

Combining brentuximab vedotin with dexamethasone, high-dose cytarabine and cisplatin as salvage treatment in relapsed or refractory Hodgkin lymphoma: the phase II HOVON/LLPC Transplant BRaVE study

Marie José Kersten,^{1,2*} Julia Driessen,^{1*} Josée M. Zijlstra,^{2,3} Wouter J. Plattel,^{2,4} Franck Morschhauser,⁵ Pieternella J. Lugtenburg,^{2,6} Pauline Brice,⁷ Martin Hutchings,⁸ Thomas Gastinne,⁹ Roberto Liu,¹ Coreline N. Burggraaf,³ Marcel Nijland,^{2,4} Sanne H. Tonino,^{1,2} Anne I.J. Arens,¹⁰ Roelf Valkema,¹¹ Harm van Tinteren,¹² Marta Lopez-Yurda,¹² Arjan Diepstra,^{2,13} Daphne De Jong^{2,14} and Anton Hagenbeek^{1,2}

¹Department of Hematology, Amsterdam UMC, University of Amsterdam, LYMMCARE (Lymphoma and Myeloma Center Amsterdam), Cancer Center Amsterdam, Amsterdam, the Netherlands; ²HOVON and Lunenburg Lymphoma Phase I/II Consortium (LLPC), the Netherlands; ³Department of Hematology, Amsterdam UMC, Vrije Universiteit Amsterdam, Cancer Center Amsterdam, Amsterdam, the Netherlands; ⁴Department of Hematology, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands; ⁵Department of Hematology, Centre Hospitalier Universitaire, Lille, France; ⁶Department of Hematology, Erasmus MC Cancer Institute, Erasmus University Medical Center, Rotterdam, the Netherlands; ⁷Department of Hematology, Hopital Saint Louis, Paris, France; ⁸Department of Hematology, Rigshospitalet, Copenhagen, Denmark; ⁹Department of Hematology, Centre Hospitalier Universitaire, Nantes, France; ¹⁰Department of Radiology and Nuclear Medicine, Radboud University Medical Center, Nijmegen, the Netherlands; ¹¹Department of Radiology and Nuclear Medicine, Erasmus University Medical Center, Rotterdam, the Netherlands; ¹²Department of Biometrics, Netherlands Cancer Institute, Amsterdam, the Netherlands; ¹³Department of Pathology and Medical Biology, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands and ¹⁴Department of Pathology, Amsterdam UMC, Vrije Universiteit Amsterdam, Cancer Center Amsterdam, Amsterdam, the Netherlands; HOVON Pathology Facility and Biobank, Amsterdam, the Netherlands

*MJK and JD contributed equally as co-first authors.

ABSTRACT

Achieving a metabolic complete response (mCR) before high-dose chemotherapy (HDC) and autologous peripheral blood stem cell transplant (auto-PBSCT) predicts progression-free survival (PFS) in relapsed/refractory classical Hodgkin lymphoma (R/R cHL). We added brentuximab vedotin (BV) to DHAP (dexamethasone, high-dose cytarabine, cisplatin) to improve the mCR rate. In a phase I dose-escalation part of the study in 12 patients, we showed that BV-DHAP is feasible. This phase II study included 55 R/R cHL patients (23 primary refractory). Treatment consisted of three 21-day cycles of BV 1.8 mg/kg on day 1, and DHAP (dexamethasone 40 mg days 1-4, cisplatin 100 mg/m² day 1 and cytarabine 2x2 g/m² day 2). Patients with a metabolic partial response (mPR) or mCR proceeded to HDC/auto-PBSCT. Based on independent central [¹⁸F]fluorodeoxyglucose (FDG) - positron emission tomography (PET) - computed tomography (CT) scan review, 42 of 52 evaluable patients (81% [95%CI: 67-90]) achieved an mCR before HDC/auto-PBSCT, five had an mPR and five had progressive disease (3 were not evaluable). After HDC/auto-PBSCT, four patients with an mPR converted to an mCR. Two-year PFS was 74% [95%CI: 63-86] and overall survival 95% [95%CI: 90-100]. Toxicity was manageable and mainly consisted of grade 3/4 hematologic toxicity, fever, nephrotoxicity, ototoxicity (grade 1/2), and transiently elevated liver enzymes during BV-DHAP. Eighteen patients developed new onset peripheral neuropathy (maximum grade 1/2); all recovered. In conclusion, BV-DHAP is a very effective salvage regimen in R/R cHL patients, but patients should be monitored closely for toxicity. (*clinicaltrials.gov* identifier: NCT02280993).



Ferrata Storti Foundation

Haematologica 2021
Volume 106(4):1129-1137

Correspondence:

MARIE JOSÉ KERSTEN
m.j.kersten@amsterdamumc.nl

Received: November 18, 2019.

Accepted: March 19, 2020.

Pre-published: April 9, 2020.

<https://doi.org/10.3324/haematol.2019.243238>

©2021 Ferrata Storti Foundation

Material published in *Haematologica* is covered by copyright. All rights are reserved to the Ferrata Storti Foundation. Use of published material is allowed under the following terms and conditions:

<https://creativecommons.org/licenses/by-nc/4.0/legalcode>.

Copies of published material are allowed for personal or internal use. Sharing published material for non-commercial purposes is subject to the following conditions:

<https://creativecommons.org/licenses/by-nc/4.0/legalcode>, sect. 3. Reproducing and sharing published material for commercial purposes is not allowed without permission in writing from the publisher.

