NCCN, Fight CRC, and Pfizer Quality Improvement Initiative: Optimizing Biomarker-Directed Therapy in Metastatic Colorectal Cancer

Request for Proposals (RFP)

1. Introduction

The National Comprehensive Cancer Network® (NCCN), Fight Colorectal Cancer (Fight CRC) and Pfizer are collaborating to offer a new grant opportunity seeking proposals for quality improvement initiatives focused on optimizing biomarker-directed therapy in metastatic colorectal cancer in accordance with established clinical practice guidelines and best evidence.

National Comprehensive Cancer Network

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 32 leading cancer centers devoted to patient care, research, and education. NCCN is dedicated to improving and facilitating quality, effective, efficient, and equitable cancer care so patients can live better lives. Through the leadership and expertise of clinical professionals at NCCN Member Institutions, NCCN develops resources that present valuable information to the numerous stakeholders in the health care delivery system. By defining and advancing high-quality cancer care, NCCN promotes the importance of continuous quality improvement and recognizes the significance of creating clinical practice guidelines appropriate for use by patients, clinicians, and other health care decision-makers around the world.

Fight CRC

Fight CRC is the leading colorectal cancer patient-empowerment and advocacy organization in the United States providing balanced and objective information on colon and rectal cancer research, treatment and policy.

Pfizer Global Medical Grants

Pfizer Global Medical Grants (GMG) supports the global healthcare community's independent initiatives (e.g., research, quality improvement or education) to improve patient outcomes in areas of unmet medical need that are aligned with Pfizer's medical and/or scientific strategies.

This RFP is being issued by all three organizations. NCCN is the lead organization for review and evaluation of proposals. A Scientific Review Committee (SRC), led by NCCN, will make decisions on which proposals will receive funding. **Grant funding and general oversight of the funded projects will be provided directly from Pfizer.**

For all grants, the grant requester (and ultimately the grantee) is responsible for the design, implementation, sponsorship and conduct of the independent initiative supported by the grant, including compliance with any regulatory requirements. NCCN, Fight CRC, and Pfizer must not be involved in any aspect of study protocol or project development, nor the conduct or monitoring of the project.

2. Background

Metastatic colorectal cancer (mCRC) is a complex, heterogeneous disease characterized by multiple gene alterations that can significantly impact a patient's prognosis and treatment option profile. Biomarker testing has transformed the landscape of mCRC care and is critical to ensuring a patient receives appropriate, evidence-based care. Recent data suggests that implementing approved biomarker-driven therapy early in a patient's treatment course is of significant benefit. Tumors that have high microsatellite instability (MSI-H) or mismatch repair deficiency (dMMR), are now eligible for immunotherapy in the first-line setting.[1,3] *BRAF* V600E mutated mCRCs have a poorer prognosis overall, but may be eligible for targeted therapy.[2] MSI-H and *BRAF* mutated tumors do not respond well to traditional chemotherapy which further highlights the importance of biomarker testing early in a patient's treatment course.[3] Recent data has uncovered potential new treatment options targeting the HER2 amplification pathway in mCRC.[4]

Given the current understanding of the role of biomarkers in mCRC, current practice guidelines recommend that all CRCs should be tested for *KRAS/NRAS/BRAF* mutations, HER2 (*ERBB2*) amplification and MSI-H or dMMR at diagnosis of metastatic disease.[5,6,7] Despite this recommendation, the execution of biomarker testing is wrought with challenges for all stakeholders including providers and patients. Testing is complex, cumbersome, and often inefficient, which leads to delays in appropriate patient care. Barriers exist throughout the biomarker testing continuum and include provider ordering, patient education, insurance coverage, tissue acquisition, data interpretation and treatment implications. These challenges are consistent in academic and community settings and lead to poor integration of evidence-based treatment, thus revealing an opportunity for improvement in a key component of delivering guideline-concordant care.

Potential strategies to optimize care delivery around biomarker directed therapy include increasing awareness of the need for biomarker testing and its impact on therapy, improving adherence to guidelines, and facilitating meaningful educational opportunities for oncology providers. Further approaches may include developing workflows to facilitate the testing process for providers as well as workflows to enhance collaboration between community and academic settings regarding biomarker testing guidelines and currently approved biomarker directed therapies. Strategies to improve patient understanding of biomarker-directed therapy are also needed. This RFP seeks to solicit projects that focus on optimizing biomarker-directed therapy according to established clinical practice guidelines in mCRC.

3. Eligibility

Geographic Scope:	United States

Eligibility Criteria:	• Primary Investigators must be from NCCN Member Institutions.
	• Proposals that foster collaboration between NCCN Member Institutions and community organizations, practices, and institutions, including NCCN Affiliate Forum members, are strongly preferred.
	  • Collaborations should foster the interactive sharing of knowledge and expertise as well as utilize the combined clinical strengths of members.
	  • Although the submitting investigator must be from an NCCN Member Institution, participating co-investigators do not need to be at an NCCN Member Institution.
	  • This can also include cross-institutional collaboration for the conduct of quality improvement initiatives.
	• Proposal submissions from Junior Faculty are encouraged.
	• Trainees may participate as a sub-investigator under the appropriate mentorship from a PI from a NCCN Member Institution.

4. Requirements

Date RFP Issued:	February 13, 2023
Clinical Area:	Metastatic Colorectal Cancer

Areas of Interest for this RFP:	The intent of this Request for Proposals (RFP) is to support proposals for quality improvement initiatives focused on optimizing biomarker-directed therapy in mCRC according to established clinical practice guidelines.
	• For this project, please see the following definitions:
	  • mCRC refers to colorectal cancer that is unresectable or has spread to other organs.
	  • Treatment will mean systemic therapies approved for use in mCRC.
	  • Clinical practice guidelines include nationally or internationally recognized published guidelines defining standards of care in this setting.
	Proposals in the following topic areas are strongly encouraged:
	• Initiatives that facilitate awareness, encourage timely testing and adherence to biomarker guidelines;
	• Initiatives aiming to improve care delivery, access to biomarker driven care in diverse and under-resourced populations;
	• Projects aiming to improve tissue acquisition and reduce turnaround time for biomarker testing;
	• Studies capitalizing on health technology to improve result collection, result interpretation and use of appropriate guideline-based treatments;

Areas of Interest for this RFP:	• Proposals seeking to facilitate community-based access to molecular tumor boards and sharing best practices and quality improvement around biomarker testing and biomarker-directed therapy; • Proposals aiming to improve interdisciplinary workflows around biomarker testing and delivery of guideline concordant care; and • Proposals to develop novel educational tools regarding biomarker directed testing or therapy for providers and/or patients. **Proposals in the following topic areas will be considered out-of-scope for this RFP:** • Clinical research projects (i.e., those evaluating the efficacy of therapeutic or diagnostic agents); • Projects involving opioids; • Projects focused on development of new biomarker technology/techniques • Projects focusing on use of circulating tumor cell DNA in biomarker testing and biomarker-directed therapy; and • Projects paying for biomarker testing.
Target Audience:	Medical Oncologists, Pathologists, Gastroenterologists, Surgical Oncologists, and allied Colorectal Cancer healthcare providers (APPs, Nurse Navigators, etc.).
Expected Approximate Monetary Range of Grant Applications:	• There is $1,000,000 available for funding of all projects. • Systemic therapy agents or drugs will not be provided. • The intent is to fund individual projects capped at $250,000 (direct and indirect costs) although smaller, lower-costs projects are encouraged. Funding greater than $250,000 will be considered for exceptional proposals with detailed budget justification. • The maximum indirect (overhead) rate is 28% and must be included in the total grant request amount. • Applicants are required to disclose additional sources of funding for this project and demonstrate that funding does not overlap. • Projects paying for new staff position(s) must include a strong rationale and a plan for sustainability in order to be considered. (Supplementing a current role is permitted, but must also include a strong rationale and sustainability plan). Note that a new FTE cannot be the main source of intervention. • The decision relative to funding is deferred to the members of the SRC as chosen by NCCN and independent of Pfizer and Fight CRC.

Key Dates:	• RFP release date: **2/13/2023** • Proposal Submission Deadline: **4/10/2023.** Please note the deadline is 23:59 Eastern Time, i.e., New York, GMT–5. • Anticipated Grant Award Notification Date: **5/22/2023** • Anticipated Study Start-up: Six Months • Period of Performance: Two years • Reporting and Dissemination of Results: Within nine months of study completion • Grants will be distributed following a fully executed agreement and submission of Final Protocol, documentation of IRB/IEC approval, regulatory approval (if applicable), exemption or waiver.
Questions:	If you have questions regarding this RFP, please direct them in writing to Nicole Zion, Clinical Research Manager, at Zion@nccn.org or Pfizer's Grant Officer, Jennifer Schreiber at Jennifer.Schreiber@pfizer.com with the subject **"NCCN Fight CRC Pfizer mCRC Project"**.
Selection Criteria:	Applications will be evaluated on the basis of: • Knowledge of and experience within the area; • Capability of carrying out the work; • Community collaboration; • Scalability, novelty, and sustainability; • Potential impact, applicability, and expected outcomes of the project; and • Dissemination strategies. Incorporation of the survivor voice/patient advocates is encouraged.

How to Submit:	• Please go to https://www.cybergrants.com/pfizer/QI and sign in. First-time users should click "REGISTER NOW".
	• Select the following Competitive Grant Program Name: **2023 ONC NCCN Fight CRC mCRC Project QI**
	• Select the following Area of Interest: **Metastatic Colorectal Cancer**
	• Requirements for submission:
	  • Complete all required sections of the online application referring to the guide included in the Appendix.
	  • If you encounter any technical difficulties with the website, please click the "Need Support?" link at the bottom of the page.
	• IMPORTANT: Be advised applications submitted through the wrong application type and/or submitted after the due date will not be reviewed by the committee.

Review and Approval Process	An NCCN Request for Proposals Development Team (RFPDT) has been formed to oversee this process and will utilize a formalized review procedure to select the proposals of highest scientific merit. The NCCN RFPDT oversaw the development of this RFP and will perform the peer review of applications. All reviews, evaluations and award decisions are independent of Pfizer and Fight CRC.
Mechanism by which Applicants will be Notified:	• All applicants will be notified via email by the dates noted above. • Applicants may be asked for additional clarification during the review period.

5. Terms and Conditions

1. RFP does not commit Fight CRC, Pfizer, or their partners, to award a grant or a grant of any particular size if one is awarded, nor to pay any costs incurred in the preparation of a response to this request.
2. If your grant is approved, your institution will be required to enter into a written grant agreement with Pfizer. Please click here to view the core terms of the agreement. These terms have been drafted to be balanced and reasonable and to further the goals of both parties. Negotiating grant agreements requires significant resources, so please ensure that your institution (including your legal department) is able and willing to abide by these terms before proceeding with submission of your application as they will need to be accepted in their entirety.
3. This RFP does not provide permission and license for the use (including the creation of derivative products) of the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) or the NCCN Biomarkers Compendium for commercial use. Grant recipients will need to maintain a separate end-user or other license agreement directly with NCCN for use of the NCCN Guidelines or Biomarkers Compendium.

6. Submission Requirements

Applications will be accepted via the online portal listed in the "How to Submit" section. Project Proposals/Protocols should be single-spaced using Calibri 12-point font and 1-inch margins. Note: There is a 15-page limit [adjust as necessary] exclusive of references.

When uploading your Full Proposal please ensure it addresses the following:

Goals and Objectives	Briefly state the overall goal of the project. Describe how this goal aligns with the focus of the RFP and the goals of the applicant organization(s). List the *overall* objectives you plan to meet with your project both in terms of learning and expected outcomes. Objectives should describe the target population as well as the outcomes you expect to achieve as a result of conducting the project.

Assessment of Need for the Project and Preliminary Data	Please include a quantitative baseline data summary, initial metrics (e.g., quality measures), or a project starting point (please cite data on gap analyses or relevant patient-level data that informs the stated objectives) in your target area. Describe the source and method used to collect the data. Describe how the data was analyzed to determine that a gap existed. If a full analysis has not yet been conducted, please include a description of your plan to obtain this information.
Target Audience	Describe the primary audience(s) targeted for this project. Indicate whom you believe will directly benefit from the project outcomes. Describe the overall population size as well as the size of your sample population.
Project Design and Methods	Describe the planned project and the way it addresses the established need. If your methods include educational activities, please describe succinctly the topic(s) and format of those activities.
Innovation	Explain what measures you have taken to assure that this project idea is original and does not duplicate other projects or materials already developed. Describe how this project builds upon existing work, pilot projects, or ongoing projects developed either by your institution or other institutions related to this project.
Evaluation and Outcomes	In terms of the metrics used for the needs assessment, describe how you will determine if the practice gap was addressed for the target group. Describe how you expect to collect and analyze the data. Quantify the amount of change expected from this project in terms of your target audience. Describe how the project outcomes will be broadly disseminated.
Project Timeline	Provide an anticipated timeline for your project including project start/end dates.

Additional Information	If there is any additional information you feel the reviewers should be aware of concerning the importance of this project, please summarize here.
Organization Detail (Environment and Mentors)	Describe the attributes of the institutions/ organizations/associations that will support and facilitate the execution of the project and the leadership of the proposed project. Articulate the specific role of each partner in the proposed project. Letters of support from partner organizations are required to be submitted with the full proposal.
Budget Detail	The budget amount requested must be in U.S. dollars (USD). While estimating your budget please keep the following items in mind: • General organizational running costs such as insurances, heating, lighting, rent, building maintenance may be included. Pfizer does not provide funding for capital purchases (infrastructure expenses such as equipment, purchases of software or software licenses, technology or bricks and mortar). Equipment hire/leasing is acceptable and may be included in project budget. • The inclusion of these costs cannot cause the amount requested to exceed the budget limit set forth in the RFP. It should be noted that grants awarded through GMG cannot be used to purchase Pfizer therapeutic agents (prescription or non-prescription). Pfizer maintains a company-wide, maximum allowed overhead rate of 28% for independent studies and projects. Please click here for details.

7. References

1. Andre, T., et al., *Pembrolizumab in microsatellite-instability-high advanced colorectal cancer.* N Engl J Med, 2020. 383 (23): p. 2207-2218.
2. Tabernero, J., et al., *Encorafenib plus cetuximab as a new standard of care for previously treated BRAF V600E- mutant metatstatic colorectal cancer: updated survival results and subgroup analysis from the BEACON study.* J Clin Oncol, 2021. 39(4): p. 273-284.

3. Diaz, L., et al., *Pembrolizumab versus chemotherapy for microsatellite instability-high or mismatch repair-deficient metastatic colorectal cancer (KEYNOTE-177): final analysis of a randomised, open-label, phase 3 study*. Lancet Oncol, 2022. 23(5): p. 659-670.
4. Meric-Bernstam, F., et al., *Pertuzumab plus trastuzumab for HER2-amplified metastatic colorectal cancer (MyPathway):an updated reports from a multicentre open-label phase 2a, multilple basket study*. Lancet Oncol, 2019. 20(4): p. 518-530.
5. National Comprehensive Cancer Network. *Colon cancer (version 3.2022)*. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed 02/07/2023
6. Cervantes, A., et al., *Metastatic colorectal cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up.* AnnOnc 2023 34:1, p10-32. DOI:https://doi.org/10.1016/j.annonc.2022.10.003
7. Morris, V., et.al., *Treatment of Metastatic Colorectal Cancer: ASCO Guideline*. Journal of Clinical Oncology 2023 41:3, 678-700