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November 28, 2019

Tamara Syrek Jensen, JD
Director, Coverage and Analysis Group
Centers for Medicare & Medicaid Services
Mail Stop # S3-02-01
7500 Security Boulevard
Baltimore, MD 21244-1850

RE: Proposed Decision Memo for Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer (CAG-00450R)

Dear Ms. Syrek Jensen:

On behalf of the American Association for Cancer Research (AACR), the first and largest scientific organization in the world dedicated to the prevention and cure of cancer through research, education, communication, and collaboration, we sincerely thank the Center for Medicare and Medicaid Services (CMS) for the opportunity to provide comments in response to the National Coverage Analysis for Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer. Our membership includes more than 44,000 basic, translational, and clinical researchers; population scientists; other health care professionals; and patient advocates residing in 120 countries.

NGS tests represent an important new paradigm in diagnostic techniques for oncology. Compared to other techniques, NGS has the potential to efficiently identify significant genetic variations across nearly the entire genome, but it is important to remind ourselves that NGS is a scientific technique, a platform. When NGS tests are used as part of well-validated test protocols, this technology can help physicians elucidate clinically actionable information to guide and inform cancer treatment for patients.

The AACR commends CMS's recognition of the importance of NGS tests and its efforts to ensure coverage of clinically and analytically valid tests. The decision summary (CAG-00450R) notes that CMS will cover FDA-approved or -cleared tests for breast or ovarian cancer patients who have not been previously tested with NGS and have risk factors for hereditary cancer, and MACs are able to determine coverage of germline NGS-tests for other cancers besides breast and ovarian if the patient has clinical indications to do so and risk factors for hereditary testing but has not been previously tested with NGS.

As described in **Section VIII CMS Analysis, Summary**, "*The evidence for cancers of the breast and ovary suggests that the use of NGS can identify germline mutations which can lead to better stratification of patients in the physician management of inherited cancers of the breast and ovary*." The summary goes on to state, "*The evidence for cancer of the breast and ovary suggests that NGS as a diagnostic tool can identify the germline mutations most likely to be targeted by a treatment regimen tailored to certain germline mutation. It is likely that the identification of such tailored treatment regimens in the clinical management of inherited cancers of the breast and ovary diagnosed by NGS will improve health outcomes of Medicare beneficiaries. Use of NGS as a diagnostic test has utility for patients in the discovery of new targeted therapies for inherited cancers and in the physician management of inherited cancers of the breast and ovary in Medicare beneficiaries. We believe that, for other cancers, the evidence is rapidly developing. We are therefore maintaining the Medicare Administrative Contractors (MACs) discretion to make coverage decisions on diagnostic uses of NGS testing for patients with inherited cancers based on new evidence that may arise.*"

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However, the AACR is concerned that as the decision memo is currently written and taken together with the coverage decision for somatic NGS tests in advanced cancers, this policy would not promote or ensure access to these tests but reduce access to NGS testing for patients with cancer. Therefore, we ask the agency to consider the following changes to the proposed coverage decision:

1) Ensure coverage of germline tests for patients with hereditary breast or ovarian cancer by clarifying proposed coverage decision;
2) Permit Medicare Administrative Contractors (MACs) to cover analytically and clinically valid NGS-based germline tests for cancer patients, including for hereditary breast and ovarian cancer;
3) Cover multiple NGS-based tests for a patient when medically appropriate and necessary; and
4) Provide NGS-based test coverage for patients with suspected or diagnosed hematologic malignancies and for minimal residual disease assessments.

Germline Testing

Germline testing in hereditary breast and ovarian cancer patients has demonstrated clinical utility in directing clinical treatment choices, leading to better outcomes for cancer patients. However, under the criteria outlined in the proposed coverage decision, no test currently in existence qualifies for coverage. Presently, there are no FDA-approved, NGS-based, germline tests for breast or ovarian cancer. Myriad Genetics myChoice CDx and FoundationFocus CDx_{BRCA} are FDA-approved companion diagnostics for PARP inhibitors used to treat advanced ovarian cancer. These tests can detect both germline and somatic mutations but cannot distinguish whether the mutation origination is germline or somatic. Therefore, they are not specifically indicated to detect germline mutations. The AACR recognizes that CMS may have intended this decision memo to cover such tests for germline testing, but that is not clear from the stated coverage criteria. Regardless, there are still no germline mutation tests that would meet the criteria for early stage breast and ovarian cancer.

Furthermore, as written, the decision would prevent MACs from covering NGS-based tests for breast or ovarian cancer (because of the conditions stipulated in Section IX Conclusion, Section B). If finalized, the lack of tests that meet the national coverage criteria combined with the restrictions placed on MACs for determining coverage for breast and ovarian cancer could lead to patients not having access to highly informative and potentially lifesaving tests.

Repeat Testing

In specific circumstances, repeat NGS testing is necessary and appropriate for optimal cancer care. The proposed manual language states that to be covered for a germline test a patient must not have been "previously tested using NGS." Similar language for somatic testing coverage may limit, if not entirely preclude, medically necessary tests from being covered. Patients may need to undergo germline testing after having already undergone somatic testing; as currently worded, this coverage determination would limit the ability of these patients to receive the testing they require. When medically necessary, cancer patients should be able to receive both somatic and germline NGS tests. In the future, disease areas outside of the oncology space may have FDA-approved NGS tests. The language in this memo could prevent the coverage of NGS-based germline testing for cancer in patients who have previously received NGS testing for other diseases. **We support a coverage approach that allows patients to have subsequent testing to ensure they receive the best available therapy over the course of their disease.**

Hematologic Malignancies

Although outside the scope of the proposed germline decision memo at hand, the somatic mutation testing coverage determination (CAG-00450N) established coverage of NGS testing for patients with "recurrent, relapsed, refractory, metastatic, or advanced stage III or IV cancer." This language is not adequately inclusive of the staging systems used for hematologic malignancies. **The AACR requests that the text of the final memo be updated to ensure that Medicare**

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beneficiaries with hematologic malignancies have access to NGS-based testing. NGS tests reflect the standard of care for many such diseases and are critical to classifying them and monitoring their progress. Furthermore, research suggests that there is value in testing patients with hematologic malignancies multiple times over the course of treatment, including at diagnosis and for monitoring for progression[1]. Such testing is often accomplished through assays for minimal residual disease (MRD), the term used to describe the small numbers of cells that remain in a patient during or after treatment. The FDA has also authorized a test for the measurement of MRD[2].

As cancer researchers and care providers, our goal is to ensure that cancer patients get the best available care. To that end, high-quality NGS-based testing should be available to all patients for whom clinical benefit will be obtained. As the science behind NGS tests continues to advance, increasing numbers of patients may benefit from their use. **CMS should carefully consider stakeholder feedback on these and future cancer diagnostic and treatment technologies with the explicit goal to set coverage policy that supports continued innovation and ensures patient access to safe, effective, and clinically useful cancer treatments.** The AACR looks forward to CMS releasing the final national coverage decision and thanks CMS for the opportunity to comment on this important issue for cancer patients.

If you have further questions, please contact Sarah K. Martin, MS, PhD, Director, Regulatory Science and Policy, Science Policy and Government Affairs, at sarah.martin@aacr.org.

Sincerely,

Kenneth C. Anderson, MD
Chair, Regulatory Science and Policy Subcommittee
American Association for Cancer Research

Margaret Foti, PhD, MD (h.c.)
Chief Executive Officer
American Association for Cancer Research

[1] Jongen-Lavrencic, M, et al. Molecular minimal residual disease in acute myeloid leukemia. N Engl J Med 2018;378: 1189-1199. https://www.nejm.org/doi/full/10.1056/NEJMoa1716863

[2] https://www.fda.gov/news-events/press-announcements/fda-authorizes-first-next-generation-sequencing-based-test-detect-very-low-levels-remaining-cancer