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 Optimizing the Use of Tyrosine Kinase Inhibitors in Relapsed or Refractory Chronic Myeloid Leukemia.

Please note that applications must be submitted in English

Date: November 23, 2020
From: Global Medical Affairs, Takeda Oncology
Re: Optimizing the Use of Tyrosine Kinase Inhibitors in Relapsed or Refractory Chronic Myeloid Leukemia

Therapeutic area: Chronic Myeloid Leukemia (CML)

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: The introduction of BCR-ABL1 tyrosine kinase inhibitors (TKIs) have drastically improved CML outcomes. With 3 generations of TKIs available for clinicians, it is important they review and understand each TKI’s risks and benefits. Understanding this risk-benefit becomes particularly important in patient’s that may become relapsed or refractory after their first line of treatment. The purpose of this call for grants is to support educational initiatives designed to improve healthcare providers (HCPs) understanding and knowledge of the latest data surrounding the risk-benefit balances of the various TKIs and how to optimally manage these TKIs.

Specific CML topics of interest for this call for grants:

- Monitoring CML patients and outcomes of patients in relapsed refractory setting (including intolerance and resistant patients with and without mutations)
- Cross TKI toxicity management including vascular toxicity

Our goal is to provide HCPs with the knowledge to enable the optimal selection of a TKI for their relapsed or refractory CML patient while taking into account each patient’s individual needs.

Summary of healthcare gaps: CML accounts for 14% of all newly diagnosed leukemia cases in the United States and the prevalence in 2020 is expected to reach 112,000 (Huang et al., 2012; American Cancer
About 95% of CML patients have the Philadelphia chromosome, a genetic aberration generated by the translocation of the ABL1 gene from chromosome 9 to the BCR region on chromosome 22, resulting in the formation of the BCR-ABL1 oncoprotein (Hughes et al., 2016; Ronson et al., 2017; Jabbour et al., 2016).

As of 2018, there are 5 currently approved BCR-ABL1 tyrosine kinase inhibitors (TKIs) for use in treating CML (Novartis 2017; Bristol-Myers Squibb 2017; Novartis 2020; Takeda 2017; Pfizer 2012). These TKIs are commonly grouped according to generations where second-generation TKIs (dasatinib, nilotinib, and bosutinib) have demonstrated activity in patients resistant or intolerant to first-generation imatinib, and third-generation ponatinib demonstrated activity in patients resistant or intolerant to second-generation TKIs. During the first-line of therapy 9-18% and 5-11% chronic phase-CML (CP-CML) patients acquired resistance to first- and second-generation TKI treatment (Brümmendorf et al., 2015; Hochhaus et al., 2013; Hughes et al., 2015). During the second-line of therapy 21-33% of CP-CML patients acquire resistance to a second-generation TKI treatment (Soverini et al., 2014). During the third-line of therapy up to 43% of CP-CML patients acquire resistance to a second-generation TKI treatment (Ribeiro et al., 2015). The results of a meta-analysis demonstrated the probabilities of achieving major cytogenetic response (MCyR) and complete cytogenetic response (CCyR) with second-generation TKIs in the third-line setting are between 29-50% and 22-26%, respectively (Lipton et al., 2015). In the third-line setting, 2nd generation TKI’s therapeutic utility may be limited and clinicians should consider other options based on the probability of response (Patel et al., 2017). Collectively, this indicates patients who are resistant or intolerant to earlier-generation TKIs experience poor long-term outcomes.

Mutations in the BCR-ABL1 oncoprotein, particularly T351I, can confer clinical resistance to all first and second generation TKIs. Second-generation TKIs are more effective than first-generation imatinib in inhibiting a variety of clinically relevant BCR-ABL1 mutants, but several key mutations, including the T315I gatekeeper mutation, still confer resistance to these drugs (Gozgot et al., 2013). Approximately 13-63% of CML patients with BCR-ABL kinase domain mutations have the T315I mutation, which confers resistance to all first- and second-generation TKIs (Ursan et al., 2015; Hochhaus et al., 2013). Mutation rates increase from 5% in first-line therapy to 43% in subsequent lines of therapy in CP-CML patients (Hochhaus et al., 2013; Ribbeiro et al., 2015). Rapid reduction of disease burden combined with maximal inhibition of BCR-ABL kinase activity should therefore minimize the mutation risk on therapy, providing a rationale for up-front therapy with more potent ABL inhibitors in patients with meaningful responses in a resistant setting and with mutations (including T315I) (O’Hare et al., 2007).

In addition to considerations related to efficacy, when selecting a TKI for a patient, it is important to consider each TKIs toxicity profile. All BCR-ABL1 TKIs have varying toxicity profiles that need to be understood and these toxicity profiles play a role in treatment decision making. One toxicity that is often a concern among providers is cardiotoxicity. Cardiotoxicity is seen with all of the BCR-ABL1 TKIs (Caocci et al., 2020; Cirimi et al., 2020; Haguet et al., 2017). Leveraging existing guidance for TKI toxicity management is important including proper screening, monitoring, and management strategies for cardiovascular care (Li et al., 2015). Being able to determine a patient’s cardiovascular risks along with understanding TKIs cardiovascular and metabolic effects should allow for an even greater improvement in the treatment of CML (Manouchehri et al., 2020).

**Target audience:** We welcome applications that target academic and community oncologists, pathologists, histologists, nurse practitioners (NP), pharmacists, physician assistants (PA), and other healthcare specialties that interact with CML patients. First priority will be given to those applications
that primarily target academic and community physicians (hematologists/oncologists) with second priority given to pathologists, and third priority given to pharmacists, NPs and PAs.

**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 CML 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**


Gozgit JM, Schrock A, Chen T-H,Clarkson T, Rivera VM, et al. Comprehensive analysis of the in vitro potency of ponatinib, and all other approved BCR-ABL tyrosine kinase inhibitors (TKIs), against a panel of single and compound BCR-ABL mutants. Poster presented at: 55th Annual Meeting of the American Society of Hematology (ASH);ASH. 2013


Novartis Pharmaceuticals Corporation. East Hanover, NJ. GLEEVEC (Imatinib) [prescribing information]. 2017.


2017.


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: [United States]

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 $300,000 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 involve 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: 11/23/2020
- Full proposal deadline: 1/15/2021
- Review of proposals by review committee starts: 1/18/2021
- Anticipated proposal notification date: 2/1/2021

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 CML)”. 