

ABSTRACT

J Clin Oncol. 2022 Dec 22;JCO2102968. doi: 10.1200/JCO.21.02968. Online ahead of print.

Outcomes of Infants and Young Children With Relapsed Medulloblastoma After Initial Craniospinal Irradiation-Sparing Approaches: An International Cohort Study.

Erker C(1), Mynarek M(2)(3), Bailey S(4), Mazewski CM(5), Baroni L(6), Massimino M(7), Hukin J(8), Aguilera D(5), Cappellano AM(9), Ramaswamy V(10), Lassaletta A(11), Perreault S(12), Kline CN(13), Rajagopal R(14), Michael G(15), Zapotocky M(16), Santa-Maria Lopez V(17), La Madrid AM(17), Cacciotti C(18)(19), Sandler ES(20), Hoffman LM(21), Klawinski D(20), Khan S(22)(23), Salloum R(10), Hoppmann AL(24), Larouche V(25), Dorris K(26), Toledano H(27), Gilheeneey SW(28), Abdelbaki MS(29)(30), Wilson B(31), Tsang DS(32), Knipstein J(33), Oren MY(34), Shah S(35), Murray JC(36), Ginn KF(37), Wang ZJ(38), Fleischhack G(39), Obrecht D(2), Tonn S(2), Harrod VL(40), Matheson K(41), Crooks B(42), Strother DR(43), Cohen KJ(44), Hansford JR(45), Mueller S(46), Margol A(15), Gajjar A(47), Dhall G(23), Finlay JL(28), Northcott PA(48), Rutkowski S(2), Clifford SC(4), Robinson G(47), Bouffet E(10), Lafay-Cousin L(43).

Author information:

- (1)Division of Hematology/Oncology, Department of Paediatrics, IWK Health Centre and Dalhousie University, Halifax, NS, Canada.
- (2)Department of Pediatric Hematology and Oncology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.
- (3)Mildred Scheel Cancer Career Center HaTriCS4, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.
- (4)Wolfson Childhood Cancer Research Centre, Newcastle University Centre for Cancer, Newcastle-upon-Tyne, United Kingdom.
- (5)Children's Healthcare of Atlanta & Emory University, Atlanta, GA.
- (6)Hospital of Pediatrics SAMIC Prof. Dr Juan P. Garrahan, Buenos Aires, Argentina.
- (7)Fondazione Istituto Di Ricovero e Cura a Carattere Scientifico, Istituto Nazionale dei Tumori, Milan, Italy.
- (8)Divisions of Neurology and Hematology, Oncology/ Bone Marrow Transplant, Department of Pediatrics, British Columbia Children's Hospital and University of British Columbia, Vancouver, BC, Canada.
- (9)Division of Pediatric Oncology/BMT, Instituto de Oncologia Pediátrica-GRAACC-UNIFESP, São Paulo, Brazil.
- (10)Division of Haematology/Oncology, Department of Paediatrics, The Hospital for Sick Children and University of Toronto, Toronto, ON, Canada.
- (11)Department of Pediatric Hematology and Oncology, Hospital Infantil Universitario Niño Jesús, Madrid, Spain.
- (12)Centre Hospitalier Universitaire Sainte, Justine, Université de Montreal, Montreal, QC, Canada.
- (13)Division of Oncology, The Children's Hospital of Philadelphia, Philadelphia, PA.
- (14)Division of Hematology-Oncology, Department of Pediatrics, University Malaya Medical Center, Kuala Lumpur, Malaysia.
- (15)Cancer and Blood Disease Institute, Children's Hospital Los Angeles, Keck School of Medicine of University of Southern California, Los Angeles, CA.
- (16)Department of Paediatric Haematology and Oncology, Second Faculty of Medicine, Charles University and University Hospital Motol, Prague, Czech Republic.
- (17)Department of Oncology, Hospital Sant Joan de Déu, Barcelona, Spain.
- (18)Division of Pediatric Hematology/Oncology, Western University, London, ON, Canada.
- (19)Dana Farber/Boston Children's Cancer and Blood Disorder Center, Boston, MA.
- (20)Nemours Children's Health, Wolfson's Children's Hospital & University of Florida, Jacksonville, FL.

- (21)Center for Cancer and Blood Disorders, Phoenix Children's Hospital, Phoenix, AZ.
- (22)Monash Children's Cancer Centre, Monash Children's Hospital. Monash Health. Center for Cancer Research, Hudson Institute of Medical Research, and Department of Molecular and Translational Science, School of Medicine, Nursing and Health Science, Monash University, Melbourne, Australia.
- (23)Division of Hematology, Oncology & Bone Marrow Transplant, Nationwide Children's Hospital, The Ohio State University, Columbus, OH.
- (24)Department of Pediatrics, Division of Hematology-Oncology, University of Alabama at Birmingham, Birmingham, AL.
- (25)Department of Pediatrics, Centre Mère-enfant Soleil du CHU de Québec, CRCHU de Québec, Université Laval, Quebec City, QC, Canada.
- (26)Children's Hospital of Colorado & University of Colorado School of Medicine, Denver, CO.
- (27)Schneider Children's Medical Center of Israel, Petah Tikva, and Sackler faculty of Medicine, Tel Aviv University, Israel.
- (28)Department of Pediatrics, Memorial Sloan-Kettering Cancer Center, New York, NY.
- (29)Division of Hematology, Oncology and Blood and Marrow Transplant, Nationwide Children's Hospital and The Ohio State University, Columbus, OH.
- (30)Division of Pediatric Hematology, Oncology, and Bone Marrow Transplant, Washington University School of Medicine in St Louis, St Louis, MO.
- (31)Department of Pediatrics, Stollery Children's Hospital, University of Alberta, Edmonton, AB, Canada.
- (32)Radiation Medicine Program, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada.
- (33)Division of Pediatric Hematology/Oncology/BMT, Medical College of Wisconsin, Milwaukee, WI.
- (34)Pediatric Hemato-Oncology Department, Sheba Medical Center at Tel HaShomer, Ramat Gan, Israel.
- (35)The University of Texas Health Science Center, Department of Pediatric Hematology-Oncology, San Antonio, TX.
- (36)Division of Pediatric Hematology/Oncology, Cook Children's Medical Center, Fort Worth, TX.
- (37)Division of Pediatric Hematology and Oncology, Children's Mercy Hospital, Kansas City, MO.
- (38)Division of Hematology and Oncology, Children's Hospital of Richmond and Virginia Commonwealth University, Richmond, VA.
- (39)Pediatric Hematology and Oncology, Pediatrics III, University Hospital of Essen, Essen, Germany.
- (40)Departments of Pediatric Hematology and Oncology, Dell Children's Medical Center of Central Texas and University of Texas, Austin, TX.
- (41)Research Methods Unit, Nova Scotia Health Authority, Halifax, NS, Canada.
- (42)Division of Haematology/Oncology, Department of Paediatrics, IWK Health Centre and Dalhousie University, Halifax, NS, Canada.
- (43)Section of Pediatric Hematology and Bone Marrow Transplantation, Alberta Children's Hospital, Calgary, AB, Canada.
- (44)Pediatric Oncology, The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD.
- (45)Children's Cancer Centre, Royal Children's Hospital; Murdoch Children's Research Institute; University of Melbourne, Melbourne, Australia.
- (46)Department of Pediatrics, University of California San Francisco, San Francisco, CA.
- (47)Department of Oncology, St Jude Children's Research Hospital, Memphis, TN.
- (48)Department of Developmental Neurobiology, St Jude Children's Research Hospital, Memphis, TN.

PURPOSE: Infant and young childhood medulloblastoma (iMB) is usually treated without craniospinal irradiation (CSI) to avoid neurocognitive late effects. Unfortunately, many children relapse. The purpose of this study was to assess salvage strategies and prognostic features of patients with iMB who relapse after CSI-sparing therapy.

METHODS: We assembled a large international cohort of 380 patients with relapsed iMB, age younger than 6 years, and initially treated without CSI. Univariable and multivariable Cox models of postrelapse survival (PRS) were conducted for those treated with curative intent using propensity score analyses to account for confounding factors.

RESULTS: The 3-year PRS, for 294 patients treated with curative intent, was 52.4% (95% CI, 46.4 to 58.3) with a median time to relapse from diagnosis of 11 months. Molecular subgrouping was available for 150 patients treated with curative intent, and 3-year PRS for sonic hedgehog (SHH), group 4, and group 3 were 60%, 84%, and 18% ($P = .0187$), respectively. In multivariable analysis, localized relapse ($P = .0073$), SHH molecular subgroup ($P = .0103$), CSI use after relapse ($P = .0161$), and age ≥ 36 months at initial diagnosis ($P = .0494$) were associated with improved survival. Most patients (73%) received salvage CSI, and although salvage chemotherapy was not significant in multivariable analysis, its use might be beneficial for a subset of children receiving salvage CSI < 35 Gy ($P = .007$).

CONCLUSION: A substantial proportion of patients with relapsed iMB are salvaged after initial CSI-sparing approaches. Patients with SHH subgroup, localized relapse, older age at initial diagnosis, and those receiving salvage CSI show improved PRS. Future prospective studies should investigate optimal CSI doses and the role of salvage chemotherapy in this population.

DOI: 10.1200/JCO.21.02968
PMID: 36548930