Oncology HTA: Canada versus UK experiences

Isabelle Chabot PhD

ARCC Conference - Toronto, 12 May 2014

Disclosure

- I worked on this analysis while a full-time employee at Pfizer.
- I am now the Principal at EvAccess, an HEOR company.
- I am a pharmacist not currently practicing.
- Angela Rocchi, Principal at Athena Research, was my collaborator in this project.
- Rx&D provided unrestricted grant to help with the dissemination of the results.
- I believe everything that I will say during this presentation.

Context

- Decision-making for life-extending therapies for patients with terminal cancers has been a source of debates
- Surrogates endpoints, life-extension benefit, high cost treatments, patients' values…
  - How to deal with "promising therapies" under conventional HTA framework?
- HTA agencies have evolved their evaluation framework to better meet the needs of patients:
  - CDR – iJODR – pCODR…
  - INESSS – pilot project in oncology…
  - NICE – end-of-life criteria…

Objectives

To review and compare Canadian and UK HTA agencies' recommendations for the reimbursement of drugs for end-of-life cancer treatments.

To determine if the source of negative recommendations was uncertainty on clinical benefit or cost effectiveness or both.

To understand to what extent clinical and cost effectiveness issues are dealt with through arrangements between payers and manufacturers.

Methods

- Comparison of reimbursement recommendations in advanced cancer from 3 HTA agencies:
  - INESSS
  - CDR/JODR/pCODR
  - NICE
- Metastatic/advanced cancer sites:
  - lung
  - breast
  - colon
  - kidney
  - blood
- Period: January 1, 2002 to June 1, 2013

Methods (cont'd)

- Variables:
  - Overall Survival (OS) gain
  - Progression-Free Survival (PFS) gain
  - Incremental Cost-Effectiveness Ratio (ICER)
  - Types of recommendations
  - Reasons for negative recommendations (if applicable)
  - Arrangements between payers and manufacturers (if applicable: risk-sharing, price negotiation, access scheme)
- Source of information:
  - Only publicly disclosed information from HTA agencies web sites was consulted
- Only the most recent recommendation was included

Results

90 recommendations reviewed

No national intravenous drug review before 2007

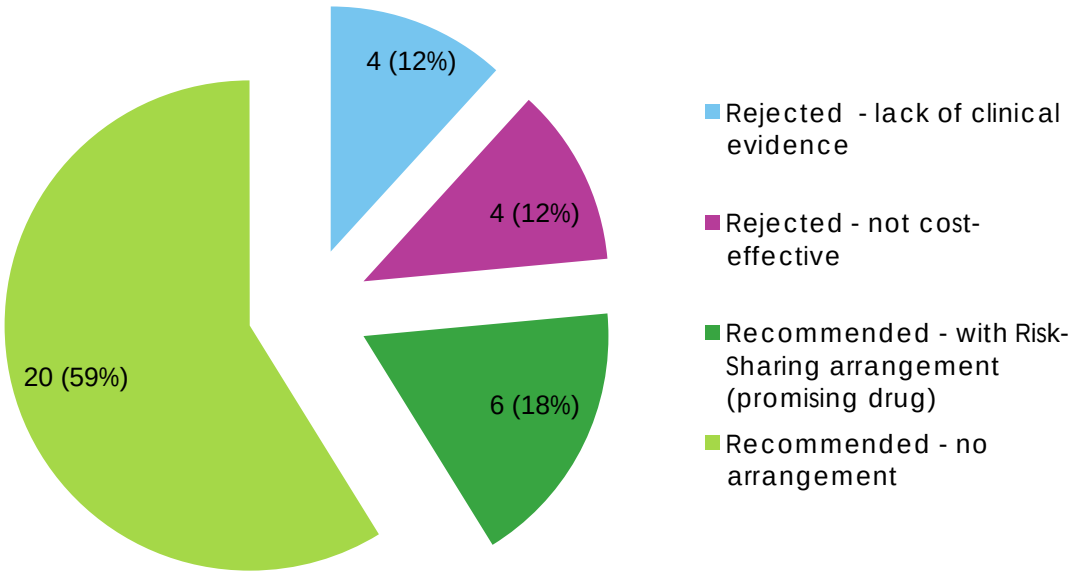
JODR: 7 drugs were reviewed but no recommendations posted (effective sample size = 20 instead of 27)

NICE does not appraise all drugs – upon referral by the Department of Health

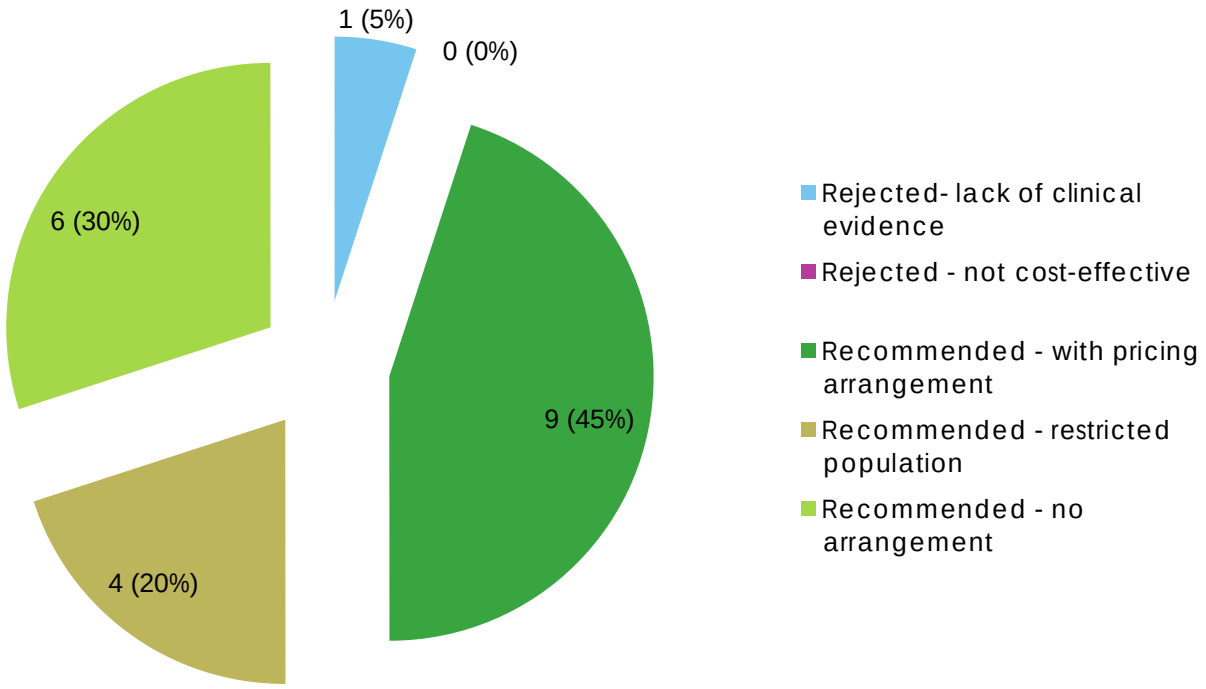
Table 1: Eligible Drugs and Indications[a]

Drug by Disease Site	Indication	INESSS (n=34)	CDR/JODR /pCODR (n=27)	NICE (n=29)
Lung (mNSCLC)				
Bevacizumab	mNSCLC (1st-line)	√	NR	NR
Erlotinib	mNSCLC (2nd line, 3rd line)	√	√	√
Erlotinib	mNSCLC (Maintenance)	√	NP	√
Pemetrexed	mNSCLC (2nd-line)	√	√	√
Pemetrexed	mNSCLC (1st-line)	√	NP	√
Pemetrexed	mNSCLC (maintenance)	√	√	√
Gefitinib	mNSCLC EGFR+	√	NP	√
Crizotinib	mNSCLC ALK+ (1st- line)	UR	√	UR
Crizotinib	mNSCLC (2nd-line)	NR	√	NR
Colorectal (mCRC)				
Bevacizumab	mCRC	NP	√	√
Cetuximab	mCRC (1st line)	NR	NR	√
Cetuximab	mCRC EGFR+ KRAS non mutated	√	√	√
Panitumumab	mCRC EGFR+ KRAS non mutated 2nd-3rd-line	√	√	√
Breast (mBC)				
Trastuzumab	mBC HER2+ (1st-line)	√	NP	√
Nab-paclitaxel	mBC (1st-line)	√	√	NR
Lapatinib	mBC HR+ HER2+ 1st-line	√	NP	√
Lapatinib	mBC HER2+ 2nd-line	√	√	NR
Eribulin	mBC (3rd-line)	√	√	√
Everolimus	mBC HR+ combo	UR		UR
Kidney (mRCC)				
Everolimus	mRCC (2nd line)	√	√	√
Pazopanib	mRCC (1st line)	√	√	√
Pazopanib	mRCC (2nd-line after cytokines)	√	NR	NR
Sunitinib	mRCC (1st line)	√	√	√
Sorafenib	mRCC (2nd-line after cytokines)	√	√	√
Sorafenib	mRCC (2nd-line after sunitinib)	√	NR	√
Temsirolimus	mRCC (poor prognosis 1st-line)	√	√	√
Bevacizumab	mRCC	NR	NR	√
Axitinib	mRCC (2nd-line)	√	√	√
Blood/plasma cell				
Lenalidomide	refractory/relapsed MM	√	NP	√
Bortezomib	refractory/relapsed MM	√	NR	√
Bortezomib	MM (initial therapy in patients not candidates for ASCT	√	NR	√
Imatinib	CML (1st-line)	√	√	√
Dasatinib	CML (2nd-line)	√	√	√
Nilotinib	CML (2nd-line)	√	NP	√
Nilotinib	CML (1st-line)	√	NR	NR
Rituximab	NHL (1st-line)	√	NR	√
Tositumomab	NHL (2nd-line)	√	NR	NR
Ibritumomab tiuxetan	NHL (2nd-line)	√	NR	NR
Bendamustine	NHL (relapse/refractory to rituximab)	√	√	UR

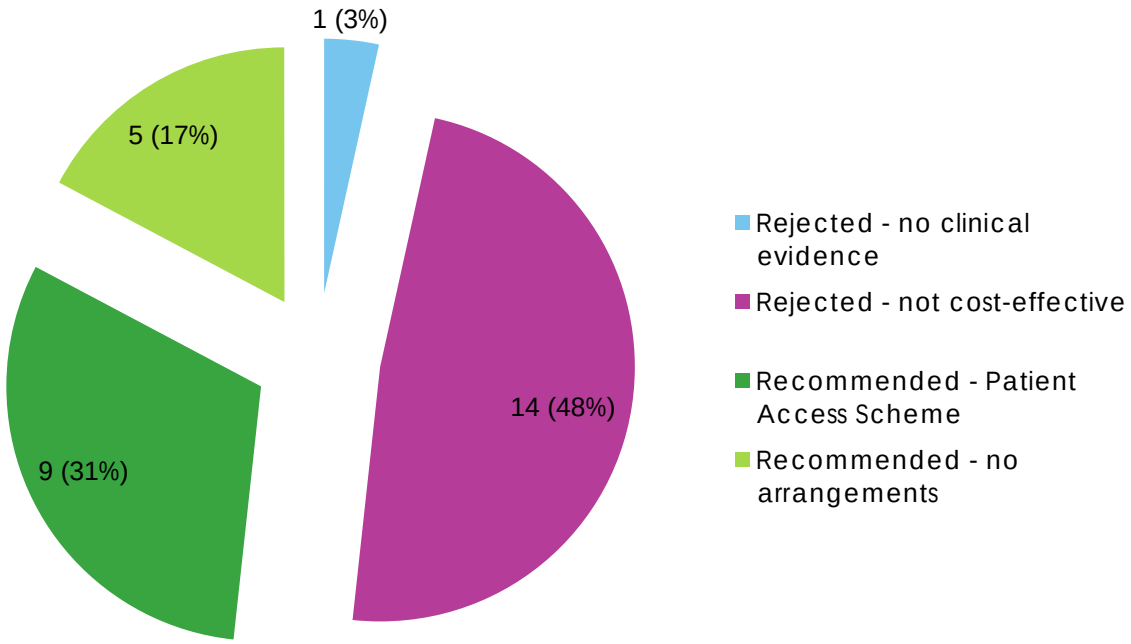
Types of recommendations INESSS (n=34)



Types of recommendations CDR/JODR/pCODR (n=20)



Types of recommendations NICE (n=29)



Clinical evidence

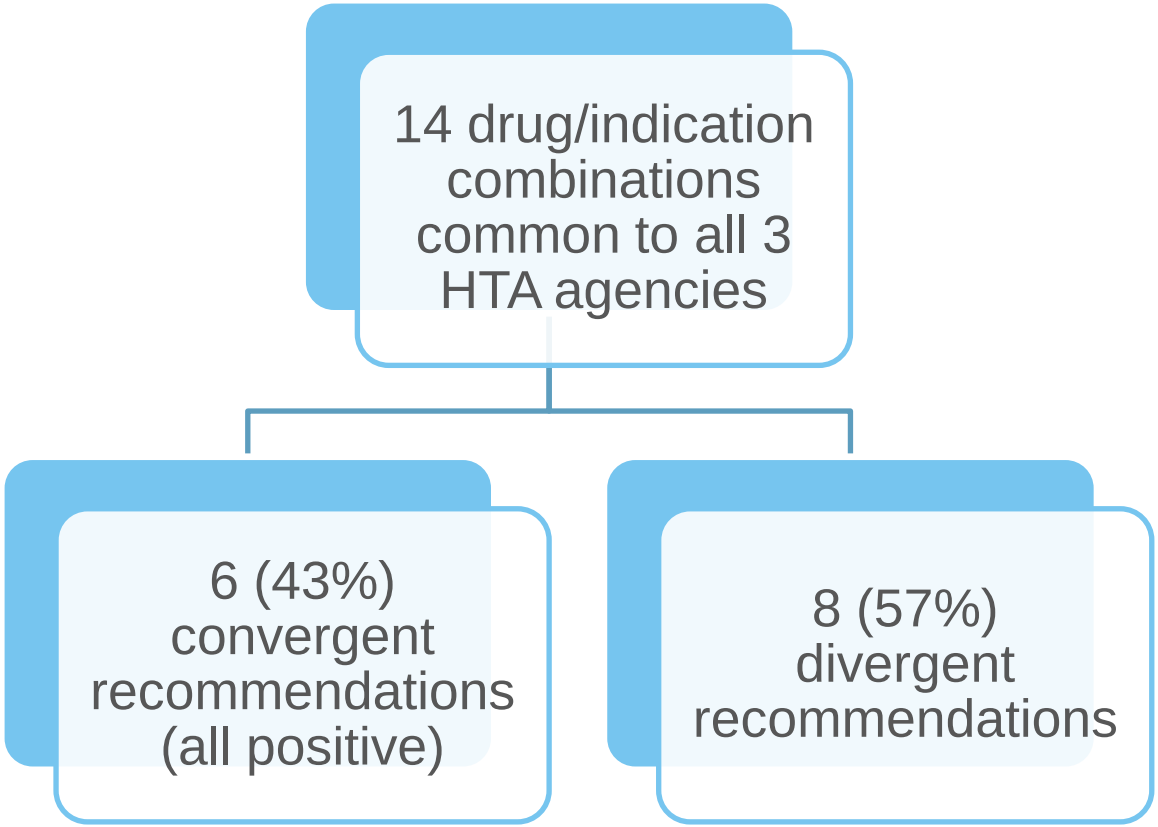
- Majority of positive recommendations include no evidence of OS benefit

Recommendations with Positive Overall Survival Benefit

Type of Recommendation	INESSS	CDR/JODR/ pCODR	NICE
All recommendations	13/34 (38%)	5/20 (25%)	10/29 (35%)
Positive recommendations	12/26 (46%)	5/19 (26%)	6/14 (44%)
Negative recommendations	1/8 (12%)	0/1 (0%)	4/15 (27%)

- Minority of drugs rejected for lacking evidence on clinical benefit:
  - INESSS – 13% (4 drugs)
  - CDR/JODR/pCODR – 5% (1 drug)
  - NICE – 3% (1 drug)

Inter-agency agreement



Interpretation

- Lack of evidence on clinical benefit: rarely a rationale for a negative recommendation
- Surrogate endpoints (PFS) are acceptable basis for clinical benefit assessment in treatments for non-curative cancers
- Differences on how HTA agencies deal with cost-effectiveness uncertainty
  - INESSS – rejected before the pilot project in oncology; then recommended with risk-sharing agreements
  - CDR/JODR/pCODR – virtually no rejection on that ground; recommended conditional to improvement of ICER
  - NICE – most of the time rejected unless a patient access scheme is agreed upon

Is access denied based on high ICER?

- INESSS – 12% rejection on ICER
  - Drug available through “patient d’exception” (case-by-case)
- CDR/JODR/pCODR – 0% rejection on ICER
  - Provincial access based on results of the negotiation at the pan-Canadian Pricing Alliance (PCPA)
- NICE – 48% rejection on ICER
  - Despite access schemes opportunities and end-of-life criteria
  - NHS Cancer Drug Funds (CDF) – England only
    - Interim process: 2011 to 2016
    - For drugs not recommended by NICE; or where the recommendation restricts the full population in the label; or when no NICE guidance issued
    - £200M/year

Conclusions

- What is the best approach to high ICERs?
  - In Canada, price negotiation through the PCPA is becoming the standard for access to cancer therapies
  - Quebec still does not benefit from any price negotiation
  - In UK, drugs rejected for high ICERs are still available through the CDF
- Where does the future land?
- Inter-HTA comparisons of recommendations can only highlight differences in the approaches used to deal with evidence uncertainty – they do not inform on differences in patient access