SCRI
Sarah Cannon Research Institute

March 25, 2013

Maria Ellis, Executive Secretary, MEDCAC
Centers for Medicare & Medicaid Services
Center for Clinical Standards and Quality, Coverage and Analysis Group
S3-02-01
7500 Security Boulevard
Baltimore, MD 21244

Dear Ms. Ellis,

I am writing to express strong support for Medicare coverage of molecular tumor profiling tests as part of the standard management of patients with cancer of unknown primary site (CUP). These molecular tests are being reviewed at the MEDCAC meeting on May 1, 2013.

Along with my colleague, Dr. F. Anthony Greco, I have been involved in the research and treatment of CUP for the last 32 years, first at the Vanderbilt University School of Medicine and then at the Sarah Cannon Research Institute. During that time, we have completed more than 25 clinical trials, published many articles in peer-reviewed medical journals, and written the chapters on CUP in most major medical textbooks. Until recently, improvements in the management of patients with CUP have included new diagnostic tests (immunohistochemical stains, MRI and PET scans) and recognition of several subsets of CUP patients in whom specific treatments result in favorable outcomes. However, in the majority of CUP patients the site of tumor origin remains unknown, and the benefits of empiric chemotherapy (the standard treatment) are modest.

Our clinical research during the last 7 years has focused on the use of molecular tumor profiling to: 1) predict the site of tumor origin, and 2) direct the selection of therapy for patients with CUP. This focus was based on our conviction that accurate identification of the site of tumor origin at the time of diagnosis would result in selection of optimal treatment for CUP patients, particularly those with relatively responsive tumor types (e.g. breast, ovary, colon).

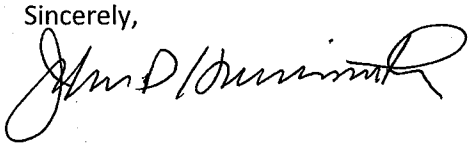
Results of a series of clinical trials have substantiated the utility of molecular tumor profiling, and are summarized as follows:

- In a group of CUP patients in whom anatomic primary sites were later identified clinically, molecular profiling of the original biopsy predicted the correct primary site in 75% (Greco et al, The Oncologist, 2012).
- Molecular tumor profiling is successful in predicting a primary site in the large majority of cases (>90%), even after all other pathologic procedures have failed to yield a prediction.
- In a large prospective multicenter phase 2 study, site-specific treatment directed by molecular profiling predictions led to a median survival of 12.5 months in a group of 194 patients, suggesting superiority to historical median survivals of 9-10 months with empiric chemotherapy (Hainsworth et al, J Clin Oncology, 2012). More importantly, patients predicted to have responsive tumor types had better results (median survival 13.4 months) than did patients with chemo-resistant tumors (median survival 7.6 months).

As targeted agents are introduced and the best treatment for different solid tumor types becomes more specific, empiric chemotherapy (developed at a time when treatment for various tumor types overlapped substantially) is unlikely to be adequate. Although evidence supporting the use of molecular tumor profiling is still developing, we feel strongly that existing evidence is strong enough to incorporate these diagnostic tests into standard management of CUP. Our trials with molecular profiling, conducted in community-based oncology practices, have met with strong support by practicing oncologists, many of whom have now incorporated tumor profiling as part of their standard CUP management.

Thank you for the opportunity to comment on this important issue. Please contact me if I can provide any further information.

Sincerely,



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