OPEN

CURRENT OPINION

Opportunities and challenges associated with the evaluation of chimeric antigen receptor T cells in real-life

Eoin McGrath[a,b], *Christian Chabannon*[b,c,d], *Sofie Terwel*[e], *Chiara Bonini*[d,f], *and Jurgen Kuball*[b,d,g]

Purpose of review
With the approval of the first chimeric antigen receptor (CAR)-T cell products on the market, the European Medicines Agency (EMA) required market authorization holders (MAHs) to monitor the long-term efficacy and safety of CAR-T cells for 15 years after administration. In 2019, the cellular therapy module of the European Society for Blood and Marrow Transplantation (EBMT) registry received a positive qualification opinion from the EMA indicating that the registry fulfills the essential needs to capture such data. We investigated its broader implication.

Recent findings
Since 2020, the cellular therapy module of the EBMT registry captures data to support postauthorization studies for MAHs and EMA. The process toward a positive qualification opinion has attracted interest from many other stakeholders, such as scientists and Health Technology Assessment bodies, and was the spin-off for a stimulating development which defined the need for a registry to comply with regulatory requirements, and also inspired ways to deal with CAR-T cell programs in terms of center qualifications and educational standards for professionals.

Summary
The positive qualified opinion of the EBMT registry by EMA to monitor long-term efficacy and safety of commercial CAR-T cells created opportunities and challenges and was serving as linking-pin to launch a novel CAR-T cell community.

Keywords
CAR T cells or chimeric antigen receptor T cells, real world data, registry

INTRODUCTION

The approval of CD19-specific chimeric antigen receptor (CAR)-T cell therapies by the U.S. Food and Drug Administration (FDA) in 2017 [1] and by the European Medicines Agency (EMA) in 2018 [2] generated excitement in the field, as it offers a new treatment modality to many patients suffering from refractory acute lymphoblastic leukemia and other B cell malignancies. CAR-T cells belong to a novel type of therapy, known as advanced therapy medicinal products (ATMPs) which are genetically modified and therefore are also often referred as gene therapy medicinal products (GTMPs). The accelerated approval process of CD19-specific CAR-T cells allowed for early access to CAR-T cells therapies for many patients. The acceptance of phase II trial data for marketing authorization by the FDA and EMA, however, also raised efficacy and

[a]EBMT Executive Office, Barcelona, [b]Legal Regulatory Affairs Committee (LRAC) of EBMT, Barcelona, Spain, [c]Institut Paoli-Calmettes, Centre de Lutte Contre le Cancer, Université d'Aix-Marseille, INSERM CBT 1409, Centre d'Investigations Cliniques en Biothérapie, Marseille, France, [d]Cellular Therapy & Immunobiology Working Party (CTIWP), [e]EBMT GoCART, Leiden, The Netherlands, [f]Università Vita-Salute San Raffaele, Milan, Italy and [g]Department of Hematology, Center for Translational Immunology, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands

Correspondence to Jurgen Kuball, Department of Hematology, Center for Translational Immunology, University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands. E-mail: J.H.E.Kuball@umcutrecht.nl

Curr Opin Oncol 2020, 32:427–433

DOI:10.1097/CCO.0000000000000665

KEY POINTS

- The cellular therapy module of the EBMT registry received a positive opinion by EMA in 2019.
- The cellular therapy module of the EBMT registry captures data to support PAS for MAHs and EMA since 2020.
- Improving data fields, data harmonization and data quality with all stakeholders will be key to the success of the registry.
- This process created the multi-stakeholder GrOup for immune effector cells such as Chimeric Antigen Receptor T cells (GoCART).

safety concerns. CD19-specific CAR-T cells have the intended potential to survive and act as guardians against recurrence of cancer throughout the lifespan of a patient. Thus, long-term toxicity could theoretically be expected many years after administration, because of continuously circulating CAR-T cells, which might slowly damage organs, or engineered T cells acquiring additional unwanted properties [3▪▪]. In addition to these safety concerns, the price tag associated with this new type of the GTMP, ranging between 250 and 500k Euro, is perceived by many stakeholders as a substantial hurdle to broader clinical implementation [4]. Of note, additional costs mediated through the high toxicity and labor intensive in and outpatient management associated with CAR-T-cell infusions are, to date, not adequately compensated by many national healthcare systems, and present an additional financial challenge. Thus, CAR-T-cell therapies are for many reasons a new and 'breathtaking' opportunity that required searching for solutions that did not exist before.

A QUALIFIED OPINION ON THE CELLULAR THERAPY MODULE OF THE EUROPEAN SOCIETY FOR BLOOD AND MARROW TRANSPLANTATION REGISTRY

In the mid-1970s, the European Society for Blood and Marrow Transplantation (EBMT) created a pan-European Registry which now captures the majority of stem-cell transplantation activities across Europe. Stem-cell transplantation is the most frequently used cellular therapy intervention, with more than 40,000 hematopoietic stem-cell infusions per year [5]. With the creation of an additional cellular therapy module half a decade ago, the EBMT registry was upgraded to allow data to capture in more detail on other cellular therapy interventions. In late 2016, the EMA reached out to the EBMT to explore solutions for registering toxicities and efficacies associated with CAR-T cell treatments up to 15 years after administration. The EMA wanted to investigate the possibility of using this new cellular therapy module of the EBMT registry for the capture of long-term follow-up data of CAR-T cells, consistent with approval requirements issued by the EMA for CAR-T-cell therapies. This strategy was part of the ongoing Patient Registry Initiative by the EMA which aims to make better use of existing registries and to capture real word data to support postauthorization studies (PAS) such as postauthorization safety studies and postauthorization efficacy studies (PAES) and regulatory decision making [6]. To test suitability, in October 2017, EBMT submitted a request to EMA to qualify the cellular therapy module. This process ended with a positive opinion on the cellular therapy module of the EBMT registry by the EMA in early 2019 (Fig. 1) [7].

ADDITIONAL WIN–WINS OF A GLOBAL REGISTRY FOR CHIMERIC ANTIGEN RECEPTOR-T CELL

The additional potential benefits of registering commercial CAR-T cells in such a global registry are manifold, and this was also evident to many stakeholders. This global CAR-T cells registry would avoid siloed data sets in private registries of market authorization holders (MAHs) or disease-focused groups, allowing for comparison of safety and efficacy data between different ATMPs, assessment of the cost-effectiveness of this rather expensive intervention between different CAR-T cell products, and comparisons with alternative interventions such as bispecific molecules and stem-cell transplantation. This knowledge would improve the quality and affordability of patient care. Such a registry could also facilitate shorter and less expensive approval procedures, which is important considering that many commercial GTMPs with small variations will enter the market in the near future at a high price [4], with many novel targets still to be discovered [8▪]. The global registry would thereby support that patients get earlier access to CAR-T cells. Marketing authorization applicants would also benefit, as they would experience a shorter and therefore less expensive approval procedures. Health authorities, payers, patients and pharmaceutical companies, would need, however, to accept that products would come to market with a higher risk of failure in terms of lower or no efficacy, and of unexpected side-effects resulting in later withdrawals. A combination of Phase II studies followed by PAS has the potential to revolutionize market approval procedures, make cumbersome Phase III studies with very small

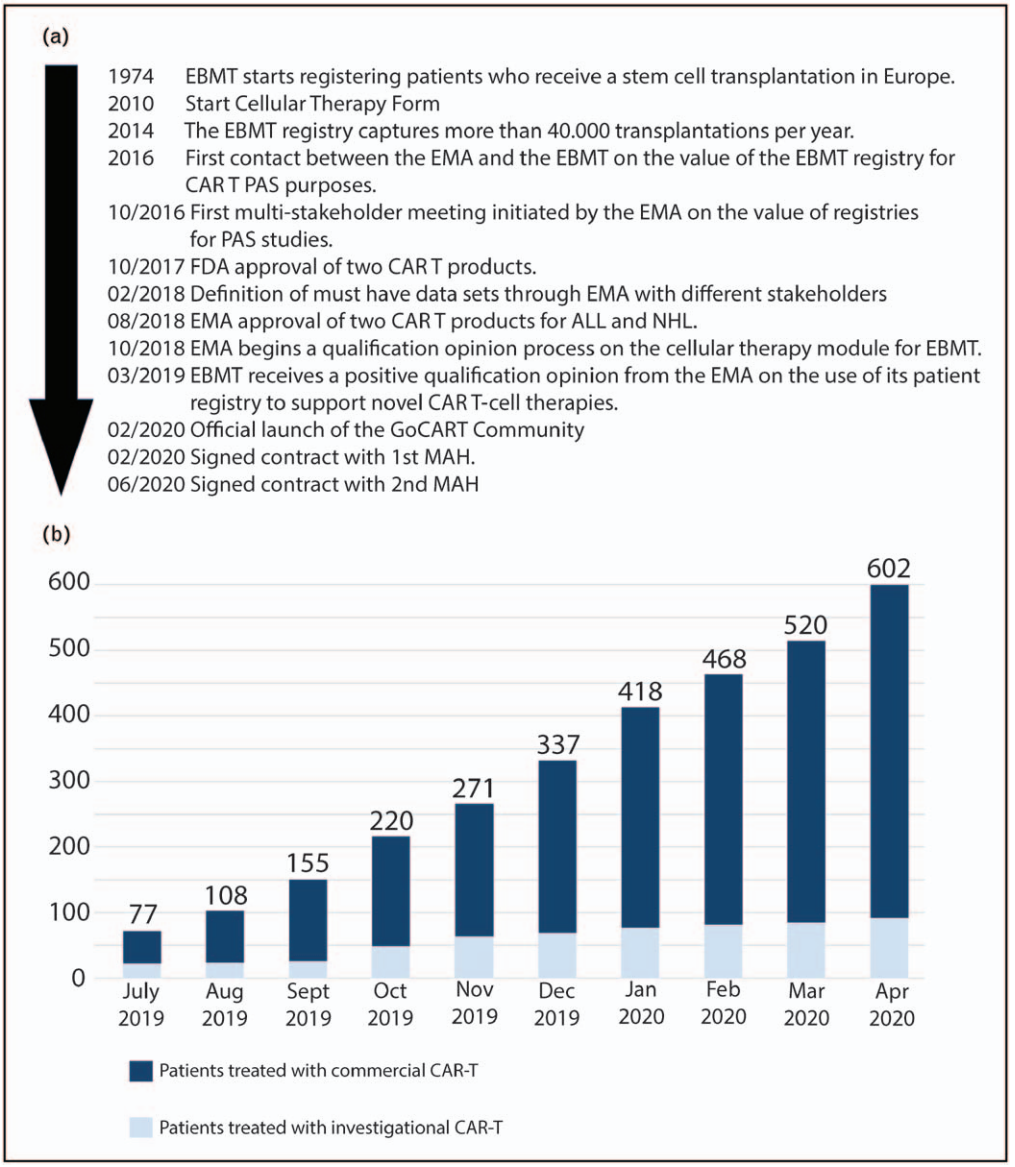

FIGURE 1. CAR-T cell and the registry (a) timelines of CAR-T cell registrations within the EBMT registry. (b) Development of reporting to the CAR-T cell registry of EBMT as reported by 05 2020 at https://www.ebmt.org/ebmt/news/how-do-i-report-patients-treated-car-t-cells-ebmt-registry-part-2.

patient populations for many products avoidable, and replace them with PAS studies where control arms consist of real-world data from patients treated with different strategies. Such concepts are also currently used to rapidly search for new drugs active against other unmet medical needs such as the novel coronavirus disease 2019 (COVID-19) [9] or colon cancer [10▪▪].

DELAYS IN IMPLEMENTING A EUROPEAN POST-AUTHORIZATION SAFETY STUDY

Although the EMA had explored the use of registries with the EBMT beginning in 2016 and had recommended approval for the first two CAR-T cell products on the market on June 29, 2018 [2], it wasn't until early 2020, when more than 300 patients had already been treated with commercial products in Europe, that the first contracts were signed between the EBMT and MAH [11]. Were there missed opportunities to assess safety, efficacy and cost-effectiveness, and what were the hurdles? First of all, the process was new to all stakeholders. Regulatory authorities, registry holders, and pharmaceutical companies needed to have a better understanding of each other's requirements. There was and is also no European regulatory framework defining requirements which may vary from

country to country or even at local level. This makes for example also the implementation of a new consent, required to allow monitoring of data and the sharing of pseudonymized data, cumbersome, and complicated. The first challenge was however to reach consensus among all stakeholders on the minimal data sets required for postmarket surveillance. This process was facilitated by a multistakeholder meeting in February 2018 when a limited data set was defined in terms of collected items and frequencies (Fig. 1). This data set collects a fraction of the data captured for clinical trials but captures the minimal essential safety and efficacy data required to support regulatory reporting obligations. Also, the approach to data collection had to be defined as primary data collection or secondary use of data. This has implications for the safety reporting obligations. For studies with primary data collection information on all adverse events should be collected and recorded and cases which are suspected to be related to the medicinal product/therapy should be reported to health authorities within established timelines. On the other hand, studies based on secondary use of data do not require the expedited reporting of suspected adverse reactions. The current approved PAS are based on secondary use of data and rely on the collection of adverse events of special interest that are defined *a priori*. Authorities will rely on the long-established pharmacovigilance networks for spontaneous reporting of suspected adverse reactions that are mandatory for all drugs, as well as summary reports of the adverse events of special interest collected in registries. The soundness of this decision is supported by an initial data set presented end 2019 by the US-based Center for International Blood and Marrow Transplant Research (CIBMTR), for patients treated with CAR-T cells and suffering from acute lymphoblastic leukemia (ALL) [12], and non-Hodgkin lymphoma [13]. The CAR-T cells registry of CIBMTR was established one year earlier than the EBMT CAR-T cells registry. It already has a five-times more cases and showed that both efficacies and reported safety events are in line with reports from Phase II studies; with a one-year delay, the EBMT registry reports on a similar growth in clinical use of approved CAR-T cells.

IMPLICATIONS FOR HOSPITAL EXEMPTION PROGRAMS AND FOR CLINICAL TRIALS

Commercial product registrations are not the only type of registration that will benefit from a pan-European CAR-T cell registry. The cellular therapy module was initially intended to capture academically based cellular immune interventions such as donor lymphocyte infusions and mesenchymal cells. Thus, the modernized registry which will need a continuous update to keep pace with all regulatory needs creates the opportunity to better capture CAR-T cell infusion related data derived from hospital exemption programs, along with commercial products. The aim of hospital exemption programs is to provide an ATMP intended for use in hospital settings when there is a high unmet medical need, and for use in an individual patient under the exclusive professional responsibility of a medical team and so are not considered suitable for the centralized market authorization process. However, to date, successes or failures are rarely transparent and are poorly monitored on a European level. The cellular therapy module allows for additional quality control for such hospital exemption programs with CAR-T cells. This is not yet mandatory in Europe, but has been requested for some ATMP programs, for example, for mesenchymal stromal cells (MSC) hospital exemption programs in The Netherlands since 2019 [14]. Mandatory reporting for hospital exemption programs to an open-access registry will undoubtedly further improve the quality of rapid access programs derived from early academic innovation in either niche indications or when commercial products are not available, as well as improve ATMP academic developments and reassure authorities that such hospital exemption programs improve rather than diminish patient care. In an ideal world, a global CAR-T cell registry should not only collect data from commercial activities and hospital exemption programs but also from clinical trials. However, a major concern of academic and commercial investigators has been that this would be a duplication of data management efforts and thus provide an extra burden to clinical centers, would not be adequately monitored for data quality, that data entered in registries would not be protected sufficiently against third parties access and have the risk of premature publications of trial data. An increase in data quality and transparent but stringent data access policies will be needed to increase the trust of the community in such early registration programs for clinical trial data. Core data sets developed by the EBMT registry could be implemented in clinical trial structures, alternatively linking both databases once a clinical trial is completed would achieve the same goal. There would be immense value for the community when capturing CAR-T cell treatment related data from approved commercial products, hospital exemption programs, and clinical trials in standardized and aligned registries.

HEALTH TECHNOLOGY ASSESSMENT AND PAYERS

A cohort of EU health technology assessment (HTA) bodies under the umbrella of the EUnetHTA Joint Action observed the qualification process of the cellular therapy module of EBMT by the EMA. HTA bodies are responsible for the systematic evaluation of properties, effects, and/or impacts of health technologies and interventions such as CAR-T cells. EUnetHTA brings together different national HTAs to create an effective and sustainable network for HTA across Europe. HTA representatives became interested in the data sets collected through the cellular therapy module of the EBMT, as these would allow for assessment of the value of CAR-T cells as compared with other treatment modalities. The EBMT has started to explore, in collaboration with EUnetHTA, whether the cellular therapy module can be of value to different HTA bodies, to conduct PAES. During the discussion with different HTAs in 2018, it became obvious that different national healthcare systems in different countries require different data sets. A registry would also allow novel reimbursement strategies for payers such as 'no cure, no pay' models, which are particularly interesting if the frequency of treatments is low, for example, for ALL where general financial discounts based on the average success of a drug have a higher risk. Therefore, the cellular therapy module of EBMT is designed in an adaptive mode, which will allow for different countries to collect somewhat different data sets in line with the requirements of their local authorities and payers. A common denominator for all of the countries is data capture, which allows for 'intention to treat' analyses. Intention to treat analysis includes every patient who was intended to receive the treatment instead of including only patients who received the treatment, as this may overestimate real-world effectiveness of an intervention, and therefore it is frequently used by authorities to assess the true medical and financial value of an intervention [15]. In the specific case of CAR-T cells, this allows for evaluation of what fraction of patients do not receive the CAR-T cell product because of disease progression, or because of a decline in the patient's status during the turnaround time for CAR-T cell production, which can last between 2 and 6 weeks. Therefore, the EBMT encourages commercial CAR-T cells to be registered as soon as the product request is submitted, or after apheresis is completed. It would be even better to register all patients in a country who are eligible for this therapy. However, because CAR-T cell centers reporting to the registry frequently rely on referring local physicians and hospitals which are not linked to the registry infrastructure, this approach does not yet seem feasible at this stage for most countries.

DATA HARMONIZATION

A major challenge when querying data is how a specific item is defined and collected. To harmonize this process across major registries, data definition groups have been established during the past decades between the EBMT and the CIBMTR, initially installed to increase quality and harmonize stem-cell transplantation data sets. Most recently the two groups started harmonizing cellular therapy registry forms across the globe. Given the fact that both organizations now capture CAR-T cells from the very same MAHs, with EBMT in the EU, and CIBMTR in the United States, this harmonization process is even more important, as the ability to easily fuse such data sets for global regulatory oversight is becoming essential. Some important details remain to be standardized, for example, what type of side-effect is captured starting from which grade and based on which grading system [16]. A more precise definition of collected data will also improve the quality of future scientific analyses.

DATA QUALITY

The EBMT registry utilizes many tools to ensure quality of collected data, including quality triggers built-in in the registry, the provision of training to data managers of member centers and procedures to check for and correct mistakes in data entry. The need to monitor at least 10% of all patients entered into the registry has been defined by the EMA as an additional requirement for PAS based on secondary use of registry data. The concept of more comprehensive monitoring of source data verification of collected data is new to most voluntary registries but is essential to making the data suitable for PAS studies and HTA evaluation, as also emphasized by EUnetHTA. As centers are normally not financially compensated for data reporting to the EBMT registry, the collaboration with MAHs in the conduct of PAS has provided EBMT the opportunity to establish a financial reimbursement for centers reporting commercial cellular therapies. This is an incentive to help professionalize data reporting and ensuring data completeness and accuracy including the introduction of regular and active data monitoring at centers participating in CAR-T PAS studies.

THE REGISTRY AND PRODUCT DETAILS

Enhancing the value of registry data by capturing product details prior to infusion would also allow for

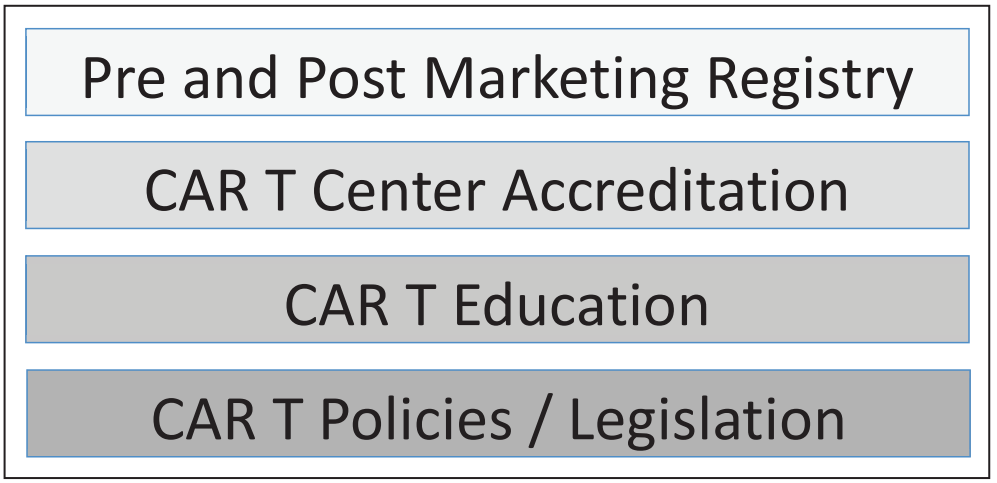

FIGURE 2. Pillars of the new GoCART Community platform. Indicated are the four major pillars of the new CAR-T cell community that came up after discussion with all stakeholders.

illustration of the variability in the production process [17] and enable a better understanding of the benefits of certain product properties, such as T-cell composition on clinical outcomes. New potency and release criteria, which are critical for the final product effectiveness and product clearance, could be defined for the future. The currently accepted product potency assay is frequently the expression of the introduced receptor which has many limitations. In addition, there is an ongoing debate about how many engineered T cells must be contained in the product to release it to patients. These questions could be addressed with such new data collections that would connect product details with clinical outcomes. However, as production details on commercial products are usually not shared to the registry by MAH, this opportunity will be most likely limited to academic developments, or to defined collaborations between an MAH and study groups [18].

OUTLOOK: FROM A NEW REGISTRY TOWARD A NEW CHIMERIC ANTIGEN RECEPTOR T-CELL COMMUNITY

To better structure the process of data collection and data access, in 2020 the EBMT launched multi-stakeholder GrOup for immune effector cells such as Chimeric Antigen Receptor T cells (GoCART), a CAR-T-cell community platform. The primary aim of GoCART is to create a public private/multistakeholder collaboration to maximize the potential of CAR-T, minimize duplication of efforts, and create a strong community for pan-EU leadership in this area (Fig. 2). The community aims to use the EBMT cellular therapy module as a central EU data registry, working in partnership with national cooperative and registry groups, as well as national organizations. In addition, it will be key to create transparent data access policies and harmonized data collection of CAR-T-cell therapies in the EBMT registry in line with the mandatory 'must have' data sets defined by EMA. Furthermore, it aims to support PAS commitments and bespoke study protocols for different stakeholders such as EMA, companies, HTA agencies, cooperative groups, and biobanks. Ensuring sustainability of the platform by continuously updating the database for new EMA qualification requirements as a suitable source for ongoing and novel postlicense evidence generation will be key to ensure its continued suitability for PAS data collections because treatment practices and stakeholder requirements are changing over time. Defining the criteria for data quality and completeness in collaboration with all stakeholders will be as important as creating partnerships with nontransplant centers, which will enable data capture on solid tumors as well as from transplant-ineligible hematology patients. Finally, it will be important to define processes and financially sound solutions which will enable continuous improvements to data quality (i.e., completeness and accuracy) and scope. The scope of the community will not, however, be limited to a pre and postauthorization registry. Developing a center qualification/accreditation process which covers immune effector cells but is not limited to a specific product, through the identification of commonalities and redundancies across the various processes for different therapies will be important. This process should be accepted by companies and authorities, and applicable to products running under a hospital exemption, as well as for commercial products. It will also be valuable to develop an educational program for physicians, data managers,

apheresis nurses, cell therapy technologists, quality managers, pharmacists, and nurses dealing with CAR-T cells, either with the supply chain or with patient care, but independent from a defined product. Finally, such a broad community has the potential to become a think tank and a source of inspiration for new European policies and legislation.

CONCLUSION

The positive qualified opinion of the EBMT registry by EMA to monitor long-term efficacy and safety of commercial CAR-T cells created opportunities and challenges and was serving as linking-pin to launch a novel CAR-T cell community. This process involved many stakeholders and managing obligations and expectations toward all stakeholders will be an exciting challenge for the upcoming years. This process will require from all, the registry holder, EMA, MAH, and healthcare professional's maximal flexibility as a comprehensive structure and legal framework need to be created that did not exist before.

Acknowledgements

We acknowledge the input of all EBMT board members and EBMT employees during the process of the implementation of the CAR-T cell registry, as well as the long-term commitment of all personnel at reporting centers.

Financial support and sponsorship

None.

Conflicts of interest

J.K. reports on grants from Novartis, Milltenyi Biotech, and Gadeta. J.K. is a inventor on multiple patents dealing with gdTCR and selection strategies of engineered immune cells. J.K. is a shareholder of Gadeta. C.B. received a Research contract from Intellia Therapeutics and participated to the advisory boards of Molmed, Intellia Therapeutics, TxCell, Novartis, GSK, Allogene. She is an inventor of patents in the field of adoptive T-cell therapy. The remaining authors have no conflict of interest.

Funding Sources

CC: Institut Paoli-Calmettes suppport to the Hematopoietic Cell Transplant program Inserm support to the ''Centre d'Investigations Cliniques en Biothérapies'', CBT-1409. CB received funding from AIRC (Ig 18458) and AIRC 5 per Mille, Rif. 22737, Italian Ministry of Research and University (PRIN 2017WC8499), Italian Ministry of Health (Research project on CAR T cells for hematological malignancies and solid tumors), JK: KWF UU 2015-7601 2017-11393 and 2019-11979, 2019-12586.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

1. FDA. FDA approves CAR-T cell therapy to treat adults with certain types of large B-cell lymphoma, 2017. https://www.fda.gov/news-events/press-announcements/fda-approves-car-t-cell-therapy-treat-adults-certain-types-large-b-cell-lymphoma.
2. EMA. First two CAR-T cell medicines recommended for approval in the European Union, 2018. https://www.ema.europa.eu/en/news/first-two-car-t-cell-medicines-recommended-approval-european-union.
3. ■■ Chabannon C, Kuball J, Bondanza A, *et al.* Hematopoietic stem cell transplantation in its 60s: a platform for cellular therapies. Sci Transl Med 2018; 10:.
Outlining the many spin-offs created from understanding the biology of stem-cell transplantation.
4. Chabannon C, Kuball J, McGrath E, *et al.* CAR-T cells: the narrow path between hope and bankruptcy? Bone Marrow Transplant 2017; 52:1588–1589.
5. Passweg JR, Baldomero H, Bader P, *et al.* Hematopoietic stem cell transplantation in Europe 2014: more than 40 000 transplants annually. Bone Marrow Transplant 2016; 51:786–792.
6. EMA. Patient registries. https://www.ema.europa.eu/en/human-regulatory/post-authorisation/patient-registries.
7. EMA. Qualification opinion on cellular therapy module of the European Society for Blood & Marrow Transplantation (EBMT) Registry, 2019. https://www.ebmt.org/ebmt/news/ebmt-receives-regulatory-qualification-european-medicine-agency-ema-use-its-patient.
8. ■ Sebestyen Z, Prinz I, Dechanet-Merville J, *et al.* Translating gammadelta (gammadelta) T cells and their receptors into cancer cell therapies. Nat Rev Drug Discov 2020; 19:169–184.
Providing inside into novel unconventional targets useful for genetic engineering T cells against cancer.
9. Angus DC, Berry S, Lewis RJ, *et al.* The randomized embedded multifactorial adaptive platform for community-acquired pneumonia (REMAP-CAP) study: rationale and design. Ann Am Thorac Soc 2020.
10. ■■ Derksen JW, May AM, Koopman M. The era of alternative designs to connect randomized clinical trials and real-world data. Nat Rev Clin Oncol 2019; 16:589.
Provides alternative clinical trial solutions.
11. EBMT. Report all CAR-T cell patients into the EBMT Registry, 2019. Available from: https://www.ebmt.org/ebmt/news/ebmt-centre-members-and-national-registries-are-requested-document-car-t-cell-therapies.
12. Grupp S, Hu ZH, Zhang Y, *et al.* Tisagenlecleucel chimeric antigen receptor (CAR) T-cell therapy for relapsed/refractory children and young adults with acute lymphoblastic leukemia (ALL): real world experience from the Center for International Blood and Marrow Transplant Research (CIBMTR) and cellular therapy (CT) registry. Blood 2019; 134(Suppl. 1):2619–12619.
13. Pasquini MC, Bleickardt E, Horowitz MM, *et al.* Tisagenlecleucel chimeric antigen receptor (CAR) T-cell therapy for adults with diffuse large B-cell lymphoma (DLBCL): real world experience from the Center for International Blood & Marrow Transplant Research (CIBMTR) cellular therapy (CT) registry. Blood 2019; 134(Suppl. 1):766–1766.
14. van der Wagen LE, Miranda-Bedate A, Janssen A, *et al.* Efficacy of MSC for steroid-refractory acute GVHD associates with MSC donor age and a defined molecular profile. Bone Marrow Transplant 2020; oinline first.
15. McCoy CE. Understanding the intention-to-treat principle in randomized controlled trials. West J Emerg Med 2017; 18:1075–1078.
16. Pennisi M, Jain T, Santomasso BD, *et al.* Comparing CAR T-cell toxicity grading systems: application of the ASTCT grading system and implications for management. Blood Adv 2020; 4:676–686.
17. Trento C, Bernardo ME, Nagler A, *et al.* Manufacturing mesenchymal stromal cells for the treatment of graft-versus-host disease: a survey among centers affiliated with the European Society for Blood and Marrow Transplantation. Biol Blood Marrow Transplant 2018; 24:2365–2370.
18. Finney OC, Brakke HM, Rawlings-Rhea S, *et al.* CD19 CAR T cell product and disease attributes predict leukemia remission durability. J Clin Invest 2019; 129:2123–2132.

