2018 UPDATE OF HEALTH TECHNOLOGY ASSESSMENT DECISIONS ACROSS THE GLOBE: A FOCUS ON ONCOLOGY

Ryan S Clark[1], PharmD, MBA, MS; Kimberly Gittings[1], PharmD, MS; Chelsey M Campbell[1], PharmD, MBA, MS; Kellie L Meyer[1], PharmD, MPH
[1]Xcenda, LLC, Palm Harbor, FL, USA

BACKGROUND

- Cancer is a highly burdensome condition affecting many individuals globally, with an estimated 17.5 million cancer cases, 8.7 million deaths, and 208.3 million disability-adjusted life-years in 2015[1]
- Oncology innovation shows no signs of decelerating; manufacturers continue to produce targeted therapies with more niche indications, and the treatment landscape is becoming increasingly complex
  - In 2017, a quarter (23/92) of the European Medicines Agency's (EMA's) positive recommendations were for cancer therapies, an increase from 13 in the previous year[2]
  - Similarly, the Food and Drug Administration (FDA) approved 16 cancer therapies in 2017, an increase from the 11 approved in 2016[3]
- Although the decision-making process differs between nations, health technology assessments (HTAs) attempt to balance oncology agents' clinical benefit alongside increased expense to produce policies that achieve optimal value

OBJECTIVES

- This analysis aimed to provide an update of 2014 and 2016 podium presentations by evaluating recent oncology-related HTA decisions and the associated rationale to identify trends in selected countries

METHODS

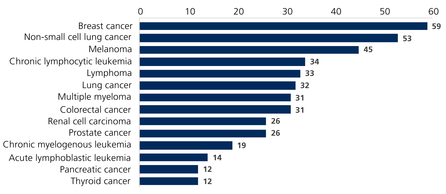
- HTA surveillance was conducted for oncology-related therapeutic agents, evaluating by primary site of origin, decision, and rationale for the decision
  - Decisions were categorized as favorable (defined as a decision that advances the product toward coverage or reimbursement), unfavorable (a decision that blocks/hinders coverage or reimbursement), or mixed (both favorable and unfavorable)
    - Major resubmissions and multiple decisions on a single agent/disease from a country were counted as separate decisions
  - Surveillance was conducted from January 1, 2012 to April 30, 2018 (76 months)
    - Previously conducted analyses were presented via podium presentations in 2014 and 2016
  - The rationale for each decision was examined to discern global trends in components of pharmaceutical product assessment and reimbursement
- HTA bodies assessed included:
  - Australia: Pharmaceutical Benefits Advisory Committee (PBAC)
  - Canada: Canadian Agency for Drugs and Technologies in Health (CADTH) pan-Canadian Oncology Drug Review (pCODR)
  - France: National Authority for Health (HAS)
  - Germany: Institute for Quality and Efficiency in Health Care (IQWiG)*
  - United Kingdom (UK): National Institute for Health and Care Excellence (NICE)

**Although the final assessment of added benefit is provided by the Federal Joint Committee (G-BA), this study examined the technology assessments conducted by IQWiG.*

RESULTS

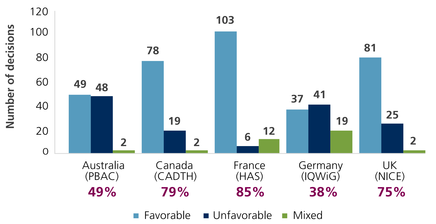
- 524 oncology-related HTA decisions were published in the study time frame for 119 different therapies and 50 primary sites of origin classifications
  - Across all countries, the most common primary sites of origin classifications included breast cancer, non-small cell lung cancer (NSCLC), and melanoma (**Figure 1**)

Figure 1. Most Common Primary Site of Origin Classifications Among Studied HTA Decisions



- Across the studied nations, 346 (66%) decisions were favorable, 141 (27%) were unfavorable, and 37 (7%) were mixed

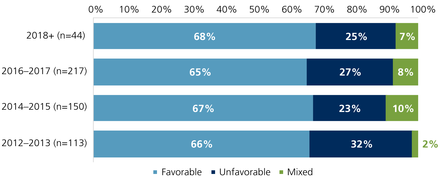
Figure 2. Global Trend of Oncology Decisions by Country



Percentages indicate percent of decisions that were favorable. Key: CADTH – Canadian Agency for Drugs and Technologies in Health; HAS – National Authority for Health; IQWiG – Institute for Quality and Efficiency in Health Care; NICE – National Institute for Health and Care Excellence; PBAC – Pharmaceutical Benefits Advisory Committee; UK – United Kingdom.

  - France had the highest percentage (85%; 103/121) of favorable decisions, followed by Canada (79%; 78/99), UK (75%; 81/108), Australia (49%; 49/99), and Germany (38%; 37/97)
- While the number of HTA decisions for oncology agents has increased every 2 years from the beginning of this study, the number of favorable decisions has remained relatively consistent
  - There are more mixed decisions in recent years than in the first 2 years of the study (**Figure 3**)

Figure 3. Percentage Breakdown of Decision Favorability by Year



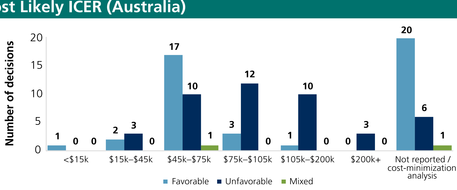
Number is equal to the number of decisions assessed within each time period.

Country-specific Observations for Recent Oncology-Related HTA Decisions

Australia

- Of the decisions where public summary documents were available, most favorable decisions fell in the $45,000 to $75,000 incremental cost-effectiveness ratio (ICER) range
  - Many assessments were submitted on a cost-minimization basis; therefore, no ICER was reported
  - For both favorable and unfavorable decisions, PBAC often will provide a more general assessment of the model's certainty and most likely ICER instead of a specific range

Figure 4. Favorable, Unfavorable, and Mixed Decisions and Their Most Likely ICER (Australia)



RESULTS (cont.)

- Economic model uncertainty plays a significant role in the level of success for a submission in Australia
  - HTA decisions in which the model had a high level of uncertainty were most often unfavorable
- Relative to other countries, PBAC frequently defers decisions to allow the manufacturer to lower the price, submit additional evidence, or allow for related technology appraisal decisions to be made

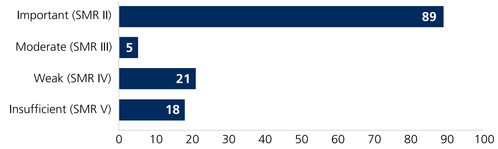
Canada

- Most (78/99; 79%) of the HTA decisions by pCODR were considered favorable, but nearly all were dependent upon cost-effectiveness of the technology being reduced to an appropriate level
- The majority of unfavorable decisions could be attributed to a small or uncertain net clinical benefit (10), limitations in the clinical trial design (5), or insufficient evidence for subgroups (2)
- Mixed decisions were split primarily due to different patient populations and whether the technology was used as monotherapy or in combination with other agents

France

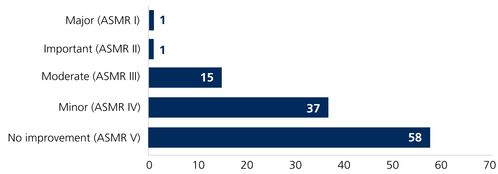
- Approximately two-thirds of decisions were considered to have an important medical benefit (SMR I), but just over half had no improvement in medical benefit (ASMR V)

Figure 5. *Service Medical Rendu* (SMR; n=133)



Note that 12 mixed decisions counted both as no benefit and as either low, moderate, or important benefit.

Figure 6. *Amelioration du Service Medical Rendu* (ASMR; n=112)



Note that 3 ASMR values were unspecified.

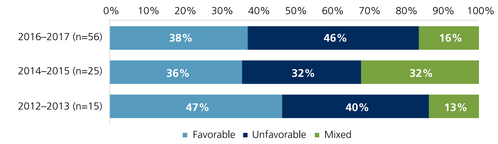
- Only 5% (6/121) of decisions had insufficient medical value and were therefore not included on the list of reimbursable drugs
  - Favorability of decisions in France is highly dependent upon definition; if ASMR V were to be considered unfavorable, then the percentage of favorability would be the lowest of all studied countries (45/121; 37%)
- Mixed decisions had differing levels of medical value when evaluated across several key domains, including:

Patient performance status or level of symptomatic involvement	Whether the technology was used as monotherapy or in combination with other agents	Various tumor expressions (eg, Philadelphia chromosome +/-)	Line of therapy	Eligibility for other treatment options

Germany

- 42% (41/97) of decisions by IQWiG found there to be no hint of added benefit, yielding an unfavorable decision
  - The percentage and number of unfavorable decisions has increased in the most recent 2 years (**Figure 8**)

Figure 8. Percentage Breakdown of Decision Favorability by Year (Germany)



Number is equal to the number of decisions assessed within each time period.

- Compared with other countries, Germany more commonly produces mixed decisions in which GBA-defined patient subgroups receive different levels of added benefit
  - Typically, specific evidence for patient subgroups is required for any level of added benefit, and without this evidence, there will be no proof of added benefit (ie, an unfavorable decision)
- The extent and probability of added benefit was often due to a presence or lack of added benefit (eg, inappropriate comparator or trial duration was too short to show benefit) in the targeted patient population, even if divided into subindications

United Kingdom

- While NICE often provides strict limitations for patient populations eligible for treatment (based on previous treatments, performance level, etc), most recent decisions have been favorable based on acceptable cost-effectiveness figures
  - Nearly all favorable ICERs were <£50,000 per quality-adjusted life-year
  - Many therapies with favorable assessments are subject to a Patient Access Scheme confidential discount agreement
- NICE varies widely in how the most likely cost-effectiveness estimate is provided, and there are often multiple ICERs reported
  - Most likely cost-effectiveness can be provided as a point estimate, range, or general statement related to the company's or Evidence Review Group's base case
- Due to recent changes to the Cancer Drugs Fund (CDF) program, NICE reviews all therapies expected to receive marketing authorization for an oncology indication
  - As a result, a relatively high number of oncologic agents have been reviewed by NICE since the program change, which now provides a pathway to be "recommended for use within the CDF" if there is potential for a positive recommendation but remaining clinical uncertainty

CONCLUSIONS

- Each 2-year period from January 2012 onward has seen an increased number of oncology-based HTA decisions, with the most common primary sites of origin being breast, NSCLC, and melanoma
- Despite the perception of increased scrutiny by HTA agencies, when considering the most recent 76 months of oncology-related HTAs, two-thirds (66%) have been favorable
  - France (85%) and Canada (79%) have the highest percentage of favorable decisions, though nearly all Canadian approvals are dependent upon the cost-effectiveness being reduced to an appropriate level
- Because of the level of complexity in cancer treatment, oncology HTAs are often nuanced and consider aspects like patient performance status, line of therapy, and tumor expression
- For countries that consider cost-effectiveness (Australia, Canada, UK), economic model uncertainty and ICER confidence are key to decision favorability
- HTA agencies continue to employ mixed decisions based on subpopulations or decisions dependent upon reducing cost-effectiveness, which enhances the importance of developing strong health economic and clinical data
- Robust evidence proving unmet need, efficacy and safety, and cost-effectiveness is critical to achieving a favorable HTA decision across multiple major markets

1. Fitzmaurice C, et al. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 32 cancer groups, 1990 to 2015. *JAMA Oncol.* 2017;3(4):524-548.
2. https://sms-oncology.com/blog/ema-anticancer-drug-recommendations-for-approval-in-2017/.
3. https://www.centerwatch.com/drug-information/fda-approved-drugs/therapeutic-area/12/oncology.

Presented at ISPOR 23rd Annual International Meeting | May 19-23, 2018 | Baltimore, MD, USA I Funded by Xcenda