**Bristol-Myers Squibb**

**Independent Medical Education**

**Request for Educational Support (RFE)**

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| **Date** | August 21, 2017 |
| **RFE Requestor Information** | Name: Sylvia Nashed, PharmD, RPh<br>Title: IME Specialist<br>Phone: 609-302-3320<br>E-mail: Sylvia.nashed@bms.com |
| **RFP Code** | RFE-17-ONC-121 |
| **Therapeutic Area** | Oncology |
| **Areas of Interest** | Immunotherapy<br>Hepatocellular Carcinoma (HCC) |
| **Educational Design** | Comprehensive educational initiative that includes a live satellite symposia at the ASCO-Gastrointestinal (GI) Cancers Symposium (January 18-20, 2018; San Francisco, CA) and web-based, and/or other enduring activities leveraging the medical content from the live meeting.<br><br>• The activities should measure improvement of learners' knowledge, confidence, performance and competency and should achieve at least a Moore's Level 4 impact. |
| **Intended Audience** | • Oncologists, Interventional Radiologists, Hepatologists<br>• Multidisciplinary Oncology Team: Post-Doctoral Fellows, NPs, PAs, PharmDs, Pharmacists, Nurses, etc. |
| **Budget** | The maximum amount of BMS funding available for this RFE is $250,000.<br>Single or multi-supported initiatives will be considered. |
| **Accreditation** | ACCME and others as appropriate to the audience(s) |
| **Geographic Coverage** | United States |
| **Deadline for Submission** | September 15, 2017 by 5pm EST |

**Background**

Hepatocellular carcinoma (HCC) is one of the most common cancers in the world, with a global incidence of over 600,000 new cases per year. The majority of HCC cases are detected at an advanced or end stage.[1] The oral multikinase inhibitor, sorafenib, has been the standard of care systemic therapy for advanced HCC as first-line treatment. Until recently, there were no therapeutic agents approved for patients who progress post-sorafenib. In April 2017, regorafenib was approved for second-line treatment. However, additional options for therapies are still needed to improve survival and quality of life in patients with advanced HCC.

In HCC, tumor-infiltrating effector CD8+ T cells have increased PD-1 expression and decreased capacity for effector function. Overexpression of PD-1 and PD-L1 in HCC is associated with a poor clinical outcome. Upregulation of PD-1 receptor and its ligand, PD-L1, is associated with poor outcomes in resectable HCC.[2]

HCC primarily develops from cirrhosis, and many patients are infected with Hepatitis B or Hepatitis C.[3] Hepatitis B and hepatitis C virus infections are associated with manifestations of immune suppression, including upregulation of PD-1, T-cell exhaustion, and spontaneous apoptosis of immune cells.[4]

The mechanistic rationale supporting cancer immunotherapy rests on the premise that tumors can be recognized as foreign rather than as self and can be effectively attacked by an activated immune system. An effective immune response in this setting is thought to rely on immune surveillance of tumor antigens expressed on cancer cells that ultimately results in an adaptive immune response and cancer cell death. Oncologists, interventional radiologists, hepatologists, as well as allied healthcare professionals are unaware of the role of immune checkpoint signaling in the regulation of tumor biology, and they consequently do not recognize the rationale for use of emerging immune checkpoint inhibitors for the management of advanced HCC. Further, they require education on efficacy and safety data of current and emerging treatment options, as well as management of toxicities associated with such treatment.

Due to the fragmented distribution of the rapidly increasing data available in the immuno-oncology area, an integration of the data in a live setting for a broad audience at a key professional meeting is warranted. Since many community oncologists and other healthcare professionals working in a multidisciplinary oncology team do not have the opportunity to attend live meetings, it is necessary and important to make the activities correlated with these meetings available through the internet/web-based modalities as well.

BMS is seeking applications for a well-designed, interactive and engaging satellite symposia live activity to be held at the 2018 ASCO-GI Cancers Symposium. The activity must include web based/enduring materials that will extend the reach to a broader target audience. The proposals must be focused on currently available systemic therapies and investigational therapies for advanced hepatocellular carcinoma, with a focus on review of clinical trial data around efficacy, safety, and tolerability. Available data on monotherapy and combination regimens for such therapies should also be

highlighted. Content must be current at the time of presentation and tailored for the intended audiences.

**Educational Needs and Professional Practice Gaps:**

The treatment of HCC with immuno-oncology (IO) is a rapidly evolving area of research. The goals of this educational initiative are to raise awareness of medical needs for patients with advanced HCC, address the educational needs of healthcare professionals, and to communicate the latest science, the rationale for IO treatment, and opportunities to incorporate IO into clinical practice.

Presentations and content must give a scientifically sound, fair and balanced overview of new and emerging therapeutic options currently available, or in development, to manage advanced HCC.

Through independent needs assessments, BMS has determined health care providers have the following educational needs and professional practice gaps:

1. Need to become aware of current unmet medical needs in management of advanced HCC
2. Limited knowledge and understanding of the mechanisms of action, pathways, and rationale for using immunotherapy in HCC
3. Need to better understand the clinical profiles of currently available systemic therapies and emerging agents for advanced HCC based on efficacy (overall response rate [ORR], complete response [CR], partial response [PR], duration of response, and overall survival), efficacy by disease etiology, safety (common adverse reactions, treatment-related discontinuations), and tolerability
4. Health care providers cannot describe the differences in safety profiles between standard of care treatment, current/emerging targeted systemic therapies, and immuno-oncologic cancer treatments
5. Need education on the management of immune-related adverse events
6. Need to understand the evolving IO research landscape, including ongoing studies in earlier stages of disease, and with loco-regional treatment

**Specific Areas of Interest**

BMS is interested in funding an innovative, interactive, educational activity that addresses the above educational needs and professional practice gaps in the treatment of advanced HCC.

*Grant Proposals should include, but not be limited to, the following information:*

- **Executive Summary: The Executive Summary should consist of 1-2 pages and highlight the key areas as described below.**

- **Needs Assessment/Gaps/Barriers:** Needs assessment should be referenced and demonstrate an understanding of the specific gaps and barriers of the target audiences. The needs assessment must be

independently developed and validated by the educational provider.

- **Target Audience and Audience Generation:** Target audience for educational program must be identified within the proposal. In addition, please describe methods for reaching target audience(s) and any unique recruitment methods that will be utilized. The anticipated or estimated participant reach should also be included, with a breakdown for each modality included in the proposal, as applicable (e.g., number of participants for the live activity, the live webcast, and enduring activity).

- **Learning Objectives:** The learning objectives must be written in terms of what the learner will achieve as a result of attending. The objectives must be clearly defined, measurable, and attainable and address the identified gaps and barriers.

- **Educational Design and Methods:** Describe the approach used to address knowledge, competence, and performance gaps that underlie identified healthcare gaps. The proposal should include strategies that ensure reinforcement of learning through use of multiple educational interventions and include practice resources and tools, as applicable.

- **Communication and Publication Plan:** Provide a description of how the provider will communicate the progress and outcomes of the educational program to the supporter. It is highly recommended to describe how the results of the activity will be presented, published, or disseminated.

- **Innovation:** Describe how this project is innovative and engages the learners to improve knowledge, competence and/or performance. Further describe how this project might build on existing work, pilot projects or ongoing projects developed either by your institution or other institutions related to this topic.

- **Program Evaluation and Outcomes Reporting:** Description of the approach to evaluate the quality of the educational program. Describe methods used for determining the impact of the educational program on closing identified healthcare gaps.
    - Please refer to "Guidance for Outcomes Report" (on the BMS grants website) for a detailed explanation of preferred outcomes reporting methods and timelines.
    - Remember that knowledge, performance and competency based outcome measures according to Moore's Levels 4 & 5 are required. Level 6 outcomes are highly favored and recommended when possible.

- **Budget:** Detailed budget with rationale of expenses, including breakdown of costs, content cost per activity, out-of-pocket cost per activity, and management cost per activity.

**Note:** The accredited provider and, if applicable, the medical education partner (MEP) or other third party executing the activities, are expected to comply with current ethical codes and regulations. They must have a conflict-of-interest policy in place to identify and resolve all conflicts of interest from all contributors and staff involved in developing the content of the activity prior to delivery of the program, and must have a separate company providing/accrediting independent medical education if they are also performing promotional activities.

*If your organization wishes to submit an educational grant request, please use the online application available on the Bristol-Myers Squibb Independent Medical Education website.*
*http://www.bms.com/responsibility/grantsandgiving*

## References


1. Giannini EG, Farinati F, Ciccarese F, et al. Prognosis of untreated hepatocellular carcinoma. *Hepatology*. 2015;61:184–190.

2. Zeng Z, Shi F, Zhou L, et al. Upregulation of circulating PD-L1/PD-1 is associated with poor post-cryoablation prognosis in patients with HBV-related hepatocellular carcinoma. *PLoS One*. 2011;6:e23621

3. McGlynn KA, Petrick JL, London T, et al. Global epidemiology of hepatocellular carcinoma: An emphasis on demographic and regional variability. *Clin Liver Dis.* 2015;19:223-238.

4. Barathan M, Gopal K, Mohamed R, et al. Chronic hepatitis C virus infection triggers spontaneous differential expression of biosignatures associated with T cell exhaustion and apoptosis signaling in peripheral blood mononucleocytes. *Apoptosis*. 2015;20:466-480.

5. El-Khoueiry A, Sangro B, Yau T, et al. Nivolumab in patients with advanced hepatocellular carcinoma (CheckMate 040): an open-label, non-comparative, phase 1/2 dose escalation and expansion trial. *Lancet.* 2017; Apr 20. pii: S0140-6736(17)31046-2.

6. Sangro B, Melero I, Yau T, et al. Safety and antitumor activity of nivolumab in patients with advanced hepatocellular carcinoma: interim analysis of dose-expansion cohorts from the phase 1/2 chechmate-040 study. Presented at, The 52nd annual meeting of the American Society of Clinical Oncology, June 3-7, 2016; Chicago, IL.

7. Sangro B, Park J, Dela Cruz C, et al. A randomized, multicenter, phase 3 study of nivolumab versus sorafenib as first-line treatment in patients with advanced hepatocellular carcinoma (HCC)-checkmate-459.Presented at: The 52nd annual meeting of the American Society of Clinical Oncology, June 3-7, 2016; Chicago, IL.

8. Bruix J, Raoul J, Sherman M, et al. Efficacy and safety of sorafenib in patients with advanced hepatocellular carcinoma: sub analyses of a phase III trial. *J Hepatol*. 2012;57:821-829.

9. Bruix J, Qin S, Merle P, et al. Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2017;389:56-66.

10. Friedman C, Proverbs-Singh T, Postow M. Treatment of the immune-related adverse effects of immune checkpoint inhibitors: A review. *JAMA Oncol*. 2016;2:1346-1353.