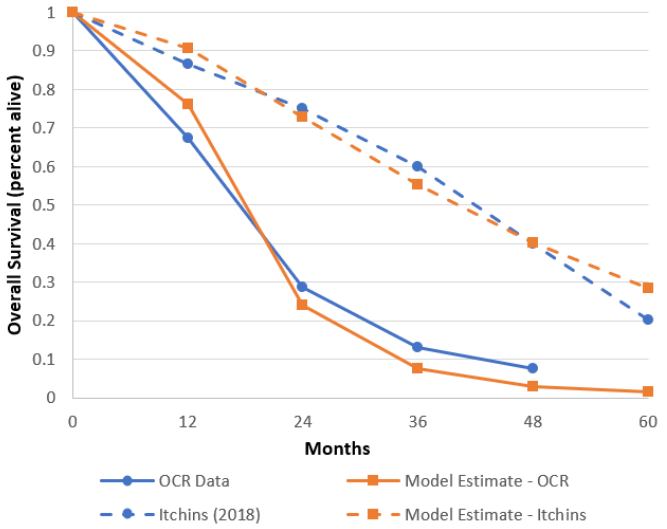
iTEN VALIDATION

Visual inspection



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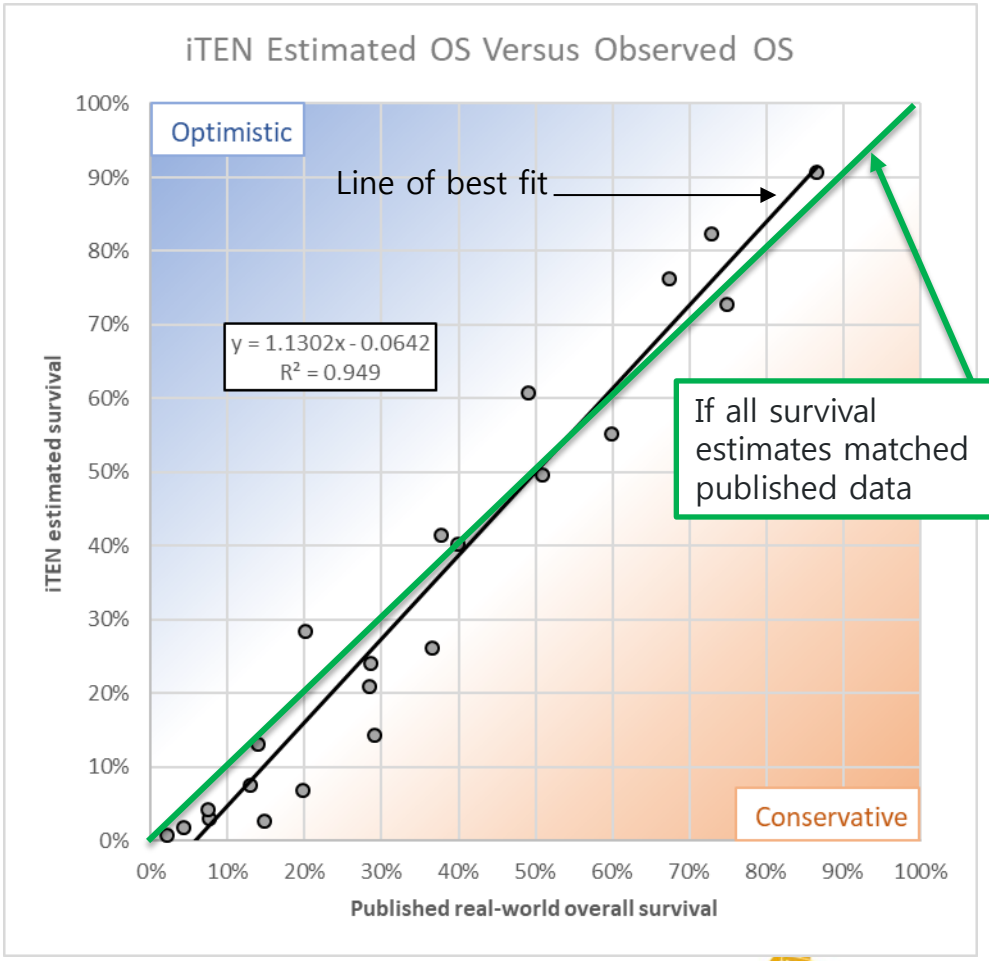

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Estimating the Cost and Survival Impact of Future Care

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Hypothetical BIA Results

Agenda	Focus	Time	Presenter
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	Panel Q&A	25 minutes	• Dr. Paul Wheatley-Price • Jaya Venkatesh

Key features of presented analysis:

- Hypothetical **5,000,000 person province**
- Assumed treatment rate:
  - **1L is 100% & 60% subsequently**

- **"2018" treatment algorithm**
  - Generated using a modified Delphi approach with 5 Canadian medical oncologists in Q1 2018
- **"2019" treatment algorithm**
  - A 2019 update to the 2018 algorithm guided by 5 Canadian medical oncologists.
- **Analyses represent the clinicians preferred treatment of patients by end 2019.**
  - Analyses for publication will focus on the projected impact to public payers

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 2018 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.*

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Impact of 2019 versus 2018 Treatment on OS

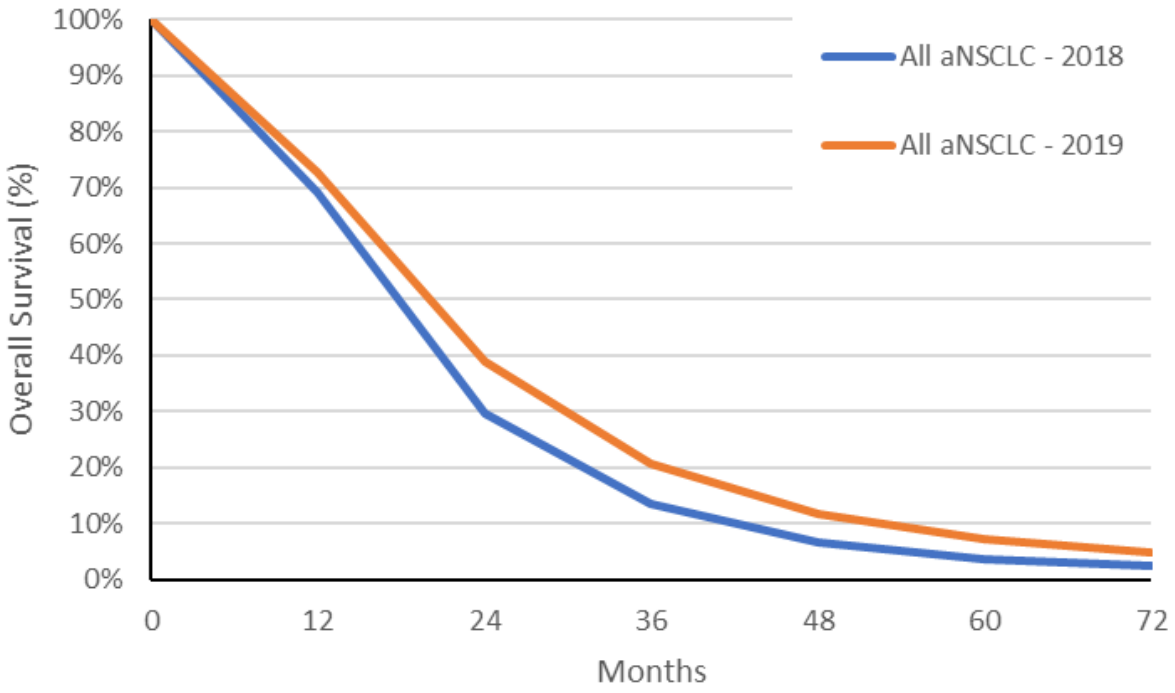
Entire aNSCLC Population

- Survival **increased**
- Most benefits realized between years 2-5

Year 1	Year 2	Year 3	Year 4	Year 5	Year 10
+5%	+31%	+56%	+74%	+97%	+358%

Assumed a 100% Treatment Rate in 1L & 60% subsequently

- *weighted average of EGFR, ALK, BRAF, and PD-L1 patient subgroups*



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Impact of 2019 versus 2018 Treatment on OS

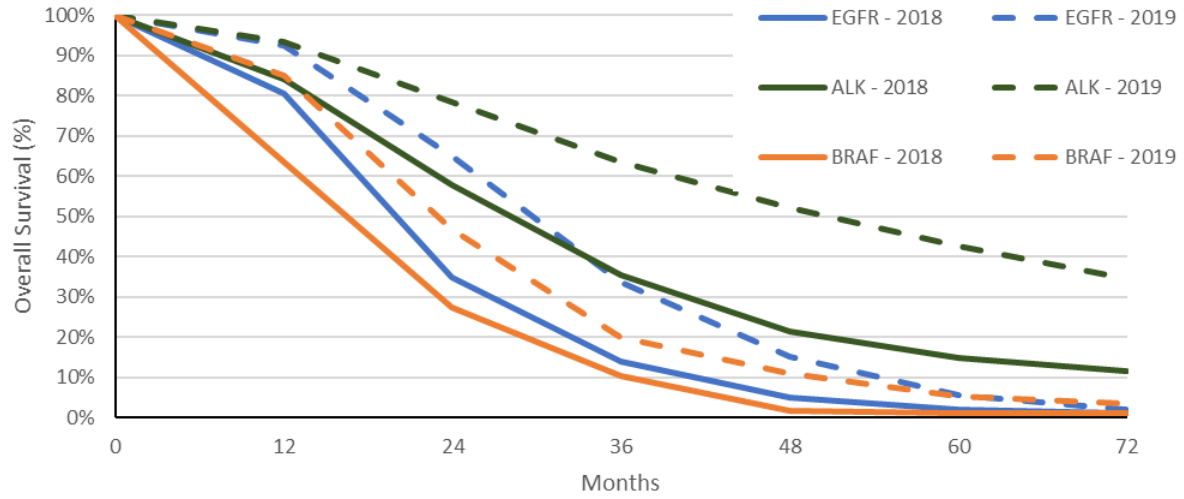
Targeted Treatment Eligible Population (*EGFR, ALK, BRAF*)

- Estimated 2.5x increase in 3-yr EGFR Survival
- More ALK patients alive at 5-yr than currently at 3-yr

	2018 OS (%, n)	2019 OS (%, n)	5-yr OS Benefit
EGFR	3-yr: 14%, 39 5-yr: 2%, 7	3-yr: 34%, 100 5-yr: 5%, 17	**193%**
ALK	3-yr: 35%, 41 5-yr: 15%, 17	3-yr: 64%, 71 5-yr: 42%, 48	**189%**
BRAF	3-yr: 10%, 4 5-yr: 1%, 1	3-yr: 20%, 8 5-yr: 5%, 2	**400%**

Assuming a 100% Treatment Rate in 1L & 60% subsequently

- *n represents the estimate patients alive after 3 & 5-years, in a 5,000,000 person province*



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Impact of 2019 versus 2018 Treatment on OS

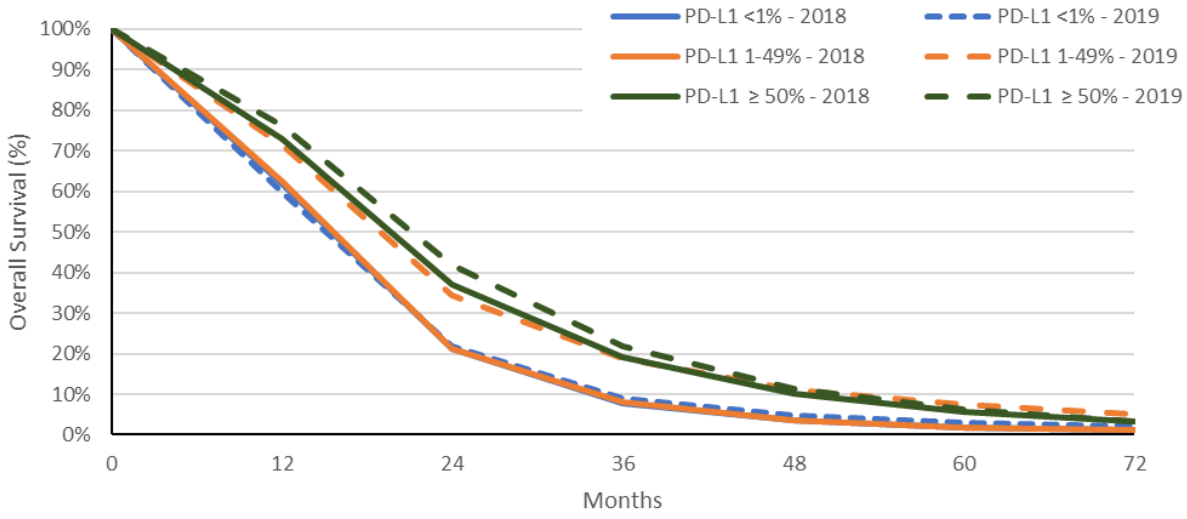
Targeted Treatment Ineligible Population (*EGFR, ALK, BRAF*)

- Largest benefit projected for the PD-L1 1-49% patient population.

PD-L1 expression	2018 OS (%, n)	2019 OS (%, n)	5-yr OS Benefit
<1%	3-yr: 8%, 47 5-yr: 2%, 10	3-yr: 9%, 49 5-yr: 3%, 15	**57%**
1-49%	3-yr: 8%, 21 5-yr: 2%, 5	3-yr: 19%, 49 5-yr: 7%, 20	**296%**
≥50%	3-yr: 19%, 70 5-yr: 6%, 20	3-yr: 22%, 82 5-yr: 6%, 23	**14%**

Assuming a 100% Treatment Rate in 1L & 60% subsequently

- *n represents the estimate patients alive after 3 & 5-years, in a 5,000,000 person province*



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Impact on Costs

- The iTEN model structure allows identification of key cost metrics, including:

Cost
❑ Costs per treated patient
❑ Costs per person in the province
❑ Drug acquisition cost per treated patient
❑ Cost per patient disaggregated by budget type
❑ Net Budget Impact

Results to follow represent a scenario wherein 100% of diagnosed patients receive 1L care & 60% alive receive care in subsequent lines

BUDGET IMPACT: Per Treated Patient Costs

Cost	
✓	Costs per treated patient
❑	Costs per person in the province
❑	Drug acquisition cost per treated patient
❑	Cost per patient disaggregated by budget type
❑	Net Budget Impact

Entire aNSCLC Population

- The **97% increase in 5-year survival** was associated with an incremental life-time cost of **$109,539** per treated patient
  - Most (**55%**) costs are incurred within the first year.

	2018	2019	Estimated Incremental Cost per aNSCLC Patient
Year 1	$81,984	$142,335	$60,351 **(+74%)**
Year 2	$45,904	$65,615	$19,710 **(+43%)**
Year 3	$15,170	$21,207	$5,857 **(+39%)**
Year 4	$6,906	$11,394	$4,488 **(+65%)**
Year 5	$3,524	$6,652	$3,128 **(+89%)**
Avg yearly (6-15)	$612	$2,213	$1,600 **(+26%)**
Total	**$159,609**	**$269,148**	**$109,539** **(+69%)**

BUDGET IMPACT: Per Person in Province

Cost	
✓	Costs per treated patient
✓	Costs per person in the province
❑	Cost per patient disaggregated by budget type
❑	Drug acquisition cost per treated patient
❑	Net Budget Impact

Entire aNSCLC Population

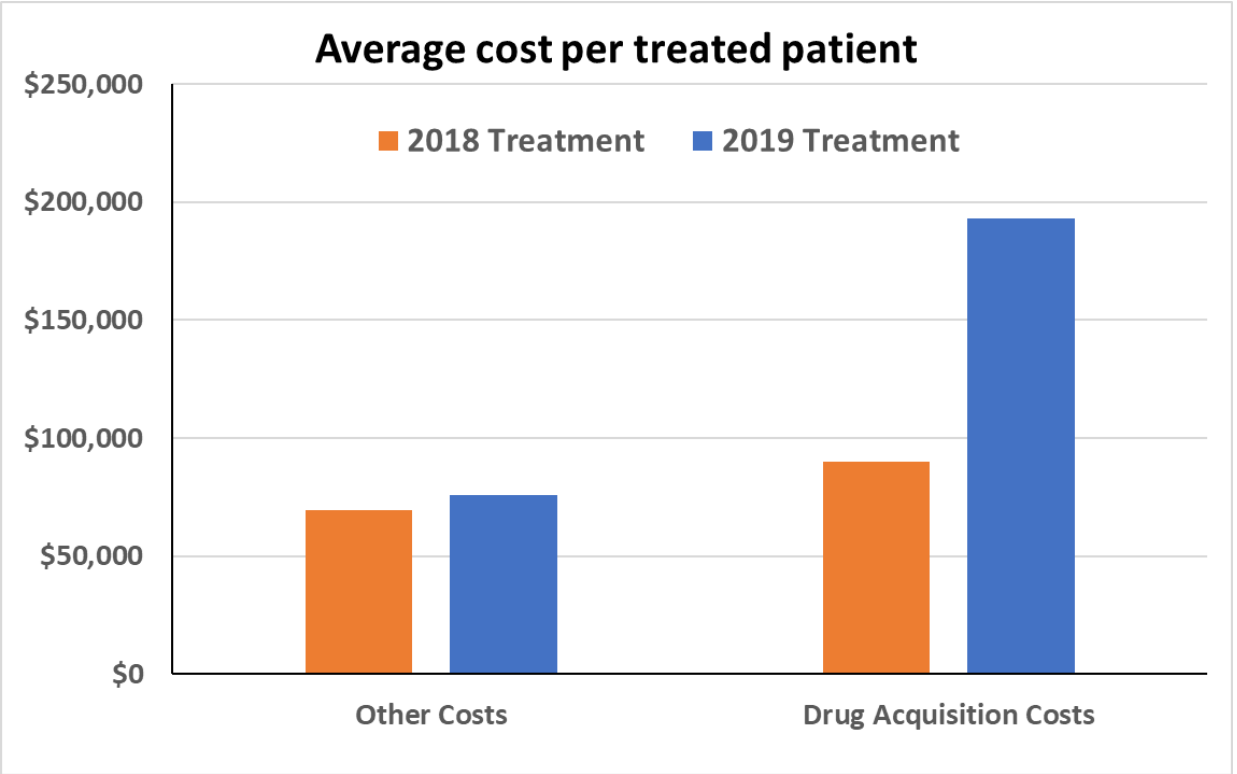
- The **97% increase in 5-year survival** was associated with an incremental **$44.65 (69%)** per province resident in the 2019 scenario.
  - *(net budget impact / 5,000,000 = cost per person)*

	2018	2019	Incremental Difference
Year 1	$33.42	$58.02	$24.60 **(+74%)**
Year 2	$18.71	$26.75	$8.04 **(+43%)**
Year 3	$6.18	$8.57	$2.39 **(+39%)**
Year 4	$2.82	$4.64	$1.83 **(+65%)**
Year 5	$1.44	$2.71	$1.28 **(+89%)**
Avg yearly (6-15)	$0.25	$0.90	$0.65 **(+26%)**
Total	$65.07	$109.72	$44.65 **(+69%)**

BUDGET IMPACT: Drug Acquisition Costs

Cost	
✓	Costs per treated patient
✓	Costs per person in the province
✓	Drug acquisition cost per treated patient
❑	Cost per patient disaggregated by budget type
❑	Net Budget Impact

- Drug acquisition costs are expected to **double**



Other costs include:

- *Medical oncologist visits, administration & clinic time, monitoring, imaging, AE management, best supportive care and end-of-life costs.*

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BUDGET IMPACT: Drug Acquisition Costs

Cost	
✓	Costs per treated patient
✓	Costs per person in the province
✓	Drug acquisition cost per treated patient
❑	Cost per patient disaggregated by budget type
❑	Net Budget Impact

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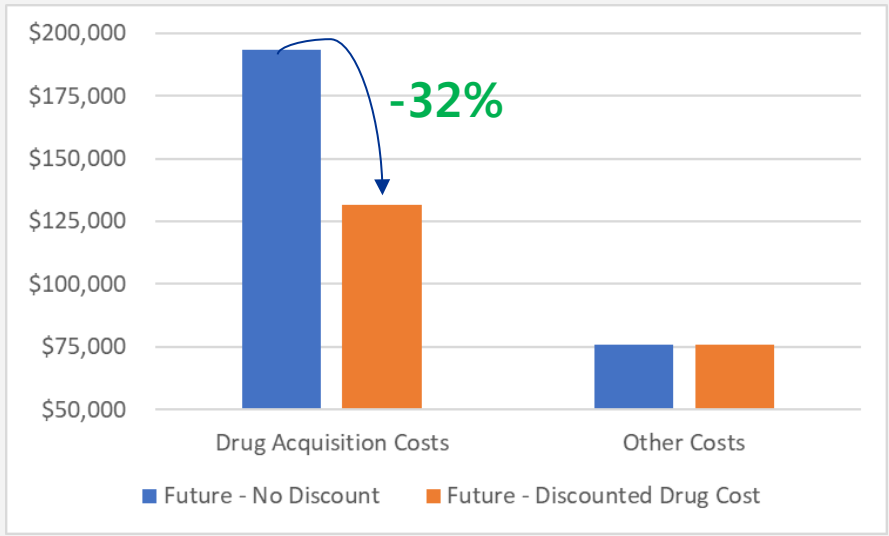
Note, these results are based upon analyses using **Ontario formulary list prices and health resource costs.**

In a hypothetical scenario with a **30% discount off branded** medicines & **50% off generic** medicines:

- Drug acquisition costs decreases reduced the incremental per-patient budget impact from **69% to 60%.**



management, best supportive care and end-of-life costs.

BUDGET IMPACT: Disaggregated Costs

Cost	
✓	Costs per treated patient
✓	Costs per person in the province
✓	Drug acquisition cost per treated patient
✓	Cost per patient disaggregated by budget type
❑	Net Budget Impact

- While drug acquisition costs increased, the cost of managing adverse events **decreased.**
- Healthcare resource utilization **increased** with **extended patient survival**

	Drug Acquisition	Medical Oncologist Visits	Administration & Chair Time Costs	Monitoring	Imaging	AE Management	BSC and EoL
2018	$90,164	$2,686	$2,745	$1,683	$624	$8,592	$53,115
2019	$193,179	$3,967	$2,644	$2,362	$843	$6,907	$59,245
Incremental	$103,015	$1,281	-$100	$679	$219	-$1,685	$6,130
Impact (%)	**114%**	**48%**	**-4%**	**40%**	**35%**	**-20%**	**12%**
Costing Source	**MOHLTC/CCO**	**MOHLTC**	**Ng (2007)[1]**	**MOHLTC**	**MOHLTC**	**OCCI**	**Chen (2010)[2]**

Notes,
1. Derived from a time in motion study at PMH. Includes attributable facility costs, overhead, medical and surgical supplies, pharmacist, pharmacist technician time, direct nursing care and required physician time,
2. BSC includes inpatient medication, hospitalization, outpatient visits, radiation therapy and community care.

BUDGET IMPACT: Net Budget Impact

Cost	
✓	Costs per treated patient
✓	Costs per person in the province
✓	Cost per patient disaggregated by budget type
✓	Drug acquisition cost per treated patient
✓	Net Budget Impact

Entire aNSCLC Population

- The **97% increase in 5-year survival** in a hypothetical 5,000,000 person province was associated with a net budget impact was **$223,273,167**.

	Drug Acquisition	Medical Oncologist Visits	Administration & Chair Time Costs	Monitoring	Imaging	AE Management	BSC and EoL	Net Budget Impact
2018	$183.78	$5.48	$5.59	$3.43	$1.27	$17.51	$108.26	**$325.33**
2019	$393.76	$8.09	$5.39	$4.81	$1.72	$14.08	$120.76	**$548.61**
Incremental	$210	$3	$0	$1	$0	-$3	$12	**$223**
Impact (%)	**114%**	**48%**	**-4%**	**40%**	**35%**	**-20%**	**12%**	**69%**

Costs are presented in millions

Notes,
1. Derived from a time in motion study at PMH. Includes attributable facility costs, overhead, medical and surgical supplies, pharmacist, pharmacist technician time, direct nursing care and required physician time,
2. BSC includes inpatient medication, hospitalization, outpatient visits, radiation therapy and community care.

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BUDGET IMPACT: Net Budget Impact

Cost	
✓	Costs per treated patient
✓	Costs per person in the province
✓	Cost per patient disaggregated by budget type
✓	Drug acquisition cost per treated patient
✓	Net Budget Impact

- Ontario aNSCLC treatment rates (Sacher *et al.,* 2015) & drug discounting reduce the net budget impact from **$223,273,167** to **$43,348,875.**
  - **Drug acquisition costs do not exceed other incurred costs.**

	Drug Acquisition	Other Costs	Net Budget Impact
2018	$21.80	$83.81	$105.61
2019	$61.55	$87.40	$148.95
Incremental	$39.75	$3.60	$43.35
Impact (%)	**182%**	**4%**	**41%**

Costs are presented in millions

- Scenario analyses like this analysis are planned to assess the impact of:
  - **Differential treatment rate assumptions**
  - **Delayed access to medicines**
  - **What therapy could look like in 5-years**

Model Demonstration

- To be completed in Excel

Agenda	Focus	Time	Presenter
	Model overview	10 minutes	Dan Moldaver & Manjusha Hurry
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	Panel Q&A	25 minutes	• Dr. Paul Wheatley-Price • Jaya Venkatesh

CONCLUSIONS

- 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 treatment sequences for aNSCLC patients.

Next Steps

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

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Question & Answer Period

- Q&A period to be held with Dr. Paul Wheatley-Price & Jaya Venkatesh

Agenda

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Question & Answer Period

Focus	#	Question
General	1	How has the landscape in lung cancer changed in the last 5 years and what does this mean for patients? What are your concerns about access challenges in Canada as a result of the significant change?
	2	How do you perceive the cost in metastatic lung cancer to shift in the years to come?
iTEN Model Related	3	What is the value of a model like iTEN model?
	4	What are the limitations of traditional individual models in informing decision making and do you feel a model like the iTEN model can help overcome those challenges / limitations?
	5	The model helps look at future-based costs across a number of treatments / regimens – how does this help to inform decision making?
	6	Do you see value in the iTEN approach (model and panel of Canadian oncologists) for pCODR, now that CDIAC has been merged?
	7	What do you think holds more value, continuously updating the model as new treatments arise or exploring a hypothetical scenario to determine the likely maximum cost?
	8	How can make the iTEN model a valuable tool for budget planning?
	9	Could this type of model be applicable and helpful in other disease areas?

Thank you

For follow-up questions, please contact either:

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