swiss medical weekly

Technical comment | Published 03 October 2024 | doi:https://doi.org/10.57187/s.3704
Cite this as: Swiss Med Wkly. 2024;154:3704

Technical comment on: Trottmann M, et al. Real-world expenditures and survival time after CAR-T treatment for large B-cell lymphoma in Switzerland: a retrospective study using insurance claims data

Caroline Arber[a], Gabriela Baerlocher[b], Yves Chalandon[c], Michael Daskalakis[d], Michel Duchosal[a], Martin Fehr[e], Sabine Gerull[f], Tayfun Güngör[g], Gayathri Nair[h], Thomas Pabst[d], Jakob R. Passweg[i], Barbara Piccolruaz[d], Christoph Renner[b], Axel Ruefer[j], Dominik Schneidawind[k], Georg Stüssi[l], Sacha Zeerleder[j], Jörg P. Halter[i], for the Swiss Blood Stem Cell Transplant and Cellular Therapies (SBST) group

[a] Service and Central Laboratory of Hematology, Service of Immuno-oncology, Departments of Oncology and Laboratory Medicine and Pathology, University Hospital Lausanne, Lausanne, Switzerland
[b] Division of Hematology/ Oncology, Clinic Hirslanden, Zurich, Switzerland
[c] Division of Hematology, Division of Pediatric Oncology and Hematology, University Hospital Geneva, Geneva, Switzerland
[d] Department of Medical Oncology, Department of Hematology and Central Hematology Laboratory, University Hospital Bern, Bern, Switzerland
[e] Division of Hematology/ Oncology, Cantonal Hospital, St. Gallen, Switzerland
[f] Division of Hematology/ Oncology, Cantonal Hospital, Aarau, Switzerland
[g] Department of Immunology/ Hematology/ Oncology/ Stem Cell Transplantation and Gene Therapy, University Children's Hospital Zurich, Zurich, Switzerland
[h] Swiss Blood Stem Cells, Swiss Transfusion SRC, Bern, Switzerland
[i] Hematology Division, University Hospital Basel, Basel, Switzerland
[j] Hematology Division, Cantonal Hospital, Lucerne, Switzerland
[k] Department of Medical Oncology and Hematology, University Hospital Zurich, Zurich, Switzerland
[l] Division of Hematology, Oncology Institute of Southern Switzerland, Ospedale San Giovanni, EOC, Bellinzona, Switzerland

We write this comment in response to the article by Trottmann and colleagues on the topic of healthcare expenditure (HCE) relating to chimeric antigen receptor T-cell (CAR-T) therapy for lymphoma [1]. CAR-T therapies have been approved by Swissmedic and subsequently introduced as a standard of care in a variety of indications for haematologic malignancies. Centres performing cellular therapies continuously optimise CAR-T product use and patient management [2, 3]; Swiss Blood Stem Cell Transplant and Cellular Therapies (SBST) maintains the national registry of all cellular therapies performed in Switzerland, ensuring annual reporting and exchange with healthcare authorities. Rigorous standards are respected by all centres, reflected by their accreditation by the International Joint Accreditation Committee of the International Society for Cell Therapy and the European Group for Blood and Marrow Transplantation (JACIE), providing state-of-the-art care to our patients [2].

With this comment, we would like to highlight and discuss several concerns raised by Swiss Stem Cell Transplant and Cell Therapy centres regarding the article by Trottmann et al. [1]. Our discussion aims to provide deeper insights into key aspects of CAR-T therapies relating to healthcare expenditure.

The dataset used in the retrospective analysis was obtained from insurance claim databases of selected insurance companies [1]. These data include only a fraction of patients who underwent CAR-T therapy for relapsed or refractory large B-cell lymphoma (LBCL) in Switzerland as their third-line treatment between October 2018 and June 2021. Insurance claim databases lack important data granularity and critical medical information.

The authors analysed healthcare expenditure across different treatment stages of CAR-T therapy (pre-, peri-, and post-infusion), but did not consider the cost of the CAR-T product. As expected, the few months before, during and after infusion were the most expensive. This is due to the nature of the indication for CAR-T therapy in relapsed/refractory LBCL in the third treatment line; most patients require active treatment and supportive care measures as a bridge to CAR-T therapy. As demonstrated in the registration trials which led to regulatory approval [4, 5], as well as by real-life results, approximately 50–60% of patients experience CAR-T failure and do not achieve long-lasting responses, and thus require additional treatment. Treatment options beyond the third line are most often novel agents or immunotherapies associated with higher costs than conventional chemotherapies, while patients also require more supportive care due to their advanced disease stage. Healthcare expenditure increases with each additional line of treatment, indicating that greater financial relief could be expected with more effective intervention at earlier stages. Therefore, it will be very interesting to see how real-life expenditure shifts once CAR-T therapy

Prof. Dr. med. Caroline Arber
Service of hematology and Service of immuno-oncology
Department of oncology
CHUV
CH-1011 Lausanne
caroline.arber-barth[at]chuv.ch

Prof. Dr. med. Jörg P. Halter
Hematology Division
University Hospital Basel
CH-4031 Basel
jhalter[at]uhbs.ch

is established broadly in the second line; clinical investigation is also ongoing into its use in the first line.

Another important consideration would be cost-effectiveness analysis by response to treatment. Patients with sustained complete response beyond 6 months after CAR-T in the third line have a high probability of long-term remission, while early failures have a dismal prognosis. In an interesting analysis conducted through the French hospital database of real-life CAR-T treatments in DLBCL patients, 207 of 362 (57.2%) patients experienced treatment failure [6]. While healthcare expenditure before and during CAR-T administration was similar in failure and non-failure groups, follow-up costs were significantly lower in the non-failure group, resulting in a close-to-zero monthly hospital cost beyond 6 months.

Trottmann et al. [1] indicate that CAR-T therapy is considered a "one and done" treatment approach. With a failure rate of 50-60% in third-line treatment, this seems unrealistic and requires rethinking at the level of insurance companies. In addition, the majority of patients require relatively intense monitoring and supportive care measures in the months following CAR-T therapy, especially those who do not achieve long-lasting responses. Trottmann et al. [1] also compared CAR-T-related healthcare expenditure with previously published healthcare expenditure for lymphoma patients in their last year of treatment. The comparison to analyses published in 2011 and 2014 does not seem pertinent. At the time, most novel treatment regimens and immunotherapies that are now part of standard care were unavailable. Thus, those cost estimates do not reflect current practice and are misleading.

SBST fully recognises that beyond clinical effectiveness, costs and benefits are an integral part of efficacy analysis of new treatments. We clearly support the analysis of economic aspects of new treatments. However, in answering those questions we believe it is imperative to consider all costs and not just those of selected insurance companies. The federal office of public health (FOPH) has conducted a health technology assessment with the objective to understand clinical efficacy, safety and cost-effectiveness of tisagenlecleucel and axicaptagene ciloleucel compared to current standard of care [7]. The report clearly highlights the difficulties encountered answering these questions with the available data, based on single arm clinical registration trials and real-world datasets. In particular, the economic evaluation was hampered by limited and low certainty evidence when comparing CAR-T cell therapies to historic controls as no randomized clinical trials are available and will likely never be.

Thus, current studies lack relevant comparators and as a result, are not conclusive. A deeper and more thorough assessment of healthcare expenditure for novel therapies is required. Insurance companies are invited to collaborate with hospitals and clinicians and contribute with their data to future collaborative studies addressing the economic impact of these novel innovative treatments. The field would also benefit from an improved understanding of biological correlates of response and non-response in CAR-T therapy. Identification of objective parameters that allow for risk stratification in the CAR-T setting may help improve patient outcomes and cost-effectiveness.

Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest related to the content of this manuscript was disclosed.

References

1. Trottmann M, Blozik E, Hilbig M, LoVerdi D, Pedruzzi M, Scherer T, et al. Real-world expenditures and survival time after CAR-T treatment for large B-cell lymphoma in Switzerland: a retrospective study using insurance claims data. Swiss Med Wkly. 2023 Sep;153(9):3441. http://dx.doi.org/10.57187/s.3441.
2. Passweg JR, Baldomero H, Ansari M, Arber C, Chalandon Y, Daskalakis M, et al.; Swiss Blood Stem Cell Transplantation Group (SBST). Hematopoietic cell transplantation and cellular therapies in Switzerland. Evolution over 25 years. A report from the stem cell transplantation and cellular therapies working groups of the SBST 1997-2021. Hematol Oncol. 2024 Jan;42(1):e3241. http://dx.doi.org/10.1002/hon.3241.
3. Duchosal MA, et al. Développements récents en hématologie, Teil 1. Swiss Medical Forum, 2023. http://dx.doi.org/10.4414/fms.2023.09462.
4. Schuster SJ, Bishop MR, Tam CS, Waller EK, Borchmann P, McGuirk JP, et al.; JULIET Investigators. Tisagenlecleucel in Adult Re-lapsed or Refractory Diffuse Large B-Cell Lymphoma. N Engl J Med. 2019 Jan;380(1):45–56. http://dx.doi.org/10.1056/NEJMoa1804980.
5. Neelapu SS, Locke FL, Bartlett NL, Lekakis LJ, Miklos DB, Jacob-son CA, et al. Axicabtagene Ciloleucel CAR T-Cell Therapy in Refrac-tory Large B-Cell Lymphoma. N Engl J Med. 2017 Dec;377(26):2531–44. http://dx.doi.org/10.1056/NEJMoa1707447.
6. Di Blasi R, Thieblemont C, Haioun C, Sackmann Sala L, Mayaud AC, Diez-Andreu P, et al. Healthcare Resource Use (HCRU) and Associated Costs Among Patients With Diffuse Large B-Cell Lymphoma (DLBCL) Treated with CAR-T Cells in France – A Real-World Study Using Data From PMSI. Value Health. 2022;25(12):S79–80. http://dx.doi.org/10.1016/j.jval.2022.09.390.
7. Nicolopoulos K, Moshi M, Min M, Stringer D, Vreugdenburg T. The CAR T-cell therapies tisagenlecleucel (Kymriah®) and axicabtagene ciloleucel (Yescarta®) for the treatment of B-cell acute lymphoblastic leukaemia, diffuse large B-cell lymphoma and primary mediastinal B-cell lymphoma. Berne: Federal Office for Public Health - HTA Report, 2024. Internet: https://www.bag.admin.ch/bag/en/home/versicherungen/krankenversicherung/krankenversicherung-leistungen-tarife/hta/hta-projekte/carttherapien.html