

Ravinet P., Aboussaid N., Chavade D. Biodimed Conseils, Paris, Ile de France, France

¹Vanier A, Fernandez J, Kelley S, et al. *Rapid access to innovative medicinal products while ensuring relevant health technology assessment. Position of the French National Authority for Health. BMJ Evid Based Med. 2023;bmjebm-2022-112091*

Context & Objectives

- ▶ Increasing number of drugs underwent HTA at an **early stage of clinical development**, especially in oncology or rare diseases, often with weak or presumptive evidence
- ▶ In Feb 2023 the TC reaffirmed its 2020 Doctrine¹: **single-arm clinical trials with indirect comparison of good methodological quality may lead to valuation in the Clinical Benefit (SMR) or Clinical Added Value (ASMR) when justified**

How did drugs with single arm trial +/- external comparison were assessed by the TC since 2020?

Table 1. TC points of attention on external comparisons

Design	• <i>A priori i.e.</i> concomitantly with the single arm trial
Data selection	• Well-performed systematic review • Similarity in studies characteristics
External control	• Corresponds to the standard of care
Data analysis	• Preferably based on individual patient data • Include a model for causal inference to control confounders on the predefined estimand • Include residual confounding analyses

Method



▶ TC appraisals with keywords "single-arm" and "non-comparative"

▶ Timeframe: 2020 to 2022 (3 full years)

▶ Criteria collected

- Orphan status
- Solicited level of SMR & ASMR
- Clinical package submitted
- Final level of SMR & ASMR

Table 2. Orphan drug status & External comparison analysis

Sample	SMR important	SMR insufficient	Mean ASMR level (when SMR important)
All appraisals (n=47)	55.3%	19.1%	4.1
Orphan status			
Orphan (n=23)	87.0%	4.3%	3.9
Non-orphan (n=24)	25.0%	33.3%	4.8
External comparison			
Provided (n=21)	42.9%	23.8%	4.4
Not available (n=26)	65.4%	15.4%	3.9

Results

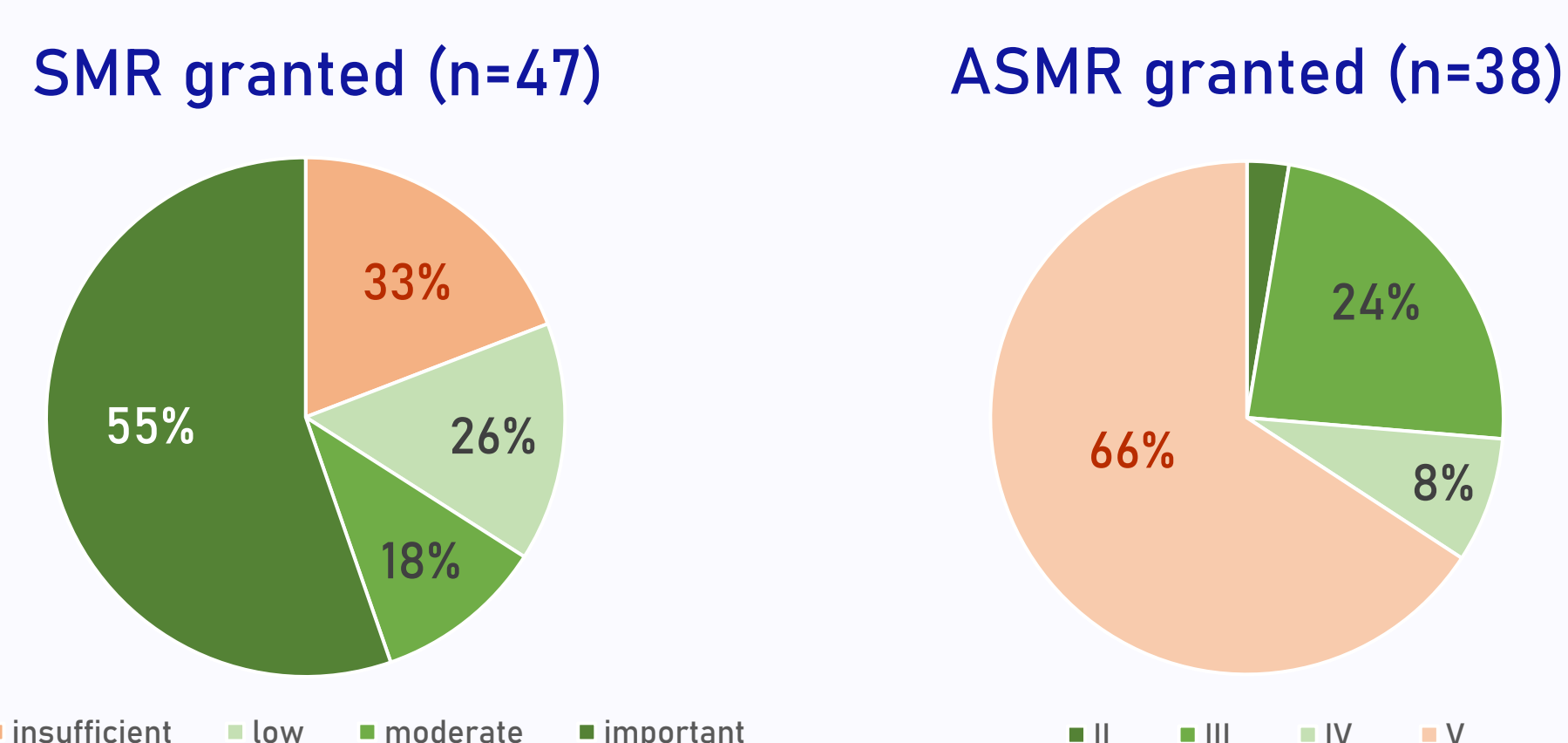


Figure 1. Detailed assessment flow-chart

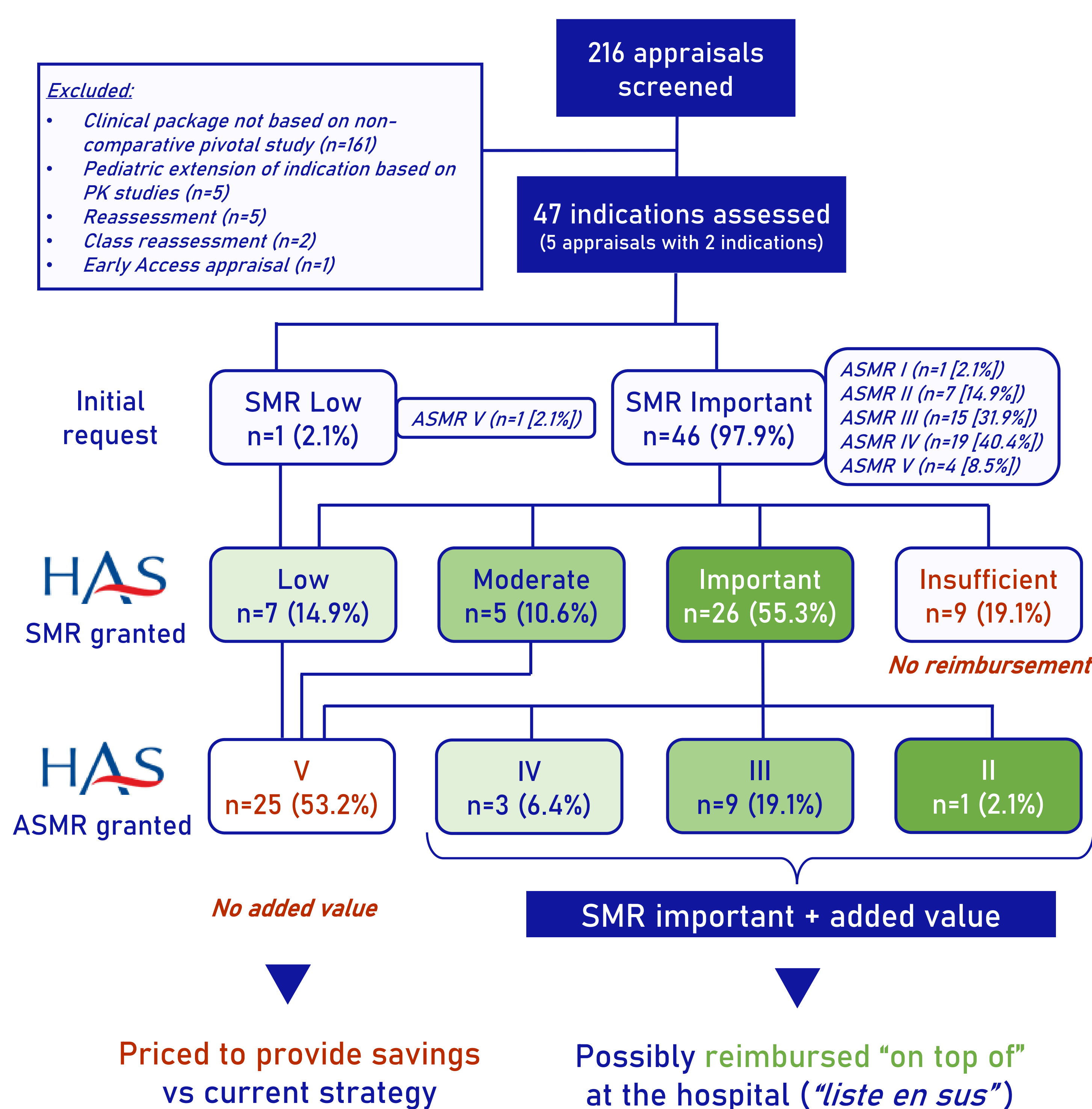
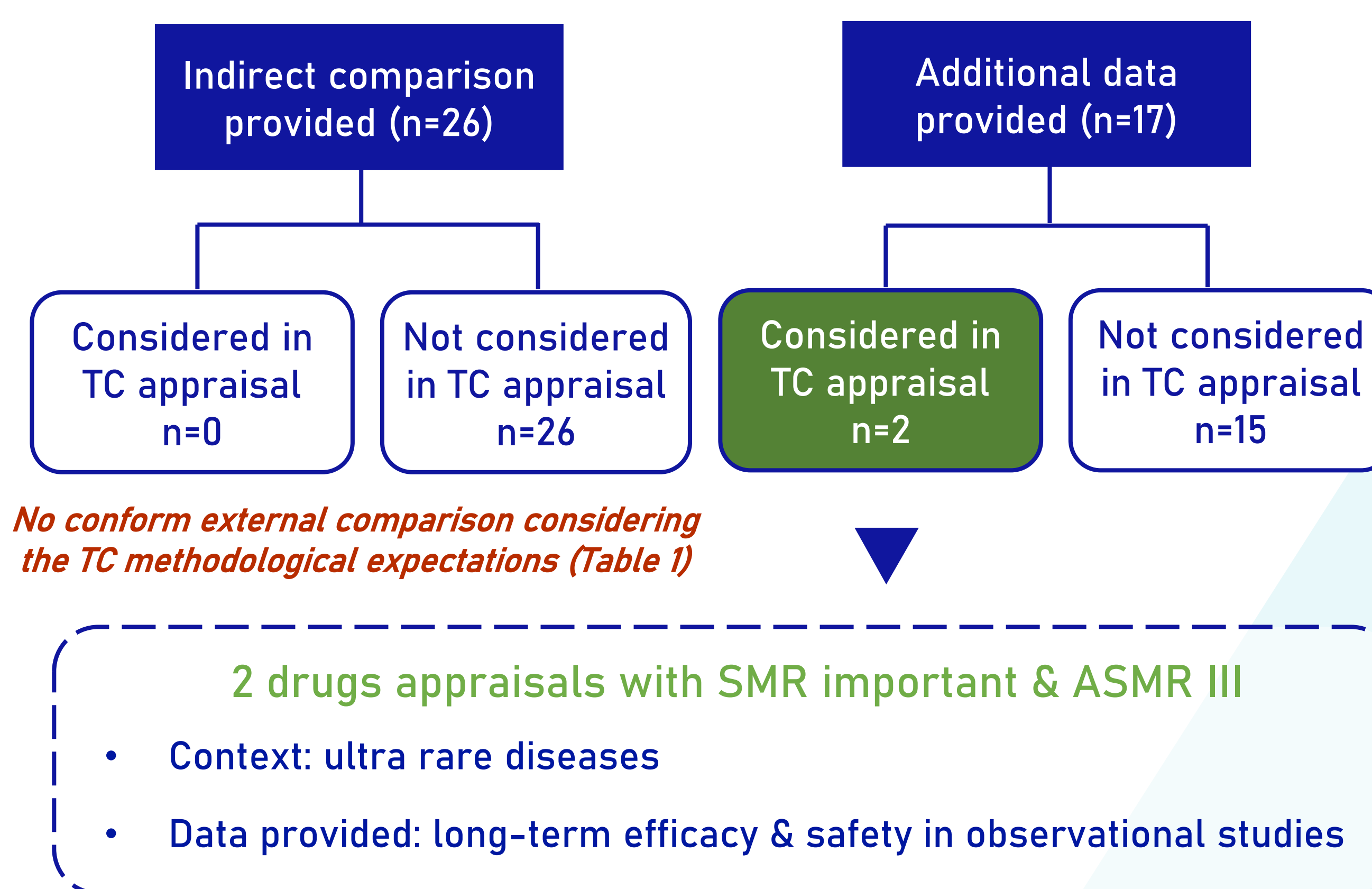


Figure 2. Additional data analysis



Conclusion

- ▶ **Medical need**, often reflected by orphan status, is highly considered to assess the SMR or ASMR
- ▶ **No external comparisons** were robust enough to supplement the single arm trial according to the TC

In Aug. 2023, an external comparison to a historical cohort led to an ASMR IV for cemiplimab in a type of skin cancer

- ▶ Additional data as long-term efficacy or safety data could be considered, case by case, depending on disease rareness