Investigating Potential Market Failure with Curative Cell and Gene Therapies

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OBJECTIVES

This research aimed to investigate the potential for market failure with currently licensed cell and gene therapies, and whether market failure may be more likely in indications with smaller patient populations.

BACKGROUND

- Cell and gene therapies (C&GTs) are transforming disease management, offering potential cures for chronic or fatal diseases. However, the nature of curative C&GTs, and the diseases for which they are mostly being deployed, may lead to market failure in indications with increasingly smaller patient populations.
- This may occur as a result of limited competition and monopoly pricing being maintained for far longer than in the traditional market for healthcare technologies.

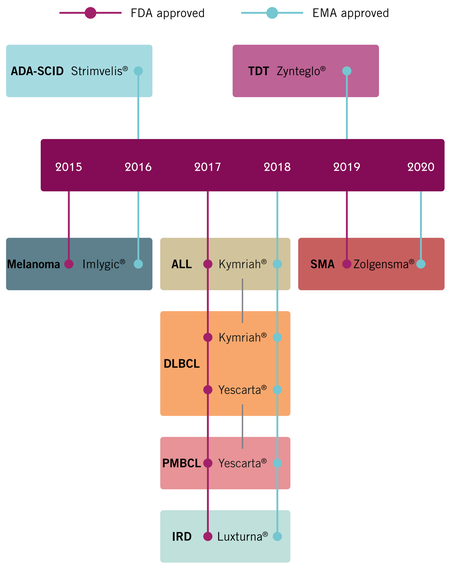
METHODS

- The European Medicines Agency (EMA) and US Food and Drug Administration (FDA) websites were searched on 12th December 2019, to identify licensed curative C&GTs, and an update was conducted on 11th June 2020.
- Non-curative therapies were excluded. Clinicaltrials.gov was then searched using the following terms: "cell therapy"; "gene therapy"; "CAR-T"; or "gene replacement therapy".
- Results were filtered by disease area to identify all Phase I/II/III trials of C&GTs that are ongoing or completed since 2015 in the indications for which there are currently licensed curative C&GTs.
- Trials were excluded if they had been withdrawn, terminated, were enrolling by invitation or with status unknown, or were investigating curative C&GTs that are already licensed. US incidence rates (per 100,000 population) for each indication were derived from various online sources.

RESULTS

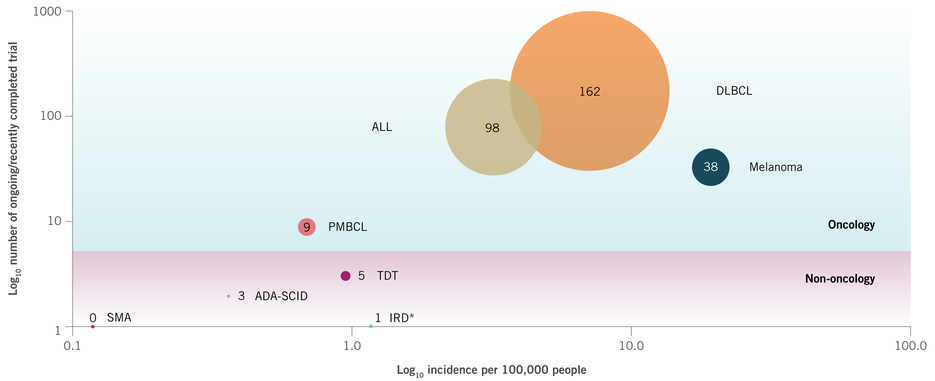
- As of 11th June 2020, seven curative C&GTs have been licensed by the FDA or EMA across eight indications: Imlygic® (melanoma); Strimvelis® (adenosine deaminase severe combined immunodeficiency [ADA-SCID]; EMA only); Kymriah® (diffuse large B-cell lymphoma [DLBCL] and acute lymphoblastic leukaemia [ALL]); Yescarta® (DLBCL and primary mediastinal B-cell lymphoma [PMBCL]); Luxturna® (inherited retinal dystrophy [IRD]); Zynteglo® (transfusion-dependent β-thalassaemia [TDT]; EMA only); and Zolgensma® (spinal muscular atrophy [SMA]) **(Figure 1)**.
- There is currently only one indication (DLBCL) with >1 curative C&GT approved; the remaining seven indications of licensed curative C&GTs each have only one curative C&GT approved.
- In terms of ongoing or completed trials for competitor C&GTs, in SMA (incidence: 0.11/100,000[1]), there were no ongoing or recently completed trials for competitor C&GTs, and in IRD (0.6–1.6/100,000[2]), there was only one ongoing Phase 1 trial **(Figure 2)**.
- Of the six indications with >1 ongoing or recently completed competitor C&GT trial, the four oncology indications had the largest number of competitor trials identified: three ongoing/recently completed trials were identified in ADA-SCID; five in TDT; nine in PMBCL; 38 in melanoma; 98 in ALL; and 162 in DLBCL **(Figure 2)**.
- The majority of ongoing or recently completed competitor C&GT trials for all indications are in early phases with 87% of the identified trials being in Phase I or I/II **(Figure 3)**.

1 Timeline of curative C&GT EMA and FDA approvals



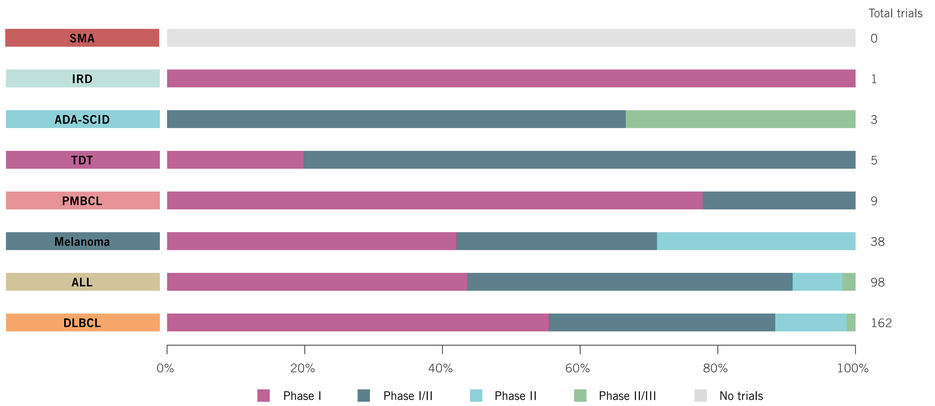
Kymriah® and Yescarta® are connected across ALL and DLBCL, or DLBCL and PMBCL, respectively, to represent that these C&GTs are approved in two indications.

2 Correlation of ongoing and recently completed C&GT trials with disease incidence



*IRD incidence is for RP in the UK; there were no studies reporting incidence of LCA. Point size and data values represent the number of ongoing/recently completely trials for the specified indication.

3 Distribution of trial phases across indications



Abbreviations: ADA-SCID: adenosine deaminase severe combined immunodeficiency; ALL: acute lymphoblastic leukaemia; C&GT: cell and gene therapies; DLBCL: diffuse large B-cell lymphoma; EMA: European Medicines Agency; FDA: Food and Drug Administration; IRD: inherited retinal dystrophy; LCA: leber congenital amaurosis; PMBCL: primary mediastinal B-cell lymphoma; RP: retinitis pigmentosa; SMA: spinal muscular atrophy; TDT: transfusion-dependent β-thalassaemia; UK: United Kingdom.

- Although the number of competitor C&GT trials does not appear to have a strong linear correlation with disease incidence, indications with a higher incidence tended to have more ongoing/recently completed competitor C&GT trials: indications with an incidence >1.6/100,000 (DLBCL,[3] ALL,[4] melanoma[5]) had >30 ongoing/recently completed competitor C&GT trials, whereas indications with an incidence <1.6/100,000[1,2,6–8] had 0–9 ongoing/recently completed competitor C&GT trials **(Figure 2)**.

CONCLUSIONS

This research identified a lack of competitor C&GTs in the pipeline for non-oncology, low incidence indications, raising the prospect of potential market failure due to a lack of competition in these indications.

With the availability of these curative therapies, incidence rates are only likely to further decrease, limiting any incentive for competition development, and increasing the risk of market failure.

Since this initial research, an additional curative C&GT was approved by the FDA for relapsed or refractory mantle cell lymphoma[9] (for which there are currently no other curative C&GTs licensed).

This was not captured in the current analysis, but the continued approval of new C&GTs demonstrates the importance of continued research into potential market failure in indications for which new curative C&GTs are in development.

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