The use and influence of real-world data on French health technology assessment.

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INTRODUCTION

The French National Authority for Health (HAS) encourages using real-world data (RWD – health data collected in routine condition) and real-world evidence (RWE - insights derived from analyzing RWD) in drug assessments[1,2] .

Since 2020, HAS views RWD as a valuable tool for assessing health solutions. In its guidance issued in 2021, the HAS clearly support RWD inclusion in evaluations[2]. This orientation has been reiterated in 2023 in the HAS doctrine[3]. However, the use of RWD/RWE in the evaluation of medications is not yet systematic in practice.

This study aimed to identify the types of RWD/RWE provided by pharmaceutical companies in their reimbursement request dossiers and to analyze their influence on therapeutic value (SMR), improvement of medical benefit (ASMR) levels assessments and price setting.

METHOD

Based on an exhaustive review of HAS files, we identified and analyzed all Transparency Committee (CT) and Economic Committee for Health Products (CEESP) evaluations and related files for breast cancer medicines published between January 2022 and February 2024. These documents were analyzed to qualitatively understand the types of RWD used in each chapter and their impact on the evaluations.

To complete the analysis, we included nine additional French "key examples" of therapies with other indications, well-known for including RWD/RWE in their submission dossiers.

Breast cancer drugs considered :
- IBRANCE® (palbociclib),
- ENHERTU® (trastuzumab déructécan),
- VERZENIOS® (abémaciclib),
- NERLYNX® (neratinib),
- LYNPARZA® (olaparib),
- KISQALI® (ribociclib),
- KEYTRUDA® (pembrolizumab),
- TRODELVY® (sacituzumab govitecan),
- ZEULIDE® (leuprorelin acetate).

"Key examples" drugs considered :
- LYNPARZA® (olaparib) in ovarian cancer,
- LIBTAYO® (cémiplimab) in epidermoid carcinoma,
- VITRAKVI® (larotrectinib) in pediatric sarcomas,
- BLYNCITO® (blinatumomab) in acute lymphoblastic leukemia,
- ABECMA® (idecabtagene vicleucel) in multiple myeloma,
- QUVIVIQ® (daridorexant) in chronic insomnia,
- AJOVY® (frémanézumab),
- AIMOVIG® (érenumab) in severe migraine,
- ENTYVIO® (védolizumab) in chronic pouchitis.

RESULTS

We identified 9 breast cancer drugs evaluated through 19 HAS assessments: 13 clinical opinions by the Transparency Committee (CT) and 6 economic evaluations by the economic committee for health products (CEESP). Additionally, we analyzed 9 "key examples" drugs in 9 HAS evaluations (9 clinical opinions dossiers) in the same way.

Clinical assessments

Transparency committee assessments for breast cancer drugs

The 13 transparency committee assessments were related to 9 oncology drugs indicated in breast cancer.

Each CT assessment dossier was subdivided into 9 distinct chapters.

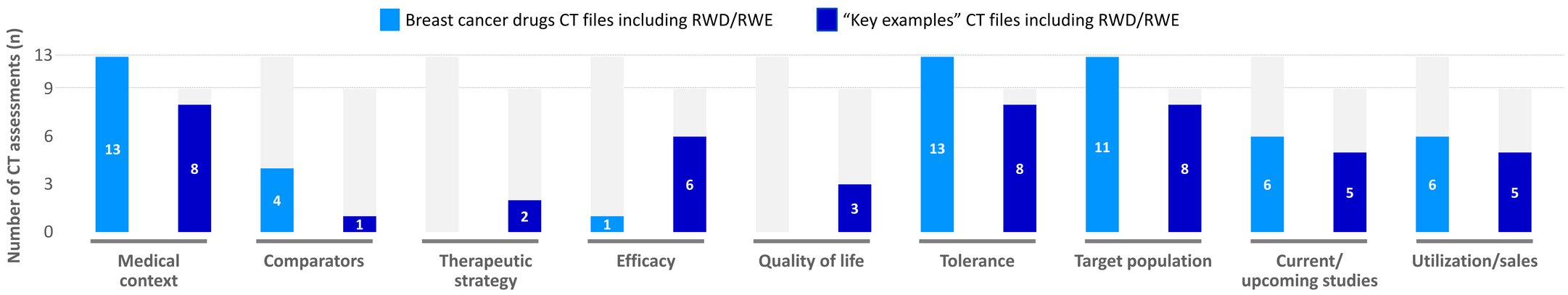
The "Medical context" (epidemiology) and "Tolerance" (drug safety) chapters were fulfilled using RWD across all assessments (100%). Additionally, RWD was included in the "Target population" section of 11 dossiers (85%) (Figure 1).

Transparency committee assessments for "key examples" drugs

A total of 9 CT evaluations of 9 drugs in various disease areas were considered as "key examples" in this study.

Through the 9 chapters of CT files, sections like "Medical context," "Tolerance," and "Target population" were estimated by RWD in 89% (n=8) of evaluations considered (Figure 1).

Figure 1. Overview of the usage of RWD/RWE across chapters of breast cancer (n=13) and "key examples" (n=9) drugs CT assessment dossiers



Across the 6 "key examples" drug assessment dossiers that included RWD in their "Efficacy" section, 5 cases (83%) were reassessments by the HAS' Transparency Committee, showing varying conclusions.

The reassessments of LIBTAYO® (cémiplimab) and VITRAKVI® (larotrectinib) showed an increase of their respective ASMR levels, that may have been due to additional "efficacy" data considered (Table 1).

Table 1. Overview of "key examples" reassessments that included RWD in "Efficacy" sections (n=5)

Product	INN	Indication	Previous assessment conclusion			Assessment conclusion after RWE inclusion			Modification
			Data selected in the Efficiency section	SMR	ASMR	Data selected in the Efficiency section	SMR	ASMR	
LYNPARZA®	olaparib	Ovarian cancer	Phase III	Important	IV	Phase III	Important	IV	No modification
LIBTAYO®	cémiplimab	Epidermoid carcinoma	Phase II non-comparative (IA) + Indirect comparison based on literature review	Important	V	Phase II non-comparative (FA) + Indirect comparison between French early access data and a historic cohort	Important	**IV**	**ASMR level increased**
VITRAKVI®	larotrectinib	Pediatric sarcomas	Phase I/II	Moderate	V	Phase I/II + External comparison between phase I/II and a French and an International cohorts	**Important**	**IV**	**SMR & ASMR levels increased**
AJOVY®	frémanezumab	Severe migraine	Phase III	Moderate	V	European observational studies (IA)	**Important**	V	**SMR level increased**
AIMOVIG®	érénumab	Severe migraine	Phase III	Moderate	V	Phase IV	**Important**	V	**SMR level increased**

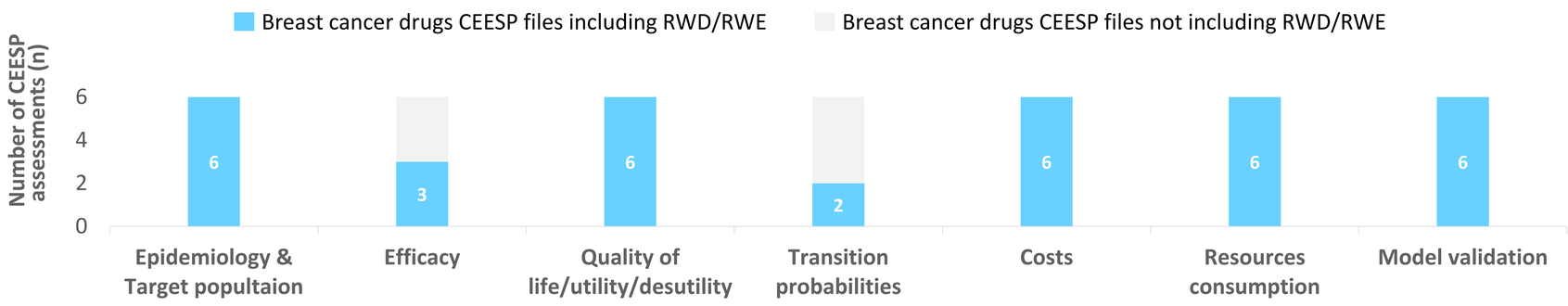
Abbreviations: ASMR: Improvement of medical benefit level ; FA: Final analysis ; IA: Intermediate analysis ; INN: International Nonproprietary Names ; SMR: Therapeutic value level

Cost-effectiveness assessments

Regarding economic evaluations, CEESP files generally included RWD, as recommended by the HAS methodological guide.

In fact, 5 (71%) out of the 7 sections, such as "Epidemiology and target population", "Quality of life, utility and disutility", "Costs", "Resources consumption" and "Model validation", systematically included these types of data through breast cancer drugs files (Figure 2).

Figure 2. Overview of the usage of RWD/RWE across chapters of breast cancer (n=6) drugs CEESP assessment files



CONCLUSION

In this study, only a third of CT dossiers' chapters ("Medical context", "Tolerance" and "Target population" sections), typically included RWD and RWE.

Through several "key examples" dossiers considered, additional "efficacy" data provided, such as RWD and RWE, contributed to the reassessment of therapeutic value (SMR) and improvement of medical benefit (ASMR) levels.

It seems that conducting rigorous indirect comparisons by including RWD in addition to clinical trial results can further strengthen the demonstration of a drug's efficacy.

REFERENCES

[1] Bégaud *et al.* (2017) – *Les données de vie réelle, un enjeu majeur pour la qualité des soins et la régulation du système de santé*

[2] HAS (2021) – *Guide méthodologique : étude en vie réelle pour l'évaluation des médicaments et dispositifs médicaux*

[3] HAS (2020 and 2023) – *Doctrine de la commission de la transparence (CT), principes d'évaluation de la CT relatifs aux médicaments en vue de leur accès au remboursement.*

Pfizer RWEality

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