Received: 8 April 2024 | Accepted: 30 May 2024

DOI: 10.1111/bjh.19590

BJHaem
BRITISH JOURNAL OF HAEMATOLOGY

SHORT REPORT

Haematological Malignancy – Clinical

Secondary primary malignancies after CD-19 directed CAR-T-cell therapy in lymphomas: A report from the Italian CART-SIE study

Angelica Barone[1] | **Annalisa Chiappella**[2] | **Beatrice Casadei**[3] | **Stefania Bramanti**[4] | **Silva Ljevar**[5] | **Patrizia Chiusolo**[6] | **Alice Di Rocco**[7] | **Maria Chiara Tisi**[8] | **Anna Maria Barbui**[9] | **Mirko Farina**[10] | **Lucia Brunello**[11] | **Maria Chiara Di Chio**[2] | **Mattia Novo**[12] | **Maurizio Musso**[13] | **Jacopo Olivieri**[14] | **Gentiana Elena Trotta**[15,2] | **Anna Dodero**[2] | **Antonella Aiello**[16] | **Paolo Corradini**[1,2]

Correspondence
Annalisa Chiappella, Division of Hematology and Stem Cell Transplantation, Fondazione IRCCS Istituto Nazionale dei Tumori, via Giacomo Venezian 1, 20133 Milano, Italy.
Email: annalisa.chiappella@istitutotumori.mi.it

Funding information
HORIZON EUROPE Health, Grant/Award Number: PNC-E3-2022-23683269-PNC-HLS-TA

Summary
Secondary primary malignancies (SPM) have been reported after anti-BCMA or anti-CD19 chimeric antigen receptor (CAR)-T-cell therapies. While the cytotoxic effect of antecedent therapies, including chemotherapy and radiotherapy, has been well established, few data are available on risk related to CAR-T immunotherapies. The study aimed to analyse the incidence of SPM in 651 patients enrolled in the Italian prospective observational CART-SIE study. SPMs were documented in 4.3% (28/651), and the most frequent SPMs were haematological malignancies. In conclusion, the frequency of SPMs in our cohort of heavily pretreated patients receiving CAR-T was relatively low and consistent with previous studies.

KEYWORDS
acute leukaemia, immunotherapy, late effects of therapy, malignant lymphomas, MDS, T-cell lymphoma

INTRODUCTION

Secondary primary malignancies (SPMs) have been extensively described in patients with haematological malignancies, due to both genetic susceptibility and DNA-damaging treatments.[1] Chemotherapy (CT), radiotherapy and autologous (ASCT) or allogeneic stem cell transplant (allogeneic SCT) have a well-characterized genotoxic effect; recently, a 5-year cumulative risk of solid tumours of 4% and of myeloid malignancies of 3% has been reported after high-dose CT and ASCT, with a 38-fold higher risk of secondary myeloid neoplasms.[2] While the role of cytotoxic therapies has been established, few data exist on SPMs after chimeric antigen receptor (CAR)-T-cell immunotherapies. In November 2023, the United States Food and Drug Administration (FDA) published a warning about a serious risk of T-cell malignancy following CAR-T cells,[3] suggesting a possible correlation between CAR transduction and malignant transformation of T lymphocytes based on reports of subsequent 'CAR-positive' T-cell non-Hodgkin lymphomas (T-NHL). The incidence of SPMs has been variably reported ranging from 0% to 15% across studies[4–9]: the FDA Adverse Events Reporting System (FAERS) database has been recently analysed and 4.3% incidence of all SPMs was reported, of which 2.7% and 0.1% were leukaemias (comprising of acute myeloid leukaemias (AML) and myelodysplastic syndromes (MDS)) and T-NHL respectively.[10]

We herein report the incidence of SPM in a large cohort of patients affected by relapsed/refractory (R/R) non-Hodgkin lymphomas treated in 21 Italian centres with currently

For affiliations refer to page 4.

in-label CAR-T cells, namely axicabtagene ciloleucel (axi-cel), tisagenlecleucel (tisa-cel) and brexucabtagene autoleucel (brexu-cel).

METHODS

The Italian CART-SIE is a multicentre prospective observational study collecting data from R/R B-NHL treated with in-label CAR-T according to the eligibility criteria, as defined by the Italian Drug Agency (detailed in Supporting Information S1). The study was conducted according to Helsinki Declaration and good clinical practice guidelines. Ethical approval was obtained by institutional review boards at each site (INT 180/19, Approval number 431/DG, 2019). All participants provided written informed consent. Potential risk factors for occurrence of SPMs were analysed, including previous treatments, cytopenias at the time of the apheresis, cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), immune effector cell-associated haematotoxicity (ICAHT) and CAR-HEMATOTOX score.[11] A cut-off of absolute neutrophil count <500/mmc and platelets <100.000/mmc was used to determine the association between pre- and post-infusion cytopenias and SPMs.

Statistical analysis

Descriptive statistics were used to summarize patient baseline characteristic, namely median and interquartile range for continuous variables, and absolute and relative frequencies for categorical variables. Univariable logistic models were used to evaluate the association between the

TABLE 1 Baseline characteristics of patients with secondary primary malignancies compared to the whole cohort.

	Overall (*N* = 651)	No second cancer (*N* = 623)	Second cancer (*N* = 28)
Age, median [Q1, Q3]	59.0 [49.0, 65.0]	59.0 [48.0, 66.0]	59.0 [51.5, 65.0]
Male sex, *n* (%)	416 (63.9%)	395 (63.4%)	21 (75.0%)
CAR-T product, *n* (%)			
Axi-cel	312 (47.9%)	298 (47.8%)	14 (50.0%)
Brexu-cel	86 (13.2%)	84 (13.5%)	2 (7.1%)
Tisa-cel	253 (38.9%)	241 (38.7%)	12 (42.9%)
Histology, *n* (%)			
DLBCL/HGBL	489 (75.1%)	465 (74.6%)	24 (85.7%)
MCL	84 (12.9%)	82 (13.2%)	2 (7.1%)
PMBCL	76 (11.7%)	74 (11.9%)	2 (7.1%)
Missing	2 (0.3%)	2 (0.3%)	0 (0%)
Disease status, *n* (%)			
Refractory	442 (67.9%)	423 (67.9%)	19 (67.9%)
Relapse	195 (30.0%)	187 (30.0%)	8 (28.6%)
Missing	14 (2.2%)	13 (2.1%)	1 (3.6%)
Ann Arbor III–IV, *n* (%)	456 (70.0%)	431 (69.2%)	25 (89.3%)
IPI ≥3, *n* (%)	218 (33.5%)	207 (33.2%)	11 (39.3%)
Extranodal sites, yes, *n* (%)	342 (52.5%)	327 (52.5%)	15 (53.6%)
Bulky disease, *n* (%)	224 (34.4%)	213 (34.2%)	11 (39.3%)
Bone marrow involvement, *n* (%)	80 (12.3%)	75 (12.0%)	5 (17.9%)
Number of previous treatments, median [Q1, Q3]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	2.00 [2.00, 3.25]
Previous ASCT, *n* (%)	200 (30.7%)	185 (29.7%)	15 (53.6%)
Bridging therapy, *n* (%)	527 (81.0%)	505 (81.1%)	22 (78.6%)
RT as bridging therapy, *n* (%)	139 (21.4%)	133 (21.3%)	6 (21.4%)
CAR-HEMATOTOX, *n* (%)			
Low	240 (36.9%)	232 (37.2%)	8 (28.6%)
High	119 (18.3%)	110 (17.7%)	9 (32.1%)
Missing	292 (44.9%)	281 (45.1%)	11 (39.3%)

Abbreviations: ASCT, autologous stem cell transplantation; DLBCL, diffuse large B-cell lymphoma; HGBL, high grade B-cell lymphoma; IPI, international prognostic index; MCL, mantle cell lymphoma; PMBCL, primary mediastinal B-cell lymphoma; RT, radiotherapy.

TABLE 2 Univariable logistic models for myeloid malignancies.

	OR	95% CI	Overall *p*-value	Non-linear *p*-value	Adjusted *p*-value*
Age, 65 vs. 49 [Q1, Q3] (*n* = 649)	0.96	0.45–2.02	0.6072	0.3719	0.916
Sex, male vs. female (*n* = 648)	1.12	0.45–2.81	0.8105		0.963
CAR-T (*n* = 651)					
Brexu-cel vs. Axi-cel	0.65	0.14–3.00	0.8551		0.963
Tisa-cel vs. Axi-cel	0.89	0.35–2.26			
Histology (*n* = 649)					
DLBCL vs. PMBCL	3.17	0.41–24.50	0.6117		0.916
HGBL vs. PMBCL	2.14	0.24–19.52			
MCL vs. PMBCL	1.83	0.16–20.59			
Disease status, relapsed vs. refractory (*n* = 637)	0.97	0.37–2.56	0.9519		0.993
Ann Arbor III–IV (*n* = 644)	8.58	1.14–64.38	0.0366		**0.030**
IPI ≥3 vs. <3 (*n* = 548)	1.38	0.55–3.45	0.4933		0.916
Extranodal sites, yes vs. no (*n* = 636)	1.41	0.58–3.46	0.4493		0.916
Bulky disease, yes vs. no (*n* = 643)	1.42	0.59–3.42	0.4350		0.916
Bone marrow involvement, yes vs. no (*n* = 355)	1.77	0.59–5.33	0.3122		0.916
Number of previous lines, 3 vs. 2 (*n* = 649)	1.94	0.75–5.00	0.0896	0.6633	0.103
ASCT, yes vs. no (*n* = 645)	3.09	1.28–7.46	0.0120		0.071
Bridging therapy, yes vs. no (*n* = 651)	1.00	0.33–3.03	1.0000		>0.999
RT as bridging therapy, yes vs. no (*n* = 527)	1.17	0.40–3.38	0.7730		0.936
HEMATOTOX, high vs. low (*n* = 359)	3.39	1.08–10.59	0.0359		**0.030**
Low platelets at the time of apheresis, yes vs. no (*n* = 648)	0.94	0.21–4.14	0.9373		0.963
Low platelets day 90 yes vs. no (*n* = 471)	9.7	3.16–29.79	0.0001		**<0.001**
Low neutrophils apheresis yes vs. no (*n* = 645)	0.00	0.00– >10 000	0.8455		0.916
Low neutrophils day 90 yes vs. no (*n* = 470)	0.78	0.10–6.04	0.8116		0.963
ICAHT, yes vs. no (*n* = 545)	5.09	1.57–16.48	0.0066		0.086
CRS, yes vs. no (*n* = 651)	0.40	0.15–1.06	0.0655		0.292
CRS, G ≥ 3 vs. <3 (*n* = 551)	0.53	0.07–4.07	0.5391		0.916
ICANS, yes vs. no (*n* = 651)	0.87	0.31–2.40	0.7828		0.963
ICANS, G ≥ 3 vs. <3 (*n* = 171)	1.15	0.19–7.06	0.8820		0.963

Abbreviations: ASCT, autologous stem cell transplantation; CRS, cytokine release syndrome; DLBCL, diffuse large B-cell lymphoma; HGBL, high grade B-cell lymphoma; ICAHT, immune effector cell-associated haematotoxicity; ICANS, immune effector cell-associated neurotoxicity; IPI, international prognostic index; MCL, mantle cell lymphoma; PMBCL, primary mediastinal B-cell lymphoma; RT, radiotherapy.

*p-values adjusted for the false discovery rate. Bold values indicate p<0.005.

incidence of second malignancies and different risk factors; the p-values were adjusted for multiple testing using the Benjamini–Hochberg method to control the false discovery rate.[12] Multivariable analysis was not possible due to a low number of events observed.

RESULTS

From 2019 to 2023, 651 patients were enrolled in the CART-SIE study; those with a minimum follow-up of 30 days after CAR-T infusion were analysed (Table 1). Median follow-up was 12.2 months (IQR: 6.22–23.29). SPMs were documented in 4.3% (28) of patients; the most frequent were haematological malignancies (n = 25, 3.8%), of which 21 were myeloid malignancies (3.2%, AML = 4, MDS = 17). Four cases (0.61%) of lymphoid neoplasms were observed: one Hodgkin lymphoma, one EBV-positive B-NHL and two (0.3%) T-NHL (large granular leukaemia = 1, T-helper follicular proliferation =1). Solid tumours were observed in three patients (0.46%), namely one EBV-positive nasopharyngeal carcinoma, one colorectal cancer and one prostate cancer in a patient with a pre-existing prostate adenoma. No cases of non-melanoma skin cancer were reported. Median time from CAR-T infusion to diagnosis of haematological malignancy was 9.2 months (range 1–39.5). Focusing on myeloid malignancies, median time to diagnosis was 9 months (range 1–39.5). Among patients with myeloid malignancies, cytogenetic and TP53 data were available in 85.6% (18) patients; complex karyotype and TP53 mutation were reported in 7 (30%) and 4 (19%) patients respectively. Only 1/21 patients had performed a next-generation sequencing (NGS) myeloid panel prior to CAR-T infusion and found a clonal

haematopoiesis of indeterminate potential (CHIP). Details on diagnosis and outcome of all patients are shown in Table S1. The 2-year cumulative incidence of second malignancies was 6.97% (95% CI: 4.58–10.63) for all SPMs and 5.09% (95% CI 3.10–8.38) for myeloid malignancies in the entire cohort. Univariable logistic regression was used to identify possible risk factors for occurrence of SPMs; a higher risk for occurrence of SPMs was found in patients with low platelets at day +90 after infusion (OR 5.89, 95% CI 2.5–13.9, $p < 0.01$), while a trend towards higher risk for SPMs was found in patients with Ann Arbor stage III–IV at diagnosis, previous ASCT, development of ICAHT and high CAR-HEMATOTOX, although not reaching statistical significance at adjusted p-values. Further information is shown in Table S2. When focusing on myeloid malignancies (as displayed in Table 2), a higher risk for occurrence was found in patients with Ann Arbor Stage III–IV ($p = 0.03$), high CAR-HEMATOTOX score ($p = 0.03$), low platelet count at day +90 post-infusion ($p < 0.01$). A trend towards higher risk for myeloid malignancies was found in patients who had received ASCT and had ICAHT after CAR-T infusion, although not reaching statistical significance. No correlation with age, CAR-T product, number of previous lines of therapy, previous RT, development of CRS or ICANS and cytopenias prior to CAR-T infusion was demonstrated. Among all patients with SPM, 10 deaths were registered, three due to recurrence of the B-cell lymphoma, seven related to SPMs (3 allogeneic SCT-related mortality, 1 progression of AML, 1 EBV-related nasopharyngeal carcinoma, 1 EBV-positive B-NHL, 1 COVID-19 infection).

DISCUSSION

The frequency of SPMs in our cohort of heavily pretreated patients was relatively low and consistent with previous studies and with recent FAERS analysis. Similarly, frequency of myeloid malignancies appeared to be consistent since with previous reports after high-dose CT and ASCT. Since all patients in our study received such treatments prior to CAR-T infusion, the late effects of CAR-T cells could not be dissected from that of antecedent cytotoxic therapies; an adequate evaluation of such late effects could not be performed in the absence of a comparative cohort of patients not progressing to CAR-T cells. Indeed, while cytotoxic therapies remain well-established critical factors in the development of secondary myeloid neoplasms due to a combination of genetic predisposition and exposure to DNA-damaging agents, it remains unclear whether therapy with CAR-T cells itself or its immunosuppressive microenvironment plays a role in malignant clone transformation; longer follow-up is required to address this question, while the presence of the CAR transgene in cases of T-cell malignancies diagnosed after CAR-T infusion should be evaluated. Late or unexplained cytopenias occurring after CAR-T require a comprehensive assessment including bone marrow aspiration and biopsy, along with an NGS myeloid panel to detect possible signs of myeloid neoplasms or other haematological conditions which could lead to cytopenias (i.e. T-LGL). Our study has some limitations: Median follow-up was short as 12 months and likely inadequate to capture the long-term risk of SPMs; moreover, a possible under-reporting of myeloid malignancies could have occurred since it was difficult to assess whether all patients with persistent cytopenias had performed a complete evaluation. In conclusion, CAR-T cells represent nowadays a promising therapeutic strategy for lymphoid malignancies and other non-malignant conditions, such as autoimmune diseases: longer follow-up, close monitoring and better comprehension of pathophysiology of SPMs are required to establish evidence-based risk stratification and treatment approach. Our data support the notion that any long-lasting cytopenia should be carefully evaluated to rule out an SPM.

AUTHOR CONTRIBUTIONS

PCo, AB and AC were involved in conception and design. AC, BC, SB, PCh, ADR, MCT, AMB, MF, LB, MCDC, MN, MM, JO, AD and AA were involved in provision of study materials or patients. AB, AC, SL, GET and PCo were involved in collection and assembly of data. SL, AB, AC and PCo were involved in data analysis and interpretation. All authors were involved in manuscript writing, final approval of manuscript and accountable for all aspects of the work.

AFFILIATIONS

[1]Chair of Hematology, University of Milan, Milan, Italy
[2]Division of Hematology and Stem Cell Transplantation, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy
[3]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy
[4]IRCCS Humanitas Research Hospital, Transplantation Unit Department of Oncology and Haematology, Rozzano, Italy
[5]Unit of Biostatistics for Clinical Research, Department of Data Science, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy
[6]Dipartimento di Scienze Microbiologiche Ed Ematologiche, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Sezione di Ematologia, Dipartimento di Scienze Radiologiche Ed Ematologiche, Università Cattolica del Sacro Cuore, Rome, Italy
[7]Department of Translational and Precision Medicine, 'Sapienza' University of Rome, Rome, Italy
[8]Hematology Unit, San Bortolo Hospital, Vicenza, Italy
[9]Azienda Socio Sanitaria Territoriale Papa Giovanni XXIII, Bergamo, Italy
[10]Unit of Hematology, ASST Spedali Civili di Brescia, Brescia, Italy
[11]SCDU Ematologia AOU SS Antonio e Biagio e Cesare Arrigo Alessandria Italy, Alessandria, Italy
[12]Division of Hematology, AOU Città Della Salute e Della Scienza di Torino, Torino, Italy
[13]UOC di Oncoematologia e TMO Dipartimento Oncologico La Maddalena Palermo, Palermo, Italy
[14]Clinica Ematologica, Centro Trapianti e Terapie Cellulari "Carlo Melzi", Azienda Sanitaria Universitaria Integrata di Udine, Udine, Italy
[15]Ematologia, Dipartimento di Biomedicina e Prevenzione, Università Degli Studi di Roma Tor Vergata, Rome, Italy
[16]Division of Pathology, Department of Advanced Diagnostics, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy

ACKNOWLEDGEMENTS

We thank Sonia Perticone and the trial office of the Fondazione Italiana Linfomi for the management of the study. We thank Anna Fedina for export data.

FUNDING INFORMATION

This study is sponsored by Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy, 'Associazione Italiana contro le Leucemie-linfomi e mieloma' (AIL) Milano; 'Società Italiana di Ematologia'. This work was supported by the European Union—Next Generation EU—NRRP M6C2—Investment 2.1 Enhancement and strengthening of biomedical research in the NHS (project #PNC-E3-2022-23 683 269-PNC-HLS-TA).

CONFLICT OF INTEREST STATEMENT

AC—Advisory boards and/or honoraria for lectures/educational events: Abbvie, Gilead Sciences, Eli Lilly, Ideogen, Hoffmann La-Roche, Janssen-Cilag, Novartis, SecuraBIO, Takeda. BC—Advisory boards and honoraria for lectures/educational events: Kite Gilead, Novartis. SB—Speaker bureau: Bristol-Myers Squibb, Gilead, Novartis; advisory board: Novartis; travel accommodation: Novartis, Roche. ADR—consulting fees: Roche, Takeda, Incyte, Kite-Gilead, Novartis, Abbvie; speakers bureaus: Roche, Kite-Gilead, Janssen, Abbvie, Eli-Lilly, Sobi, Incyte, Recordati Rare Disease; advisory board: Takeda, Kite-Gilead, Roche, Abbvie, Novartis. PCo—Speaker and/or participating in advisory board: AbbVie, ADC Theraputics, Amgen, BeiGene, Celgene, Daiichi Sankyo, Eli Lilly, Gilead/Kite, GSK, Incyte, Janssen, Jazz Pharma, Novartis, Pfizer, Roche, Sanofi, SOBI, Takeda. The other authors declare that they have no conflict of interest.

DATA AVAILABILITY STATEMENT

The dataset analysed during the current study is available from the corresponding author on reasonable request.

ETHICS APPROVAL STATEMENT

The study was conducted according to Helsinki Declaration and good clinical practice guidelines.

PATIENT CONSENT STATEMENT

All participants provided written informed consent.

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

N/A.

CLINICAL TRIAL REGISTRATION

Ethical approval was obtained by institutional review boards at each site (INT 180/19, Approval number 431/DG, 2019).

ORCID

Angelica Barone https://orcid.org/0009-0004-1623-3842
Annalisa Chiappella https://orcid.org/0000-0002-2977-0098
Patrizia Chiusolo https://orcid.org/0000-0002-1355-1587
Mirko Farina https://orcid.org/0000-0002-2980-9028
Paolo Corradini https://orcid.org/0000-0002-9186-1353

REFERENCES

1. Martelin E, Volin L, Itälä-Remes M, Niittyvuopio R, Lindström V, Heiskanen J, et al. Incidence and risk factors of secondary cancers after allogeneic stem cell transplantation: analysis of a single centre cohort with a long follow-up. Bone Marrow Transplant. 2019;54(2):334–7. https://doi.org/10.1038/s41409-018-0290-6
2. Trab T, Baech J, Jakobsen LH, Husby S, Severinsen MT, Eloranta S, et al. Second primary malignancies in patients with lymphoma in Denmark after high-dose chemotherapy and autologous haematopoietic stem-cell transplantation: a population-based, retrospective cohort study. Lancet Haematol. 2023;10(10):e838–e848.
3. Administration UFAD. *FDA Investigating Serious Risk of T-cell Malignancy Following BCMA- Directed or CD19-Directed Autologous Chimeric Antigen Receptor (CAR) T cell Immunotherapies*. 2023.
4. Neelapu SS, Jacobson CA, Ghobadi A, Miklos DB, Lekakis LJ, Oluwole OO, et al. Five-year follow-up of ZUMA-1 supports the curative potential of axicabtagene ciloleucel in refractory large B-cell lymphoma. Blood. 2023;141(19):2307–15. https://doi.org/10.1182/blood.2022018893
5. Jacobson CA, Locke FL, Ma L, Asubonteng J, Hu ZH, Siddiqi T, et al. Real-world evidence of Axicabtagene Ciloleucel for the treatment of large B cell lymphoma in the United States. Transpl Cellular Therapy. 2022;28(9):581.e1–581.e8.
6. Ghilardi G, Fraietta JA, Gerson JN, van Deerlin VM, Morrissette JJD, Caponetti GC, et al. T cell lymphoma and secondary primary malignancy risk after commercial CAR T cell therapy. Nat Med. 2024;30:984–9. https://doi.org/10.1038/s41591-024-02826-w
7. Chong EA, Ruella M, Schuster SJ. Lymphoma program investigators at the University of Pennsylvania. Five-year outcomes for refractory B-cell lymphomas with CAR T-cell therapy. N Engl J Med. 2021;384(7):673–4. https://doi.org/10.1056/NEJMc2030164
8. Jaeger U, Tam CS, Borchmann P, McGuirk JP, Johansen M, Waller EK, et al. Long-term safety for patients with tisagenlecleucel-treated relapsed/refractory diffuse large B-cell lymphoma. Blood Adv. 2022;6(16):4816–20. https://doi.org/10.1182/bloodadvances.2021006193
9. Wang M, Munoz J, Goy A, Locke FL, Jacobson CA, Hill BT, et al. Three-year follow-up of KTE-X19 in patients with relapsed/refractory mantle cell lymphoma, including high-risk subgroups, in the ZUMA-2 study. J Clin Oncol. 2022;41(3):555–67.
10. Elsallab M, Ellithi M, Lunning MA, D'Angelo C, Ma J, Perales MA, et al. Second primary malignancies after commercial CAR T cell therapy: analysis of FDA adverse events reporting system (FAERS). Blood. 2024;143:2099–105. https://doi.org/10.1182/blood.2024024166
11. Rejeski K, Perez A, Sesques P, Hoster E, Berger C, Jentzsch L, et al. CAR-HEMATOTOX: a model for CAR T-cell–related hematologic toxicity in relapsed/refractory large B-cell lymphoma. Blood. 2021;138(24):2499–513. https://doi.org/10.1182/blood.2020010543
12. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J R Stat Soc B Methodol. 1995;57(1):289–300. https://doi.org/10.1111/j.2517-6161.1995.tb02031.x

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Barone A, Chiappella A, Casadei B, Bramanti S, Ljevar S, Chiusolo P, et al. Secondary primary malignancies after CD-19 directed CAR-T-cell therapy in lymphomas: A report from the Italian CART-SIE study. Br J Haematol. 2024;00:1–5. https://doi.org/10.1111/bjh.19590