DO PAYER AND PRESCRIBER ENDPOINT PREFERENCES ALIGN?: IMMUNE CHECKPOINT INHIBITORS IN NON-SMALL CELL LUNG CANCER

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Yulia Privolnev, MA[1]
Boaz N. Adler, MPH[2]

1. Decision Resources Group, Toronto, Canada
2. Decision Resources Group, New York, NY, USA

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BACKGROUND & OBJECTIVE

- The health technology assessment (HTA) bar is rising across the EU5 (France, Germany, Italy, Spain, UK). As payers balance clinical need with budgetary constraints, proving added benefit over currently available therapies is vital for new agents entering high-cost therapeutic markets and some payers are more rigid than others when it comes to what data will be accepted and used to inform decision-making.
- This study examines the impact of clinical outcomes, particularly primary and secondary endpoints, on payer decision-making for immune checkpoint inhibitors approved to treat non-small cell lung cancer (NSCLC) in the EU5, and how that aligns with what efficacy data drives prescribing for NSCLC.

METHODS

- 59 national and regional EU5 HTAs for approved immune checkpoint inhibitors—Opdivo (nivolumab), Keytruda (pembrolizumab), and Tecentriq (atezolizumab)—from 2016 to 2019 were collected using Decision Resource Group's Market Access Platform and Global Market Access Solution platform.
  - Due to a lack of transparency into Italy's Agenzia Italiana del Farmaco (AIFA) decision rationale, only HTA decisions from Italian regions were included. For Spain, national-level informe de posicionamiento terapéutico (therapeutic positioning reports) and regional-level HTA decisions were both included. In Germany, both Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG) and Gemeinsamer Bundesausschuss (G-BA) decisions were included. In the UK, National Institute for Health and Care Excellence (NICE) and Scottish Medicines Consortium (SMC) decisions were included.
  - The decisions were analyzed for clinical and nonclinical factors that influenced HTA outcomes, particularly which primary and secondary endpoints were considered when making the HTA decision, such as overall survival (OS), progression-free survival (PFS), objective response rate (ORR), and other response-related endpoints.
- In April 2018, 251 oncologists (France=50, Germany=50, Italy=50, Spain=51, United Kingdom=50) were surveyed in an online survey regarding their prescribing patterns, including which clinical and nonclinical outcomes most influence their prescribing.
- Also in April 2018, 10 decision makers involved in the reimbursement and pricing of NSCLC drugs in the EU5 (France=2, Germany=2, Italy=2, Spain=2, United Kingdom=2) were interviewed over the telephone regarding their views about the relative importance of clinical vs other factors (e.g. cost) for HTA decisions in this indication.

RESULTS

- Of the 59 HTA decisions that were identified, the majority of decisions were either recommendations (or positive added benefit ratings, or ASMR IV or above) or were recommendations with restrictions. Only one decision was a rejection (Figure 1).
- OS was the most important efficacy endpoint influencing payer decision-making (86% [n=51] of decisions cited the OS outcome in their rationale), with PFS considered 58% (n=34) of the time and ORR considered only 32% (n=19) of the time. Four of the EU5 countries considered PFS for the majority of HTA decisions (75-100%), with the exception of Germany, where it was considered in 16% (n=4) of decisions (Table 1).
- Data from the HTA results is in line with what interviewed payers outlined as key endpoints influencing HTA decision-making in their country, with all interviewed payers but the German ones reiterating the importance of PFS as a surrogate endpoint. Payers' perspectives on ORR and other response-related endpoints (such duration of response) were mixed, with some valuing the data gleaned from respond endpoints more than others (Table 2). Notably, Spanish and French HTA decisions considered ORR in the majority of their decisions (75%), and France's Haute Autorité de Santé (HAS) was the only agency that considered other response endpoints in a majority of decisions (63%).
- Overall, for surveyed physicians, clinical factors (notably efficacy outcomes such as OS and PFS and, to a lesser extent, a deep and/or durable response) outweighed nonclinical factors in influencing prescribing of immune checkpoint inhibitors for NSCLC. Improvement in OS was the most important driver in all EU5 countries (48-58%) and PFS was second (12-34%). The strongest preference for OS was in the UK. Only 4-16% of oncologists chose response-related endpoints as the most influential driver of prescribing (Figure 2).
- Furthermore, when ranking their second-most important factor that influences prescribing, 14-30% chose PFS, 10-22% chose deep and/or durable response, indicating that while OS may be the most commonly ranked top prescribing driver, PFS and response remain important factors (Figure 3).

- Payer and physician preferences did not align in every country. **German oncologists ranked PFS as more important (34%) than their peers did (12-22%) and had the joint-lowest ranking of importance for OS at 48%, despite the fact that only 16% of German HTA decisions that were analyzed considered PFS in the decision rationale (although PFS data was provided).** Although less receptive to response rate than their colleagues, German physicians placed more importance on response rate than their payer counterparts.

TABLE 1: KEY ENDPOINTS INFLUENCING HTA DECISION RATIONALE

	FRANCE (n=8)		GERMANY (n=25)		ITALY (n=2)		SPAIN (n=12)		UK (n=12)		EU5 TOTAL (n=59)	
ENDPOINT	KEY DRIVER (Y/N)	% OF DECISIONS	KEY DRIVER (Y/N)	% OF DECISIONS	KEY DRIVER (Y/N)	% OF DECISIONS	KEY DRIVER (Y/N)	% OF DECISIONS	KEY DRIVER (Y/N)	% OF DECISIONS	KEY DRIVER (Y/N)	% OF DECISIONS
Overall survival (OS)	✓	100%	✓	72%	✓	100%	✓	100%	✓	100%	✓	86%
Progression-free survival (PFS)	✓	88%	✗	16%	✓	100%	✓	100%	✓	75%	✓	58%
Objective response rate (ORR)	✓	75%	✗	0%	✗	0%	✓	75%	✗	25%	✗	32%
Other response-related endpoints	✓	63%	✗	0%	✗	0%	✗	42%	✗	25%	✗	24%

FIGURE 1: HTA DECISIONS FOR NSCLC IMMUNE CHECKPOINT INHIBITORS

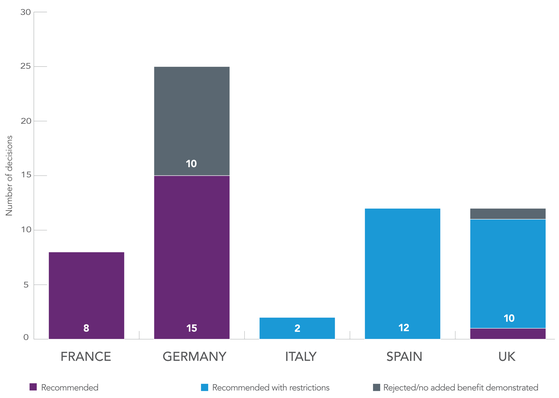


TABLE 2: INTERVIEWED PAYER INSIGHT ON THE PREFERRED CLINICAL ENDPOINTS

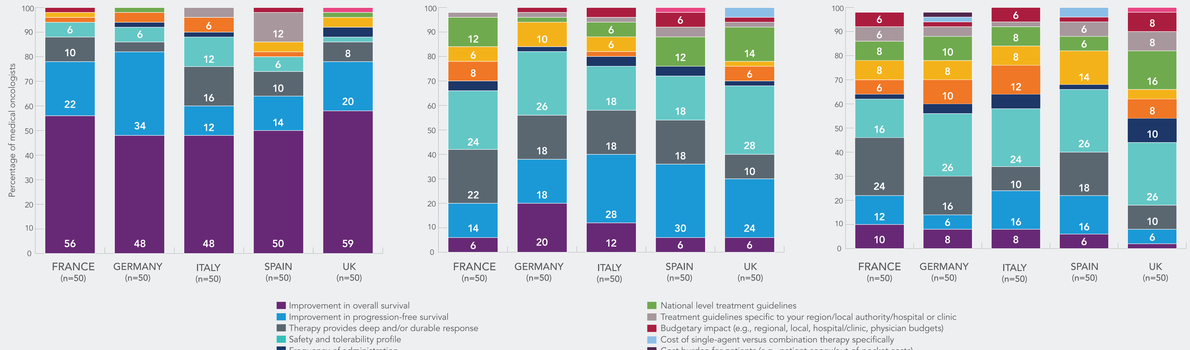
COUNTRY	PAYER INSIGHT
France	"We need a significant improvement versus an active comparator to justify a high cost. We need a significant increase in overall survival. If a drug can improve on the OS results of existing therapies, payers will support the reimbursement of the new agent, and the budget impact will not be an issue." — *HAS advisor, France*
Germany	"Emerging drugs need H2H data in patient-relative endpoints; the most important end points for NSCLC are OS and then QOL. Most emerging immune checkpoint inhibitors will receive a no additional benefit rating due to the wrong efficacy endpoint, so that is quite disappointing. Nearly all have had the wrong end points. They just have data for PFS, response rate, objective response rate, and duration of response—not OS." — *G-BA advisor, Germany*
Italy	"Overall survival is the most important efficacy endpoint. However, it can be substituted with progression-free survival in the first line of treatment because progression-free survival at this point is not biased by prior lines of therapy. In the second line, progression-free survival is still a good end point. Quality of life is another endpoint that is highly valued by payers; it is related to the toxicity profile of the drugs." — *PTOR member, Italy*
Spain	"National and regional payers in Spain mainly care about incremental benefit and incremental efficacy in terms of overall survival or progression free survival, as well as toxicity and tolerability. I think it is necessary to present overall survival in order to see the real value of an immune checkpoint inhibitor treating NSCLC. Especially if the comparator has OS data." — *DGFPS advisor, Spain*
United Kingdom	"To demonstrate additional benefit over a current therapy, manufacturers should show good cost-effectiveness, with an improvement in PFS or OS within a subgroup or in an indication in which there are few alternatives. Overall survival is still important. Progression-free survival is accepted in the U.K., but overall survival is still something that we look for ideally for tumors, and especially for lung cancer where the survival is not that long anyway." — *NICE advisor, United Kingdom*

FIGURE 2:

MOST IMPORTANT DRIVERS OF CHOICE OF IMMUNE CHECKPOINT INHIBITOR FOR NSCLC

SECOND-MOST IMPORTANT DRIVERS OF CHOICE OF IMMUNE CHECKPOINT INHIBITOR FOR NSCLC

THIRD-MOST IMPORTANT DRIVERS OF CHOICE OF IMMUNE CHECKPOINT INHIBITOR FOR NSCLC



CONCLUSION

- Surveyed oncologists and HTA decisions both cited OS as the most influential factor affecting decision-making for ICIs in NSCLC. However, there was some divergence in how influential other endpoints (PFS, different response types, safety and tolerability) were between the agencies and the oncologists practicing in those geographies, particularly in Germany.

REFERENCE

1. European Access & Reimbursement: Navigating Reimbursement for and Maximizing Market Access to Immune Checkpoint Inhibitors in Europe: Physician and Payer Insights. Decision Resources Group, Burlington, MA, USA. July 2018.