



DESCAR-T

Dispositif d'Enregistrement et de Suivi des CAR-T
French CAR-T registry

26e conférence thématique organisée par le Collège des
Economistes de la Santé - 25/04/2024

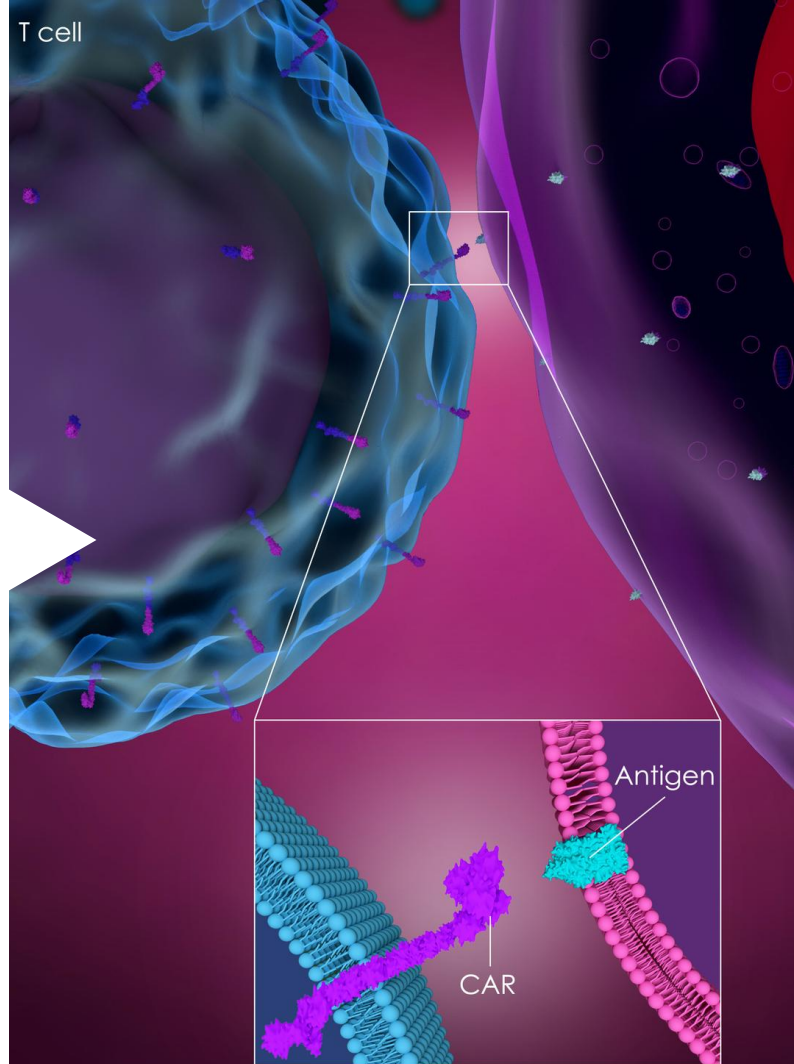
La place des registres dans les accords de performance

Fabienne Di Giambattista

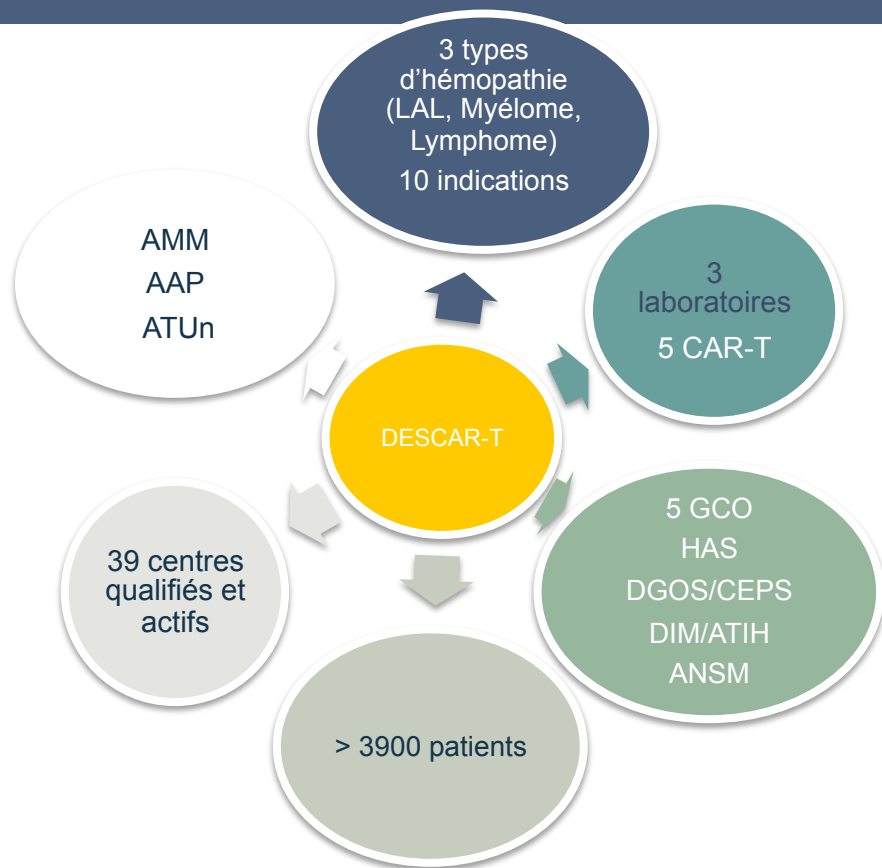
GRAALL
LILA GOELAND SAKK



T cell



Le registre national DESCAR-T



Indépendance nationale et scientifique

Les groupes coopérateurs :



Les 3 laboratoires partenaires: KITE
GILEAD, NOVARTIS et BMS

DESCAR-T : 3 dimensions originelles

Scientifique

Améliorer les connaissances et la compréhension des mécanismes associés à l'efficacité et à la toxicité de l'utilisation des CAR-T en vie réelle

- 31 projets académiques
- 11 projets industriels (**Bras comparateurs**)
- 16 présentations orales en congrès + 12 posters
- **7 publications (Nature Medicine, Blood Advances.....)**

Réglementaire

Demande de la HAS : description de la survie globale des patients en intention de traitement par CAR-T et autres objectifs secondaires d'efficacité et de toxicité

- 20 rapports cliniques depuis le lancement du registre

Administratif/ Médico-économique

- Exports DIM + FICHCOMP → ATIH
- Paiement des hôpitaux

- **ATIH** : remontées de données via les DIM
- **DGOS**: chiffres / état d'avancement trimestriel

Valorisation scientifique et médicale

DESCAR-T, le registre national des patients traités par CAR-T cells

nature
medicine

ARTICLES

<https://doi.org/10.1038/s41591-022-01969-9>

OPEN

A real-world comparison of tisagenlecleucel and axicabtagene ciloleucel CAR T cells in relapsed or refractory diffuse large B cell lymphoma

Emmanuel Bachy^{1,2,5,22}, Steven Le Goull¹, Roberta Di Blasi¹, Pierre Sesques¹, Guillaume Mansot¹, Guillaume Cartron¹, David Beauvais¹, Cristina Castilla Lorente¹, Marie Thérèse Rubio¹, Pierre Borles¹, Jacques Olivier Bay¹, Stéphanie Guidet¹, Sylvain Choquet¹, René-Olivier Casanovas¹, Mohamad Mohty¹, Adrien Chauchet¹, Magalie Joris¹, Michaël Louch¹, Sylvain Carras¹, Julie Abraham¹, Thomas Gastinne¹, Laurianne Drieu La Rochelle¹, Bénédicte Deau-Fischer¹, Olivier Hermine¹, Jean Jacques Tudesq¹, Elodie Gat², Florence Broussais¹, Catherine Thieblemont¹, Roch Houq¹ and Franck Morschhauser^{1,2,5}

Abstract Axicabtagene ciloleucel (axi-cel) and tisagenlecleucel (tisa-cel) have both demonstrated impressive clinical activity in relapsed/refractory (R/R) diffuse large B cell lymphoma (DLBCL). In this study, we analyzed the outcome of CAR T cell therapy for large B-cell lymphoma was 50%, with ~80% of deaths occurring beyond day 28 after infusion. Infections are responsible for the majority of NRM after CAR T-cell infusion for large B-cell lymphomas (56%).

Florence Broussais¹, Jacques Olivier Bay², Nicolas Boitard¹, Franck Morschhauser¹, Marie Robin¹, Gabrielle Roth-Salomon Abouier¹, Thibaut Leguay¹, Stéphanie Nguyen
Steven Le Goull¹

1. Hospices Civils de Lyon, France; 2. Hospices Civils de Lyon, France; 3. Hospices Civils de Lyon, France; 4. Hospices Civils de Lyon, France; 5. Hospices Civils de Lyon, France; 6. Hospices Civils de Lyon, France; 7. Hospices Civils de Lyon, France; 8. Hospices Civils de Lyon, France; 9. Hospices Civils de Lyon, France; 10. Hospices Civils de Lyon, France; 11. Hospices Civils de Lyon, France; 12. Hospices Civils de Lyon, France; 13. Hospices Civils de Lyon, France; 14. Hospices Civils de Lyon, France; 15. Hospices Civils de Lyon, France; 16. Hospices Civils de Lyon, France; 17. Hospices Civils de Lyon, France; 18. Hospices Civils de Lyon, France; 19. Hospices Civils de Lyon, France; 20. Hospices Civils de Lyon, France; 21. Hospices Civils de Lyon, France; 22. Hospices Civils de Lyon, France

Key Points

- The NRM rate estimate after CAR T-cell therapy for large B-cell lymphoma was 50%, with ~80% of deaths occurring beyond day 28 after infusion.
- Infections are responsible for the majority of NRM after CAR T-cell infusion for large B-cell lymphomas (56%).

Introduction DLBCL is the most common lymphoma subtype, accounting for about 40% of all non-Hodgkin lymphomas. CAR T cell therapies targeting CD19 have shown impressive efficacy and manageable toxicity for the treatment of various lymphoma subtypes, such as mantle cell lymphoma, follicular lymphoma, and DLBCL^{1–3}. Tisagenlecleucel (tisa-cel) and axicabtagene ciloleucel (axi-cel) T products that were initially approved for the treatment of DLBCL in the 1st line of treatment. Tisa-cel is a 1B3 co-stimulatory second-generation CAR T cell whereas axi-cel is a CD19-targeted CAR T cell. The results of the JULIET⁴ and ZUMA-1⁵ studies demonstrated both ORR/CR/CRi of 52/64% and 42/54% at 6 weeks, respectively^{4,5}. The recent tisa-cel and axi-cel, respectively^{6,7}. The use of ZUMA-1 after 5 years suggested that ~40%

Conclusion This study compares the efficacy and safety of tisa-cel and axi-cel in a real-world setting. The results show that both CAR T cell products have similar efficacy and safety profiles in relapsed or refractory DLBCL. The study highlights the need for further research to optimize CAR T cell therapy for DLBCL.

REGULAR ARTICLE

Nonrelapse mortality after CAR T-cell therapy for large B-cell lymphoma: a LYSA study from the DESCAR-T registry

Jean Lemona¹, Emmanuel Bachy¹, Guillaume Carton¹, David Beauvais¹, Thomas Gastinne¹, Roberta Di Blasi¹, Marie Thérèse Rubio¹, Stéphanie Guidet¹, Mohamad Mohty¹, René-Olivier Casanovas¹, Magalie Joris¹, Cristina Castilla Lorente¹, Corinne Heuson¹, Steven Le Goull¹, Franck Morschhauser¹, Catherine Thieblemont¹, and Roch Houq¹

Abstract CD19 chimeric antigen receptor (CAR) T cells can induce prolonged remissions and potentially cure a significant proportion of patients with relapsed/refractory large B-cell lymphoma. However, some patients may die of causes unrelated to lymphoma after CAR T-cell therapy. To date, little is known about the nonrelapse mortality (NRM) after CAR-T-cell therapy using the French DESCAR-T registry, we analyzed the incidence and causes of NRM and identified risk factors of NRM. We report on 957 patients who received standard-of-care axicabtagene ciloleucel (n = 589) or tisagenlecleucel (n = 359) between July 2018 and April 2022, in 27 French centers. With a median follow-up of 12.4 months, overall NRM occurred in 46 patients (5.0% of all patients; early before day 28 after infusion in 9 patients (59%) (4.1% of all patients and 9.1% of overall NRM). Causes of overall NRM were distributed as follows: 50% infections (29% of overall NRM), 22% with COVID-19, 10% cytokine release syndrome, 6% stroke, 6% cerebral hemorrhage, 6% second malignancy, 6% immune effector cell associated neurotoxicity, and 10% deaths from other causes. We and elevated ferritin level at lymphodepletion were associated with an increased risk of overall NRM. Our results may help physicians in patient selection and management in order to reduce the NRM after CAR T-cell therapy.

Introduction CD19 chimeric antigen receptor (CAR) T cells can induce prolonged remissions and potentially cure a significant proportion of patients with relapsed/refractory large B-cell lymphoma. However, some patients may die of causes unrelated to lymphoma after CAR T-cell therapy. To date, little is known about the nonrelapse mortality (NRM) after CAR-T-cell therapy using the French DESCAR-T registry, we analyzed the incidence and causes of NRM and identified risk factors of NRM. We report on 957 patients who received standard-of-care axicabtagene ciloleucel (n = 589) or tisagenlecleucel (n = 359) between July 2018 and April 2022, in 27 French centers. With a median follow-up of 12.4 months, overall NRM occurred in 46 patients (5.0% of all patients; early before day 28 after infusion in 9 patients (59%) (4.1% of all patients and 9.1% of overall NRM). Causes of overall NRM were distributed as follows: 50% infections (29% of overall NRM), 22% with COVID-19, 10% cytokine release syndrome, 6% stroke, 6% cerebral hemorrhage, 6% second malignancy, 6% immune effector cell associated neurotoxicity, and 10% deaths from other causes. We and elevated ferritin level at lymphodepletion were associated with an increased risk of overall NRM. Our results may help physicians in patient selection and management in order to reduce the NRM after CAR T-cell therapy.

blood advances

Transfusion needs after CAR T-cell therapy for large B-cell lymphoma: factors and outcome. A DESCAR-T study

Tracking no: ADV-2023-01177293

Check for updates

blood advances

Regular Article

Outcomes of patients with aggressive B-cell lymphoma after failure of anti-CD19 CAR T-cell therapy: a DESCAR-T analysis

Check for updates

blood advances

Regular Article

CD19 chimeric antigen receptor (CAR) T cells represent a major advance in the treatment of relapsed/refractory aggressive B-cell lymphoma. However, a significant number of patients experience failure. Among 550 patients registered in the French registry DESCAR-T, 228 (43.3%) experienced progression/relapse with a median follow-up of 19 months. At registration, 82.6% of patients presented an age-adjusted International Prognostic Index ≥ 2, 57.1% received ≥ 3 lines of treatment, prior CAR T-cell treatment occurred after a median of 2.7 months from registration. Median progression-free survival was 2.8 months, and median overall survival (OS) was 4.2 months. High LDH at infusion, time to CAR T-cell failure, and high ferritin were associated with inferior outcomes. The poor outcome of patients relapsing after CAR T-cell treatment, highlighting the need for further research.

blood advances

Regular Article

Mesquite Continuing Medical Education online

in support of improving patient care, this activity has been approved and implemented by Mesquite LLC (an Accredited Provider of continuing medical education (CME) for the American College of Physicians (ACP) and the American Nurses Credentialing Center (ANCC) to provide continuing education for the healthcare team.

Comparaison indirecte / bras synthétique

nature
medicine

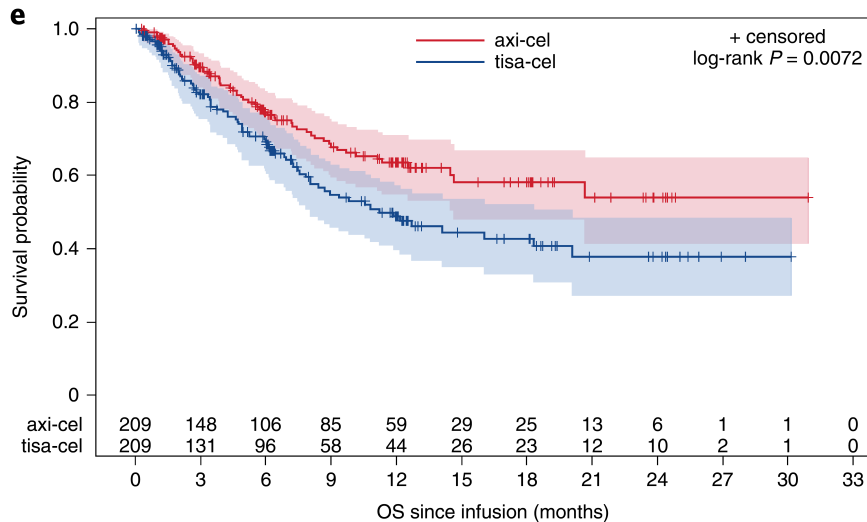
ARTICLES

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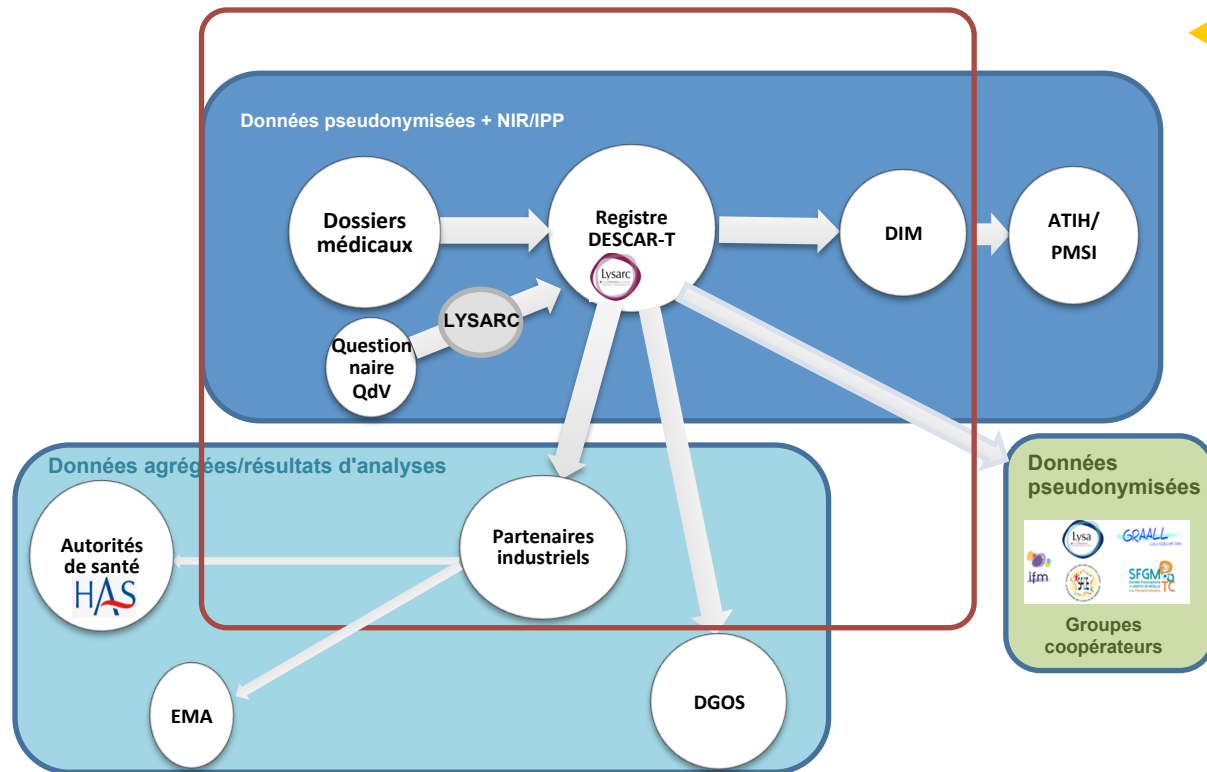
OPEN

A real-world comparison of tisagenlecleucel and axicabtagene ciloleucel CAR T cells in relapsed or refractory diffuse large B cell lymphoma



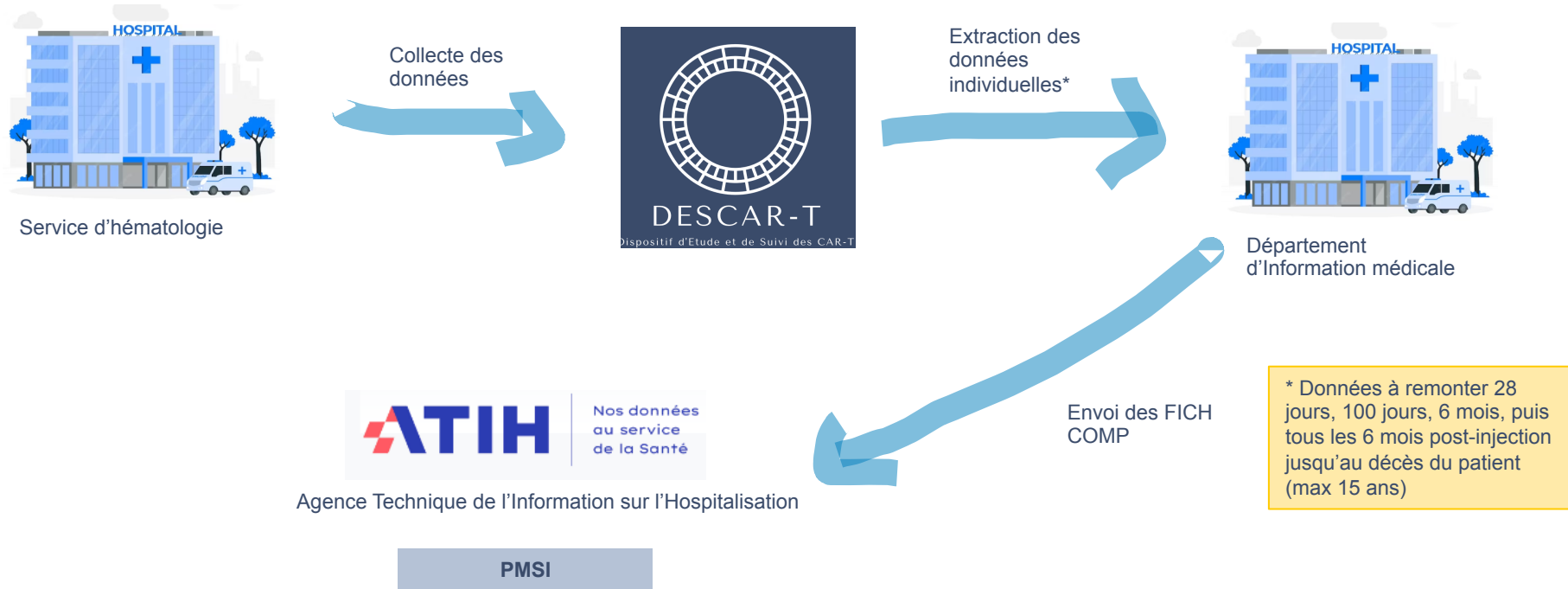
- Comparaison de 2 CAR-T à partir du registre DESCAR-T (phase 3 impossible)
- Indépendance académique
- Qualité scientifique (revue majeure, IF=83)
- Changement de pratique +++

Circuit des données



Périmètre du Registre DESCAR-T

Circuit des données vers l'ATIH



* Selon Article L.162-17-1-2 du code de la SS, Arrêtés du 30/04/2019 et 08/07/2019

Les bonnes raisons de s'appuyer sur un registre de vie réelle pour un contrat de performance

- Acteur national indépendant propriétaire du registre
- Gouvernance académique
- Interactions déjà existantes avec les Autorités de Santé
- Flux de données déjà en place
- Exhaustivité des cas
- Couverture de plusieurs produits concernant la même pathologie
- Grande motivation des services spécialisés pour la collecte des données
- Large set de données de qualité
- Données disponibles assez rapidement (une fois le registre lancé)
- Evite les saisies multiples
- Des analyses statistiques réalisées par l'équipe du registre



Les conditions pour qu'un registre participe efficacement à un contrat de performance

- Choix de l'indicateur en fonction de sa disponibilité dans la base
- Ne pas envisager de collecte rétrospective, ou d'ajout de nouvelles données
- Bien définir l'indicateur et les besoins : population, données agrégées ou individuelles, échéances, (taux de décès ≠ plusieurs tables statistiques avec plan d'analyse)
- Circuit clair, interlocuteurs précisés, **demandes réalistes**

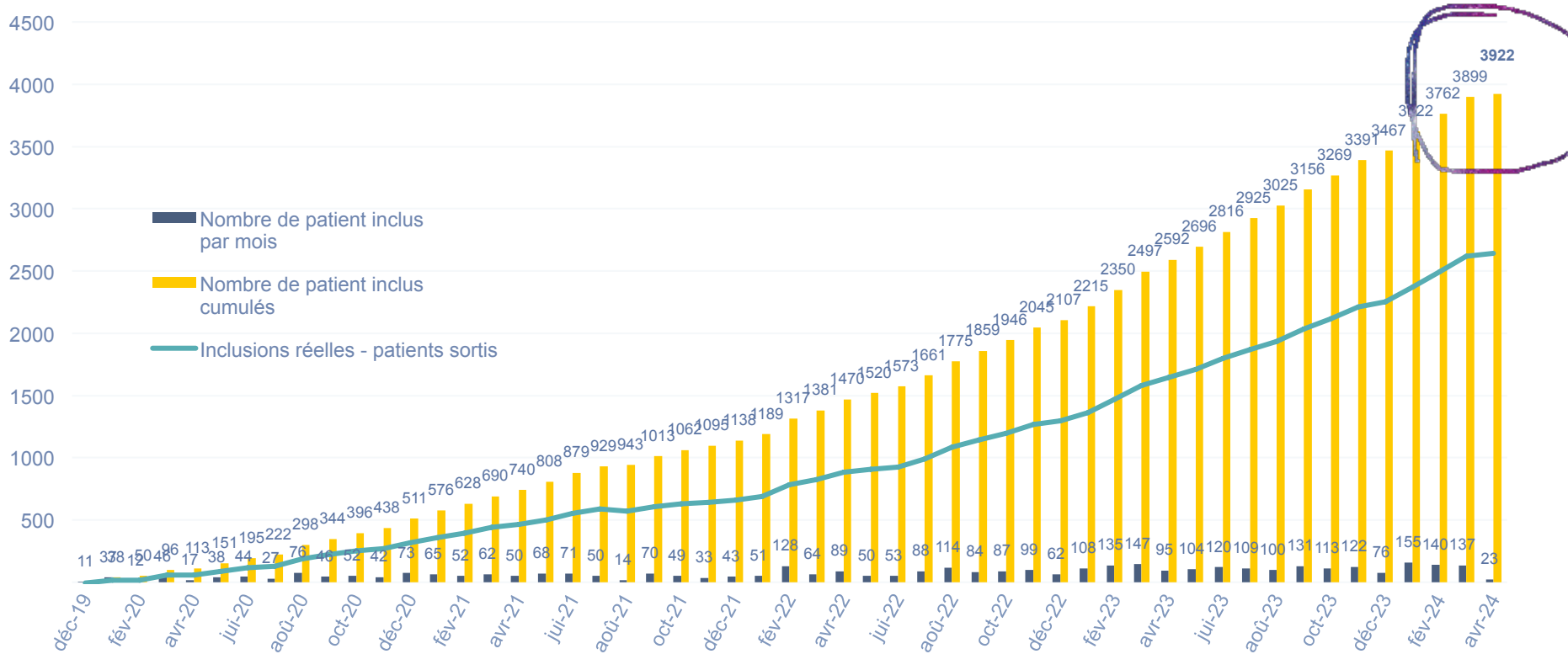


- S'assurer de la **faisabilité organisationnelle et financière**, tant au niveau du détenteur du registre que des centres contributeurs
- Pérennité du registre
- Quelle **formalisation avec l'industriel concerné** (contrat, financement, responsabilité en tant que détenteur de l'AMM) ?

- Niveau de conformité aux critères méthodologiques de la HAS pour la vie réelle
- Positionnement des pouvoirs publics vis-à-vis des données de vie réelle



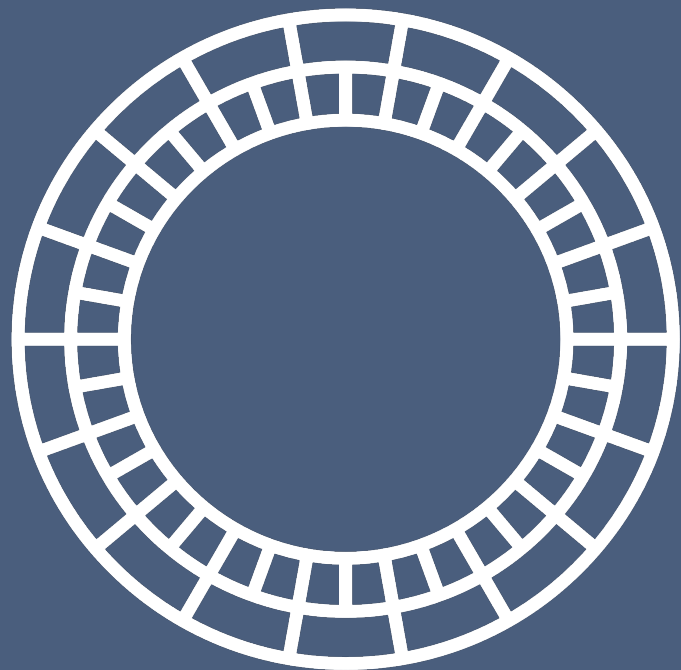
Une croissance exponentielle des CAR-T



Perspectives



- DESCAR-T est une preuve de concept : **écosystème complexe de collecte et d'utilisation de données de vie réelle**
- Participe au pilotage médico-économique des CAR-T, médicaments coûteux (et possiblement dangereux)
- Ouvre la voie à un nouveau business-model public/privé pour répondre aux enjeux de santé publique dans le cadre d'une expansion des molécules innovantes et de leur coût
- Un outil complémentaire pour maîtriser le coût de traitements qui ne tiendraient pas leur promesse ?



DESCAR-T

Dispositif d'Etude et de Suivi des CAR-T
French CAR-T registry



Merci pour votre
attention



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