# Insights on early access refusal in France

Goda Kijauskaite, Orestis Lazos, Catherine Kielar
Avalere Health, London, UK

HTA28

## Introduction

The French Health Technology Assessment agency, Haute Autorité de Santé (HAS), has established an early access (EA) program designed to expedite the availability of innovative treatments for serious diseases that lack effective treatment options. Although numerous therapies receive EA approval, some applications are denied. It is essential to understand the factors contributing to these rejections to strengthen future EA submissions and apply relevant learnings to drug development and access strategy.

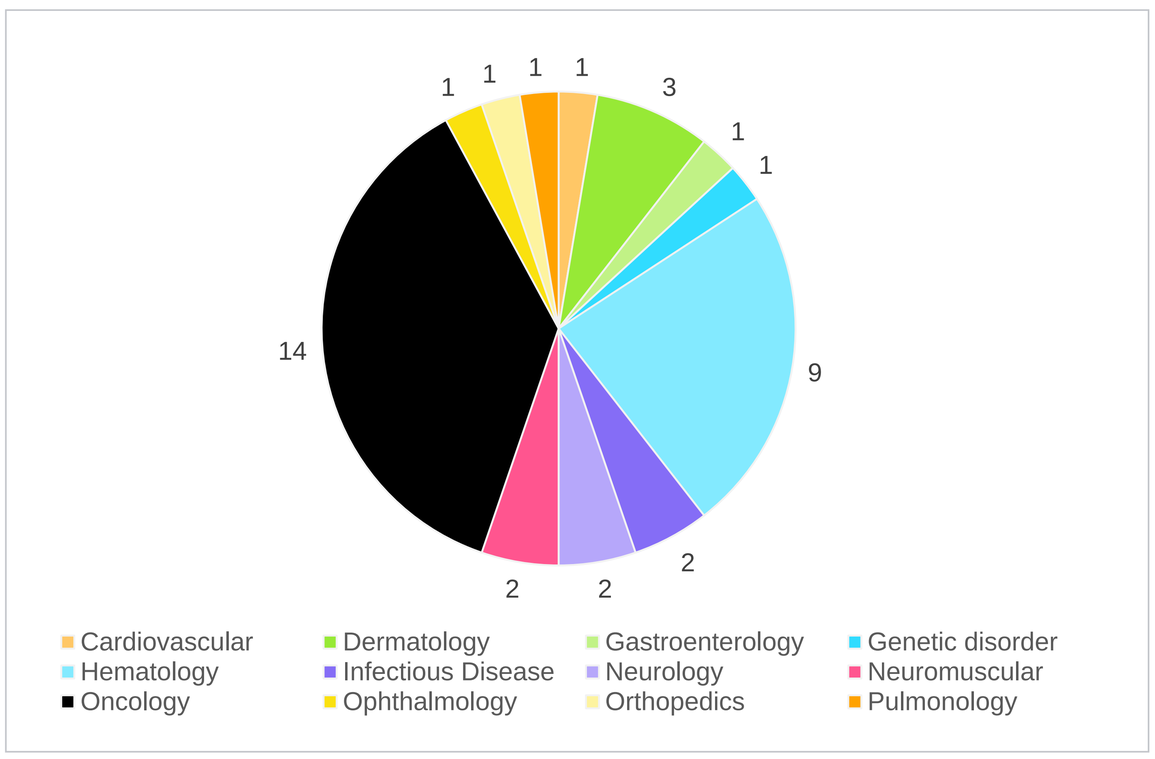
## Methods

This retrospective study evaluated all refusal cases within HAS's EA program from 2021 to May 2024. A total of 38 cases were identified through a systematic review of the HAS website. Selected cases were assessed in detail to identify patterns related to the drivers of the decision and to provide relevant insights for manufacturers, particularly regarding the criteria for evaluating EA requests and the commentary provided by the Transparency Committee (TC). Extracted information included the indication in question, disease area, and commentary on the criteria for EA assessment: the seriousness of the condition, availability of alternative treatments, innovation status, and the proposed clinical development plan (CDP). In cases where a TC health technology assessment (HTA) was conducted on the indication for which EA was requested, service médical rendu (SMR) and amélioration du service médical rendu (ASMR) scores were extracted to identify any parallels between EA request and HTA outcomes.

## Results

Out of 38 decisions reviewed (Figure 1), oncology (n=14), hematology (n=9), and dermatology (n=3) were selected for in-depth review.

Figure 1: Breakdown of disease areas in EA case studies

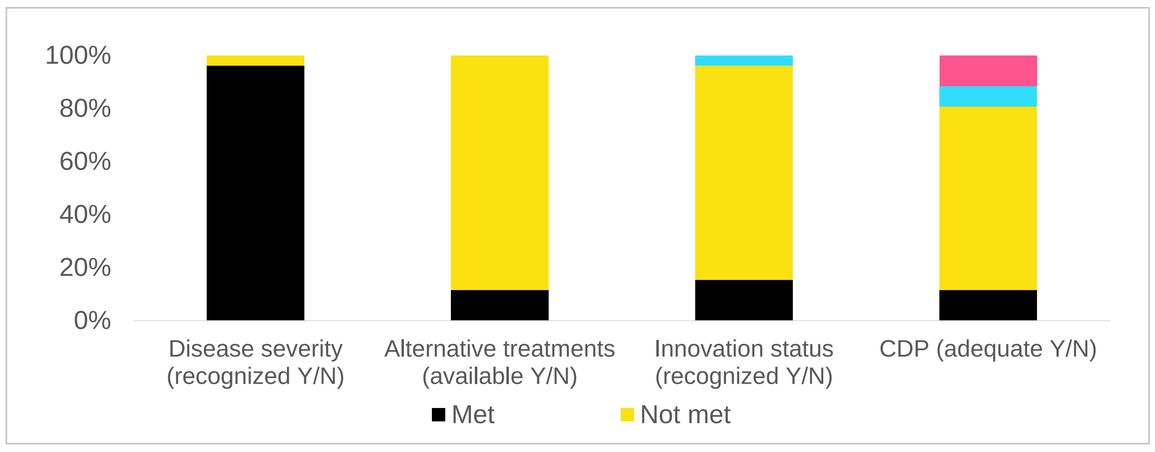



According to the HAS early access doctrine, all criteria must be met for early access approval[1], however, most applications failed to meet majority of the criteria (Figure 2). Specifically, the TC recognized disease severity in all but one EA request (in atopic dermatitis), however, the availability of alternative treatments (either in early or regular access), lack of innovation, and inadequate CDP were noted in over 70% of cases.

Regarding the availability of alternative treatments criterion, the TC noted whether treatments were already available to patients in France, in either regular or early access, or through compassionate use, rarely commenting on the efficacy and safety of the available treatments. This suggests that, related to this criterion, the key driver for EA decisions is whether there is urgency to provide access to a drug, or if it could be deferred (ie, by pursuing regular access). For example, EA was refused for Hemgenix (etranacogene dezaparvovec) for the treatment of hemophilia B, as the TC noted that despite meeting the severity of the disease and innovative status criteria, as well as having an adequate CDP, the availability of other treatments meant that access could be deferred.

Unlike other HTA agencies, the TC determines a drug's innovative status and adequate CDP regarding its expected incremental efficacy, safety, health-related quality of life (HRQoL), or practicality of the drug in the care pathway. The TC consistently applied this point of view, noting a lack of incremental comparative benefit in either completed or ongoing trials in most cases to justify not considering drugs as innovative. Furthermore, regarding the assessment of the CDP, methodological issues, biases, lack of comparative efficacy, or benefit in patient-relevant endpoints were cited.

Figure 2: TC conclusion for each EA assessment criterion across reviewed application (n=26)

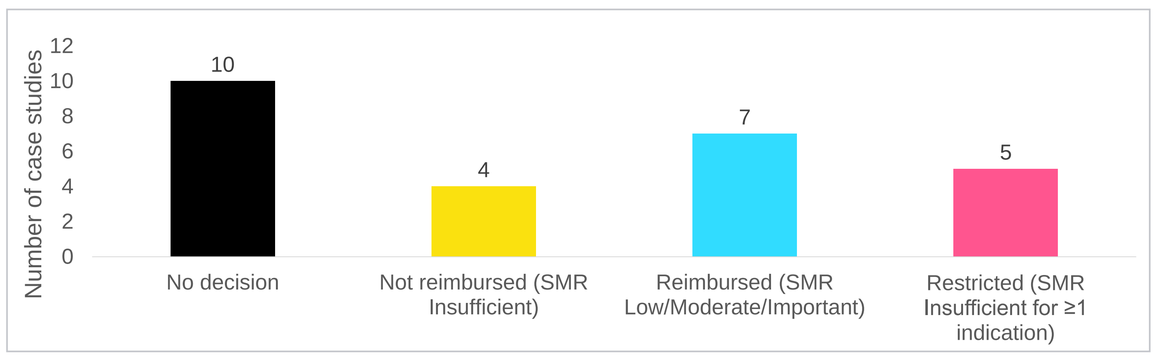



HAS is the final decision-maker for granting EA, and while by and large it adopts the TC's recommendation, in one instance, we observed that there was divergence between TC and HAS, with TC providing a favorable opinion, while HAS concluded that EA should be refused. Specifically in the assessment of Scemblix (asciminib)[2] for the treatment of Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML-CP) in chronic phase with a T315I mutation, in relapse, refractory or intolerant to ponatinib or for whom treatment with ponatinib is contraindicated, HAS agreed with the TC on the criteria of severity of the condition, lack of alternative treatments (noting that despite the option of allogeneic stem cell transplantation, its implementation depends on donor availability; therefore, it cannot be considered an appropriate treatment), however, it did not accept that Scemblix can be considered innovative in light of the available data and development plan. Specifically, HAS determined that the development plan was unsuitable for EA because the primary efficacy data were derived from a maximally tolerated dose-finding study, the ongoing non-comparative Phase 3b study lacked efficacy as a primary endpoint, and the study included a small number of patients with the targeted indication.

**The link between EA refusals and HTA outcomes**

TC decisions (Figure 3) were also reviewed to examine an association between the reasons and commentary for EA refusal and HTA outcome; however, there was, at best, a tangential association between the two.

Figure 3: HTA outcome of EA refusal cases




A potential explanation is that the remit of the TC when conducting HTA vs EA assessment as well as the drivers of HTA outcomes (SMR, ASMR) are different, and more nuanced for HTA. It is conceivable that some of the reasons for EA refusal may also carry over when a drug undergoes HTA, therefore, while we do not consider EA assessment results as predictive of HTA, they warrant consideration.

**Strategic recommendations**

**Strive to establish comparative effectiveness early:** When there are alternative treatments available, prioritize submitting evidence showcasing comparative benefits to strengthen the need for early access.

**Leverage early access feedback for strategic planning:** Even unsuccessful EA submissions can yield valuable insights into currently relevant comparators, guiding future clinical development plans and evidence generation activities to achieve a successful reimbursement outcome.

## Conclusions

This study provides valuable insights into the refusal patterns within HAS's EA program. Understanding the evaluation criteria and strategic considerations can help manufacturers optimize their approaches to navigate the EA landscape and enhance patient access to innovative therapies.

**Scan here for poster references**

Poster presented at ISPOR EU, 17–20 November 2024, Barcelona, Spain