LEARNINGS FROM TC OPINIONS OF DRUGS EVALUATED FOR EAP UNDER NEW PROCESS

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CONTEXT

In France, since 1992, patients can benefit from an early access to innovation, ahead of the marketing authorization or final reimbursement. This early access program (EAP) was reformed on July 1, 2021. HAS is now involved in granting EAP (HAS decision) while continuing to assess drugs for reimbursement (Transparency Committee (TC) opinions). According to HAS, it ensures consistency between derogation-based schemes (EAP) and the common law funding scheme (based on TC opinions).

To determine if a medication can be granted EA, the 5 criteria listed below are assessed. This is done by ANSM (1st criteria) or by TC (Criteria 2 to 5).

Eligibility criteria for EAP[1]

When no marketing authorisation, efficacy and safety are strongly presumed ;	☒
Indicated in a severe, rare or incapacitating disease ;	☒
No appropriate treatment;	☒
Initiation of treatment cannot be delayed;	☒
Medicinal product is presumptively innovative, particularly compared to any clinically relevant comparator	☒

For reimbursement, TC will assess :

- Actual clinical benefit ("SMR" in French) which determines whether or not medication is reimbursed,
- Clinical added value ("ASMR" in French) compared to available treatments which is used to define the framework for price negotiations.

Assessments performed during TC opinion[2]

ACTUAL CLINICAL BENEFIT (SMR)

- severity of the disease/condition ;
- efficacy ; adverse effects ;
- intended role in the therapeutic strategy in comparison with other available therapies ;
- public health benefits

CLINICAL ADDED VALUE (ASMR)

with regards to available treatments (reference medicinal product or better treatment modalities) conditional to:

- quality of the demonstration ;
- effect size in terms of clinical efficacy, quality of life and safety,
- clinical relevance

OBJECTIVES

This study aimed at analyzing TC opinion of drugs which have also been assessed for EA under new process.

METHODS

We conducted a retrospective analysis of all drugs which had, between July 1, 2021 and May 31, 2023: 1) an assessment for EAP with corresponding HAS decision published 2) the TC appraisal with corresponding opinion published.

RESULTS

72 opinions were identified. Among drugs granted EA,

- the majority had an important SMR (64/72). However, there was also: 1 insufficient, 4 weak and 3 moderate SMRs.
- Regarding ASMR, the majority had a clinical added value either important (ASMR II ; 1/72), moderate (ASMR III ; 31/72) or minor (IV ; 23/72). The remaining drugs (16/72) had an ASMR V (no clinical added value).

FIGURE 1: SMR of drugs granted EA

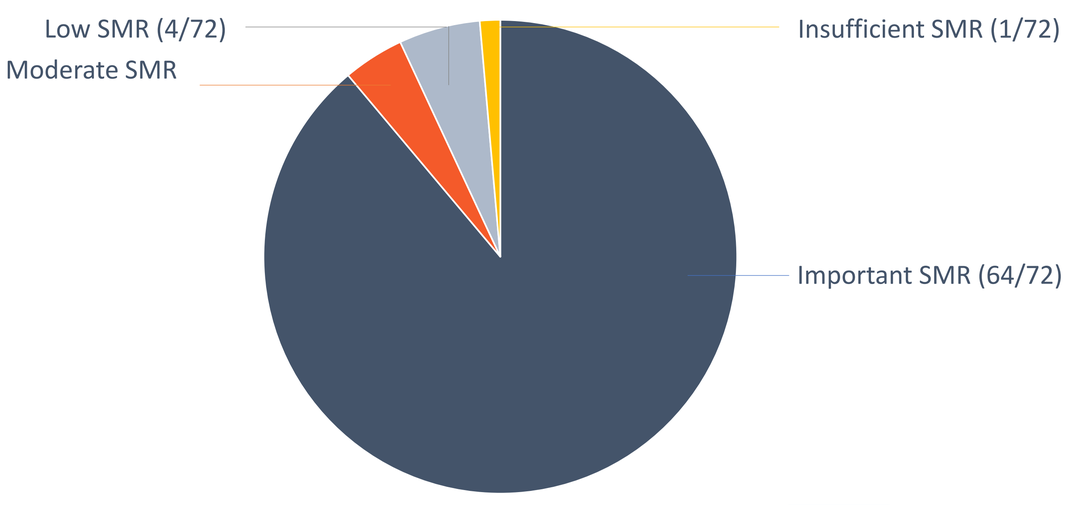

FIGURE 2 : ASMR of frugs granted EA

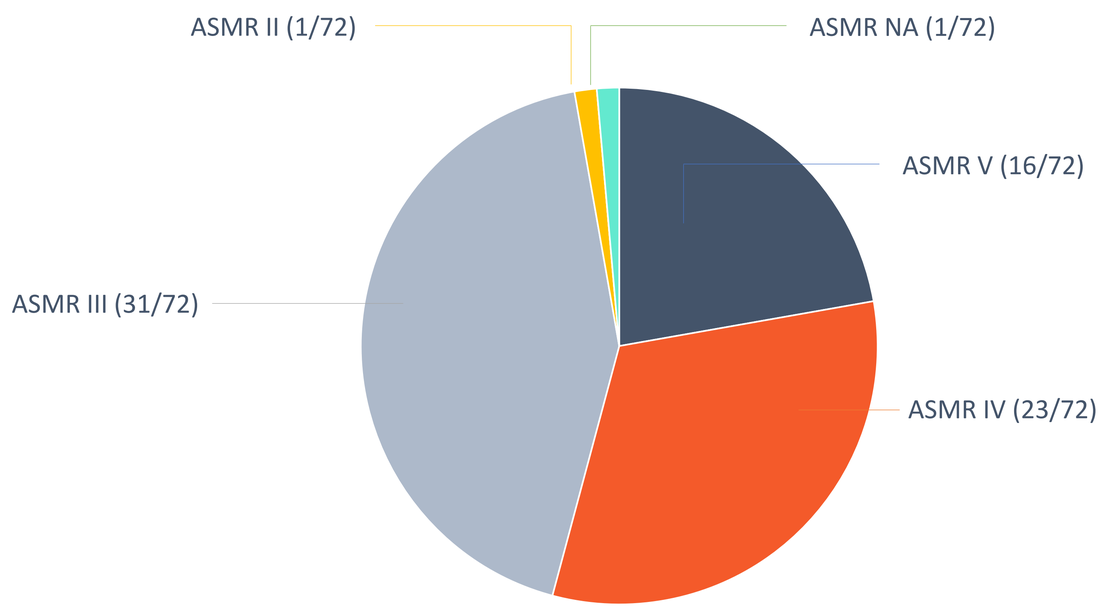

TABLE 1 : MEDICATIONS GRANTED NO CAV (ASMR V) AND EXPLANATIONS

Medication (trade name)	Explanation
YESCARTA®	Data from a non comparative Phase II study. Phase 3 randomized study data awaited.
RYBREVANT®*	Data from a non comparative Phase II study. Phase 3 randomized study data awaited.
LUMYKRAS®*	Data from a non comparative Phase II study. Phase 3 randomized study data awaited.
KYMRIAH®	Data from a non comparative Phase II study. Phase 3 randomized study data awaited.
CARVYKTI®	Data from a non comparative Phase II study. Phase 3 randomized study data awaited.
WEGOVY®	Uncertainties on cardiovascular risks. Results of a phase 3 study awaited.
OXBRYTA®*	EA granted by College (i.e. not the TC). Post-inscription study requested
TECVAYLI®	Data from a non comparative Phase II study. Phase 3 randomized study data awaited.
NEXVIADYME®	Only treatment for infantile forms. Phase 3 study data awaited.
AMVUTTRA ®	No clinically relevant comparators. New data awaited.
TECARTUS ®	Data from a non comparative Phase II study. Phase 3 randomized study data awaited.

* Moderate SMR

DISCUSSION

- Contrary to previous study (presented in 2022) one drug had an insufficient SMR (Ronapreve) and some drugs had a low or moderate SMR. This was mainly explained by some weakness in the quality of current clinical data.
- Most drugs granted an EA had an ASMR III or IV. This was expected considering the EA criteria : 'Presumptively innovative" which needs to rely on clinical data.
- There were 11 situations (on top of the 5 situations shown during previous study) where the EA was granted whereas no ASMR was acknowledged. In **all** cases new clinical data was awaited. In 9/11 cases, current evaluation had been based on a non comparative phase II study whereas, there was an ongoing comparative randomized study ongoing. In this situation, drug can be considered as **presumably** innovative based on the phase II data which **supported the assumption of better efficacy** than currently available treatments) and having a suitable development plan (phase 3 ongoing). Therefore, they fulfill the criteria for the derogation-based schemes (EAP). However, for the assessment in the scope of the common law funding scheme, phase II non comparative data is not sufficient to **demonstrate** a clinical added value at the time of the 1st evaluation.
- Even though there is no inconsistency between the 2 assessments, this situation can lead to difficulties as drugs granted EA can be available for a period of time but later on may not be available anymore as they are granted an ASMR which does not allow for a adequate funding.

CONCLUSION

As already seen previously, with the new process consistency between authorization of EA and TC opinion is ensured. When drugs which were authorized for EA and are granted an ASMR V (no clinical added value) there was a good reason for that (mainly the fact that phase 3 clinical trials were ongoing and new data with a demonstrative value, awaited.
This can raise some difficulties to have a continuity between derogation-based schemes (EAP) and the common law funding schemes. This situation is being addressed in the new coming law in France with a "transitory funding".

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COI : Estival A and Caron A are employees at CEMKA, one of the first French consulting firms in the field of evaluation of products, programs and organizations in Health. The study was not sponsored.

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