How could ATMPs demonstrate an economic benefit for payers and what are the real-world examples of this?

An analysis of payer considerations underlying HTA decisions for Yescarta and Alofisel in the UK, Italy and France

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INTRODUCTION

Advanced therapy medicinal products (ATMPS) include cell, gene, tissue-engineered and somatic-cell therapy medicines. These innovative treatments, generally given as one-off, often claim life-long benefits for patients and even curative potential for difficult-to-treat conditions.

However, as they are significantly more expensive and are associated with higher evidentiary uncertainty than other medicinal products, they present greater challenges to manufacturers when it comes to demonstrate economic benefit to payers.

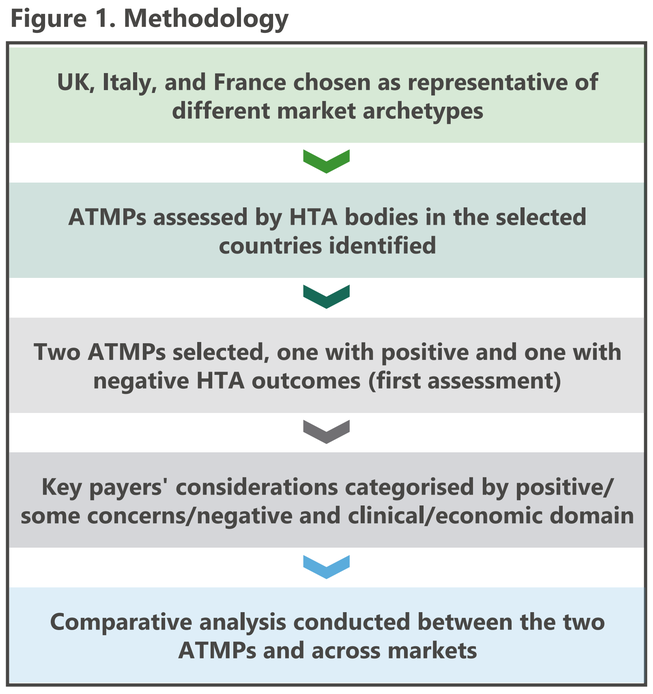
OBJECTIVES

The objective of this study is to explore the role of economic benefit in the HTA decisions across diverse market types: cost-effectiveness driven (UK), budget-impact driven (Italy), and clinical-differentiation driven (France). More specifically, the objective is to understand whether the clinical or the economic domain yields most of the key payer considerations underlying these decisions and whether this varies across markets representing different payer archetypes.

METHODS

UK, Italy, and France were chosen as representative market archetypes for cost-effectiveness, budget impact, and clinical-differentiation, respectively. ATMPs assessed by HTA bodies within these markets were identified using NICE, AIFA, and HAS databases. From these, two ATMPs were selected to illustrate contrasting examples from a P&R perspective, specifically one with a negative HTA outcome and another with a positive HTA outcome. Only the initial assessment was considered, and reassessments were excluded. Key payers' considerations on evidence package were extracted from HTA reports and were categorised as positive, some concerns/ uncertainties, or negative and as pertaining to the clinical vs the economic domain. A comparative analysis was conducted between the two selected ATMPs across the three markets.

Figure 1. Methodology



RESULTS

Yescarta (first indication) and Alofisel have been evaluated and are associated with positive and negative HTA outcomes, respectively, in the selected markets. Across markets, Yescarta's positive HTA outcomes are either linked to conditions or facilitated by MEAs, while Alofisel is only reimbursed in France and only for a sub-group.

Key payer considerations on Yescarta's value and evidence package, underlying HTA decisions, mainly pertain to the clinical domain in all markets. Positive considerations are focussed on clinical benefit or include recognition of unmet need; concerns are around the size of the added clinical benefit and its long-term maintenance due to lack of direct comparative data and short trial length.

Similarly, key payer considerations on Alofisel, which are mainly negative, pertain to the clinical domain, i.e., are related to the size and long-term maintenance of the clinical benefit and to the quality of clinical evidence (e.g., generalisability of the result). In France and UK, for both Yescarta and Alofisel, there are some concerns pertaining to the economic domain, but these are caused by uncertainties over cost-effectiveness that result from uncertainties in the clinical benefit in the first place.

Figure 2. Selected ATMPs based on HTA decisions in France[1], Italy[2] and the UK[3]

Treatment	Indication	France	Italy	UK
Yescarta	R/R DLBCL and PMBCL after two or more lines of systemic therapy	Coverage with evidence development	Payment at results	Cancer Drugs Fund
Alofisel	Complex perianal fistulas with inadequate response to at least one conventional or biologic therapy in adults with non-active/mildly active luminal Crohn's disease	Reimbursement only for a subgroup	No reimbursement	

Positive result | Partially negative result | Negative result

Figure 3. Key payer considerations underlying HTA decisions in France[2], Italy[3] and the UK[4]

Treatment		Yescarta	Alofisel
Evidence		Zuma 1, phase 1/2 - non controlled	Admire-CD, phase 3 RCT
Key payer considerations on drugs' value and evidence package	France	• ASMR III - moderate added clinical benefit • Unmet need and clinical efficacy recognised	• Unmet need recognised • RCT
	France	• Uncertainty over clinical benefit's size (no direct comparative data), its long-term maintenance, and results' generalizability • Toxicity and no long-term tolerability data	• ASMR IV – minor clinical benefit • Lack of long-term data
	France	• ICER – €114,509/QALY gained - considered very high, however low patient number limits budget impact • Uncertainty in the ICER due to short follow-up, survival data extrapolation methods and lack of comparative data	Lack of evidence in patients with inadequate response to conventional therapies alone due to small sample size
	Italy	• Moderate unmet need, important added therapeutic value, moderate quality of evidence • Full innovation rating	• Moderate unmet need, scarce added therapeutic value, low quality of evidence • Uncertainty over the generalisability and significance of the efficacy results
	Italy	ICER is €54,699 once confidential discounts and effect of payment at result are considered	
	UK	• Meets NICE's criteria to be considered a life-extending treatment at the end of life • Unmet need and clinical efficacy recognised	• Only modest benefit vs placebo • Uncertainty over long-term benefit and generalisability of the results to UK clinical practice
	UK	• Uncertainty in comparative clinical effectiveness and, consequentially, in CE due to immature survival data, lack of direct comparative data, and inappropriate long term survival extrapolation method • ICER > £50K/QALY gained	• Uncertainty over the clinical benefit makes CE highly uncertain • Unlikely to be cost-effective

Positive | Some concerns/ uncertainties | Negative | Clinical domain | Economic domain

CONCLUSIONS

Across markets, the level of clinical benefit is the key determining factor in HTA decisions for ATMPs. However, ATMPs often do not have the right level of evidence to support demonstration of clinical benefit and, consequentially of economic benefit, at the time of launch.

For this reason, alternative reimbursement schemes, such as coverage with evidence development, and payments methods are utilised by payers to allow access to these innovative treatments despite the uncertainties.

However, if the uncertainty over the clinical benefit is too high, these will not even be considered, as it was the case for Alofisel. This is especially true in markets where clinical benefit is assessed first and is a gateway to the discussion on economics.

REFERENCES

1. France HTA agency: https://www.has-sante.fr/
2. Italian HTA agency: https://www.aifa.gov.it/
3. UK HTA agency: https://www.nice.org.uk/

***Abbreviations**; AIFA= Italian Medicines Agency; ASMR: Improvement in medical benefit; ATMP= Advanced therapy medicinal products; CDF= Cancer Drugs Fund; CE= Cost-effectiveness; DLBCL= Diffuse large B cell lymphoma; HAS= Haute Autorité de Santé; HTA= Health technology assessment; ICER= Incremental cost-effectiveness ratio; NICE= National Institute of Health Care and Excellence; P&R=Price and reimbursement; PMBCL= Primary mediastinal large B cell lymphoma; QALY= Quality-adjusted life year; RCT= Randomised controlled trial*

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