INESSS
LE SAVOIR PREND FORME

HOW RWE CAN INFORM REIMBURSEMENT QUESTIONS? PERSPECTIVE OF AN HTA BODY

CAPT, TORONTO

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Institut national d'excellence en santé et en services sociaux
Québec

INSTITUT NATIONAL D'EXCELLENCE EN SANTÉ ET EN SERVICES SOCIAUX?

Institut national d'excellence en santé et en services sociaux Québec

ABOUT INESSS

MISSION

Promote clinical excellence and the efficient use of resources in the health and social services sector

VISION

Be the reference to inform decisions and practices

VALUES

Excellence
Independence
Openness
Scientific rigour
Transparency
Integrity
Equity

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MANDATES

INESSS assesses, in particular, the clinical advantages and the costs of:

- technologies
- medication
- interventions used in health care and personal social services

It issues recommendations concerning their adoption, use and coverage by the public plan

It develops guides to clinical practice in order to ensure their optimal use in the Québec healthcare network

THE TEAM

The Institute : more than 220 people animated by the pursuit of clinical excellence

Science professionals :

- health
- social services
- biostatistics
- knowledge transfer
- pharmacotherapy
- methodology
- pharmacoeconomics
- economic analysis
- pharmacy

Advisors:

- communications
- scientific information
- information technology
- technological support

Scientific coordinators

And support staff

INFORM DECISIONS AND PRACTICES: HOW?

By mobilizing collaborators

- scientific
- economic
- contextual
- experiential

Knowledge

- societal
- ethical
- political

Considerations

A multidimensional recommendation…

… to a complex decision-making need

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LEGISLATIVE CONTEXT OF MEDICATION EVALUATION

Act of INESSS

Specifically, the mission of the Institute consists of :

- Making recommendations to the Minister of Health and Social Services with a view to updating the **list of medications** referred to in section 60 of the Act respecting prescription drug insurance (R.S.Q., chapter A-29.01) and the **lists of medications** refered to in section 116 of LSSSS (chapter S-4.2)
- In exercising the functions described in paragraph 8 of section 5, the Institute must first assess the **therapeutic value** of a medication

EVALUATION PROCESS

Based on evidence

- what scientific literature says

Adjustments to Québec's context

- treatments and impacts on pharmacoeconomy
- healthcare services organisation
- resources availability
- clinician experience... care trajectory

Adjustment measures according to patient's needs and preferences

- ability to pay
- with respect to the drug plan object

PATIENTS PERSPECTIVE: ASSOCIATED TO THERAPEUTIC VALUE

Experience of patients and caregivers:

- Need to feed deliberations from different sources
- Improvement of our practices

→ In addition to clinical, economic and ethical lighting, experiential lighting is added

MULTIPLE-CRITERIA DECISION ANALYSIS
MCDA

Aspects of the law appraised in accordance to specific criteria supporting the deliberative process of our scientific steering committee

1. Importance of health needs

2. Medication's ability to generate a clinical benefit in regard of those needs

Those two criteria are used in determining the crucial aspect of the law called **therapeutic value qualified**

- similar
- added

If INESSS considers that therapeutic value is not demonstrated to its own satisfaction, it will convey a notification to the minister of health and social services in this regard.

MULTIPLE-CRITERIA DECISION ANALYSIS
MCDA

3. Medication efficiency
   - price appropriateness and cost-effectiveness

4. Importance of benefits for the population

5. System capacity to offer the medication

6. Organizational capacity to offer the medication
   - Listing consequences on population health and on different components of the health and social services system

MULTIPLE-CRITERIA DECISION ANALYSIS
MCDA

- Deliberative process on all aspects of the law including
  - opportunities in listing medication on the lists with regard to the general drug plan: to ensure reasonable and equitable access to drugs as required by the medical condition of people
  - relation between therapeutic value and economic value and budget impact analysis
  - qualitative and quantitative judgement

NEW EVALUATION PROCESS

- Updated drug evaluation framework published in July 2018
  - key steps and basic principles explaining the process
  - integration of the 5 aspects of the law into 6 deliberative criteria
  - stowage of guide and submission forms
  - simplification of the scheme of recommendations ... same argument

- Multi-source drugs
  - Status quo ... 9 updates with submission deadlines

- Biosimilars
  - modification of the evaluation process

RWE IN OUR PROCESS

- More than economic concern
  - exposure to « bad drugs »
  - more harm than asset in accordance with patient preferences
- Not always a regulator's concern

efficacy

innocuity

uncertainty on long term outcomes… OS

Must we deny the patients of treatments potentially safe and effective during the time the evidence is coming?

RWE AND PURPOSE

- Are we ready to live and accept the results issued by RWE?
  - what if the results are not what expected?
    - re-negociate?
    - desinvest?
- Are we conscious than while we collect RWD, the environment changes
  - more experienced clinicians
  - new therapies, new sequencing
  - will we find what we are looking for ?

RWE AND PURPOSE

- Does HTA have the ability to do that?
  - access to data
- Does the government want and have the ability to receive that?
  - in HTA recommandations
  - in signed agreement
  - in managing this information

WHY RWE

- A way to ⬇ uncertainties
  - confirm long term outcomes
  - reassessment
    - review recommandation/sequencing
  - re-negociate prices according to efficiency

- A way to identify best responders
  - when results are fantastic in small number

FROM THE PAST INTO THE FUTURE

- « The unmet need is big but the actual data do not give us confidence that the medication can fulfill that need »
  - In the past : therapeutic value not assessed
  - In the future :
    - refusal of listing?
    - positive recommandation with condition?
      - clinical monitoring

Évaluation des médicaments : étapes clés

Évaluation des médicaments aux fins d'inscription	Décision du ministre de la santé et des services sociaux sur l'inscription des médicaments	Mise à jour par la Régie d'assurance maladie du Québec (RAMQ) de la liste des médicaments assurés	Évaluation des médicaments en condition réelle d'utilisation	Élaboration de recommandations, guide d'usage optimal, et d'outils destinés au professionnel de la santé
Principales données et informations utilisées:				
Études cliniques soumises par les fabriquants Opinions d'experts (comité scientifique permanent aux fins d'inscription)	Avis au ministre soumis par l'INESSS	Décision du ministre	Banque de données administratives	Données scientifiques Données contextuelles (banque de données administratives) Données expérientielles

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Canadian Association for Population Therapeutics (CAPT) Conference
Taking Action with Real World Evidence (RWE): From Analysis to Impact
MaRS, Toronto, October 22-23, 2018

How RWE can Inform Reimbursement Questions: A Case Study Approach

Michael A.S. Jewett

DEPARTMENT OF SURGICAL ONCOLOGY(UROLOGY)

PRINCESS MARGARET CANCER CENTRE
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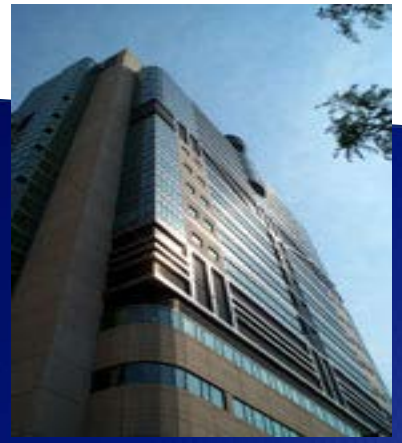
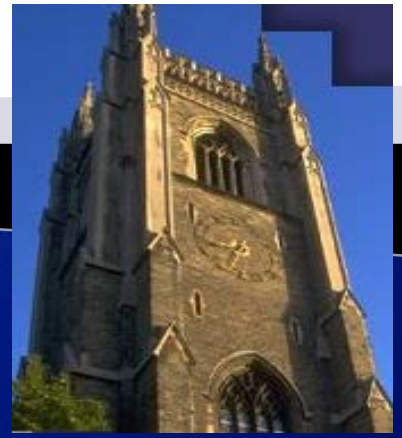
THE UNIVERSITY OF TORONTO





KCRNC KIDNEY CANCER RESEARCH NETWORK OF CANADA

RRCRC RÉSEAU DE RECHERCHE SUR LE CANCER DU REIN DU CANADA

Canadian Kidney Cancer information system (CKCis)

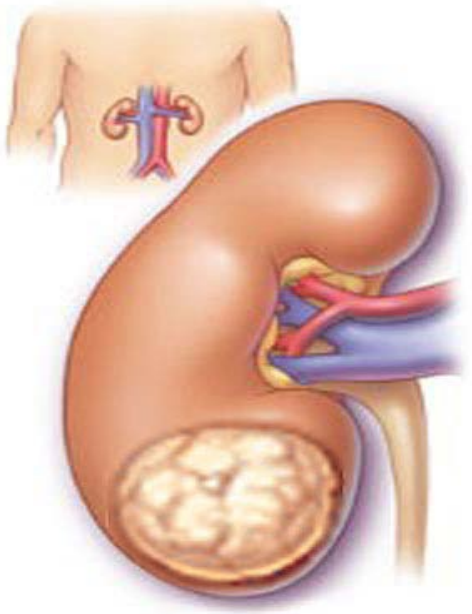
Brief History and Present Status

Initial vision

1st Canadian Kidney Cancer Forum 2008

June 2012

CIHR Network Catalyst Grant Announced for Kidney Cancer Research Network of Canada



Kidney Cancer Research Network of Canada (KCRNC)

Working with

Kidney Cancer Canada

www.kidneycancercanada.org

Why a National Information System Database?

Benefit of a national database

- Ability to evaluate our outcomes
- Ability to understand our needs
- Ability to identify our strength and weakness
- Ability to identify differences across the country
- Ability to study **real-time data**

- Should be linked to a biobank in interested institutions
  - Provides a unique opportunity to develop Canadian research programs
  - Allows to improves our knowledge of the disease

Renal Cancer Database meeting

Toronto, January 2008

- **Invitation to participate to broad group of participants**
  - **CPAC (Canadian Partnership Against Cancer)**
  - **CIHI (Canadian Institute for Health information)**
  - **Canada Health Infoway**
  - **Privacy officer**
  - **Thyroid Cancer Registry of Canada**

- **Initiative supported by Pfizer**

Environmental Assessment

- **Environmental scan of current technologies at the participating institutions**
- **Every institution has a different IT infrastructure**
- **Many institutions have other priorities (i.e. many cancer IT projects pending)**
- **Institutions would like to have a solution that is embedded into their EPR**
  - **Not a third party system**
  - **Prefer internal long-term support/maintenance**
  - **Inherent EPR integration (no additional interfacing)**
  - **Congruent with long-term goals**

NEED AN ADAPTABLE SOLUTION

Some Existing Models

Name	scope	participation
CIHI Discharge Abstract Database (DAD)	National	~850 sites
Canadian Joint Replacement Registry (CJRR)	National	~450 surgeons
Retinoblastoma World Survey	International	14 countries
CCO Interactive Symptom Assessment and Collection (ISAAC)	Provincial	5 sites

Implementation Plan

- Establish a Steering & Operations committees
- Define research questions
- Define data set
- Develop work flow for data entry/import and access
- Determine hosting and support for central system
- Define Governance Model
- Define and develop outcomes and data quality reports
- Address Privacy requirements
- Develop database and user interface

Potential sites

Sites	Urologist	Medical Oncologist
McGill University health Center	S. Tanguay	J. Sturgeon
University Health Network	A. Finelli	J. Knox
Halifax	R. Rendon	L. Wood
Montreal University	P. Karakiewick	N. Blais
Laval University	L. Lacombe	E. Levesque
London	S. Pautler	M. MacKenzie
Hamilton	A. Kapoor	S. Hotte
Vancouver	P. Black	C. Kollmansberger
Calgary	B. Donnelly	D. Heng
Winnipeg	D. Drachenberg	R. Wong
Ottawa	C. Morash	N. Reaume
Edmonton	R. Moore	S. North
Sunnybrook	L. Klotz	C. Bjarnason

Core data set

- Patient Demographics
- Initial Consultation information
- Initial Diagnosis
- Lab Values form
- Operative Report
- Pathology report
- Radiology/Imaging
- Radiation Therapy
- Systemic treatment
- Adverse Event form
- Follow-up

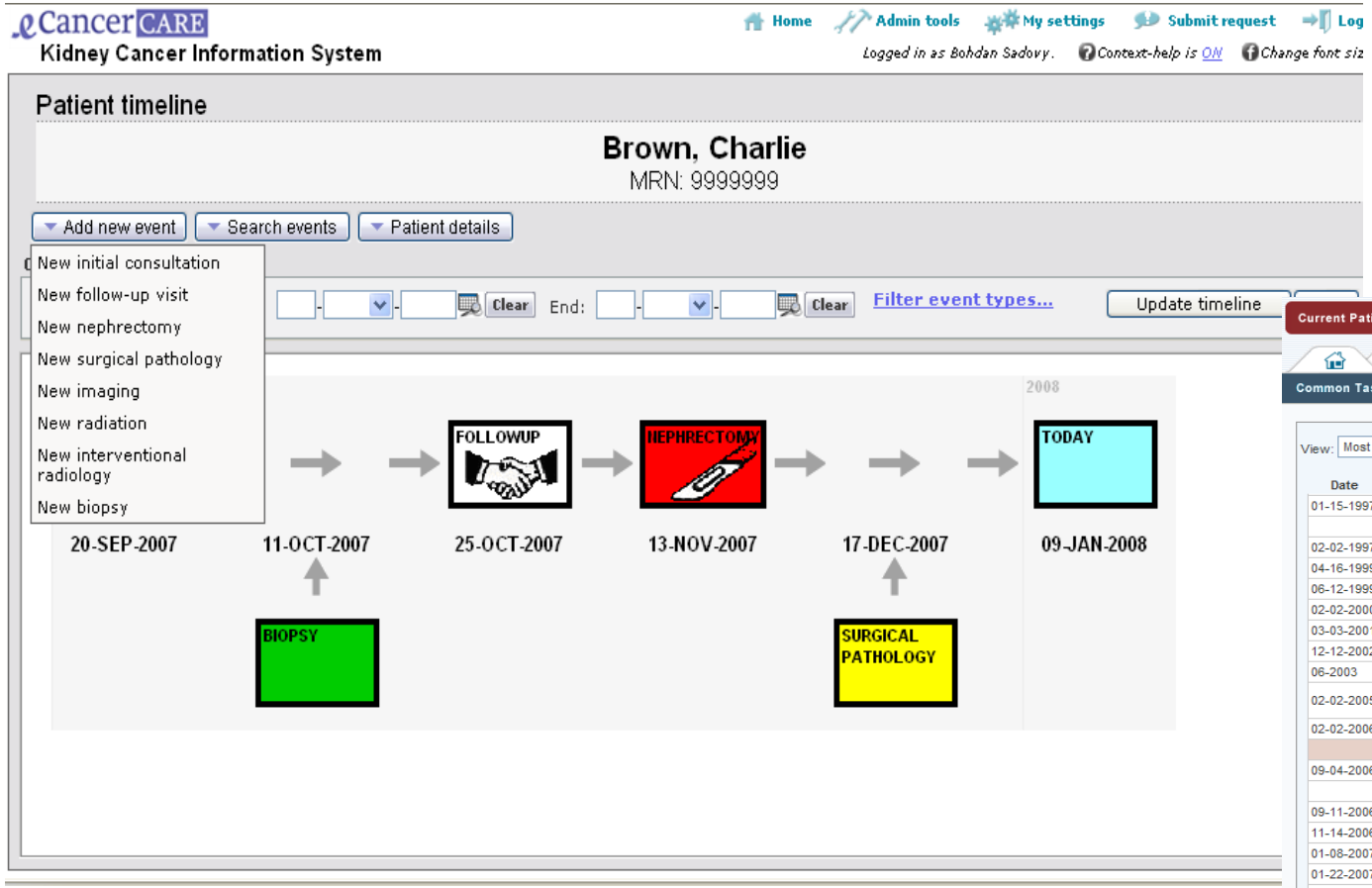
Potential Research Questions

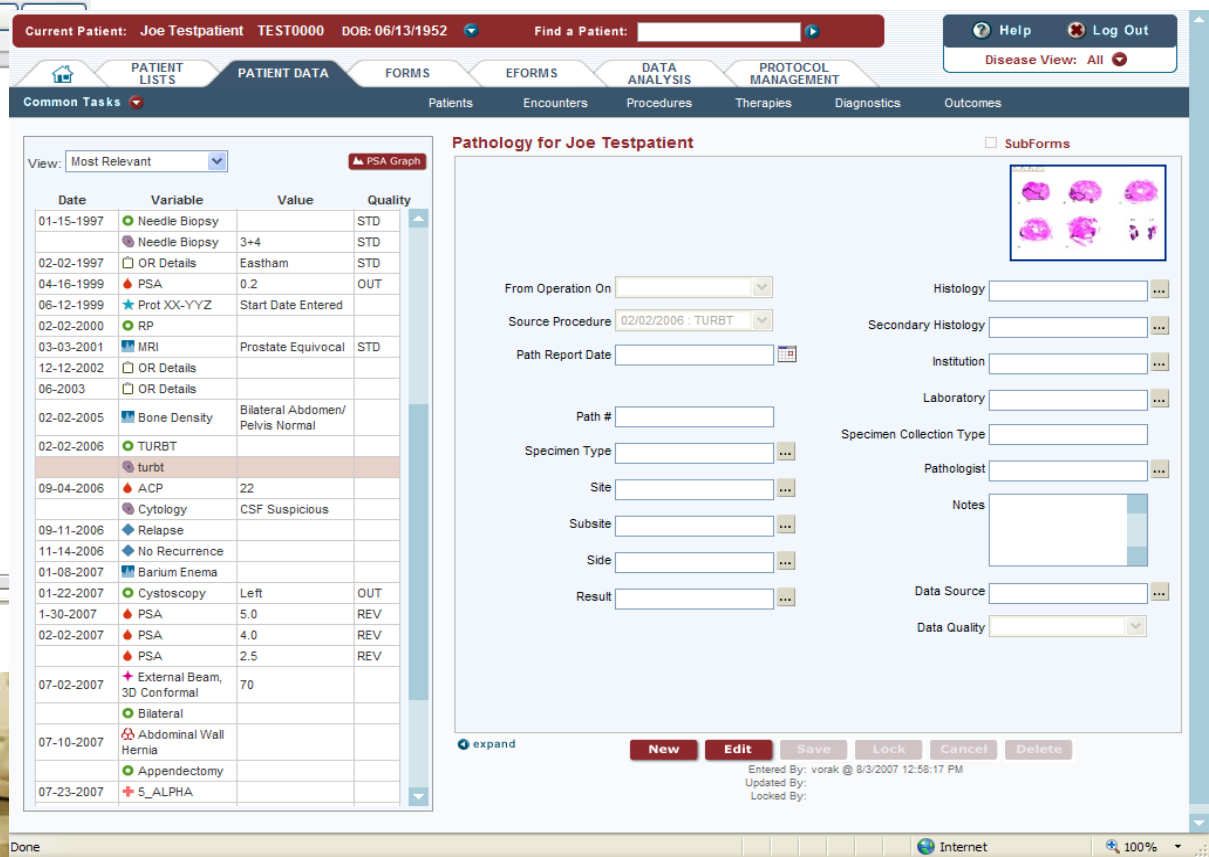
- Analyze the PFS, DSS and OS for all stages of kidney cancer in Canada
- Evaluate treatment outcome of first line metastatic RCC (mRCC) in an effort to provide effectiveness data to drug funding organizations.
- Evaluate practice pattern across Canada for the management of stage T1a and T1b RCC
- Evaluate impact of partial nephrectomy, ablative techniques and radical nephrectomy on renal function
- Evaluate treatment options and outcome for second and third line therapy of mRCC
- Evaluate treatment outcome by pathologic subtypes of mRCC
- Validate previously identified prognostic factors for PFS and OS in an independent, prospective database
- Evaluate toxicity of systemic therapy and potentially correlate them with renal function, body surface area, genetic single nucleotide polymorphisms (when biobank available)
- Evaluate the role of pre-surgical targeted therapy
- Evaluate the impact of surgery in metastatic RCC
- Evaluate the use of biopsy in management of localized and metastatic RCC
- Evaluate and compare the complications associated with the different surgical techniques of partial nephrectomy
- Locally advanced disease: Evaluate the impact of lymph node dissection and adrenalectomy
- Evaluate the impact of warm and cold ischemia duration on renal function
- Evaluate the outcome of unclassified and collecting duct Ca

Data collection methods

- Secure access to institution data
- Add or modify data with ability to mark data as completed for reporting purposes
- Multiple permission models
- Direct web data entry
- Import data from local system
  - Pre-determined format that will be accepted
  - Tool will allow users to upload a data files, to eliminate any duplicate data entry efforts

Databases options





Database/User Interface development

- Framework for database development
  - Handle multiple permission models
  - Set up to segregate multiple institution's data
  - User friendly interface
  - Comprehensive audit trails
  - Secure connections (SSL)
  - Implementation includes health care standards SNOMED and HL7

Data Governance Model

- Proposed Model
  - Each institution will have access to their own data
  - Each institution will have the possibility to the aggregate data from all the institutions; depending on the type of report required, different levels of approval will be required. Approval model will need to be defined
- Designated resource will pull the reports on a cost recovery basis. (CIHI model) Depending on financial support

Privacy/REB

- Privacy Impact Assessment required
- Data sharing agreements
- Determine the role of REB and consent requirements

Outcomes and Data Quality Reporting

- Annual Report
  - Include general outcomes
  - Participation trends (by date/province/service)
  - Future directions
- Data Quality
  - Summary of data element changes
  - Method of data submission
  - Description of data validation, including checks for duplicate records, missing and/or invalid data and inconsistencies in data imports
  - Data validation with CIHI Discharge Abstract Database

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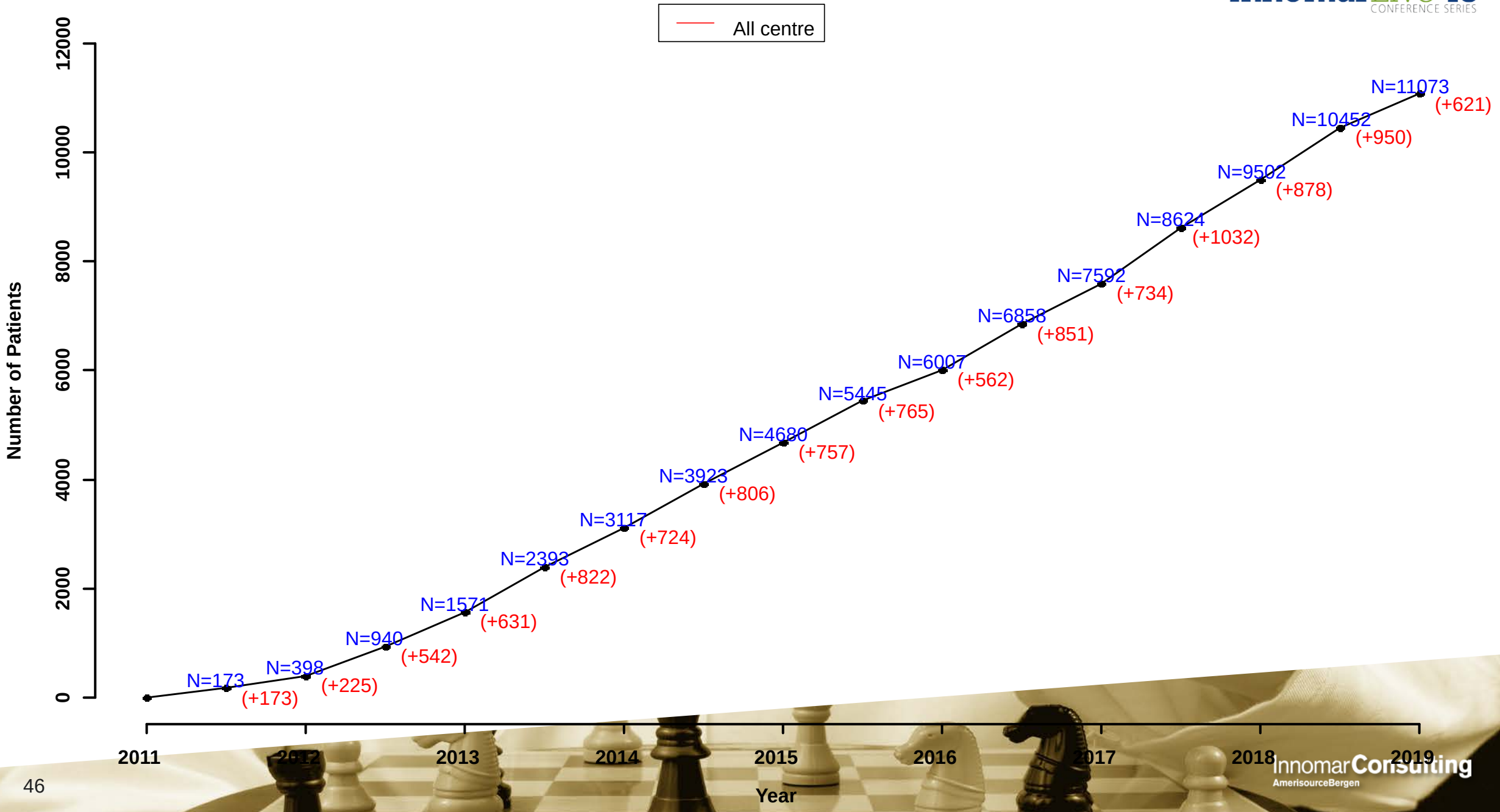
Canadian Kidney Cancer information system (CKCis)

Numbers and Publications to Date

October 16, 2018

Accrual to CKCis

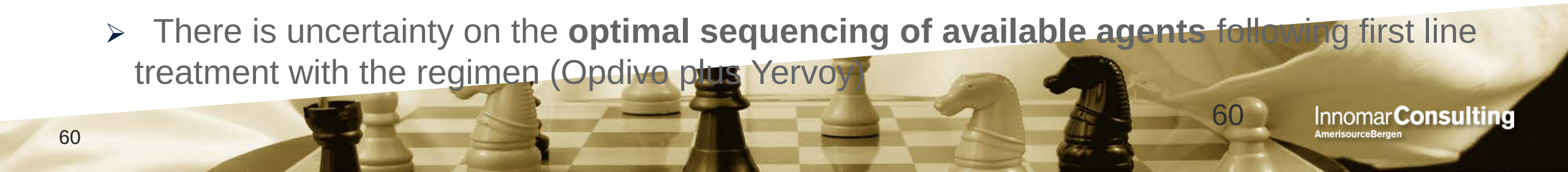


How RWE Can help implementing innovation

Case Study: Opdivo in combination with Yervoy Access Program in Renal Cell Carcinoma

Context on Opdivo (nivolumab) in combination with Yervoy (ipilimumab) in Renal Cell Carcinoma (RCC)

- **Opdivo in combination with Yervoy was approved by Health Canada on July 06, 2018 for the following indication:**
  - Intermediate/poor-risk advanced or metastatic RCC when used in combination with ipilimumab
- **pCODR issued an initial recommendation on Aug 30, 2018 :**
  - for the treatment of previously untreated intermediate or poor-risk advanced RCC with clear cell component
- **pCODR initial recommendation identified some implementation challenges including:**
  - There is uncertainty on the **optimal sequencing of available agents** following first line treatment with the regimen (Opdivo plus Yervoy)



60

Access Program (CLYvER) Objectives

- Supporting access to OPDIVO (nivolumab 3mg/kg) in combination with low-dose YERVOY (ipilimumab 1 mg/kg) for the treatment for previously untreated patients with intermediate or poor risk RCC as defined by the IMDC prognostic risk criteria
- Enable the collection of real-world evidence on patient outcomes supported through local registries (CKCis registry) to **help inform optimal usage of this Innovation as well as subsequent treatment algorithm**

Data Collection Priorities

To collect efficacy and safety data for:

- Subsequent treatment following Opdivo in combination with Yervoy in first-line RCC
- Opdivo in combination with Yervoy in special populations (non-clear cell histology, stable autoimmune disease, CNS metastases)
- Real World setting compared to clinical trial results

62

The Canadian Kidney Cancer information system (CKCis): Past and Future RWE Applications

October 23, 2018

Robert Bick
Vice Chair, Kidney Cancer Canada
Co Chair, CanCertainty

Information • Support • Advocacy
For Canadians touched by Kidney Cancer

Disclosure

- I have no actual or potential conflict of interest in relation to this topic or presentation

Canadian Kidney Cancer information system (CKCis)

- A web-based nat'l registry containing retrospective and prospective de-identified patient data collected from consented patients
- CKCis has been in operation for 8 years - 15 Cdn centres accrue patients: 11000+ pts enrolled
- Flexible database platform

pCODR Provincial Advisory Group: Request for Advice

PAG submitted in April 2017 a RFA for the Final Recommendation of axitinib which was originally posted on March 2013

Is there evidence to fund axitinib as an alternative to everolimus for the second-line treatment of metastatic clear cell renal carcinoma?

Kidney Cancer Canada was invited to provide input on the RFA. We requested that CKCis investigators make as a research priority the RFA question.

Background

- **2013 pERC recommendation re: axitinib:** funding for patients unable to tolerate or who have a contraindication to everolimus.

Vs

- **Management of advanced kidney cancer: Canadian Kidney Cancer Forum 2013 Consensus Update**: *At this time, there is no evidence to help determine which second-line therapy after VEGFr TKI is superior, thus everolimus or axitinib would be suitable choices..*

CKCis Analysis/Results

- CKCis identified a study cohort of patients who were pretreated with either sunitinib or pazopanib.
- Axitinib was given second line in 108 patients while everolimus was used in 229 patients.
- Time to treatment failure (TTF) was found to be longer in the axitinib group while Overall Survival (OS) was similar in both groups.

Conclusion of CKCis Investigators: “Axitinib should be considered an option for all patients in Canada post 1stL VEGF-Targeted Therapy without the limitations of the existing pCODR recommendation”.

pCODR Clinical Guidance Panel Conclusions:

“The Clinical Guidance Panel is of the opinion that there is appropriate real world evidence and expert judgment to justify axitinib as an equal alternative to everolimus in the second line setting.”

What if we had done this prospectively?

What If pERC had “conditionally” approved axitinib (without the imposed access restrictions)? CKCis could have been deployed to prospectively resolve the uncertainties.

- Shortly before the pERC recommendation in 2013 re: axitinib, CKCis had been launched and pt data was being collected
- In 2013 KCC did formally propose the prospective use of CKCis data to resolve uncertainties, including sequencing questions and non-evidence based restrictions on access
- Our pitch was to CCO, proposing to use CKCis to inform the Evidence Building Program.

Piloting “Conditional” Reimbursement with Evidence Development

- We are urging pCODR to allow for the prospective collection of real world data: survival, side effects and toxicities, cost-effectiveness and utilization -- to resolve uncertainty encountered during the review of current and forthcoming treatments for mRCC.

- KCC and the KCRNC are prepared to work with the pCPA and pCODR to support evidence-building on an ongoing basis

Why Kidney Cancer?

1. Existing high quality patient registry with proven capability to inform reimbursement decision-making

2. The treatment paradigm for kidney cancer is undergoing significant and rapid change. There will be uncertainty…but also tremendous opportunity to improved treatment/outcomes.

3. It is a relatively small cancer (#10 in incidence). Of the 6,600 Cdns being diagnosed with RCC this year, approximately 25% will be diagnosed as stage IV. The financial risk to payers to pilot a “conditional listings” process with evidence development is small.

We Are Not Alone

Patient groups and clinician networks are building patient registries:

- eCancerCare, the platform developed by Techna (an institute of UHN, with UoT) is a suite of secure web-based software tools streamlining the collection of high-quality, structured point-of-care data for disease management and research.
- It has been deployed in ALL GYNE CANCER, ALL GU CANCERS, LYMPHOMA, MULTIPLE MYLEMA, LEUKEMIA (IN PROGRESS), OCULAR, LUNG, GI AND BREAST
- Bladder Cancer Canada has partnered with clinicians to build the **Canadian Bladder Cancer Information System** (CBCIS)
- The Brain Tumour Foundation of Canada is fundraising and building the **Canadian Brain Tumour Registry**