Risk of subsequent primary leukaemias among 69,460 five-year survivors of childhood cancer diagnosed from 1940 to 2008 in Europe

Allodji, Rodrigue S; Hawkins, Mike M; Bright, Chloe J; Fidler-Benaoudia, Miranda M; Winter, David L; Alessi, Daniela; Fresneau, Brice; Journy, Neige; Morsellino, Vera; Bárdi, Edit; Bautz, Andrea; Byrne, Julianne; Feijen, Elizabeth Lieke Am; Teepen, Jop C; Vu-Bezin, Giao; Rubino, Carole; Garwicz, Stanislaw; Grabow, Desiree; Gudmundsdottir, Thorgerdur; Guha, Joyeeta

DOI:
10.1016/j.ejca.2019.05.013

RISK OF SUBSEQUENT PRIMARY LEUKEMIAS AMONG 69,460 5-YEAR SURVIVORS OF CHILDHOOD CANCER IN EUROPE: A COHORT STUDY WITHIN PANCARESURFUP

Rodrigue S Allodji[1,3,27], Mike M Hawkins[1], Chloe J Bright[1], David L Winter[1], Daniela Alessi[2], Brice Fresneau[3,4], Miranda M Fidler-Benaoudia[1,5], Vera Morsellino[6], Edit Bárdi[7,8], Andrea Bautz[9], Julianne Byrne[10], Elizabeth AM Feijen[11,12], Giao Vu-Bezin[3], Carole Rubino[3], Stanislaw Garwicz[13†], Desiree Grabow[14], Thorgerdur Gudmundsdottir[8,15], Joyeeta Guha[1], Eva-Maria Hau[16,17], Momcilo Jankovic[18], Peter Kaatsch[14], Melanie Kaiser[14], Helena Linge[13], Monica Muraca[6], Neige Journy[3], Damien Llanas[3], Cristina Veres[3], Hilde Øfstaas[19], Ibrahima Diallo[3], Imene Mansouri[3], Cecile M Ronckers[11,12], Roderick Skinner[20], Jop C Teepen[11,12], Monica Terenziani[21], Finn Wesenberg[22], Thomas Wiebe[13], Carlotta Sacerdote[2], Zsuzsanna Jakab[23], Riccardo Haupt[6], Päivi Lähteenmäki[24], Lorna Zadravec Zaletel[25], Claudia E Kuehni[16,17], Jeanette F Winther[9,26], Leontien C Kremer[11,12], Lars Hjorth[13], Nadia Haddy[1,3], Florent de Vathaire[3], Raoul C Reulen[1]

Affiliations:

[1]Centre for Childhood Cancer Survivor Studies, Institute of Applied Health Research, Robert Aitken Building, University of Birmingham, Birmingham, UK.
[2]Childhood Cancer Registry of Piedmont, Cancer Epidemiology Unit, Department of Medical Sciences, University of Turin and AOU Città della Salute e della Scienza di Torino, Italy.
[3]Cancer and Radiation Team, Center for Research in Epidemiology and Population Health, INSERM U1018, University Paris Saclay, Gustave Roussy, Villejuif, France.
[4]Department of Pediatric oncology, Gustave Roussy, Université Paris-Saclay, Villejuif, France
[5]Department of Cancer Epidemiology and Prevention Research, Alberta Health Services, Calgary, Alberta, Canada
[6]Epidemiology and Biostatistics Unit, Istituto Giannina Gaslini, Genova, Italy.
[7]2nd Department of Pediatrics, Semmelweis University, Budapest, Hungary.
[8]Kepler Universitätsklinikum, Linz, Austria.
[9]Danish Cancer Society Research Center, Childhood Cancer research group, Copenhagen, Denmark.
[10]Boyne Research Institute, Drogheda, Ireland.
[11]Department of Pediatric Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, The Netherlands.
[12]Princess Máxima Center for Pediatric Oncology, Utrecht, The Netherlands.
[13]Lund University, Skane University Hospital, Department of Clinical Sciences, Paediatrics, Lund, Sweden.
[14]German Childhood Cancer Registry (GCCR), Institute of Medical Biostatistics, Epidemiology and Informatics, University Medical Center, Mainz, Germany.
[15]Children´s Hospital, Landspitali University Hospital, Reykjavik, Iceland.
[16]Swiss Childhood Cancer Registry, Institute of Social and Preventive Medicine, University of Bern, Switzerland.
[17]Department of Paediatrics, University Children's Hospital of Bern, University of Bern, Switzerland
[18]Foundation MBBM, Hemato-Oncology Center, University of Milano-Bicocca, via Cadore 38, 20900 Monza (MB), Italy.
[19]Norwegian National Advisory Unit on solid tumors in children, Norway.
[20]Great North Children's Hospital, Newcastle upon Tyne Hospitals NHS Foundation Trust, and Northern Institute of Cancer Research, Newcastle University, Newcastle upon Tyne, UK.
[21]Pediatric Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori , Milano, Italy.
[22]Norwegian Cancer Registry and Dept. of Pediatric Medicine, Oslo University Hospital and Institute of Clinical Medicine, Faculty of medicine, University of Oslo, Norway.
[23]Hungarian Childhood Cancer Registry, 2nd Department of Pediatrics, Semmelweis University, Budapest, Hungary.
[24]Turku University and Turku University Hospital, Department of Pediatric and Adolescent Medicine, Turku, Finland.
[25]Institute of Oncology, Ljubljana, Slovenia.
[26]Department of Clinical Medicine, Faculty of Health, Aarhus University, Aarhus, Denmark.
[27]Polytechnic School of Abomey-Calavi (EPAC), University of Abomey-Calavi, 01 P.O. Box 2009, Cotonou, Benin
[†]Deceased 27th November 2018 to whom this research is dedicated.

Background

Survivors of childhood cancers are at risk of developing subsequent primary leukemias (SPLs), but the long-term risks after 20 years following treatment are still unclear. We investigated the risk of SPLs in 5-year childhood cancer survivors using a large-scale pan-European (PanCareSurFup) cohort and evaluated variations in the risk by cancer and demographic factors.

Methods

This largest-ever assembled cohort comprises 69,460 5-year childhood cancer survivors from 12 European countries. Standardized incidence ratios (SIRs) and absolute excess risks (AERs) were calculated. Cumulative incidence was calculated accounting for competing risk of death.

Results

One hundred and fifteen survivors developed a SPL including 86 subsequent primary myeloid leukemias (SPML) and 17 subsequent primary lymphoid leukemias (SPLL); of these SPLs, 31 occurred beyond 20 years from first childhood cancer diagnosis. Compared with the general population, childhood cancer survivors had a 4-fold increased risk (SIR = 3.7; 95%CI: 3.1-4.5) of developing leukemia, and eight leukemias per 100,000 person-years (AER = 7.5; 95%CI: 6-9.2) occurred in excess of that expected. The risks remained significantly elevated beyond 20 years from first primary malignancy. Overall, the risk ratio for SPML (SIR = 5.8; 95%CI: 4.6-7.1) was higher than that for all other SPLs combined.

Conclusions

We demonstrate that beyond 20 years after childhood cancer diagnosis survivors experience an increased risk for SPLs compared to that expected from the general population. Our findings show that awareness for symptoms potentially related to subsequent leukemias among long-term survivors of childhood cancer needs to continue well into middle age.