Swedish Health Technology Assessment Outcomes and Considerations for Advanced Therapy Medicinal Products

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Background

Advanced therapy medicinal products (ATMPs) are breakthrough interventions that are based on gene, cell and tissue manipulation. They often show great therapeutic potential, but outcomes are often uncertain. This is due to limited available clinical data, while the cost of therapy may be substantial [1,2]. The aim of this study was to identify key considerations and challenges in the HTA of ATMPs in Sweden.

Methods

- A review of the European Medicines Agency (EMA) was conducted to identify ATMPs issued marketing authorization between January 2009 and June 2022
- Identified therapies were used to guide a targeted review of the Swedish Dental and Pharmaceutical Benefits Agency (TLV) and the New Therapies Council (NTc) websites.
- Assessment criteria and final recommendations were extracted from the relevant documents to determine variables of interest.
- The variables of interest were the analysed to identify any potential relationships with the health technology assessment (HTA) outcome.

Results

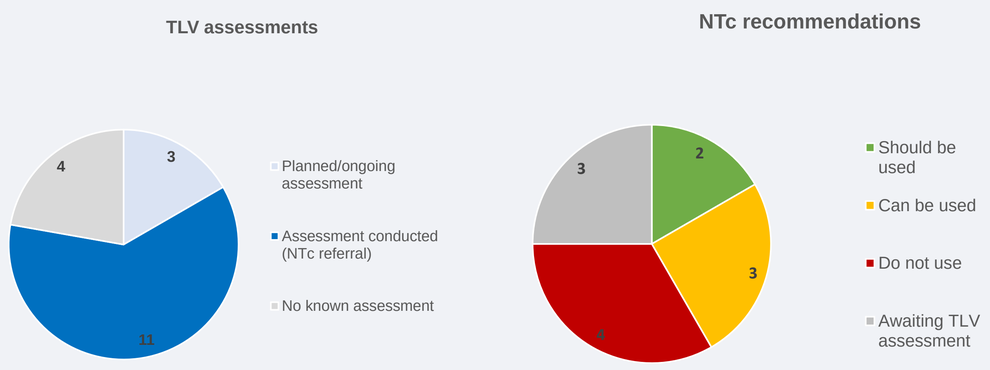
- Marketing authorisation was issued to 15 ATMPs (19 indications) in the study timeframe (Table 1).

Table 1: ATMPs issued marketing authorization by the EMA (January 2009 – June 2022)

Drug	Disease area	Date of marketing authorisation	Type of ATMP
Carvykti®	Multiple myeloma	25/05/2022	Gene therapy
Zyntelgo®	Beta Thalassaemia	06/2019	Gene therapy
Holoclar®	Limbal stem-cell deficiency	17/02/2015	Tissue engineered product
Strimvelis®	ADA-SCID	26/05/2016	Gene therapy
Tecartus®	Mantle cell lymphoma	14/12/2021	Gene therapy
Yescarta®	DLBCL	23/08/2018	Gene therapy
	PMBCL	23/08/2018	
Spherox®	Defects to the knee cartilage	10/07/2017	Tissue engineered product
Imlygic®	Melanoma	16/12/2015	Gene therapy
Alofisel®	Crohn's disease (complex anal fistula)	23/03/2018	somatic Stem cell therapy
Kymriah®	ALL	22/08/2018	Gene therapy
	DLBCL	22/08/2018	
Luxturna®	Inherited retinal dystrophy	21/11/2018	Gene therapy
Zolgesma®	Spinal muscular atrophy	18/05/2020	Gene therapy
Libmedly®	MLD	17/12/2020	Gene therapy
Breyanzi®	DLBCL	04/04/2022	Gene therapy
	PMBLC	04/04/2022	
	FL3B	04/04/2022	
Abecma®	Multiple Myeloma	18/08/2021	Gene therapy

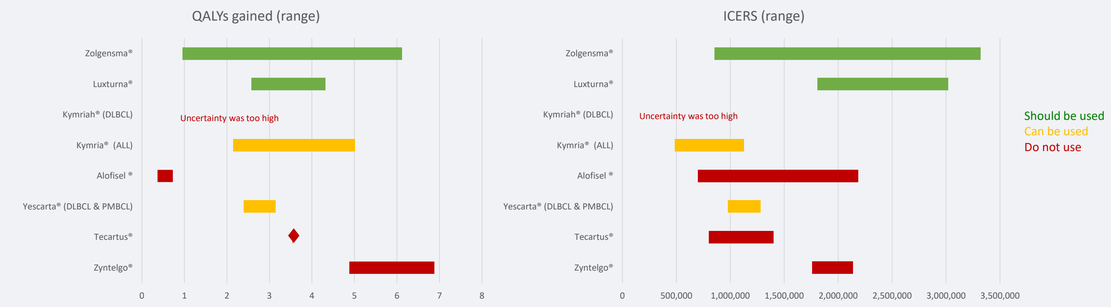
- A TLV assessment and NTc recommendation was identified for 9 (11 indications) and seven (9 indications) ATMPs, respectively (Figure 1).
- Of the ATMPs for which no TLV assessment was found, one was provided in Sweden (Imlygic®). As Imlygic® was introduced prior to the routine assessment of high-cost hospital drugs, it was removed from further analysis.

Figure 1: TLV assessment and NTc recommendations identified



- Mean time-to-access (marketing authorisation to NTc recommendation was 11,72 months (median = 12.46 months).

Figure 2: QALYs gained and ICERS from TLV health economic assessments



- All ATMPs with a "rare" or "very rare" presence of condition had a positive recommendation of use. The only exception was Kymriah® (DLBCL) had a "rare" presence of condition and a negative recommendation of use (Table 2).
- A price agreement was in place for all ATMPs with a positive recommendation of use (Table 2).
- The condition severity was deemed to be "high" or "very high" for all ATMPs, except Zyntelgo® (condition severity deemed "moderate") (Table 2).
- The reliability of clinical documentation and health economic assessment were deemed low for all therapies (Table 2).
- The range of the QALYs gained and the ICERS were quite large for most ATMPs (Figure 2).

Table 2: Overview of variables of interest from TLV and NTc assessments

Drug	Condition severity	Treatment effect size	Reliability of clinical documentation	Presence of condition	Price agreement	ΔQALYs (lower)	ΔQALYs (upper)	ICER (lower) (SEK)	ICER (upper) (SEK)	Reliability of health economic assessment	NTc reccomendation
Zyntelgo®	Moderate	Large	Low	Less common	No	4.88	6.88	1,761,000	2,137,000	Low	Do not use
Tecartus®	Very High	-	Low (high uncertainty)	Common	No	3.54	-	800,000	1,400,000	Very low	Do not use
Yescarta® (DLBCL & PMBCL)	Very high	Large	Low	Rare	Yes	2.39	3.14	977,908	1,281,575	low	Can be used
Alofisel®	High	Small	Low	Common	No	0.37	0.73	699,329	2,183,393	Low	Do not use
Kymria® (ALL)	Very high	Large	Low	Very rare	Yes	2.15	5.01	487,240	1,127,596	Low	Can be used
Kymriah® (DLBCL)	Very High	Cannot be assessed	Too low to assess	Rare	No	Uncertainty too high				Very low	Do not use
Luxturna®	High	Moderate	Moderate	Very rare	Yes	2.58	4.32	1,805,512	3,017,482	Low	Should be used
Zolgensma®	Very high	Large	Low	Very rare	Yes	6.12	0.96	854,976	3,321,184	Low	Should be used

Discussion

- Most authorized ATMPs are available in Sweden and the majority went through an HTA process.
- The time-to-access was approximately one year which could indicate that patient access is long given the severity of these conditions.
- All ATMPs issued with a positive recommendation of use were deemed to have a "rare" or "very rare" presence of condition. This could indicate that a key consideration for the market access is prevalence. Kymriah® (DLBCL) was an exception, with a "rare" presence of condition and a negative recommendation for use. However, the uncertainty for Kymriah® (DLBCL indication) was deemed too high to assess several variables, which may have had some relation to the negative recommendation of use.
- All ATMPs with a positive recommendation of use had a price agreement in place, and vice versa. The recommendations for use are based on a negotiated confidential price rather than the list price. As such, the presence of a price negotiation could be a key consideration for a successful HTA outcome.
- No potential relationship could be discerned for the other variables of interest and the HTA outcomes of ATMPs.
- However, notably a low reliability clinical and health economic information did not seem to be a challenge for a positive recommendation of use.

Conclusions

- More than half of the ATMPs issued marketing authorization are available in Sweden
- It is difficult to predict the HTA outcome for ATMPs based on available assessments.
- All positive recommendations in this study are preceded by a negotiated confidential net price

References

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2. Gonçalves E. (2020). Advanced therapy medicinal products: value judgement and ethical evaluation in health technology assessment. *The European journal of health economics : HEPAC : health economics in prevention and care*, *21*(3), 311–320. https://doi.org/10.1007/s10198-019-01147-x