

Call for Grants

The intent of this document is to encourage organizations with a focus in continuing medical education (CME) for healthcare professionals to submit an application for funding that is related to **New developments shaping treatment decisions in relapsed/refractory Hodgkin Lymphoma.**

Please note that applications must be submitted in English

Date: December 14, 2020

From: Global Medical Affairs, Takeda Oncology

Re: New developments shaping treatment decisions in relapsed/refractory Hodgkin Lymphoma

Therapeutic area: Hodgkin Lymphoma

Background: The mission of the Takeda Oncology Call for Grants program is to partner with qualified organizations to meet unmet educational needs, encourage improvement in patient outcomes, and/or promote excellence in patient care. The initiatives funded are independent, meaning that projects are the full responsibility of the recipient organization. Takeda has no influence over any aspect of the project and only asks for reports about the results and impact of the projects in order to share them publicly.

Eligibility: Collaborations within institutions, and between different organizations, are encouraged. All partners must have a relevant role, with the requesting organization being the primary contact with Takeda and responsible for ensuring the grant agreement is adhered to. All funding will be awarded to the requesting organization. For collaborative applications, all partners must submit a letter describing their competencies, experience and roles within the project.

Educational objective: There are many treatment options available for Hodgkin lymphoma (HL). While Hodgkin lymphoma is treatable, especially in its early stages, each treatment failure complicates the subsequent course of therapy. The purpose of this call for grants is to support educational programs designed to improve healthcare professionals (HCPs) knowledge of key factors known to influence treatment selection in relapsed/refractory HL patients.

Specific topics of interest for this call for grants:

- Rationalizing decisions on first salvage therapy options in HL
- Combining various mechanisms of actions to achieve optimal outcomes in relapsed/refractory patients
- Treatment sequencing scenarios for common relapsed/refractory patient types
- Value of post-autologous stem cell transplant (ASCT) consolidation therapy in light of novel frontline treatment options
- Impact of real-world evidence (RWE) on treatment selection in relapsed/refractory HL
- The role of allogeneic stem cell transplant (allo-SCT) in the era of increasing use of newer agents in HL

Our goal is to provide HCPs with the knowledge to enable them to select optimal treatment (sequences) for individual patients with relapsed/refractory Hodgkin Lymphoma.

Summary of healthcare gaps: Hodgkin lymphoma (HL), a relatively uncommon B cell malignancy, has the second highest societal burden of all malignancies (Hanly et al., 2014). This high societal burden is due to the relatively young age of many patients and lost productivity due to premature mortality. In 40 – 48% of newly diagnosed HL patients this disease has already reached an advanced stage (stage III/IV disease or earlier stage disease with high-risk features) (Bray et al., 2018; Global Cancer Observatory; Engert et al., 2005). Multi-agent chemotherapy regimens are a mainstay therapy in the first-line, second-line, and salvage treatment of patients with advanced HL (NCCN 2020; Eichenauer et al., 2014). The salvage therapy options for patients with advanced HL are limited and associated with substantial treatment burden. For most patients with R/R HL, salvage treatment choices are not optimal, and often consist of high-dose chemotherapy followed by autologous stem cell transplant (ASCT) (NCCN 2020; Eichenauer et al., 2014; Majhail et al., 2006). Many of the multi-agent chemotherapy regimens used in R/R HL patients are associated with severe toxicities and side effects (Borchmann et al., 1998; Nikolaenko et al., 2017; Gotti et al., 2013).

Patients who relapse after ASCT or patients not eligible for transplant historically have experienced poor outcomes. After ASCT failure, the median survival is 16 – 29 months (Martínez et al., 2013; Arai et al., 2013). If a patient relapses within 1 year of ASCT, the median survival is less than a year (Arai et al., 2013). Allogenic SCT can be an option after ASCT, but the toxicity is high (Sureda et al., 2011; Genadieva-Stavrik et al., 2016; Jacobsohn et al., 2007; Lee et al., 2017). After an allogenic SCT, about half of patients will experience graft versus host disease and 1 in 2 will relapse or have disease progression (Sureda et al., 2011; Genadieva-Stavrik et al., 2016). Treatment options for R/R HL in elderly patients are limited as they are often deemed ineligible for ASCT due to frailty and level of comorbidities (Boli et al., 2013). With the introduction of novel agents to the therapy of HL, such as checkpoint inhibitors and antibody drug conjugates, new options are available for patients after ASCT and patients ineligible for ASCT (Dahi 2019).

Pre-transplant risk factors have been identified that place a patient at a high risk for failing ASCT. Disease-related and patient-related pre-transplant risk factors may increase the chance of early post-transplant progression or death (Josting et al., 2010, Sureda et al., 2005, Moskowitz et al., 2001, Devillier et al., 2012). Increasing numbers of risk factors further elevate the risk of relapse following ASCT (Moskowitz et al., 2001; Josting et al., 2010). Effective pre-transplant treatment options that achieve CR are needed to improve the success of transplant (Czyz et al., 2004; Devillier et al., 2012). Novel agents are also investigated to improve the outcomes of ASCT: Recent approaches for salvage therapy combine novel agents and classical chemotherapy to increase the amount of patients achieving a CR pre-transplant. Consolidative therapy after ASCT for patients with increased risk for relapse demonstrated reduction in the risk of progression after ASCT (Voorhees et al., 2020; Castagna et al., 2020; Moskowitz et al., 2019).

Several novel agents are approved by EMA and FDA for treatment of r/r HL in different lines of therapy (Vassilakopoulos et al., 2020). The application of the novel agents as monotherapy improved the prognosis of r/r HL patients (Kallam et al., 2019). Open questions remain, such as if efficacy can be further improved by combining several novel agents or what the optimal sequencing of traditional chemotherapy regimens, the different novel agents, ASCT, and allo SCT will be in the future (Wang et al., 2018; Voorhees et al., 2020).

As not all these questions are investigated in clinical trials, evidence from RWE is of increasing importance for treatment decisions in r/r HL (Vassilakopoulos et al., 2020; Bair et al., 2017).

Target audience: We welcome applications that target academic and community oncologists, pathologists, histologists, nurses, pharmacists and other healthcare specialties. First priority will be given to those applications that primarily target physicians (hematologists/oncologists) with second priority given to other healthcare professionals.

Educational format: Virtual formats will be accepted, with a preference for a combined format involving an interactive virtual component and an online enduring component that enable interaction between attendees, encourage discussion and sharing of resources related to HCPs perceived and real needs in terms of finding the optimal treatment plan for patients. Innovative learning formats that incorporate the patient perspective and assist HCPs to develop a treatment plan after considering individual patient symptoms, needs and preferences are also encouraged.

Outcomes measures: The educational evaluation plan must be designed to objectively measure improvements in HCP knowledge and competence (level 3 and above). The evaluation plan will include quantitative and qualitative evidence that the educational program has had an impact on HCP behavior.

References:

- Arai S, Fanale M, deVos S, Engert A, Illidge T, Borchmann P, et al. Defining a Hodgkin lymphoma population for novel therapeutics after relapse from autologous hematopoietic cell transplant. *Leukemia & Lymphoma*. 2013/6/5;54(11): 2531-2533.
- Bair SM, Strelec L, Nagle SJ, et al. Outcomes of patients with relapsed/refractory Hodgkin lymphoma progressing after autologous stem-cell transplant in the current era of novel therapeutics: a retrospective analysis. *Am J Hematol* 2017; 92: 879–884.
- Böll B, Goergen H, Arndt N, Meissner J, Krause SW, Schnell R, et al. Relapsed Hodgkin Lymphoma in Older Patients: A Comprehensive Analysis From the German Hodgkin Study Group. *Journal of Clinical Oncology*. 2013/12/10;31(35): 4431-4437..
- Borchmann P, Schnell R, Diehl V, Engert A. New drugs in the treatment of Hodgkin's disease. *Annals of Oncology*. 1998/1/1;9(suppl 5): S103-S108.
- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*. 2018/9/12;68(6): 394-424.
- Castagna L, Santoro A, Carlo-Stella C. Salvage Therapy for Hodgkin's Lymphoma: A Review of Current Regimens and Outcomes. *J Blood Med*. 2020; 11: 389–403.
- Czyz J. Outcome and prognostic factors in advanced Hodgkin's disease treated with high-dose chemotherapy and autologous stem cell transplantation: a study of 341 patients. *Annals of Oncology*. 2004/8/1;15(8): 1222-1230.
- Dahi PB, Moskowitz CH, Giralto SA, Lazarus HM (2019) Novel agents positively impact chemotherapy and transplantation in Hodgkin lymphoma, *Expert Review of Hematology*, 12:4, 255-264.
- Devillier R, Coso D, Castagna L, Brenot Rossi I, Anastasia A, Chiti A, et al. Positron emission tomography response at the time of autologous stem cell transplantation predicts outcome of patients with relapsed and/or refractory Hodgkin's lymphoma responding to prior salvage therapy. *Haematologica*. 2012/1/22;97(7): 1073-1079.

Eichenauer DA, Engert A, Andre M, Federico M, Illidge T, Hutchings M, et al. Hodgkin's lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*. 2014/7/25;25(suppl 3): iii70-iii75.

Engert A, Ballova V, Haverkamp H, Pfistner B, Josting A, Dühmke E, et al. Hodgkin's Lymphoma in Elderly Patients: A Comprehensive Retrospective Analysis From the German Hodgkin's Study Group. *Journal of Clinical Oncology*. 2005/8;23(22): 5052-5060.

Genadieva-Stavrik S, Boumendil A, Dreger P, Peggs K, Briones J, Corradini P, et al. Myeloablative versus reduced intensity allogeneic stem cell transplantation for relapsed/refractory Hodgkin's lymphoma in recent years: a retrospective analysis of the Lymphoma Working Party of the European Group for Blood and Marrow Transplantation. *Annals of Oncology*. 2016/10/24;27(12): 2251-2257.

Global Cancer Observatory.

Gotti M, Fiaccadori V, Bono E, Landini B, Varettoni M, Arcaini L, et al. Therapy-Related Late Adverse Events in Hodgkin's Lymphoma. *Lymphoma*. 2013;2013: 1-7.

Hanly P, Soerjomataram I, Sharp L. Measuring the societal burden of cancer: The cost of lost productivity due to premature cancer-related mortality in Europe. *International Journal of Cancer*. 2014/9/4;136(4): E136-E145.

Jacobsohn DA, Vogelsang GB. Acute graft versus host disease. *Orphanet Journal of Rare Diseases*. 2007/9/4;2(1).

Josting A, Müller H, Borchmann P, Baars JW, Metzner B, Döhner H, et al. Dose Intensity of Chemotherapy in Patients With Relapsed Hodgkin's Lymphoma. *Journal of Clinical Oncology*. 2010/12;28(34): 5074-5080.

Kallam A, Vose JM. Hope After Salvage Therapy Fails: Novel Agents for Relapsed/Refractory Hodgkin Lymphoma. *Oncology (Williston Park)*. 2019 May 14;33(5):192-8.

Lee SJ. Classification systems for chronic graft-versus-host disease. *Blood*. 2017/1/5;129(1): 30-37.

Majhail NS, Weisdorf DJ, Defor TE, Miller JS, McGlave PB, Slungaard A, et al. Long-Term Results of Autologous Stem Cell Transplantation for Primary Refractory or Relapsed Hodgkin's Lymphoma. *Biology of Blood and Marrow Transplantation*. 2006/10;12(10): 1065-1072.

Martínez C, Canals C, Sarina B, Alessandrino EP, Karakasis D, Pulsoni A, et al. Identification of prognostic factors predicting outcome in Hodgkin's lymphoma patients relapsing after autologous stem cell transplantation†. *Annals of Oncology*. 2013/5/26;24(9): 2430-2434.

Medula Osea (GEL/TAMO) and the Lymphoma Working Party of the European Group for Blood and Marrow Transplantation. *Haematologica*. 2011/10/11;97(2): 310-317. NCCN clinical practice guidelines Hodgkin lymphoma v1.2020. https://www.nccn.org/professionals/physician_gls/default.aspx. 2020

Moskowitz AJ, Herrera AF, Beaven AW. Relapsed and Refractory Classical Hodgkin Lymphoma: Keeping Pace with Novel Agents and New Options for Salvage Therapy. *American Society of Clinical Oncology Educational Book 39 (May 17, 2019)* 477-486.

Moskowitz CH, Nimer SD, Zelenetz AD, Trippett T, Hedrick EE, Filippa DA, et al. A 2-step comprehensive high-dose chemoradiotherapy second-line program for relapsed and refractory Hodgkin disease: analysis by intent to treat and development of a prognostic model. *Blood*. 2001/2/1;97(3): 616-623.

Nikolaenko L, Chen R, Herrera AF. Current strategies for salvage treatment for relapsed classical Hodgkin lymphoma. *Therapeutic Advances in Hematology*. 2017/8/29;8(10): 293-302.

Sureda A, Canals C, Arranz R, Caballero D, Ribera JM, Brune M, et al. Allogeneic stem cell transplantation after reduced intensity conditioning in patients with relapsed or refractory Hodgkin's lymphoma. Results of the HDR-ALLO study - a prospective clinical trial by the Grupo Espanol de Linfomas/Trasplante de

Sureda A, Constans M, Iriondo A, Arranz R, Caballero MD, Vidal MJ, et al. Prognostic factors affecting long-term outcome after stem cell transplantation in Hodgkin's lymphoma autografted after a first relapse. *Annals of Oncology*. 2005/4/1;16(4): 625-633.

Vassilakopoulos TP, Asimakopoulos JV, Konstantopoulos K, Angelopoulou MK. Optimizing outcomes in relapsed/refractory Hodgkin lymphoma: a review of current and forthcoming therapeutic strategies. *Ther Adv Hematol*. 2020; 11: 2040620720902911.

Voorhees TJ, Beaven AW. Therapeutic Updates for Relapsed and Refractory Classical Hodgkin Lymphoma. *Cancers (Basel)*. 2020 Oct; 12(10): 2887.

Wang, Y., Nowakowski, G.S., Wang, M.L. et al. Advances in CD30- and PD-1-targeted therapies for classical Hodgkin lymphoma. *J Hematol Oncol* 11, 57 (2018). <https://doi.org/10.1186/s13045-018-0601-9>.

Submission requirements: When responding, please follow the established guidelines for the Takeda medical education grant submission process. All applications must be submitted at <http://www.takedaoncology.com/partnerships/grants--donations/>

The education must be accredited by the appropriate accrediting bodies, be fully compliant with ACCME criteria and the Standards for Commercial Support and must be in accordance with the U.S. Food and Drug Administration's Guidance on Industry-Supported Scientific and Educational Activities. If accepted, must attest to the terms, conditions and purposes of an educational grant as described in the Takeda letter of agreement.

Geographic region: [Europe, Latin America, & Asia Pacific]

Length of proposed project: 12 months

Expected approximate monetary range of awarded proposals: Projects (consisting of multiple smaller educational pieces in a variety of formats or one large educational piece) requesting up to \$120,000 will be considered. The amount of the grant Takeda Oncology will fund for any project will depend on the Review Committee's evaluation of the proposal and costs involved and will be stated clearly in the approval notification.

Preference will be given to proposals that address ALL of the following:

- 1. Overview of requesting organization:** Please describe the organization requesting the grant, including its history, current mission, a list of key officers and staff who will direct the program; and descriptions of any other participating organizations/partners. Describe any experience your organization has in working in this area.
- 2. Abstract:** Please provide a summary (750-word maximum) of your proposed project, including a brief assessment of needs in the target population.
- 3. Goals and implementation plan:** Provide a clear description of program goals, implementation plan, target audience, and an anticipated timeline of project activities and milestones. Please indicate whether the project will be integrated into an existing program; if yes, please describe the existing

program, how this project will be integrated, and the additional impact that is expected if funding is awarded.

4. **Budget:** Please provide a detailed itemized budget for the proposed project. Please also include a narrative justification for the requested amount.
5. **Reach and impact:** Please describe the planned reach for your program, as well as the estimated impact the program will have on your intended audience. Please include any currently available baseline data.
6. **Collaboration:** If your project is collaborative in nature, please describe the roles and capabilities of each partner.
7. **Evaluation:** Specify how you will define and measure success for each of the proposed activities; indicate how the program will be measured and evaluated, and how results will be reported.
8. **Reporting:** Please specify the descriptive and evaluative reporting results that you will provide. For projects that are funded for longer than six-months, interim reporting is required. A final report is due at the end of the funded activities, including reporting of funding used to inform reconciliation of unused funding.
9. **Sustainability/replicability:** Describe any plans to broadly disseminate the proposed program's results and ensure sustainability beyond the funding period. Describe how the proposed program could serve as a model in other geographic regions or to serve different populations.
10. **Terms and conditions:** Please take note that every Call for Grants released by Takeda Oncology is governed by specific terms and conditions. Please review these terms and conditions, posted here [LINK TO TERMS AND CONDITIONS].
11. **Additional submission requirements:**
 - Letter of commitment from any partner organizations
 - Most recent audited financial statement
 - IRS 501(c)(3) letter (if applicable)
 - Current annual report
 - Current operating budget
 - Biographies of key staff

Key dates: Call for Grants release date: 12/14/2020
Full proposal deadline: 1/29/2021
Review of proposals by review committee starts: 2/1/2021
Anticipated proposal notification date: 2/19/2021

Grants will be distributed following the execution of a fully signed Letter of Agreement.

How to submit: Instructions on submitting can be found at:
<http://www.takedaoncology.com/partnerships/grants--donations/>

Questions: If you have any questions, please direct them in writing to Sarah Willette, Manager Congresses, Outreach and Medical Education (sarah.willette@takeda.com) with the subject line "(Call for Grants HL)".