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Exploring Uncertainties and Solutions Allowing Patient Access to CAR T-Cell Therapies: Learning Today How to Improve Tomorrow

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BACKGROUND

- Only two CAR T-cell therapies have been launched to date, tisagenlecleucel (tisa-cel, Kymriah®) and axicabtagene ciloleucel (axi-cel, Yescarta®).
- Despite promising efficacy data in populations with high unmet need (Figure 1), market access and reimbursement of these therapies has proven challenging.
- The pipeline is booming, with 250 CAR T-cell therapies currently in clinical development around the world for diseases with high unmet need.
- Developing these therapies in accordance with payers' needs will be crucial in order to support optimal patient access while making the best use of healthcare resources.

Figure 1 – Clinical profile of tisa-cel and axi-cel

CAR T-cell therapy	tisa-cel	tisa-cel	axi-cel
Indication	ALL	DLBCL	DLBCL/PMBCL
Evaluable patients	79	99	101
Trial design	Phase 2, single-arm		
Median follow-up	4.8 months	9.4 months	7.9 months
ORR	83%	50%	72%
CR	63%	32%	51%
mDOR	Not reached	Not reached	9.2 months
CRS ≥G3	48%	23%	13%
Neurotoxicity ≥G3	13%	11%	31%
Therapy-related deaths	None	None	4

ALL – Acute Lymphoblastic Leukaemia; DLBCL – Diffuse Large B-cell Lymphoma; – PMBCL – Primary Mediastinal B-cell Lymphoma

OBJECTIVES

To understand how payers around the world have been appraising CAR T-cell therapies, identify uncertainties in the assessments and how these were overcome in order to allow patient access, with the aim of informing future development of CAR T-cell therapies.

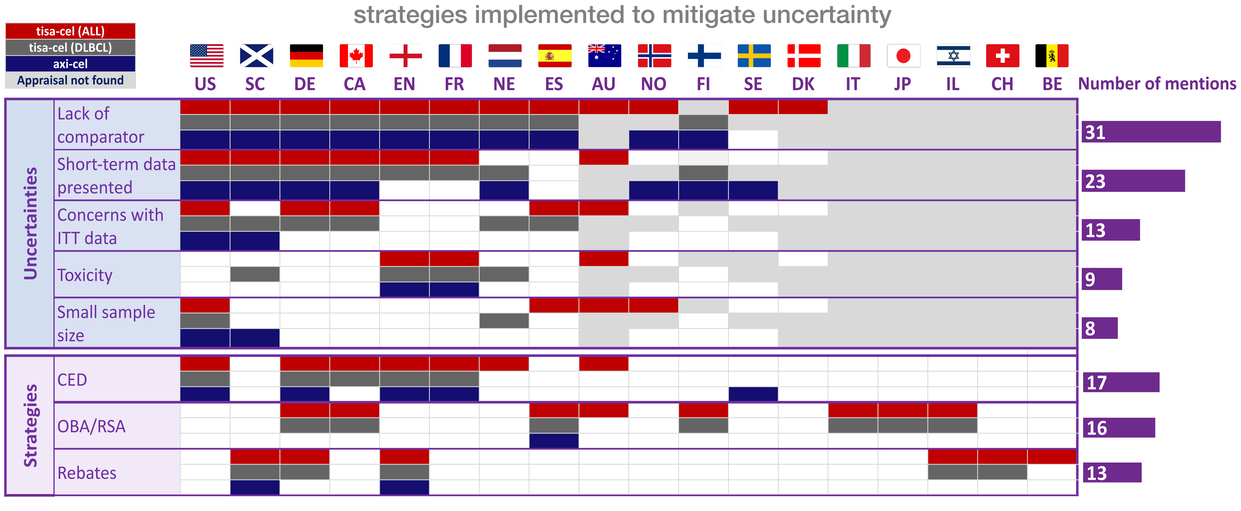
METHODS

We conducted a review of HTA appraisal documents and press releases up to 15 October 2019, identifying the outcome of each appraisal of tisa-cel and axi-cel, the rationale behind the decision and whether any solutions were implemented to ensure patient access. We used translation software to review non-English materials.

RESULTS

- To date, we identified 32 HTA sources detailing appraisal details of tisa-cel and axi-cel. The most called out source of uncertainty was lack of a comparator arm in the clinical trials, followed by short-term data presented, concerns with the intent-to-treat (ITT) data, toxicity of these therapies and small sample size (Figure 2).
- Despite low quality of evidence, the high unmet need in ALL led to perceived clinical benefit that was high (e.g. Denmark), moderate (e.g. France) or even unquantifiable (e.g. Germany), with reimbursement generally approved due to low budget impact.
- The cost-effectiveness of CAR T-cell therapy in DLBCL appears to be lower and the budget impact higher than in ALL, which has led to reimbursement denials at first iteration (e.g. England, Netherlands).
- Proposed solutions to allow sustainable patient access range from patient access schemes in the form of rebates (e.g. UK, Scotland), coverage with evidence development (e.g. France, Germany, US) or performance-based arrangements (e.g. Spain, Italy, Israel, Japan).
- The list price of tisa-cel ranges from $311k in Japan, to $350 in most European countries and $373 or $475 in the US, for DLBCL and ALL respectively. Available data on discounts to list price suggests 14 to 30% discount.
- Axi-cel is obtaining a slight price premium compared to tisa-cel in European countries (≈$360k), attributed to better quality of the evidence.
- According to available evidence, innovative payment models have consisted of either a refund if patients don't respond (e.g. Germany) or spread payments dependent on successful infusion or ongoing response up to 18 months.

Figure 2 – Sources of uncertainty as mentioned in HTA resources and strategies implemented to mitigate uncertainty



US - United States; SC – Scotland; DE – Germany; CA – Canada; EN – England; FR – France; NE – Netherlands; ES – Spain; AU – Australia; NO – Norway; FI – Finland; SE – Sweden; DK – Denmark; IT – Italy; JP – Japan; IL – Israel; BE – Belgium; CH – SwitzerlandOBA – Outcomes-based arrangements; RSA – Risk-sharing agreements; CED: Coverage with evidence development/registries

CONCLUSIONS

Developers could increase development time by investing in longer trials with a comparator arm, engaging early-on with payers to discuss where trade-offs can be agreed, in order to enable sustainable patient access. Additional data will be available at time of presentation.

LIMITATIONS

Sources of uncertainty and mitigation strategies were obtained from published secondary research and therefore might be underreported.

REFERENCES

1. Kymriah Summary of Product Characteristics, Yescarta Summary of Product Characteristics, HTA appraisals, news articles