ESMO-MCBS Evaluation and French Derogatory Access Decision: Is There a Correlation?

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INTRODUCTION

In July 2021, France reformed its early access system to accelerate access to promising medicines, establishing **2 main routes**:

- **Early Access (EA)**: a transitional access, possible before or after marketing authorization, intended to bridge over to routine reimbursement.
- **Compassionate Use (CU)**: a route to address unmet medical need when no appropriate alternative exists.

The ESMO-Magnitude of Clinical Benefit Scale **(ESMO-MCBS)** is a validated tool[1,2] used to assess the clinical value of cancer drugs, based on **substantial benefit (SB)**. If previous studies shown that higher MCBS scores positively associate with favourable reimbursement decisions, no study evaluated its role for EA decision.

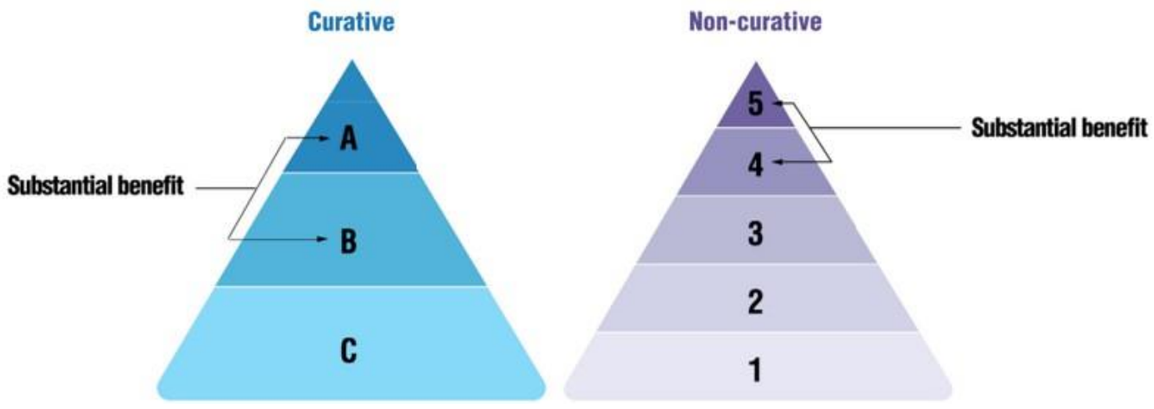

Figure 1: ESMO-MCBS scores for solid tumors, according to curative and non-curative setting

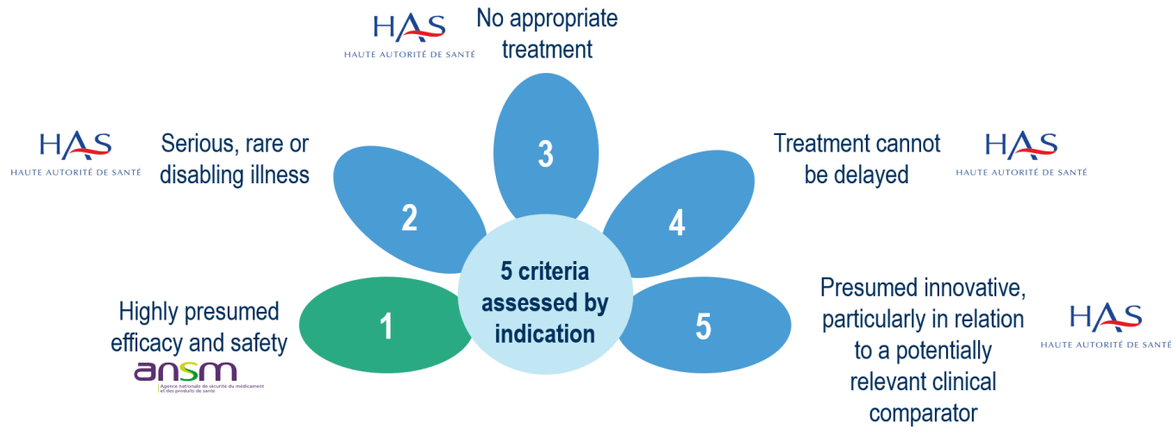

Figure 2: Early Access (EA) eligibility criteria in France

→ Objective: Our study evaluated whether Substantial Benefit, as defined by ESMO-MCBS, predicts early access decisions in France.

METHODS

Inclusion criteria:

- French early access applications for **solid tumors** (except antidotes) between **July 2021 and April 2025**
- With available ESMO-MCBS score

Outcomes:

- **Correlation** between SB and early access decisions, in terms of overall agreement (concordance), positive and negative predictive value
- Qualitative analysis of **discrepancies**
- **Decision timelines** between ESMO-MCBS and early access decisions

RESULTS

From July 2021 to April 2025, 77 indications for French early access applications for solid tumors had an available ESMO-MCBS score.

The cohort was predominantly in the non-curative setting (81%), consisting mainly of targeted therapies (60%) or immunotherapies (39%). Most of the trials were phase III (78%).

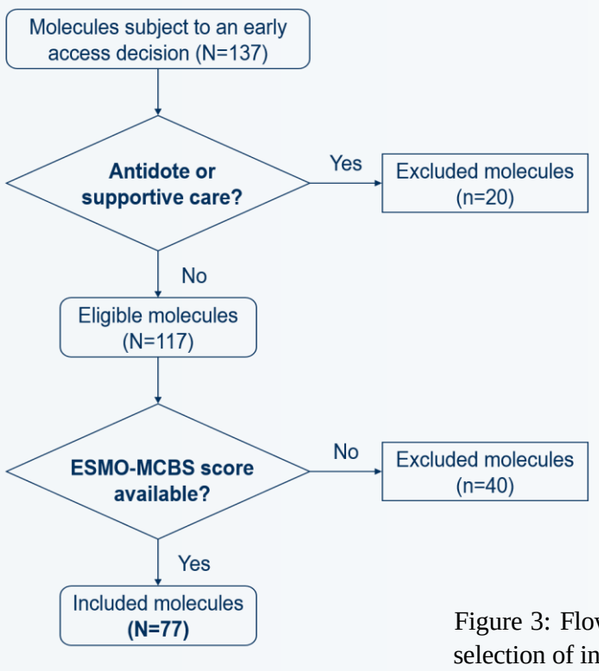

Figure 3: Flowchart of selection of indications

Table 1: Overall concordance between the ESMO-MCBS score and the French early access decisions

	Early access decision		
	Acceptance	**Refusal**	**Total**
Substantial Benefit	33	10	**43**
Absence of Substantial Benefit	22	12	**34**
Total	**55**	**22**	77

- With a concordance of 58.4% $CI_{95\%}$=[47.5% − 69.4%] between the ESMO-MCBS and the EA decision, the concordance was **modest**. This means that in 45/77 cases, the MCBS prediction align with the final decision of EA, whereas discordance occurs in 32 cases.
- The Positive Predictive Value (PPV) was 77% $CI_{95\%}$=[62% − 87%], meaning that **if a drug is assigned a substantial benefit by the ESMO-MCBS, it strongly suggests the EA decision will be granted**.
- In contrast, the Negative Predictive Value (NPV) was 35% $CI_{95\%}$=[21% − 53%], meaning that a low **MCBS score is only a very modest predictor of refusal**. Notably, an EA was approved in 22 cases despite a lack of substantial benefit.
- For discrepancies, the reasons for EA rejection despite a SB score were the possibility to defer the treatment (80%), the lack of innovation (70%), existing alternatives (70%), and a negative risk-benefit profile (20%).
- ESMO-MCBS preceded EA decisions in **71%** of cases, with a median delay of **134 days**.

CONCLUSIONS

ESMO-MCBS showed only **moderate alignment** with EA decisions. This study shows that the regulatory decision is a **multi-criteria assessment** that may consider other factors like unmet medical need and existing alternatives beyond the clinical benefit. However, the high PPV makes the MCBS an effective **initial screen** for highly promising drugs. Therefore, we suggest the MCBS serves as a valuable **complementary tool** for guiding early access assessments rather than a sole determinant.

REFERENCES

1. ESMO-Magnitude of Clinical Benefit Scale version 2.0 (ESMO-MCBS v2.0) Cherny, N.I et al. Annals of Oncology, Volume 36, Issue 8, 866 - 908
2. Methodological and reporting standards for quality-of-life data eligible for European Society for Medical Oncology-Magnitude of Clinical Benefit Scale (ESMO-MCBS) credit Oosting, S.F. et al. Annals of Oncology, Volume 34, Issue 4, 431-439