Review of published efficiency opinions of the French economic and public health assessment committee (CEESP) in oncology

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BACKGROUND

- Since 2004, cancer has been the leading cause of premature death in France, compared with cardiovascular diseases.[1] According to the National Cancer Institute, about 382,000 new cases of cancer were estimated in France in 2018.[1]
- Over the last 15 years, in France, the implementation of 3 national cancer plans has led to major advances and broad mobilization of the various actors.[2]
- Thus, products belonging to the oncology therapeutic areas constitute a major market in France. This is reflected in particular by the important market access of anti-cancer drugs.
- Since 2013, manufacturers are requested to submit to the French economic and public health assessment committee (Commission Evaluation Economique et de Santé Publique - CEESP) a pharmacoeconomic evaluation for any innovative health product claiming an clinical added value (Amélioration du Service Médical Rendu - ASMR) level ≤III with a substantial impact on healthcare expenditures (≥€20 million the second year).
- The objective of this study was to review the CEESP efficiency opinions and provide a summary of the methodological concerns (MCs) reported in oncology indications.

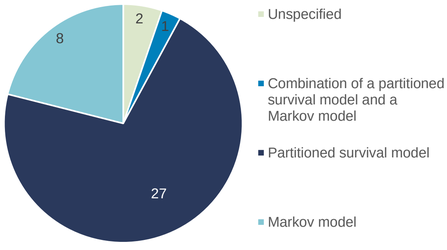
METHODS

- All opinions published by the CEESP until May 2019 were retrieved from the website of the French Health Agency (Haute Autorité de Santé – HAS).
- For each opinion, the data of interest, such as the therapeutic area, the type of analyses presented, the ASMR obtained, etc., were extracted.
- The MCs raised by the CEESP were also extracted and subsequently classified according to their impact (major, important and minor) and their dimension (e.g. clinical data, programming). The purpose of the concern (e.g. robustness, representativeness) was also extracted.
- The main results were summarised with a focus on the products with oncology indications.

RESULTS

- Overall, 88 CEESP opinions were identified on HAS website. Among them, 38 opinions were related to oncology.
- About 3 out of 4 models used are ‘partitionned survival model’, as described in Figure 1.

Figure 1. Model types used in oncology cost-effectiveness analysis assessed by CEESP



- In the 38 dossiers, 262 MCs were raised overall: 22 major (8.4%), 84 important (32.1%), 156 minor (59.5%).
- Table 1 describes the distribution of the MCs raised, according to the dimension.

- **Relevant findings**:
  - 19 Oncology Products (OP) applied for a first inscription, 13 were evaluated for a new indication, 2 assessments were required by the Economic Committee for Health Products (Comité Economique des Produits de Santé - CEPS)
  - 13 OP claimed a ASMR level-II and 23 a level-III
  - 1 OP granted a level-II AMSR, 13 granted a level-III and 21 granted a level-IV or V
  - 12 OP targeted a first line indication and 23 a second line or more
  - 12 OP were assessed in combination with another molecule

Table 1. Dimension of the 262 MCs raised (n=38 oncology efficiency opinions)

Dimension	Major MCs	Important MCs	Minor MCs
Economic analysis and outcome choice	-	1	1
Sensitivity analysis	1	13	16
Costs	-	3	29
Clinical data	11	20	17
Time on treatment	-	1	8
Clinical expert	1	-	-
Time horizon	-	-	1
Assumptions	-	5	10
Comparators	3	3	7
Modelling	-	1	4
Assessment objective	-	2	1
Perspective	-	-	1
Simulated population	2	6	12
Transition probabilities	-	1	-
Literature search	-	-	2
Model results	3	3	5
Model structure	-	3	5
Safety	-	6	9
Utilities	1	10	20
Validity (internal and external) & study limits	-	6	8
Total	**22**	**84**	**156**

- Among the 38 CEESP oncology efficiency opinions assessed, 14 reported ≥1 major MC (37%); in these 14 efficiency opinions, the mean number of major MC was 1.6.
- Most of the major MCs were related to clinical data (11/22, 50%). Most of them were attributable to the lack of robustness (4/11, 36%), or to use of non-comparative results from the clinical trial (2/11, 18%).
- The other purposes of the major MC included:
  - estimation method of utility values
  - uncertainty surrounding the data (lack of deterministic and probabilistic analysis)
  - absence of (at least) one clinically relevant comparator
  - representativeness of the population
  - pairwise comparison for ICER calculation
  - anonymity of clinical experts
- Regarding important MCs, most of them were attributable to clinical data (20/84, 24%), especially lack of robustness (6/84, 7%), lack of sensitivity analysis (9/84, 11%) and utility derivation method (6/84, 7%).

DISCUSSION

- In France, authority decision making is much driven by the clinical benefit of the strategy over existing products.
- The quality and robustness of clinical data appears to be a crucial aspect of oncology efficiency opinions.
- Indeed, among the 38 opinions reviewed, around half of major MCs and around a quarter of the important MCs were related to the clinical data, especially about their robustness.

CONCLUSIONS

- The review of opinions emphasises the impact of robustness of clinical data on the CEESP assessment.
- Conduct of high quality sensitivity analyses was also raised as a key driver, to quantify the uncertainty around the results.
- The consideration of all clinically relevant comparator(s) in the analysis, as well as the representativeness of the clinical trials patients and the transferability to the French patients were also mentioned as a key aspect.

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