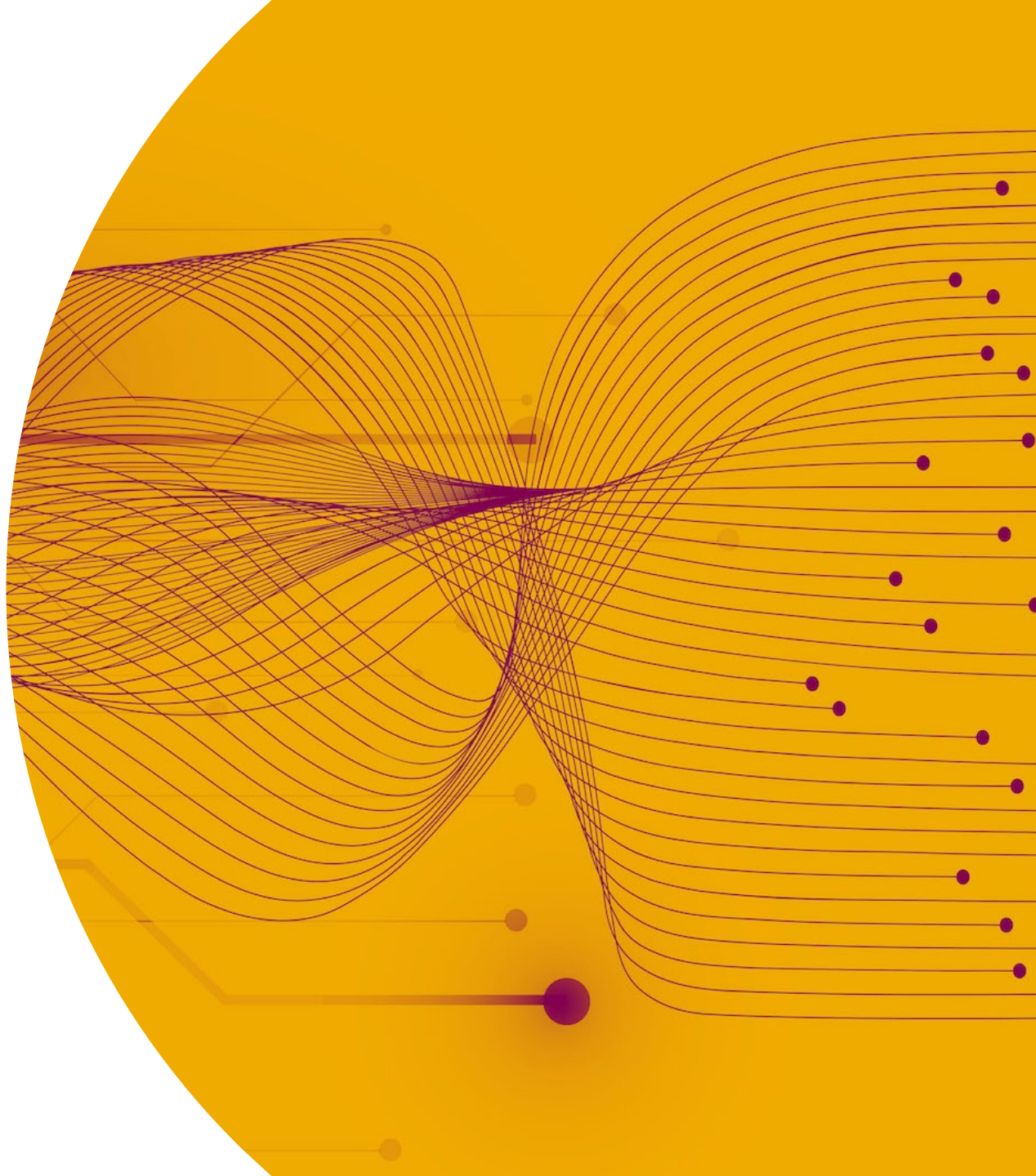
AstraZeneca

How industry supports innovation in drug reimbursement decision-making in Canada

Cal Shephard

October 20th, 2023



Cal Shephard

Senior Manager, Market Access Strategy & Health Economics at AstraZeneca Canada

- At AZ since November 2020
- Focus on gynecological and genitourinary cancers
- Previously Lead, Health Economics at CADTH
- Experience in market access consulting in the UK and Canada
- MSc in Health Economics from City, University of London

Agenda

1. Introduction to AstraZeneca Canada
2. How drugs are reimbursed in Canada
3. The importance of real-world evidence
4. Eliciting patient preferences
5. Stakeholder engagement

Objective

To demonstrate how industry supports innovation in drug reimbursement decision-making in Canada

Introduction to AstraZeneca Canada

About AstraZeneca Canada

1,300
employees across Canada

9th
consecutive year recognized as one of *Greater Toronto's Top Employers*

90%
of AZ's clinical pipeline today follows a precision medicine approach

$148M
in Canadian health sciences research in 2022

130+
global clinical studies led by our AZ and Alexion R&D hubs in Mississauga.

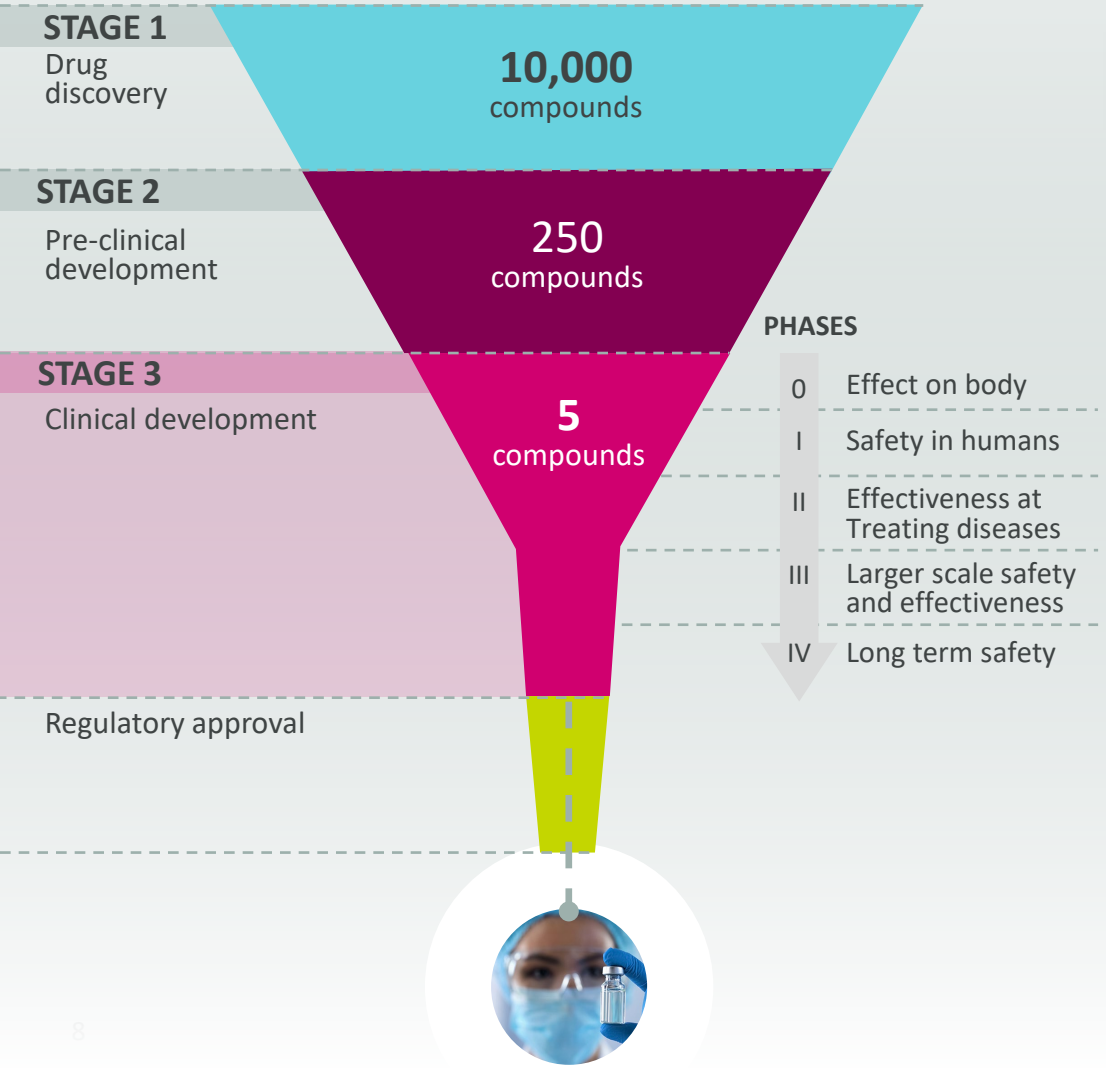
174
active clinical studies in Canada involving roughly 2,800 patients

Our Global R&D centres

The Mississauga site is a strategic Clinical Hub for AstraZeneca Globally

Clinical Hub in Canada – Mississauga site

Drug Development path



Leading **130+ global clinical studies** which screened over 110,000 patients in 50+ countries around the world

Investigational compounds under study

Oncology: Enhertu, Dato-Dxd, ceralasertib, Imfinzi, Koselugo, Tagrisso, Lynparza, Imjudo, tremelimumab, capivasertib, adavosertib, monalizumab, Recentin, savolitinib, camizestrant

Hematology: TNB-486, Calquence

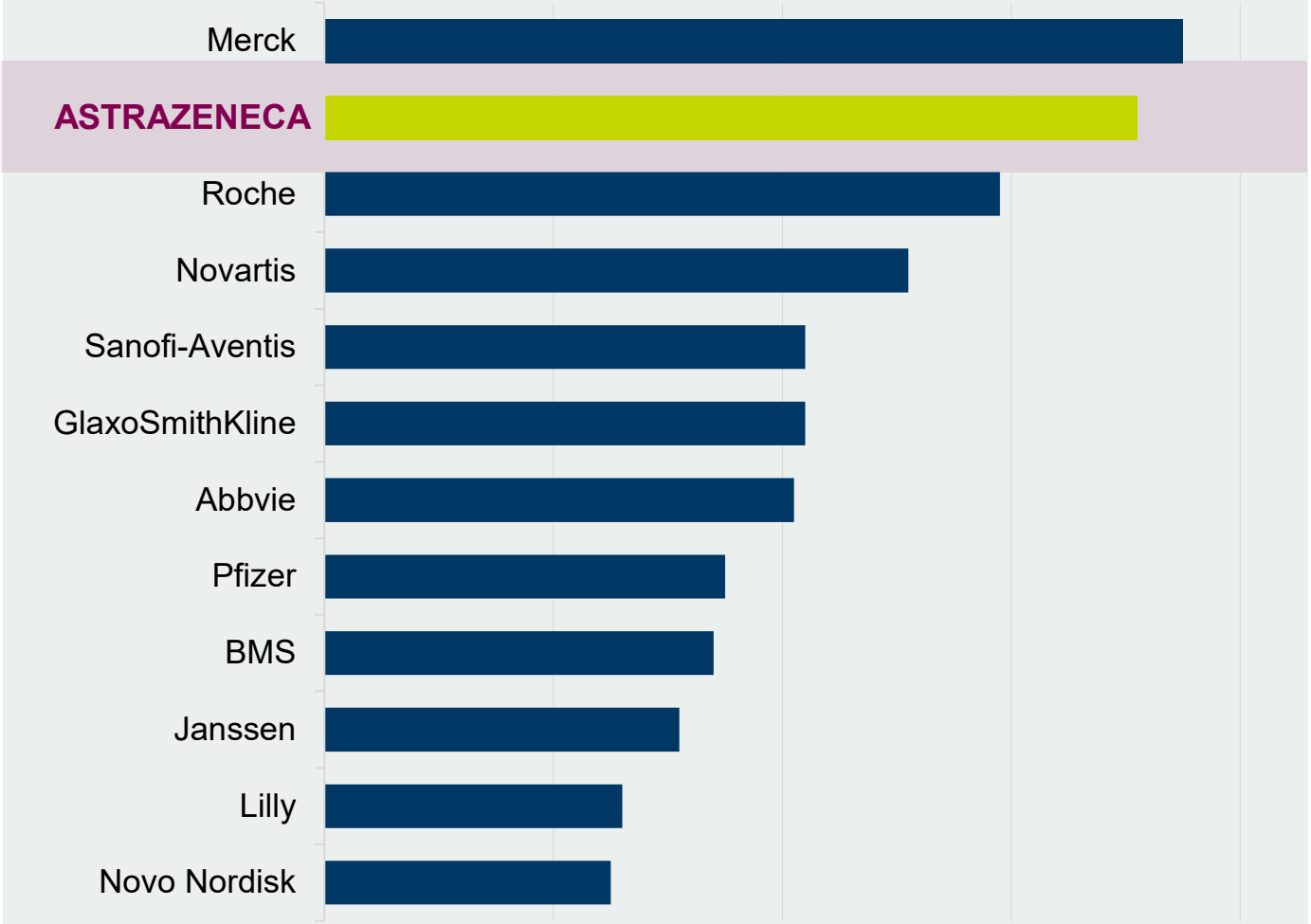
V&I: Evusheld, Vaxzevria, Beyfortus

R&I: Breztri, tozorakimab, brazikumab, Tezspire, PT-0009, Fasenra

CVRM: Andexxa, AZD8233, cotadutide, dapagliflozin, Lokelma, verinurad, zibotentan

A rapidly growing clinical footprint in Canada

Canadian Clinical Studies
Total Studies 2019-2021



174
Active clinical studies in Canada

264
Canadian hospitals, clinics, sites

2,800
Canadian patients

4th
Largest clinical footprint within AZ

Expanding our Canadian scientific footprint

AstraZeneca

Expansion of Mississauga
AZ R&D Hub

ALEXION®
AstraZeneca Rare Disease

Creation of new Mississauga
Alexion Development Hub

70

Canadian real world evidence (RWE) studies in 2022

20+

RWE partnerships with leading hospitals and research institutions

70

External-sponsored research studies (ESRs)

Princess Margaret Cancer Centre

UHN

CHUM

Centre hospitalier de l'Université de Montréal

IC/ES

McGill University Health Centre

Alberta Health Services

BC CANCER

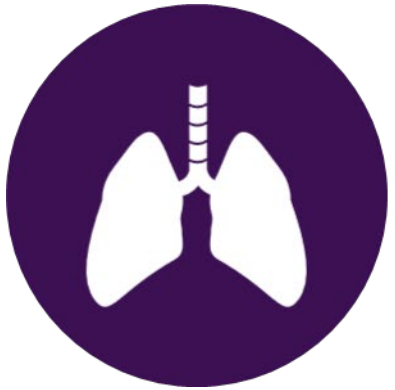
Leading in our therapy areas

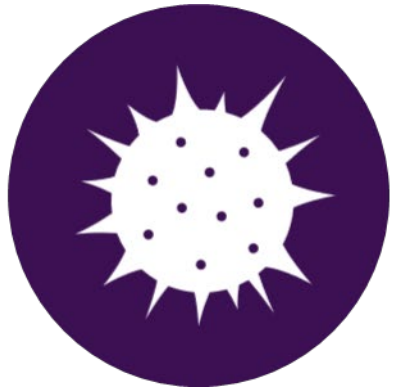
We’re creating novel therapies that help people with cancer, other chronic and rare diseases – areas where we believe we can make the most meaningful difference to patients.

Oncology

Leading a revolution in oncology to redefine cancer care

BioPharmaceuticals





Our aim is to transform care for billions of people living with chronic diseases and delivering long-lasting immunity

Cardiovascular, Renal & Metabolism

Respiratory & Immunology

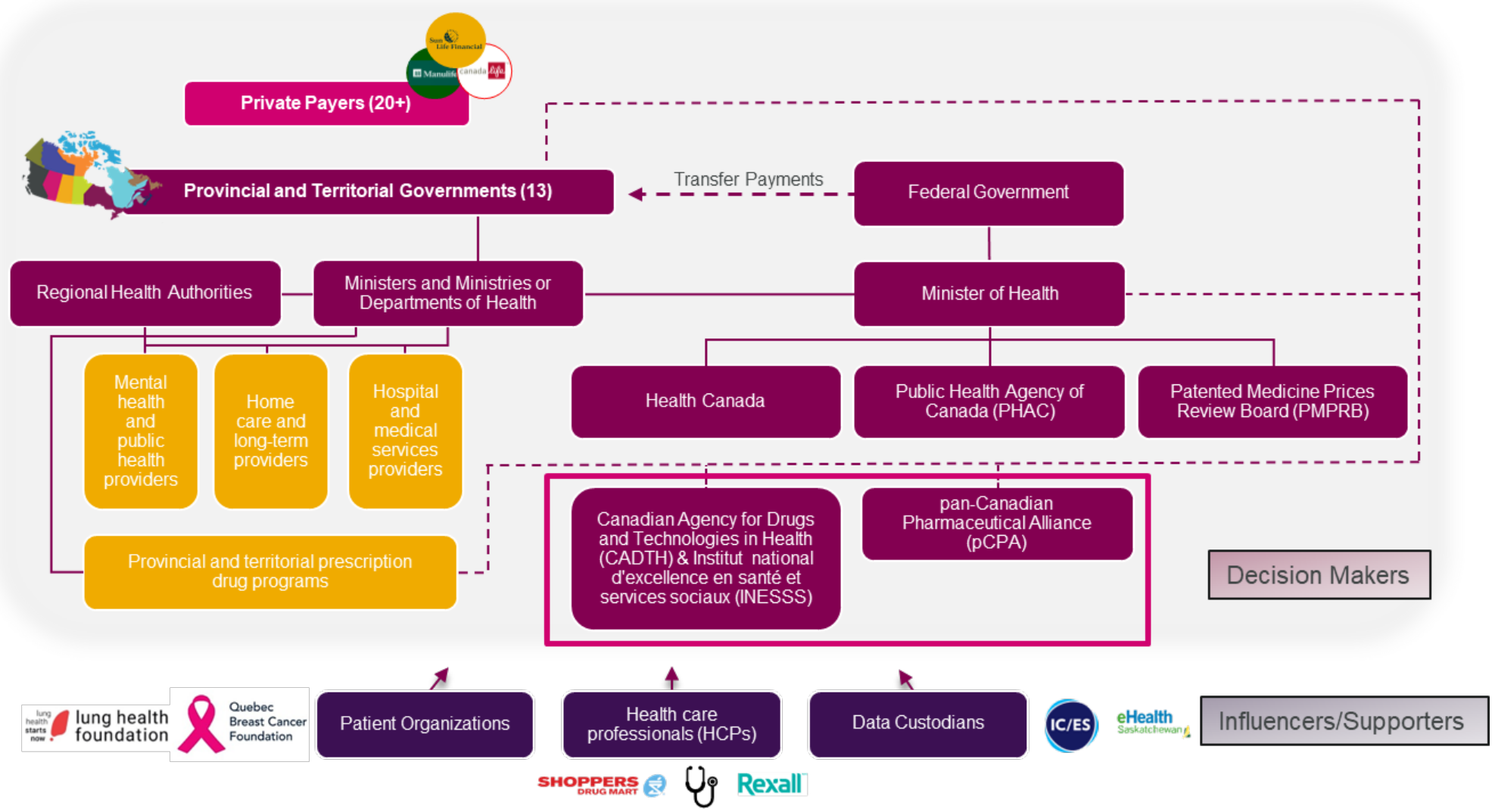
Vaccines & Immune Therapies

Rare Disease

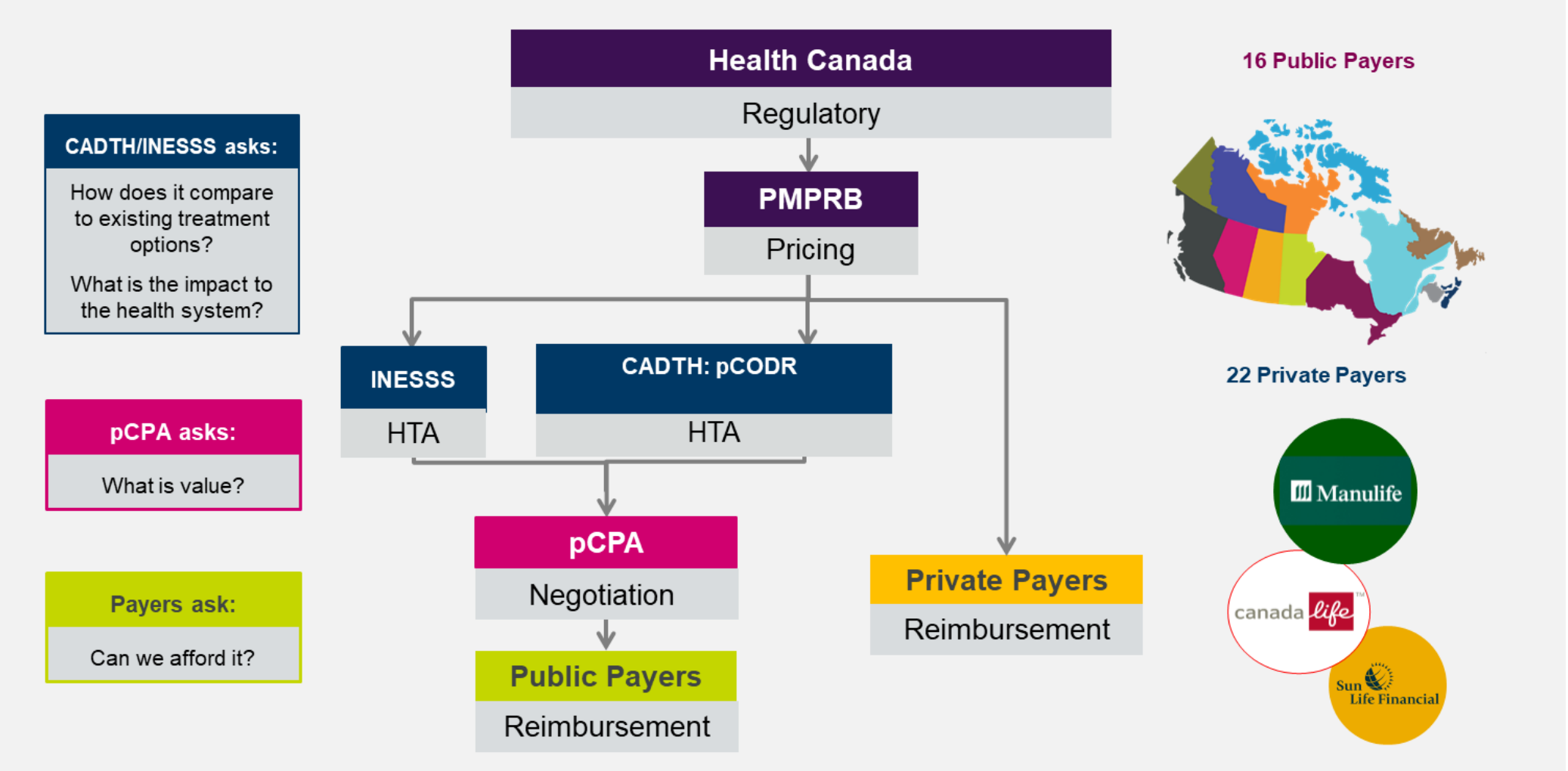
We aim to transform the lives of people affected by rare diseases

How drugs are reimbursed in Canada

Many stakeholders influence access to medicines in Canada



Canadian Pharmaceutical Reimbursement Pathway



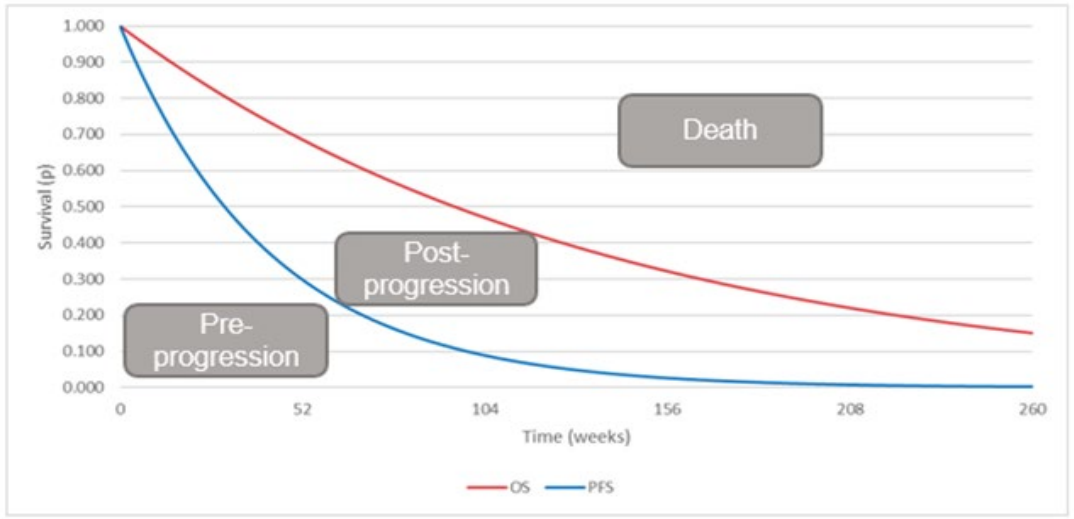
Market access professionals conduct the following activities to support reimbursement in Canada

- Clinical submission dossiers
- Cost-effectiveness analyses
- Budget impact analyses
- Indirect treatment comparisons
- Expert advisory boards
- Real World Evidence Studies
- Engaging with key stakeholders

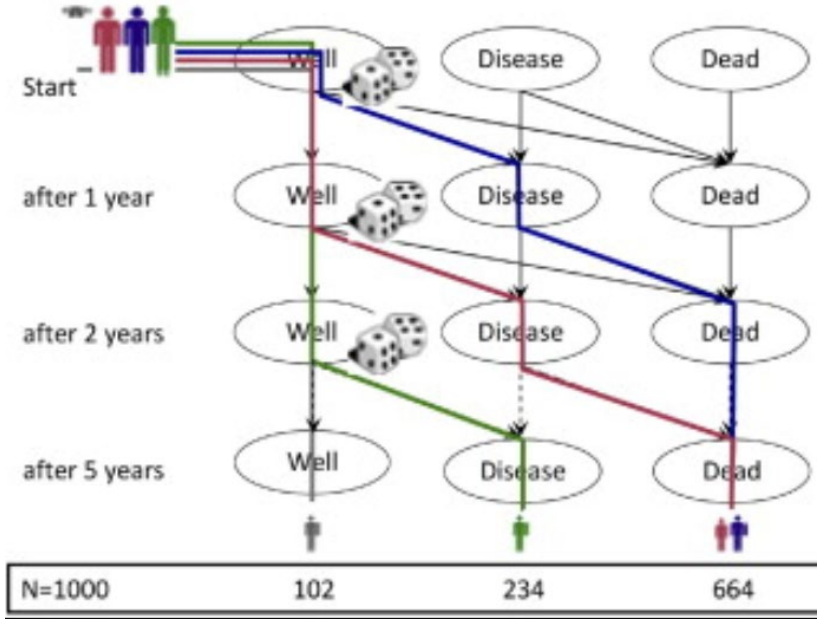
What is cost-effectiveness analysis?

Incremental Cost-Effectiveness Ratio (ICER) = $\dfrac{\text{Incremental Costs}}{\text{Incremental QALYs}}$

Partitioned-Survival Model

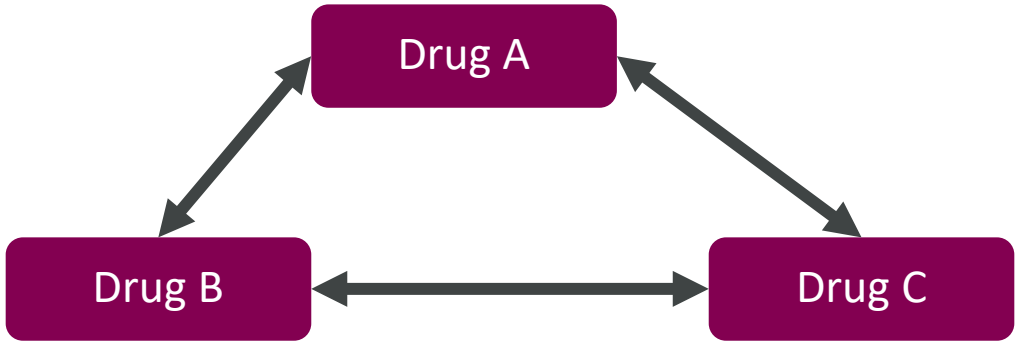


Semi-Markov Model



What is indirect treatment comparison?

- The clinical trial compares Drug A with Drug B
- What if we wanted to compare Drug A with another comparator Drug C
- If there is another trial comparing Drug B with Drug C then this may be possible



The Importance of Real-World Evidence

What is Real World Evidence?

- Real-world evidence is the clinical evidence about the usage and potential benefits or risks of a medical product derived from analysis of real-world data (RWD) relating to patient health status and/or the delivery of health care routinely collected from a variety of sources.

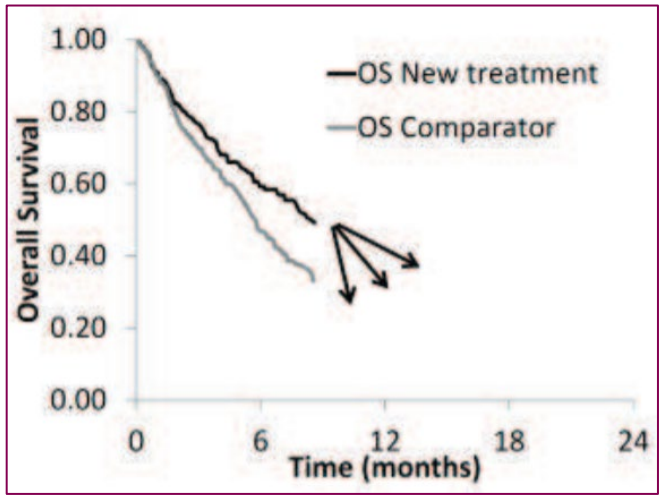
- Examples of RWD include data derived from electronic health records, medical claims data, data from product or disease registries, and data gathered from other sources that can inform on health status.

Source: FDA. https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence

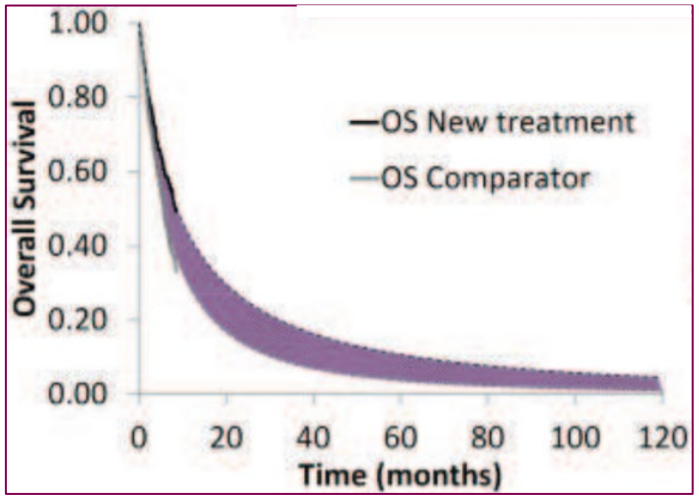
Real world evidence is critical to Canadian HTA submissions

- Cost-utility analyses submitted to CADTH or INESSS are required to use a lifetime horizon
- At launch trial data on the effects of a new drug typically don’t typically have long enough follow up to assess clinical efficacy over a lifetime horizon or are even immature, increasing payer uncertainty
- Including a real-world evidence study as part of the submission package can pre-emptively mitigate against expected criticisms of existing data

Real world evidence can help justify long-term survival assumptions



Longer survival benefit



Shorter survival benefit

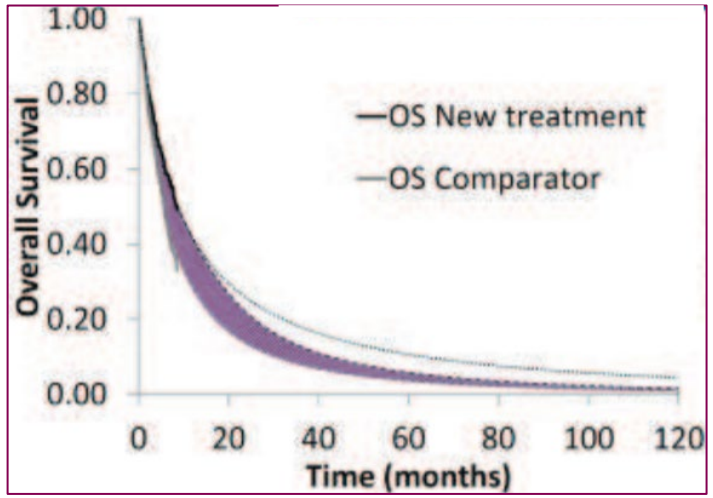


Image from: Beca, Husereau, Chan, Hawkins & Hoch (2018) Oncology modeling for fun and profit! Key steps for busy analysts in health technology assessment. *Pharmacoeconomics* **36:**7-15

Why real-world evidence is critical to Canadian HTA submissions

- Clinical trials do not always perfectly replicate the Canadian treatment landscape. We're at risk of:

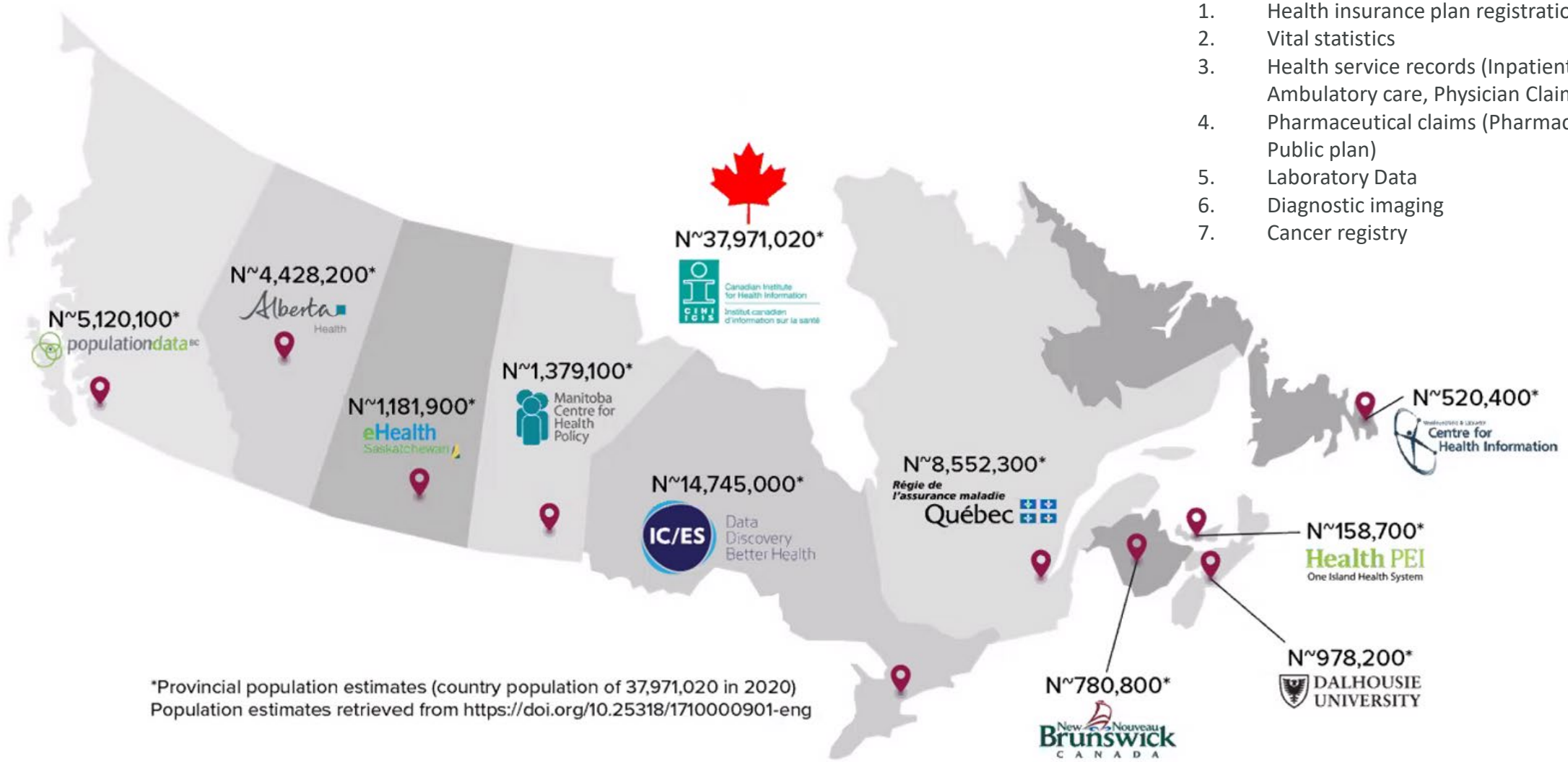
1. Misidentifying comparators
2. Not understanding the impact of different pre-treatments
3. Incorrectly estimating the cost of healthcare resource use and subsequent treatment
4. Incorrectly estimating the efficacy of SoC

- Real World Evidence can help better inform us about the Canadian treatment landscape

Sources of Real-World Evidence in Canada

Canadian RWE typically includes the following data:

1. Health insurance plan registration
2. Vital statistics
3. Health service records (Inpatient, Ambulatory care, Physician Claims)
4. Pharmaceutical claims (Pharmacy-level, Public plan)
5. Laboratory Data
6. Diagnostic imaging
7. Cancer registry



Eliciting Patient Preferences

We partner with patient advocates in an effort to improve experiences and outcomes for patients

Shape healthcare systems and policies to improve outcomes for patients

Demonstrate our company's commitment to the communities of people impacted by the diseases we treat or aim to treat

Support access to our **innovative medicines** including supporting patient advocacy groups who wish to input into HTA submissions

Deepen our collective **understanding of patients' lived experiences** to inform our strategy and solutions to **improve the patient experience**

Preference research and data helps us better understand what patients want from treatment

- Patients are the end users of medicines.
- Patients have different experiences, perspectives and wants from their treatment.
- It cannot be assumed all patients want the same thing.
- Different patients have different attitudes to the trade off between the benefits of drug treatment and the impacts of adverse events

Source: European Medicines Agency. Accessible from: https://www.ema.europa.eu/en/documents/presentation/presentation-patient-preference-research-k-morrigan-mpe_en-0.pdf

Patient preferences relate to data generated directly from patients on how they make choices on different treatment options and attributes

Patient Characteristics

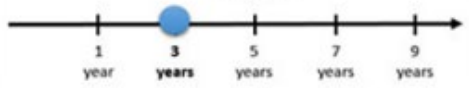
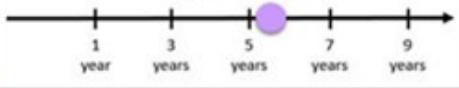
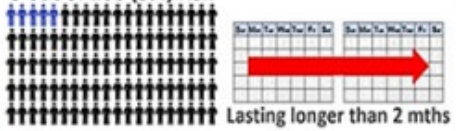
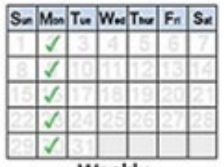
- Disease severity
- Age
- Gender
- Race
- Rural vs. Urban
- Work/parenting/caregiver commitments

Attributes of treatment

- Progression-free survival
- Overall survival
- Side effect profile
- Mode of administration
- Frequency of administration

Source: European Medicines Agency. Accessible from: https://www.ema.europa.eu/en/documents/presentation/presentation-patient-preference-research-k-morrigan-mpe_en-0.pdf

Discreet Choice Experiment

Factors	Treatment A	Treatment B	Neither of these treatments
Average overall survival	7 years 	3 years 	
Average remission period	5 years 3 months 	9 months 	
Mild or Moderate side-effects	60 out of 100 (60%) risk 	20 out of 100 (20%) risk 	
Severe side-effects	5 out of 100 (5%) risk 	10 out of 100 (10%) risk 	
How treatment is taken	 Intravenous drip (Hospital / clinic) Time: 2-3 hours	 Subcutaneous Injection (Hospital / clinic) Time: 15 mins	
Frequency of taking treatment	 Fortnightly	 Weekly	
Average out of pocket costs to you over a year	£0	£0	
I would choose	○ Treatment A	○ Treatment B	○ Neither

Source: European Medicines Agency. Accessible from: https://www.ema.europa.eu/en/documents/presentation/presentation-patient-preference-research-k-morrigan-mpe_en-0.pdf

How can patient preference data be used?

- Benefit risk assessments
- Frames and provides context for decision-making (in a more robust way).
- Answer specific questions for committees (such as value patients place on administration, survival gains or QoL).
- Is the treatment acceptable to patients?

Source: European Medicines Agency. Accessible from: https://www.ema.europa.eu/en/documents/presentation/presentation-patient-preference-research-k-morrigan-mpe_en-0.pdf

Stakeholder Engagement

AstraZeneca needs to work with various stakeholders given the changing nature of drugs and reimbursement pathways

Identify the Issue	Engage Stakeholders	Educate Decision Makers	Assess Readiness
Identify the issue through local assessment	Build patient/PAG awareness and advocacy	Gain support from regulators and policymakers through education of need	Build up political support for change
	Gain industry collaboration to drive policy change		
	Work with medical and scientific community to substantiate endpoint value		

The Canadian healthcare system needs to adapt to the coming avalanche of early-stage cancer trials which use surrogate endpoints as the primary endpoint

- It is often unfeasible to use traditional endpoints such as OS in early-stage cancer trials
- Early-stage oncology trials usually assess efficacy using surrogate endpoints (e.g. pCR, DFS, EFS etc.)
- Surrogate endpoints may reduce clinical trial duration by ~11 months and it is often infeasible to demonstrate overall survival benefit as it would often be confounded by subsequent lines of therapy and mandatory cross-over
- Despite the increasing use of surrogate endpoints by regulatory agencies for drug approval, HTA bodies often preferentially weigh traditional clinical outcomes

Championing Oncology Relevant Endpoints (CORE) in Canada: Surrogate endpoints in clinical trials and reimbursement decisions for early-stage cancers

- IQVIA Canada, in partnership with AstraZeneca Canada, conducted this study to quantify and examine how traditional and surrogate endpoints used in early- stage oncology clinical trials are evaluated in Canadian reimbursement decision-making.

- Retrospective analyses were conducted with the following objectives:
  - To assess the use of surrogate endpoints in early-stage oncology clinical trials
  - To assess endpoints considered by CADTH when making informed reimbursement recommendations

An independent study of clinical trials in early-stage disease for solid tumours was conducted to assess the use of surrogate endpoints

Selection Criteria

Trial type: Interventional clinical trials

Trial timing: Start date of Jan 2017 - Mar 2022

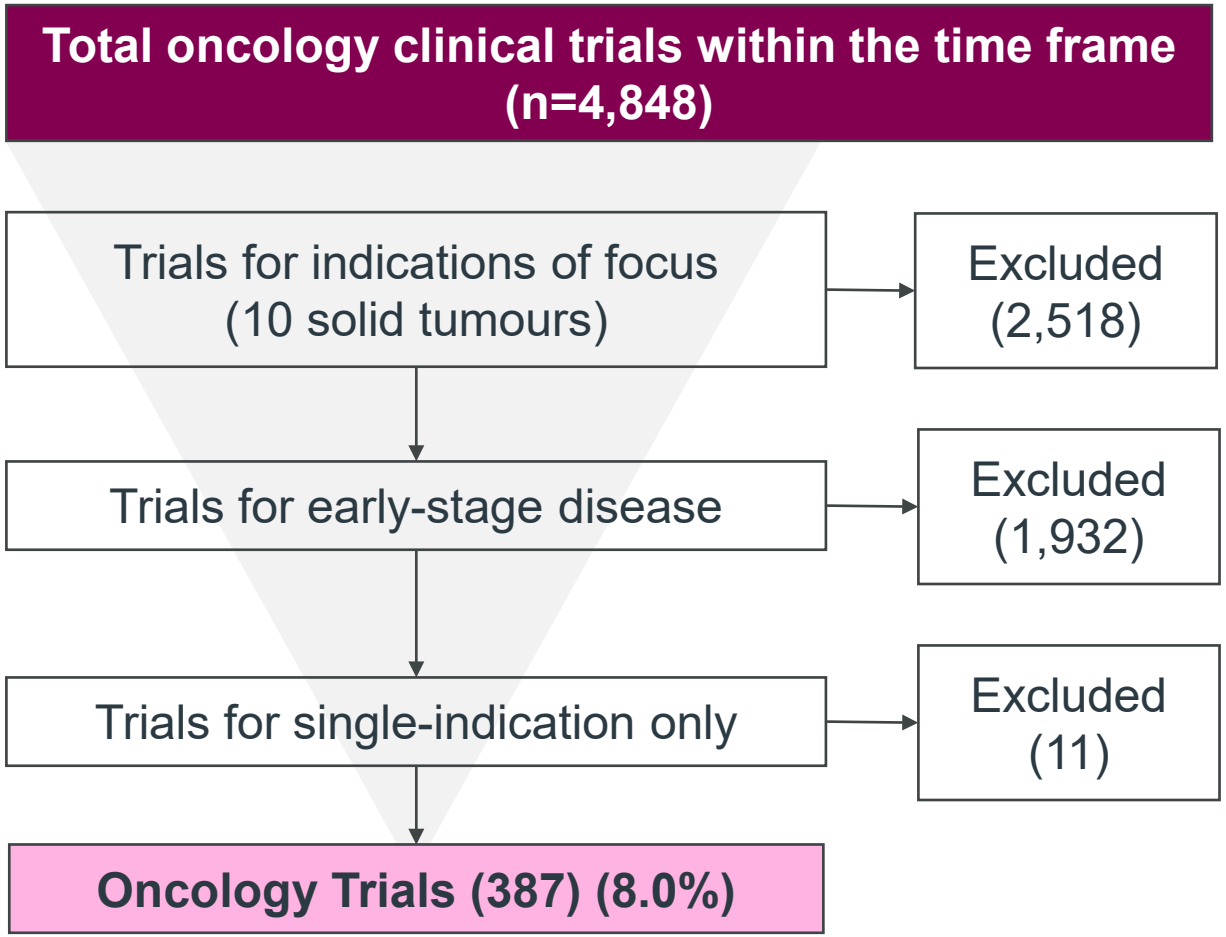
Sponsor: Industry

Study Phase: Phase 2 and 3

Status: not withdrawn, suspended or completed

Top 10 tumor types: Lung, Breast, Prostate, Melanoma, Ovarian, Colorectal, Pancreatic, Esophageal, Gastric, Bladder (single indication)

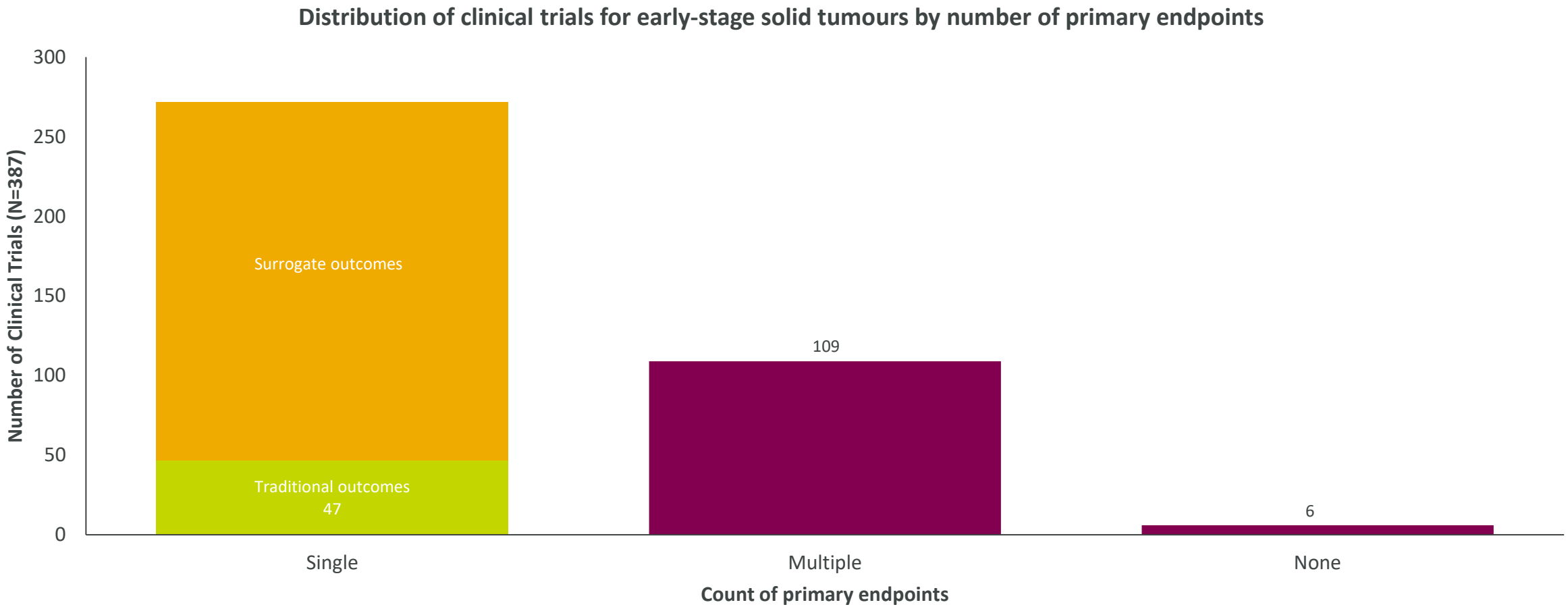
Disease stage: Early stage, non metastatic, non invasive, localized, Stage I-III



Source: clinicaltrials.gov

Analysis conducted by IQVIA, and sponsored by AstraZeneca

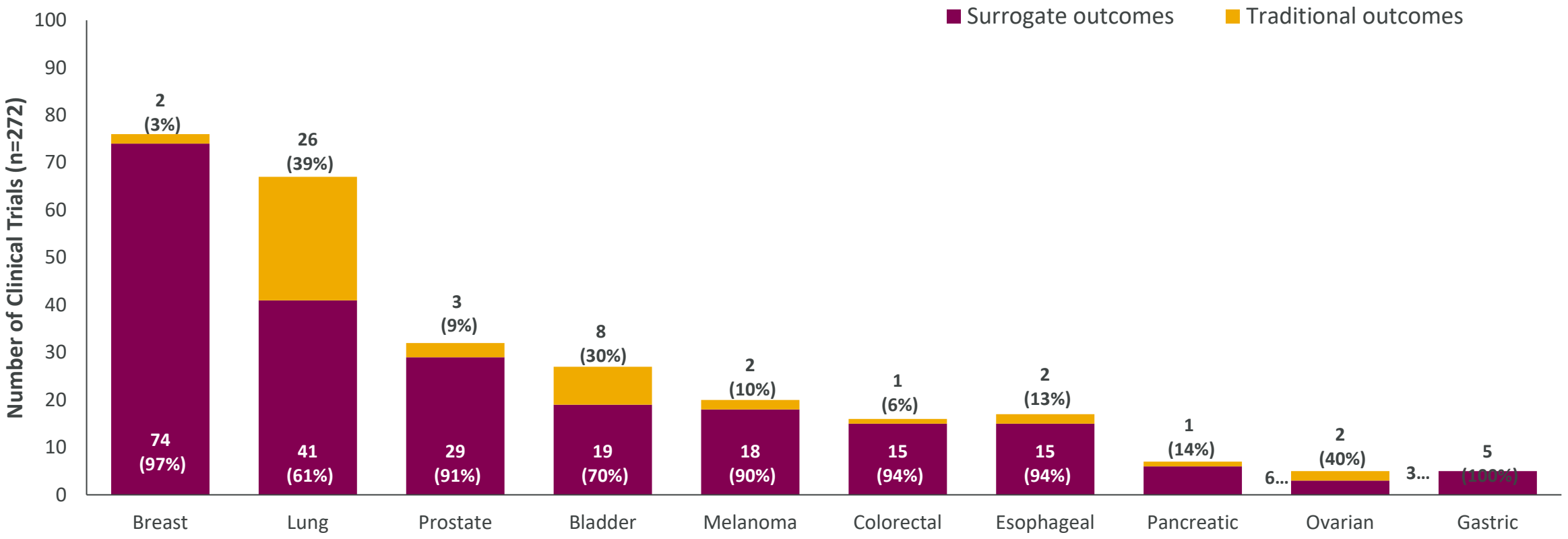
70% of early-stage oncology trials had a single primary endpoint and of these 83% used a surrogate endpoint



Source: clinicaltrials.gov

Analysis conducted by IQVIA, and sponsored by AstraZeneca

Surrogate endpoints for early-stage cancers can be seen across tumour types, with significant representation in breast and prostate

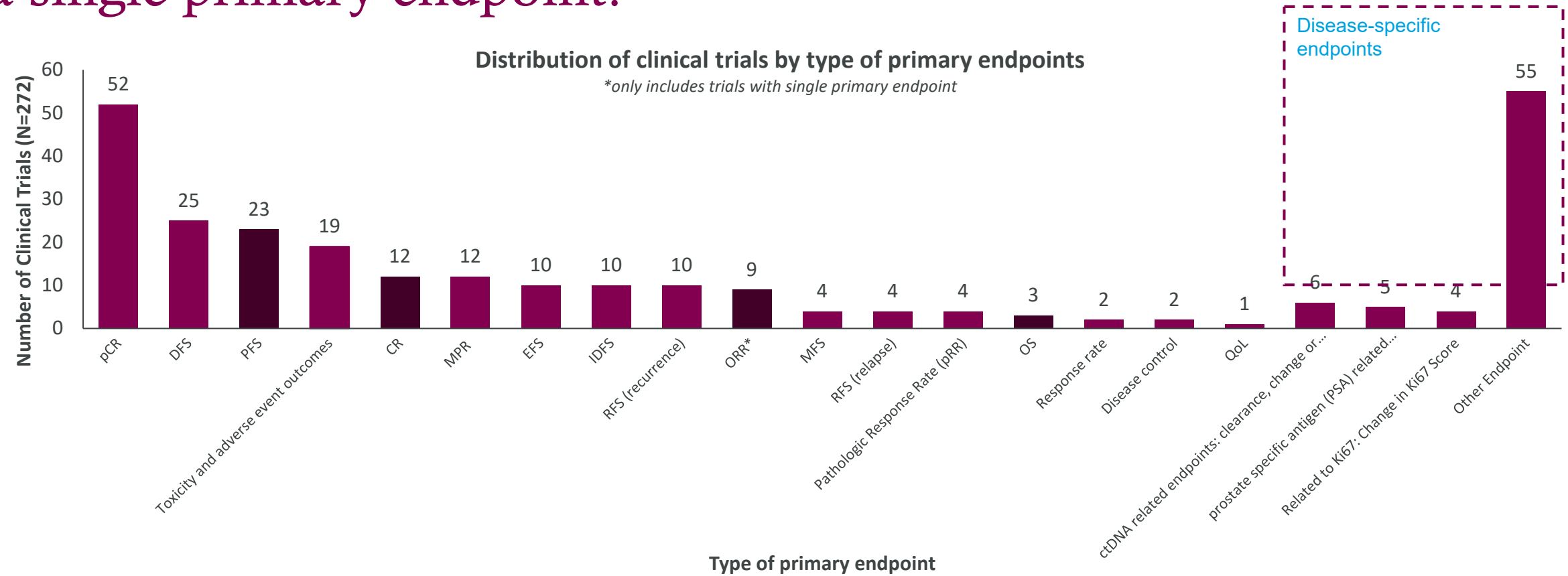


Notes: 1 trial with gastro-esophageal cancer was merged with esophageal cancer

Source: clinicaltrials.gov

Analysis conducted by IQVIA, and sponsored by AstraZeneca

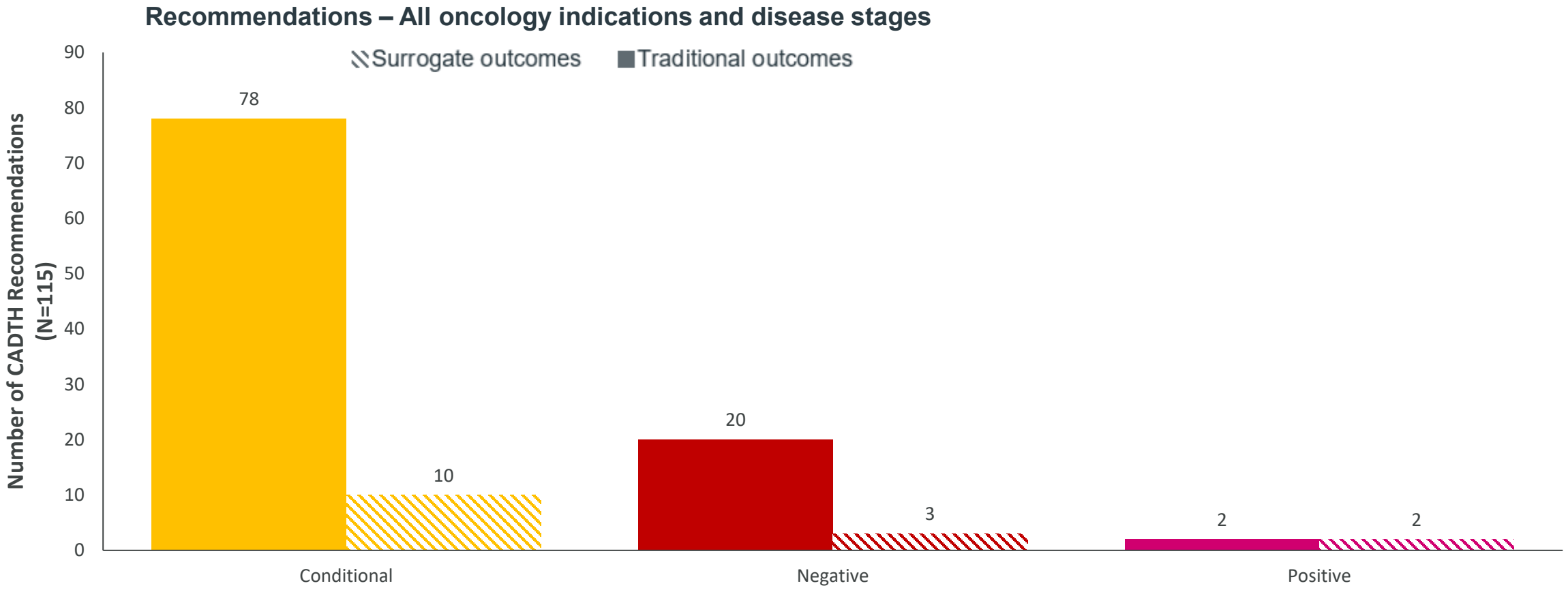
Pathologic complete response (pCR) was the most common surrogate endpoint among early-stage oncology clinical trials with a single primary endpoint.



Abbreviations: *CR; complete response; DFS, Disease free survival; EFS, event free survival; IDFS, Invasive disease free survival; MFS, Metastasis free survival; MPR, major pathological response; ORR, overall response rate; OS, overall survival; pCR, Pathologic complete response; PFS, progression free survival; QoL, quality of life; RFS (recurrence free survival); RFS (relapse free survival) *Includes eight clinical trials for lung cancer and one for melanoma*

Source: clinicaltrials.gov
Analysis conducted by IQVIA, and sponsored by AstraZeneca

A study of CADTH recommendations for oncology therapies highlighted historic trends in submitted evidence across all indications



Source: IQVIA's Market Access Metrics database & CADTH

 Analysis conducted by IQVIA, and sponsored by AstraZeneca

A study of CADTH recommendations in early-stage disease for solid tumours was conducted to estimate the potential impact of surrogate endpoints on HTA decisions

Selection Criteria

Document type: CADTH Final Recommendation

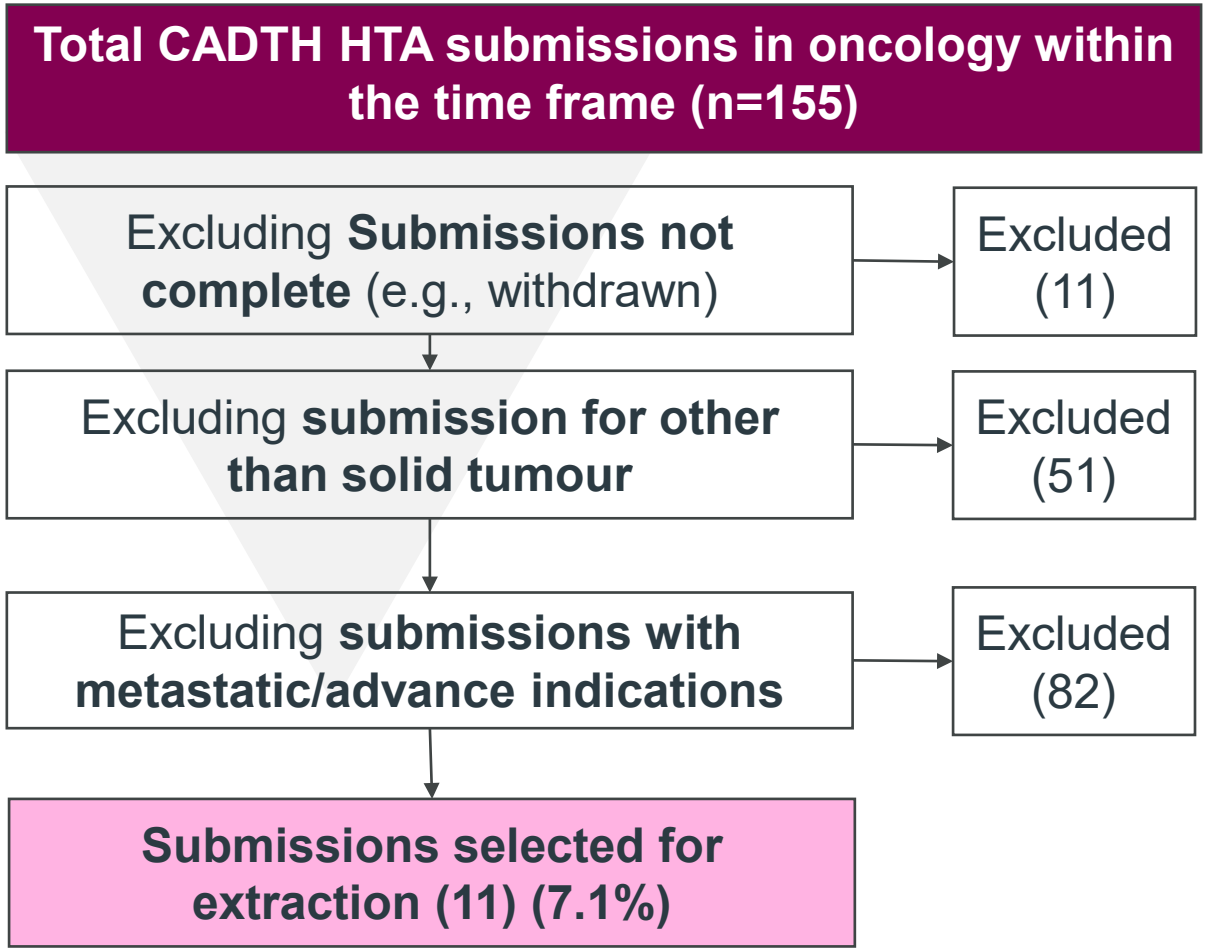
Timing: Jan 2017 - Mar 2022

Study Phase: Phase 2 and 3

Status: "Completed" (i.e. not withdrawn or suspended), first submission (i.e. not resubmission)

Tumour types: Solid tumours

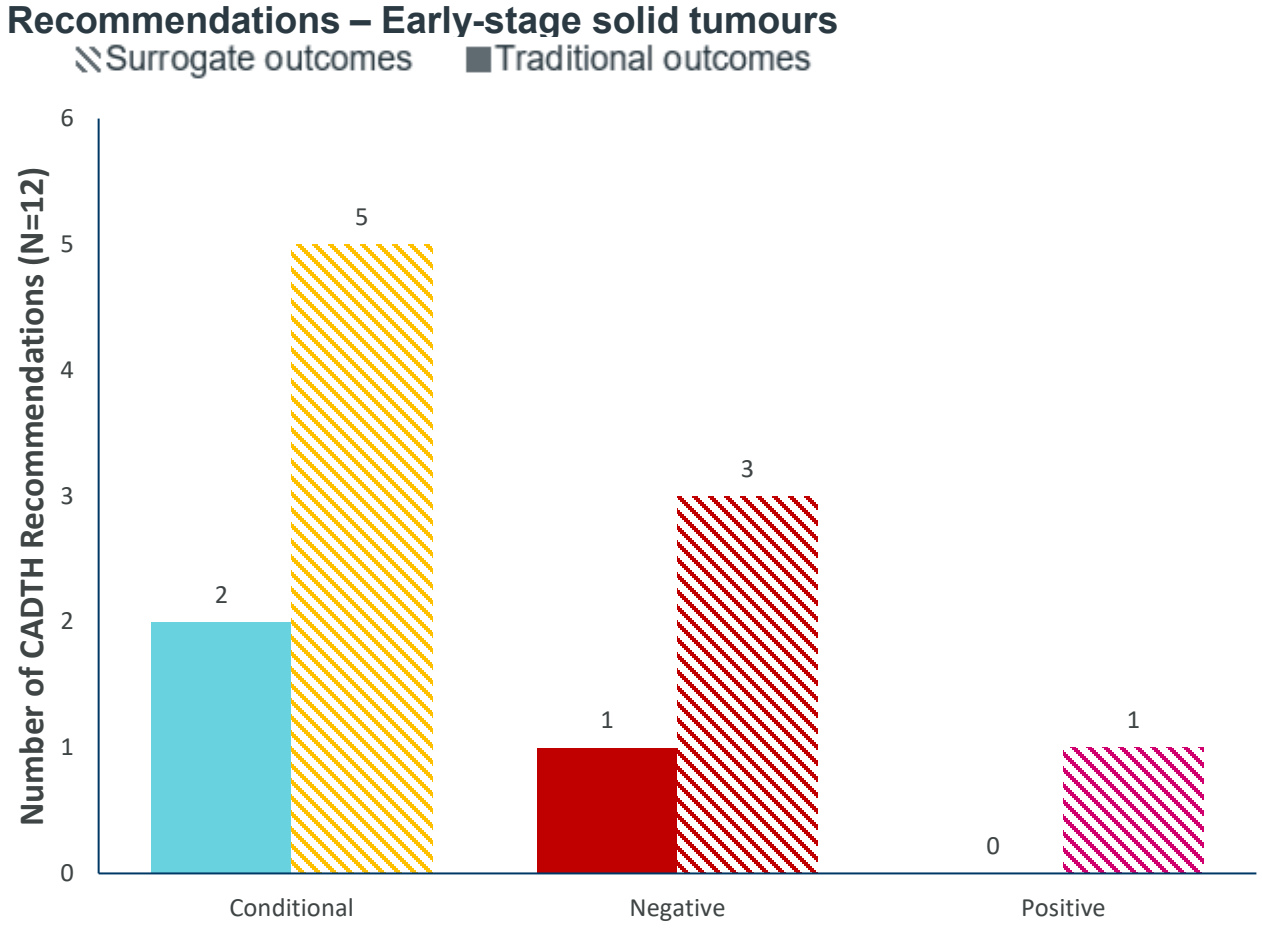
Disease stage: Early stage, non metastatic, non invasive, localized, Stage I-III

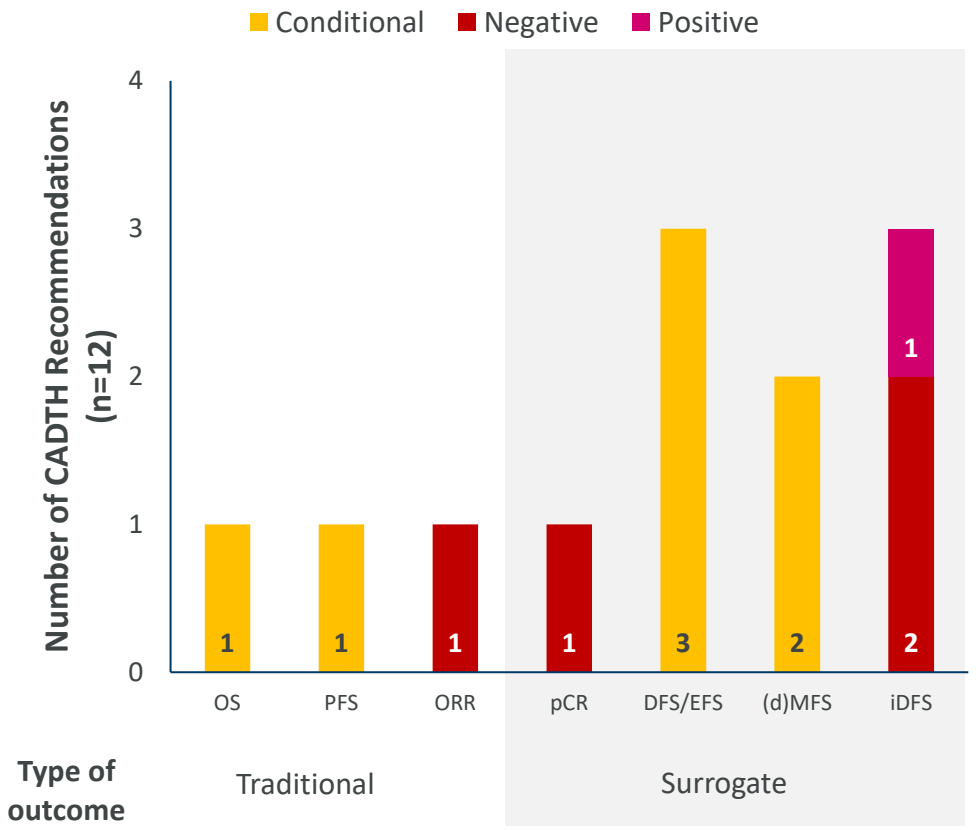


Source: IQVIA's Market Access Metrics database & CADTH

Analysis conducted by IQVIA, and sponsored by AstraZeneca

Recommendations for early-stage cancers demonstrate a proportionally higher use of non-traditional endpoints





***Abbreviations**: DFS=disease-free survival; EFS=event-free survival; IDFS=invasive disease-free survival; (d)MFS= (distant) metastasis-free survival; ORR=Objective response rate; OS=Overall survival; pCR=Pathologic complete response; PFS=Progress-free survival*

Source: IQVIA's Market Access Metrics database & CADTH
Analysis conducted by IQVIA, and sponsored by AstraZeneca

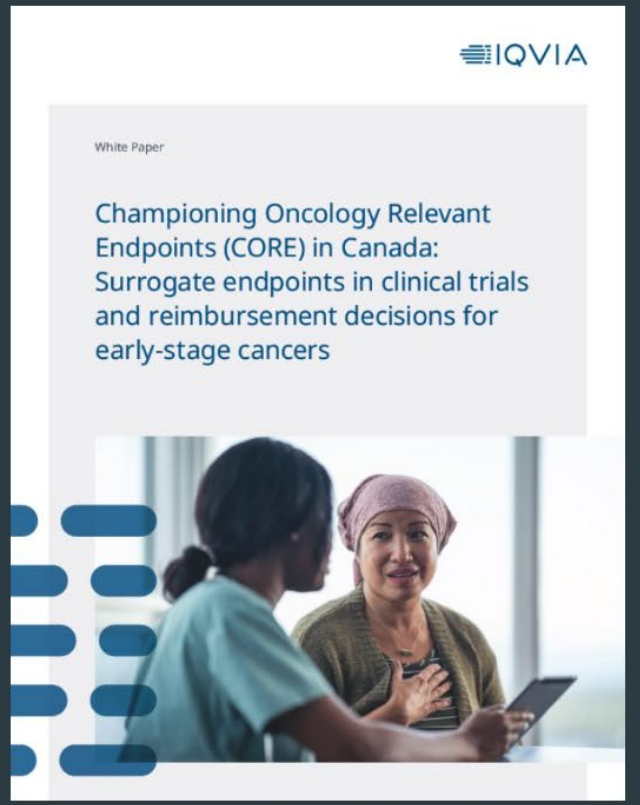
Championing Oncology Relevant Endpoints Whitepaper

WHITE PAPER

Championing Oncology Relevant Endpoints (CORE) in Canada

Surrogate endpoints in clinical trials and reimbursement decisions for early-stage cancers

Feb 20, 2023

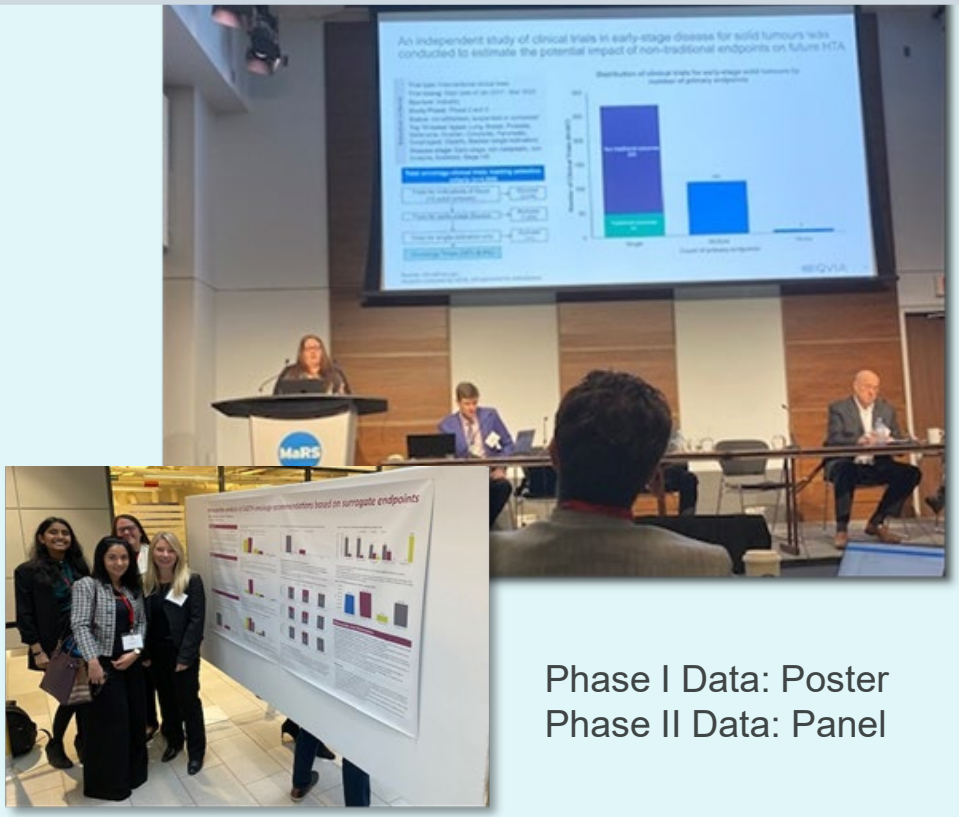


https://www.iqvia.com/locations/canada/library/white-papers/championing-oncology-relevant-endpoints-in-canada

Stakeholder Engagement (1/2)

Canadian Association of Population Therapeutics

Conference – *Oct. 2022*

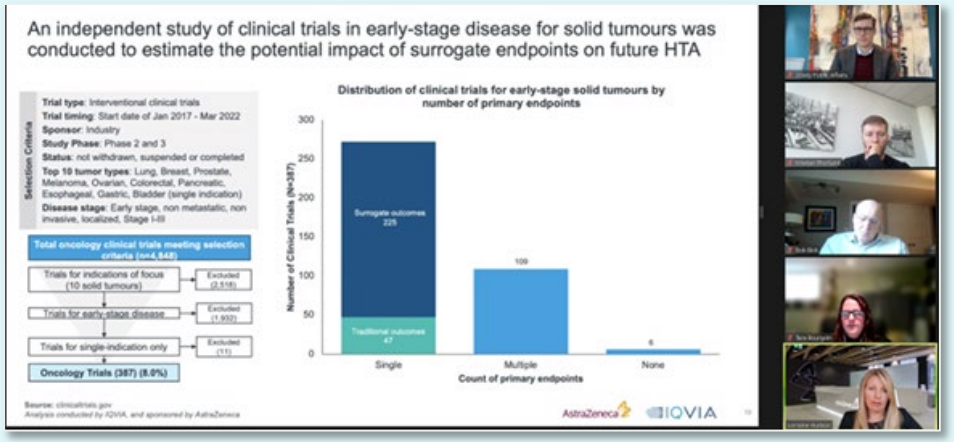


Phase I Data: Poster

Phase II Data: Panel

CanCertainty

Hot Topics Webinar - *Feb. 2023*



Stakeholder Engagement (2/2)

ISPOR Conference Panel
May 2023

ISPOR 2023
May 7-10, 2023 | Boston, MA, USA

CADTH Conference Panel
May 2023

2023 CADTH Symposium
Shaping Future-Ready Health Systems
May 16 to 18, 2023
Shaw Centre, Ottawa, Ontario

Manuscript in progress…

Summary

- Industry members such as AstraZeneca contribute to innovation in drug reimbursement decision-making through:
  - Conducting real world evidence studies
  - Looking at better ways to amplify the patient voice through patient preference studies
  - Engaging with stakeholders as the nature of drugs and their reimbursement changes

Questions

THANK YOU!