PATIENT ENGAGEMENT AND OUTCOMES: TAKING IT TO THE NEXT LEVEL

The Canadian Association for Population Therapeutics

October 24, 2017

PANEL MEMBERS:

- **Christina Sit**

  Program Manager, Lung Cancer Canada

- **Jo Nanson**

  Patient Representative, Expert Review Committee, pCODR

- **Seema Nagpal**, BSc. Pharm, M.Sc, Ph.D

  Epidemiologist and Senior Leader, Public Policy, Diabetes Canada

Christina Sit

- Program manager at Lung Cancer Canada
- Portfolio includes patient education, awareness, stakeholder relations advocacy
- Responsible for making patient group submissions to pCODR

Jo Nanson

- Retired doctoral psychologist
- Work experience: Royal Victoria Hospital in Saskatoon and private practice; worked closely with Saskatoon Cancer Centre providing psychological services to children and young adults with cancer
- member of the expert review committee of pCODR for six years
- a breast cancer survivor and member of a breast cancer Dragon boat team

Seema Nagpal

- Attained Pharmacy and Community Health and Epidemiology degrees from Dalhousie University
- Attained PhD in Population Health from the University of Ottawa
- Has worked at CADTH, the Canadian Medical Association, Health Canada and the Queen Elizabeth Health Science Centre prior to becoming the Epidemiologist and Senior leader, Public Policy at Diabetes Canada

(MY) HISTORICAL PERSPECTIVE ON PATIENT ENGAGEMENT

- Prior to 1990 – almost none
- 1992, Montréal Breast Cancer Conference; women demanded role in decision-making for care and research agenda
- Breast cancer advocacy groups formed
- Research on women's attitudes to share decision-making undertaken
- Rapid increase in the number of advocacy groups; initial advocacy initiatives led by women but men followed (eventually)

(MY) HISTORICAL PERSPECTIVE ON PATIENT ENGAGEMENT

- My personal epiphany in 1995
- Engagement of patients on Ottawa cancer centre committees
- Now an expectation that all cancer centres have a Patient and Family Advisory Committee
- CCO Provincial Patient and Family Advisory Committee

(MY) HISTORICAL PERSPECTIVE ON PATIENT ENGAGEMENT AND HTA

- New Drug Funding Program in Ontario started in 1995
- Inaugural Policy Advisory Committee(1997) had patient representatives but MOHLTC committee to evaluate drugs did not
- Committees merged in 2004 but patients were not initially included in the CCO/CED
- Ultimately, patients were invited to participate in that committee and CCO/CED processes became the model for the current pCODR

ONCOLOGY DRUG FUNDING DECISIONS IN CANADA

Patented Medicine Prices Review Board – acceptance of manufacturer's price

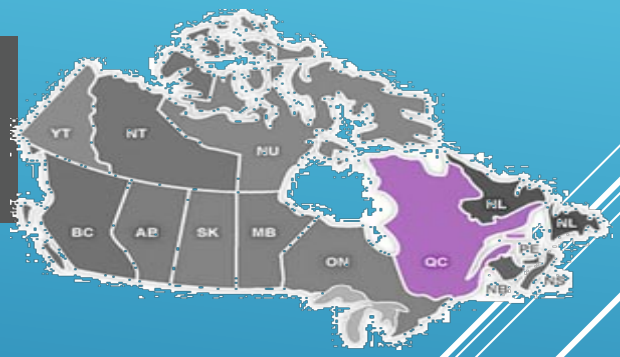
Health Canada

Santé Canada

National Regulatory body – reviews and approves new medicines based on efficacy, safety +/- magnitude of benefit

pCODR

INESSS
LE SAVOIR PREND FORME



Pan-Canadian Oncology Drug Review (pCODR)

l'Institut d'excellence en santé et services sociaux

Rigorous evidence review of:

1. Clinical effectiveness (Clinical Panel, systematic review)
2. Alignment with Patient values
3. Cost effectiveness (Economic Panel)
4. Feasibility of adoption

Expert Review Committee (pERC) delivers recommendation:

1. For reimbursement
2. For reimbursement with conditions
3. Against reimbursement

www.cadth.ca/pcodr/

www.inesss.qc.ca/

NEW DRUGS APPROVED BY FDA/EMEA FOR LUNG CA

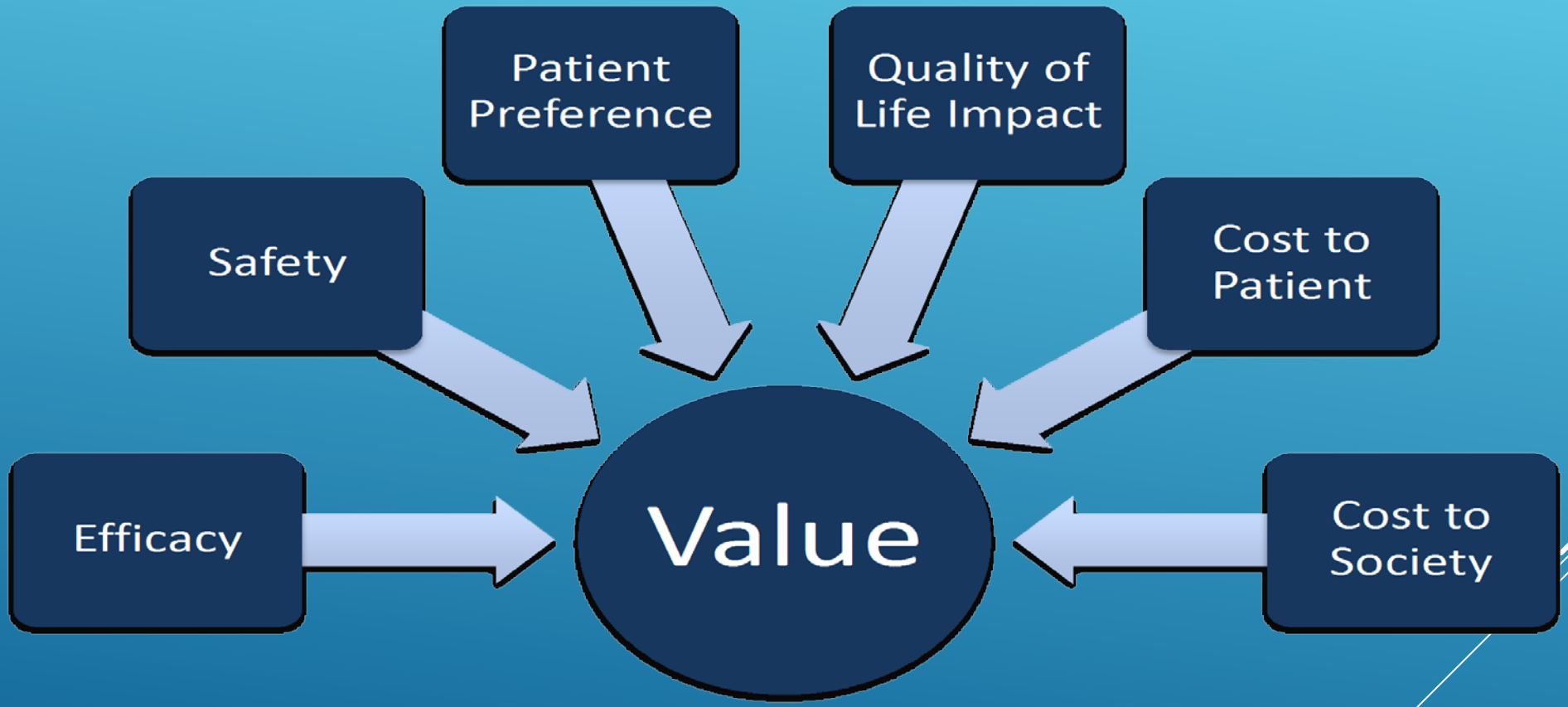
AGENT	OS Gain	Indication	Competitors
Necitumumab (EGFR mAb) + Gemcitabine/Cisplatin	HR 0.84 + MST 1.6 m	1L Squamous	PlatinumDoublet +/-/or Pembrolizumab
Ramucirumab (VEGFR mAb) + Docetaxel	HR 0.86	2L NSCLC	Nivolumab Pembrolizumab Docetaxel
Nintedanib (VEGFR TKI) + Docetaxel (-ve all NSCLC)			Nivolumab Pembrolizumab Docetaxel
Nivolumab (PD-1 mAb)			Pembrolizumab Docetaxel
Pembrolizumab (PD-1 mAb)			Nivolumab Docetaxel
	HR 0.60 + MST n/a	1L PDL1+ NSCLC	Platinum Doublet
Osimertinib (T790M TKI)	61% ORR Median PFS 9.6 m	2L T790M EGFR+	Platinum Doublet Other T790Mis
Ceritinib (ALK TKI)	54% ORR mPFS 7.9 m	2L ALK+	Platinum Doublet Other ALK TKIs
Alectinib (ALK TKI)	48% ORR	2L ALK+	Platinum Doublet Ceritinib

***Can* we pay for it all?**

***Should* we pay for it all?**

What is good value?

How SHOULD Medical Decisions be made? 2.0



IASLC Task Force on Quality and Value

HOW WILL WE ACHIEVE SUSTAINABILITY?

Reduce costs of drug development

Negotiate prices!

Guideline-based treatment

Choose wisely

Contain Costs

Prioritize Value (maximize benefit)

Prevention, Cure > Palliation

Maintain high bar for clinical benefit (ASCO: <0.8 HR OS, Median OS gain >2.5 m)

Select patients with greatest benefit (biomarkers, performance status)

MY PERSPECTIVE ON PATIENT ENGAGEMENT IN HTA

- Brings the reality of the cancer experience to the discussion of new treatments
- Provides a patient perspective on what progression free survival means
- Patient and caregiver input are both invaluable
- Patients and their care providers are realistic
- Benefits to patients may be different from traditional HTA measures

DIABETES CANADA™

Seema Nagpal, BSc. Pharm, M.Sc., Ph.D.
Epidemiologist & Senior Leader, Public Policy

Discloser

- Diabetes Canada receives funds from general fundraising, donations, foundations, provincial governments, and private corporations including, but not exclusively, pharmaceutical companies. These pharmaceutical companies include: AstraZeneca, Bayer, Boeringer Ingelheim, Eli Lily, Janssen, Merck, Novartis, Novo Nordisk, Sanofi, Stonebridge, Valiant.

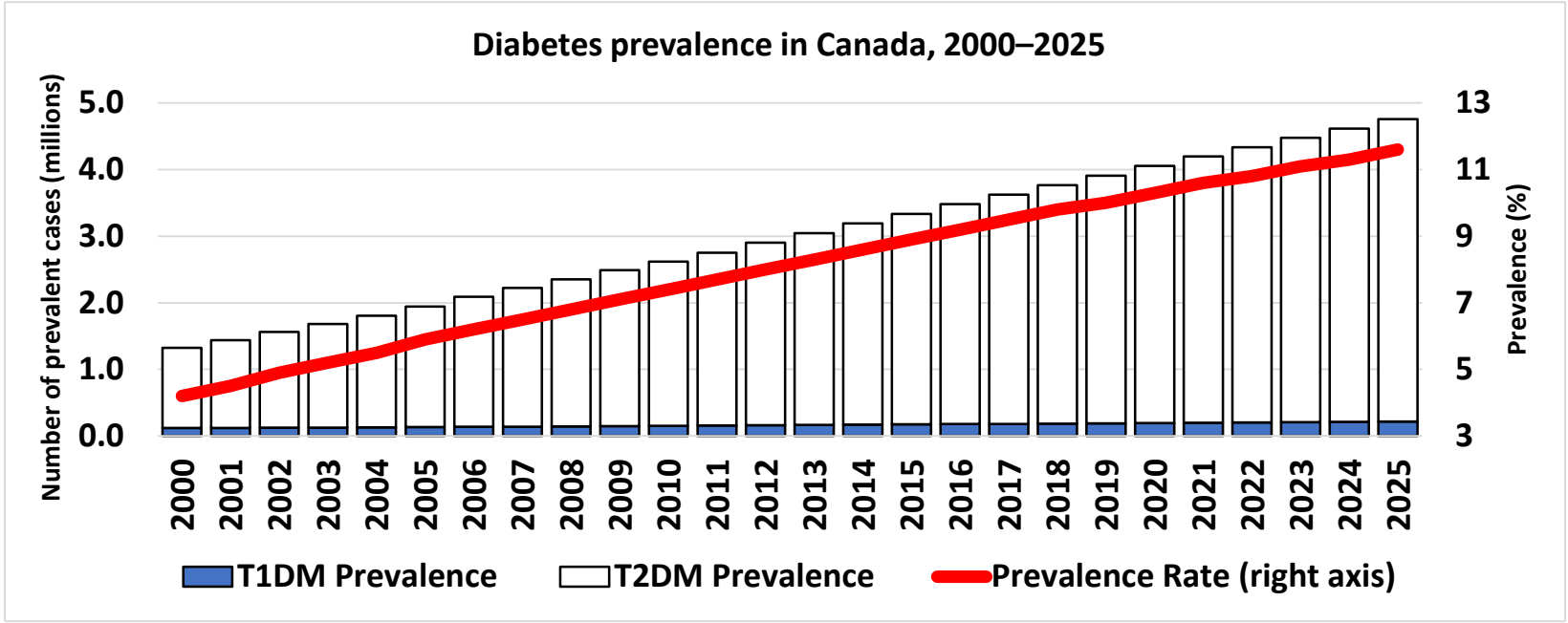
- Diabetes Canada does not receive any funding for submission of patient input submissions.

DIABETES CANADA

On Feb, 13, 2017 the Canadian Diabetes Association became Diabetes Canada

Our ultimate, long-term goal is to End Diabetes through prevention and cure.

The Evolving Diabetes Epidemic in Canada



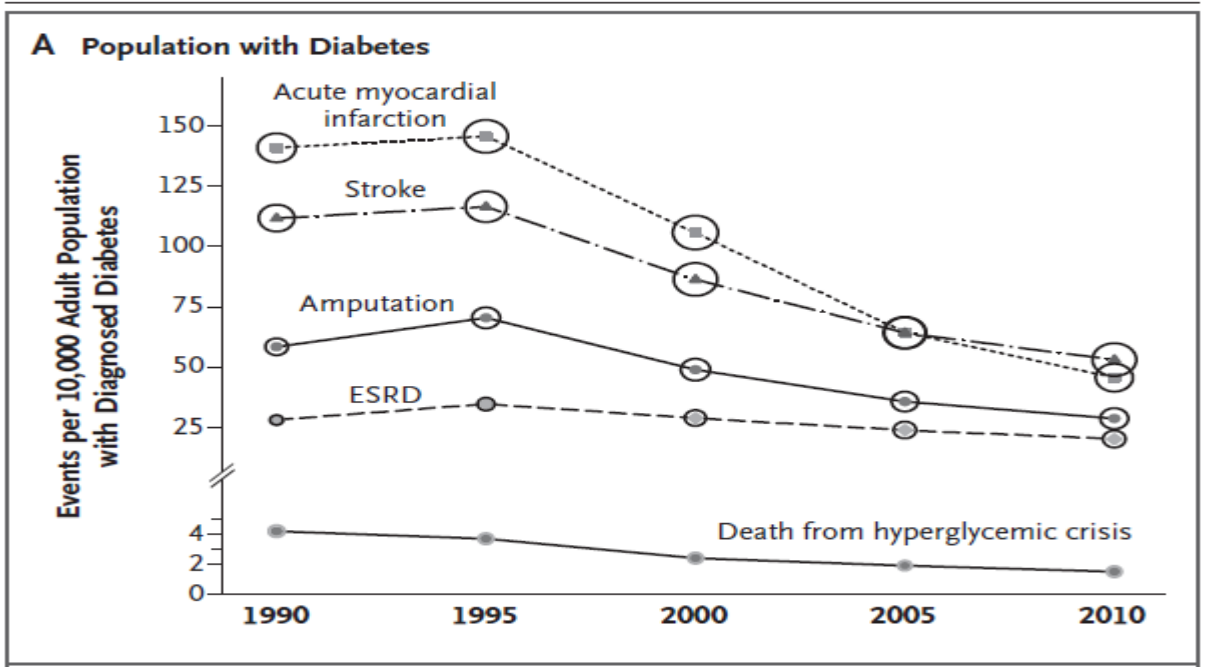
2015 Report on Diabetes: Driving Change. Diabetes Canada

Growth Drivers of Type 2 Diabetes

1. Genetics Factors
2. Lifestyle Factors
3. Environmental Factors

Overcrowding in the diabetes pool

Falling Complication Rates over Time



Gregg et al. N Engl J Med 2014; 370:1514-1523

Diabetes Canada believes that the needs of patients must be at the centre of health policy decisions.

- Healthcare funding decisions are made in an environment of limited fiscal resources
- There must be choice.
- There must be balance.

CDR Patient input

- Challenges
  - Wide range of opinions and experience with the disease and drug treatment
  - Not many with drug experience
  - Exact indication is unknown so difficult to ask specific questions that inform the review
  - Resources are limited
  - How does the value of the drug to the patient get incorporated into a cost effectiveness recommendation

What do patients want?

- HCCC – draft
  - FIT framework (Flexible, Involvement, Transparency)

- **Patient Engagement**
  - Patients are meaningfully involved at the decision-making table as partners in the process

HTA evolves to Health Technology Management

- The promise of a brighter future and patient engagement
- How will this happen?
  - Patient engagement at every stage
    - Governance and Priority-Setting
    - Assessment and Evaluation Throughout the Technology Life Cycle
    - Partners in knowledge translation
    - Partners in continuous improvement

But where are the patients with development of HTM?

- The proposal was developed within CADTH and with input from provinces
- How are patients involved with the next steps of operationalizing this initiative?
- What structural changes are required to ensure patients are not asked for input but are real partners

DIABETES CANADA™

Thank You!

CANADA

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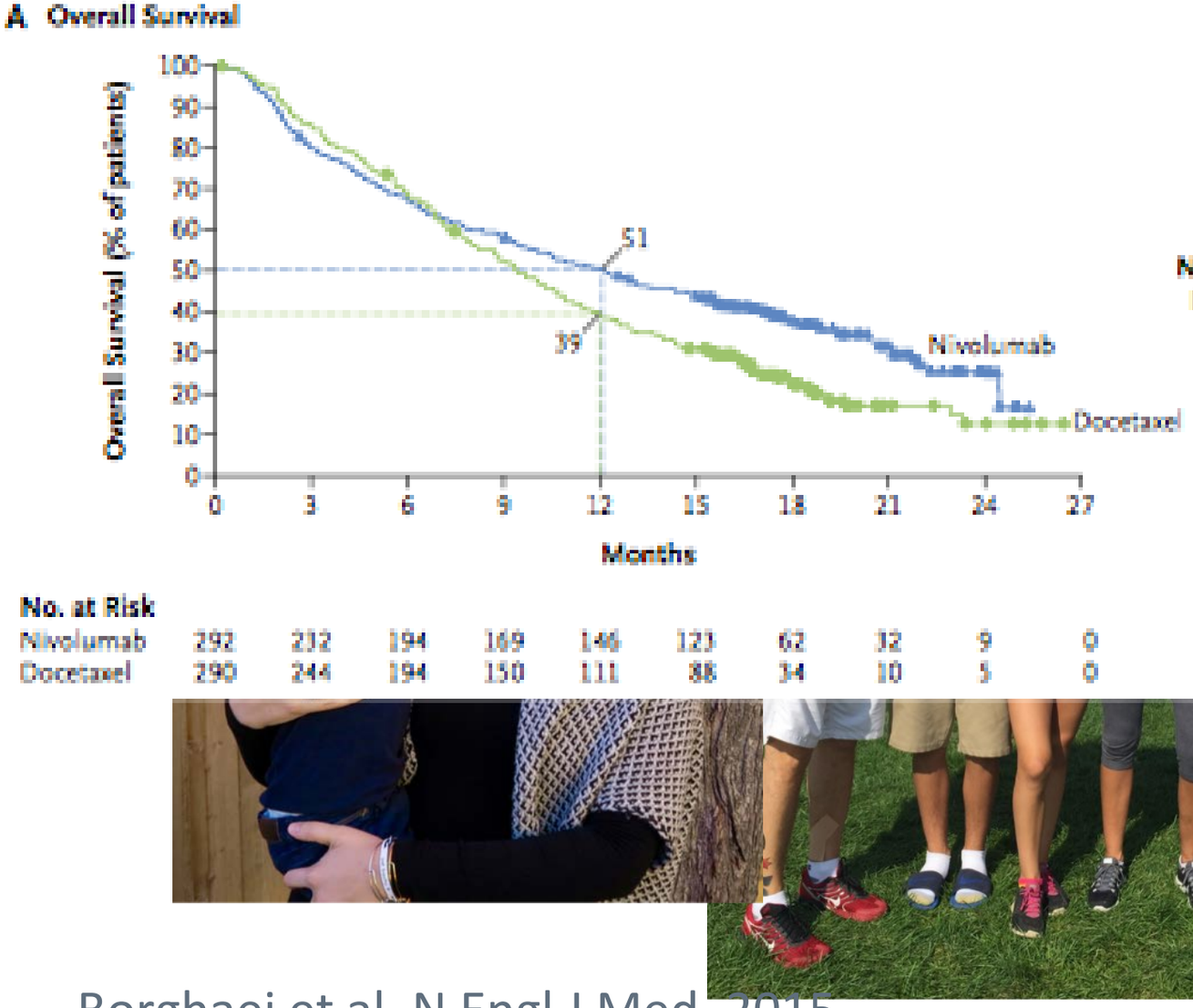

	No. of Deaths/ Total No. of Patients	Median Overall Survival (95% CI)	1-Yr Overall Survival Rate (95% CI)
		mo	%
Nivolumab	190/292	12.2 (9.7–15.0)	51 (45–56)
Docetaxel	223/290	9.4 (8.1–10.7)	39 (33–45)

Hazard ratio for death, 0.73 (96% CI, 0.59–0.89)
P=0.002

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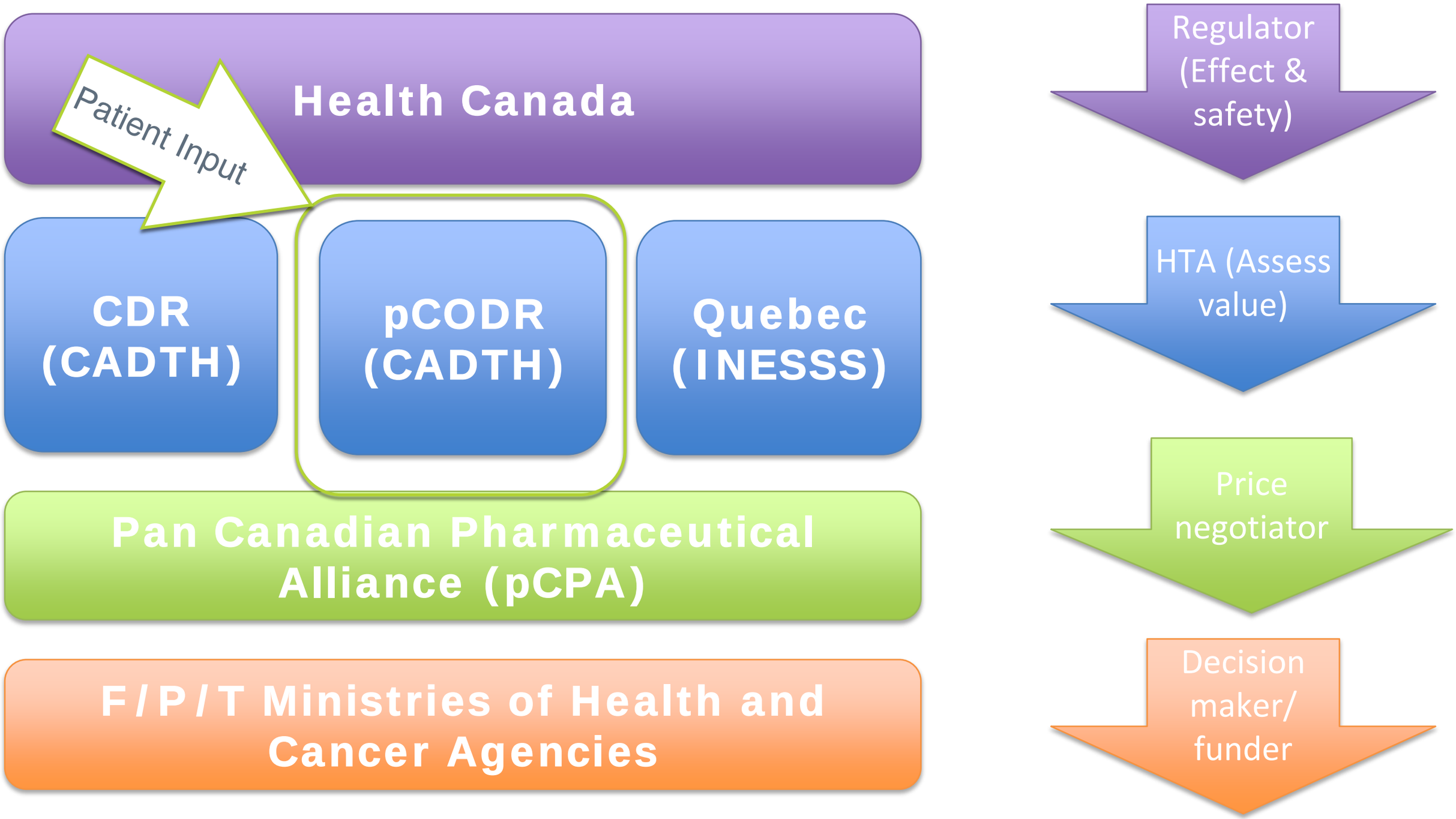
Borghaei et al, N Engl J Med, 2015

Drug Access—Who Does What in Canada?



Beyond Data: Questions answered by patient group submission

- Experience patients have with this type of cancer - impact on their lives
- Patient experience with current therapy
- Impact on caregivers
- What are the expectations for the new drug
- What experience have patients had to date with the new drug
- Additional information

Challenges in lung cancer!

- Limited Canadian experience with drug
- Low survivorship
- Time past between close of trial and submission
- Small target patient population drug under consideration is a targeted therapy

→ Low number of Canadian patients able to participate

Quantitative

Faces of Lung Cancer Survey

- 91 patients
- 72 caregivers
- Collected information on disease attitudes, experiences and challenges

QUANTITATIVE

Qualitative

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- Physicians
  - Clinical trial participants
  - Patients of LCC's Medical Advisory Committee
- Other Patient Groups
  - Canada
  - International
- Online forums

Giving meaning to data: Eg. Pemrolizumab

KEYNOTE 010[2]	All Patients with PD-L1 TPS of ≥1%			Patients with PD-L1 TPS ≥50%		
HrQoL		n=210	n=146	n=90	n=103	n=60
QLQ-C30 LS Mean Change from baseline at 12 weeks (95% CI)	(-3.7 to 1.4)	-2.5 (-5.1 to 0.0)	-3.8 (-6.7 to 0.9)	1.5 (-2.5 to 5.5)	-3.0 (-6.8 to 0.7)	-6.9 (-11.5 to -2.2
LS Mean Difference[D] (CI); p-value				8.3 (2.4 to 14.3) p=0.006	3.8 (-1.9 to 9.6) p=0.19	-
Harms Outcomes, n (%)	Pembro 2mg/kg (n=339)	Pembro 10mg/kg (n=343)	Docetaxel (n=309)			
TRAE Grade ≥3	43 (13)	55 (16)	109 (35)			
TRAE (any grade)	215 (63)	226 (66)	251 (81)			
WDTRAE	15 (4)	17 (5)	31 (10)			

Abbreviations: AE = adverse event, CI = confidence interval, HR = hazard ratio, HRQoL = health-related quality o life, LS - least squares; NA - not applicable; NR = not reported, Pembro - pembrolizumab; QLQ-C30 - EORTC Quality of Life Questionnaire C-30; SD = standard deviation, TRAE = treatment-related adverse event, WDTRAE = withdrawal due to treatment-related adverse event; "-" docetaxel is the treatment reference group.

Notes:
[A] Data cut-off date is September 30, 2015.
[B] HR is for pembrolizumab versus docetaxel, where a HR < 1 favours pembrolizumab 2mg/kg or 10mg/kg.
[C] Result is not statistically significant because it did not meet the pre-specified criterion declaring statistical significance for PFS (p<0.001).
[D] Pembrolizumab treatment group versus docetaxel.

HrQoL

Change from baseline

Efficacy

After a median follow-up time of 13.1 months (range, 8.6-17.7), a total of 521 patients had died: 172 (50%) in the pembrolizumab 2mg/kg group, 156 (45%) in the 10mg/kg group, and 193 (56%) in the docetaxel group.

Overall, compared to docetaxel, pembrolizumab significantly prolonged OS, regardless of dose, among all patients (t was greater in the TPS ≥50% patient subgroup. The tre other patient subgroups examined, however, the difference between treatment groups did not reach statistical significance in the following patients subgroups: those with squamous cell histology, mutant EGFR status, aged ≥70 years,* and an ECOG status of 0. The subgroups analysis was pre-specified for ECOG PS, EGFR status and age of tumour sample. For tumour histology it was a post-hoc exploratory subgroup analysis. Further, the use of archived versus new tumour sample tissue for PD-L1 testing did not appear to affect treatment benefit.

Magnitude of benefit

Considering all patients (TPS ≥1%), a total of 776 PFS events were observed during the follow-up period; 226 (77%) in the 2mg/kg pembrolizuma oup, and 256 (75%) in the docetaxel group. No differen nent groups. Compared to docetaxel, pembrolizumab a FS benefit among patients with a TPS ≥50%, but not s expression level. The results of subgroup analyses benefit in the following subgroups of patients: male gender, ECOG of 1, and those patients with EGFR wi

Statistically significant PFS benefit

Fewer all grade and grade 3 - 5 treatment-related adverse events

* At the ubgroup analysis for patients aged ≥ trial publication and was pre-specified.

Note:
The current slide and next slide have been placed onto separate slides for ease of review
They will be on the same slide but animated during actual presentation.

Giving meaning to data

HrQoL

Change from baseline

Pembrolizumab allowed patients to get out of bed and find a “new normal”

The ability to get out of bed, put clothes on like a “real person” and “fix my hair” was significant. As one patient put it, “When you are on chemotherapy you can be at home but there is no difference to being in the hospital. You still can’t do things.” Pembrolizumab gave patients and their families a new, “good” quality of life by giving them a chance to still do some of the they were able to do before a lung cancer diagnosis. It established a “new normal”.

Pembrilzumab offered the possibility of returning to work

Patients were often concerned with taking time off for their disease. On chemotherapy, the side effects can be so strong, that there is no chance the patient can work. For those that responded on pembrolizumab, the question of returning to work became an option not possible for many lung cancer patients. For CC this was a very big concern and he was happy that his treatments allowed him to continue to teach at an Canadian University, coach Little League, play hockey. Other patients shared this desire.

Magnitude of benefit

Statistically significant PFS benefit

Pembrolizumab offered a chance to fulfil life hopes and dreams.

For CC that meant being a father to their young children, “32 months on Keytruda, everything went down 96%. I’m spoiled…my daughter gets to treat [stage IV lung cancer] as a chronic illness. She wants to be an oncologist.”

It also allows for patients to start a new mission. Many of the patients interviewed for this submission indicated that they wanted to help increase lung cancer awareness or serve as a peer to others living with lung cancer. This is significant not because that want to contribute and help. It is significant in that a they are ABLE to help.

“Stable became my new favourite word!”

When you have cancer, perspective can be everything. One patient reported that while her tumour never did shrink despite multiple rounds of treatment, after each scan the results were stable. This was “my new normal” and “better than the alternative.” Even small chores and “getting back to the basics of life” were a triumph. Stable is an important point to emphasize as patients have high expectations of immunotherapy. They hear about complete responders and pin great hopes of being the same. Education needs to occur to ensure that patients and their families understand that stable is still a win.

Fewer all grade and grade 3 - 5 treatment-related adverse events

The side effects of pembrolizumab did not inhibit life

LL reported that her side effects were “really, really light.” She has experienced some dizziness and some itchiness but otherwise Keytruda has “given me my life back.” She likes to exercise and the only thing holding her back now is due to ageing.

The majority of patients interviewed and reviewed during the environmental scan have reported no side effects to mild side effects that are easily managed. In a few cases there have been stronger side effects that had to be managed either by OTC or prescription drugs. Even of those however, most found that the management was tolerable and did not interfere with day to day life.

THE FACES OF LUNG CANCER REPORT

RESEARCH AND ANALYSIS OF THE LUNG CANCER 'WAITING GAME'

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2016

DATE OF FROM FDA APPROVAL TO HEALTH CANADA APPROVAL

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Figure 6 – Date of FDA approval to Health Canada approval

DRUG Generic name (brand name)	INDICATION	FDA APPROVAL DATE	ADDITIONAL DAYS UNTIL HEALTH CANADA APPROVAL DATE	pCODR Status	Phase Data Used
afatinib (Giotrif®)	For the first line treatment of epidermal growth factor receptor (EGFR) mutation positive, advanced non-small cell lung cancer (NSCLC) patients	July 12, 2013	**November 1, 2013 (112 days)**	Final Recommendation May 2, 2014: Recommended pending cost effectiveness	3
alectinib (Alecensaro®) 2nd line*	As monotherapy for the treatment of patients with anaplastic lymphoma kinase (ALK) positive, locally advanced (not amenable to curative therapy) or metastatic NSCLC who have progressed on or are intolerant to crizotinib until loss of clinical benefit	December 11, 2015	**September 29, 2016 (293 days)**	Pending	3
alectinib (Alecensaro®) 2nd line with central nervous system (CNS) metastases	As monotherapy for the treatment of patients with ALK positive, locally advanced or metastatic NSCLC who have progressed on or are intolerant to crizotinib and have central nervous system (CNS) metastases	December 11, 2015	**September 29, 2016 (293 days)**	Final Recommendation: Not recommended	2
ceritinib (Zykadia®) 2nd line	For treatment as monotherapy in patients with ALK positive locally advanced (not amenable to curative therapy) or metastatic NSCLC who have progressed on or who were intolerant to crizotinib	April 29, 2014	**March 27, 2015 (332 days)**	Final Recommendation December 3, 2015: Not Recommended	2
ceritinib (Zykadia®) Resubmission 2nd line	For treatment as monotherapy in patients with ALK positive locally advanced (not amenable to curative therapy) or metastatic NSCLC who have progressed on or who were intolerant to crizotinib	April 29, 2014	**March 27, 2015 (332 days)**	Final Recommendation March 21, 2017: Recommended, pending cost effectiveness	3
crizotinib (Xalkori®) 2nd line	As monotherapy for use in patients with ALK positive advanced (not amenable to curative therapy) or metastatic NSCLC	August 26, 2011	**April 25, 2012 (243 days)**	Final Recommendation May 2, 2013: Recommended, pending cost effectiveness	3
crizotinib (Xalkori®) 1st line	As monotherapy for use in patients with ALK positive advanced (not amenable to curative therapy) or metastatic NSCLC	August 26, 2011	**April 25, 2012 (243 days)**	Final Recommendation July 21, 2015: Recommended, pending cost effectiveness	3

DATE OF FROM FDA APPROVAL TO HEALTH CANADA APPROVAL

Continued... **Figure 6 – Date of FDA approval to Health Canada approval**

DRUG Generic name (brand name)	INDICATION	FDA APPROVAL DATE	ADDITIONAL DAYS UNTIL HEALTH CANADA APPROVAL DATE	pCODR Status	Phase Data Used
dabrafenib (Tafinlar®) + trametinib (Mekinist®) 2nd line	In combination for the treatment of patients with advanced NSCLC with a BRAF V600 mutation and who have been previously treated with chemotherapy	June 22, 2017 (approved in any line of therapy)	**May 16, 2017 (-37 days) [approved only after failure of prior chemotherapy]**	Initial Recommendation: Not recommended	2
nivolumab (Opdivo®) 2nd line	For the treatment of patients with advanced or metastatic NSCLC who progressed on or after chemotherapy	March 4, 2015	**Februrary 26, 2017 (725 days)**	Final Recommendation June 3, 2016: Recommended and publicly funded in most provinces	3
osimertinib (Tagrisso®) 2nd line	For the treatment of patients with locally advanced or metastatic EGFR T790M mutation positive NSCLC who have progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy	November 13, 2015	**July 5, 2016 (235 days)**	Final Recommendation May 4, 2017: Recommended pending cost effectiveness	3
pembrolizumab (Keytruda®) 2nd line	For the treatment of patients with metastatic NSCLC whose tumours express PD-L1 (as determined by a validated test) and who have disease progression on or after platinum-containing chemotherapy	September 4, 2014	**April 15, 2016 (589 days)**	Final Recommendation: Recommended pending cost effectiveness but not yet funded	2/3
pembrolizumab (Keytruda®) 1st line	For previously untreated patients with metastatic NSCLC whose tumours express PD-L1 and who do not harbour a sensitizing EGFR mutation or ALK translocation.	October 24, 2016	**July 12, 2017 (261 days)**	Final Recommendation: Recommended, pending cost effectiveness but not yet funded	3
ramucirumab (Cyramza®) 2nd line	For the treatment of patients with advanced or metastatic NSCLC who progressed on or after platinum-based chemotherapy in combination with docetaxel	April 21, 2014	**July 16, 2015 (451 days)**	Closed, not submitted	3

Significant Delays In Access

Figure 8 – Number of days from date of FDA approval to date of provincial coverage

DRUG Generic name (brand name)	FDA APPROVAL DATE	BC	AB	SK	MB	ON	QC	NS	NB	NL	PEI
afatinib (Giotrif®) 2nd line	July 12, 2013	446	445	430	461	403	1027	535	426	689	1200
alectinib (Alecensaro®) 2nd line	December 11, 2015	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded
alectinib (Alecensaro®) with CNS metastasis	December 11, 2015	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded
ceritinib (Zykadia®) 2nd line	April 29, 2014	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded
crizotinib (Xalkori®) 2nd line	August 26, 2011	918	797	769	783	767	892	828	805	949	1711
crizotinib (Xalkori®) 1st line	August 26, 2011	1746	1763	1773	1794	1749	1627	1711	1879	1808	Not Funded
dabrafenib (Tafinlar®) + trametinib (Mekinist®) 2nd line	June 22, 2017	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded
nivolumab (Opdivo®) 2nd line	March 4, 2015	728	761	750	740	748	Not Funded	759	790	883	Not Funded
osimertinib (Tagrisso®) 2nd line	November 13, 2015	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded
pembrolizumab (Keytruda®) 2nd line	September 4, 2014	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded
pembrolizumab (Keytruda®) 1st line	October 24, 2016	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded
pemetrexed (Alimta®) 2nd line	July 2, 2009	1764	1764	1705	1795	1734	1917	1734	1887	1734	2335
ramucirumab (Cyramza®) 2nd line	April 21, 2014	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded	Not Funded

LUNG CANCER CANADA
AWARENESS. SUPPORT. EDUCATION.

- Negative funding PCODR recommendation
- Submitted on phase 2 data - Targeted therapies with high response rates

Innovation in treatment have given Canadian Lung Cancer Patients Real Hope But....

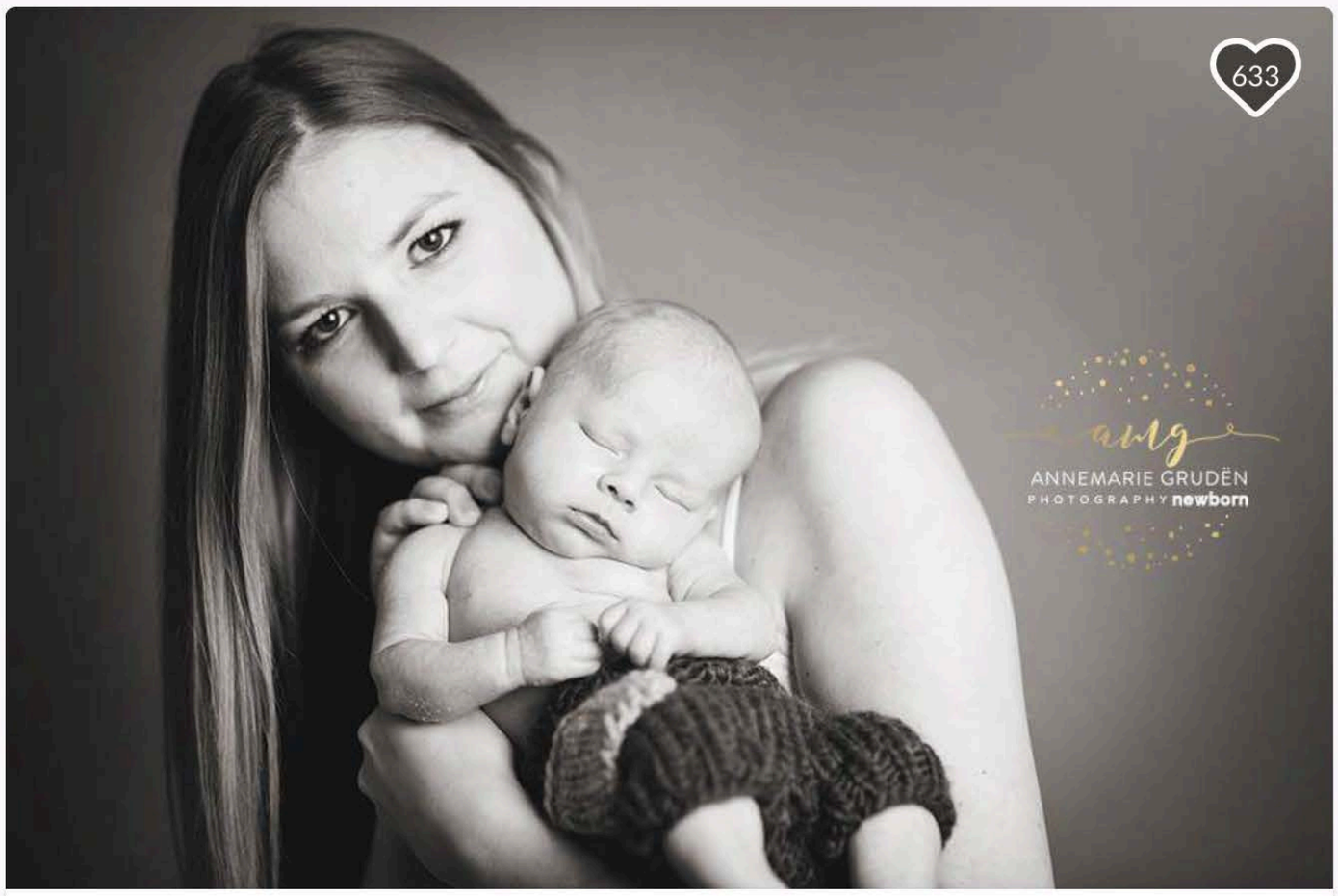
- Healthcare system has not innovated on pace with treatments
- Significant barriers to access that are growing
  - Treatments approved on phase 2 data denied public coverage
  - CDIAC
  - Private plans
- High cost of treatment

Lung Cancer patients have no time to wait!

Lung Cancer is not a Go Fund Me Disease!

gofundme | Search | Start a Fundraiser

Share | Tweet | Donate



Kayla's Fight Club

Share | Tweet | 2.9K shares

$42,731 of $65k goal

Raised by 629 people in 9 months

Donate Now

Share on Facebook

Created January 16, 2017

April-Dawn Bradford

on behalf of Kayla Bradford

Medical

Carleton Place, ON

Top Supporters

First Donor

JM

Jo-Ann McKenna

$100

COLLABORATION = INNOVATION

- Change paradigm of drug evaluation
- Targeted therapies and phase 2 data
- Develop new economic models for drug funding
- All stakeholders (clinicians to patients to government) have a voice, and a responsibility

CANADA

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