



March 1, 2010

Nita Collins, R.N.
Palmetto GBA
J1 Part B Medical Affairs
P.O. Box 1476
Augusta, GA 30903-1476

Reference: LCD ID # DL30695, Circulating Tumor Cell Marker Assays

Dear Ms. Collins:

On behalf of the members of the American Clinical Laboratory Association (ACLA), I am submitting comments on the draft local coverage determination denying coverage for circulating tumor cell assays because of insufficient published evidence-based data (clinical utility) to justify coverage.

The level of evidence required to justify coverage of diagnostic testing can vary depending on the applications of the particular diagnostic test. Where a test is being used to confirm a diagnosis, less rigorous may be sufficient to demonstrate the utility of the test. Where significant therapeutic decisions may be made based on the test results, a higher level of evidence may be required. However, there are already well accepted standards for judging most clinical, diagnostic testing, standards which focus on two necessary and complementary requirements. First, does the test consistently and accurately measure the analyte for which it is testing? Second, does it consistently identify the clinical condition associated with the analyte in the patient population for whom the test is intended? Beyond analytical and clinical validity, an assessment of the utility of a diagnostic test should be informed evidence of the extent to which the results of the test can influence patient management. The perceived benefits gained from lengthy, comprehensive evidentiary methodologies must be balanced against the significant opportunity costs such methodologies often can impose, including disincentives to medical innovation and delayed or denied access to diagnostics that could have avoided or mitigated negative health outcomes and their associated costs.

There is a broad spectrum of evidence that can and should be considered in evaluating diagnostic tests. While randomized clinical trials (RCTs) may be the “gold” standard for some procedures and therapies, they have significant limitations when applied to many diagnostic situations. The difficulties of constructing RCTs are complicated by rapid changes in therapeutic approaches where the drug regimens used to treat patients are in constant states of revisions. Scientifically sound alternative approaches must be considered.

Consistent with the above, CTC markers are tests that should be evaluated on their own merit (*i.e.*, to monitor patient prognosis), rather than the particular courses of therapy chosen by the physician. These tests assist physicians to monitor patient prognosis for malignant solid tumors, and provide valuable insight towards the patient’s response to the current course of therapy. The test is performed on whole blood, and provides a real-time perspective of disease status. They are not intended to replace physician judgment as a standard of care to determine treatment for every patient, nor are they intended to inform/suggest a particular treatment change; rather, they

complement the battery of information available to the physician and aid in the clinical decision-making process. There is a large body of evidence supporting the use of CTC assays as a predictor of patient prognosis and overall survival in patients with metastatic breast, prostate and colorectal cancers.¹

CTC assays have been integrated into the treatment paradigm for many physicians, and provide invaluable information to physicians in determining patient care decisions. Palmetto GBA should evaluate CTC markers on a case by case basis to allow Medicare beneficiaries under its jurisdiction access to this technology. A coverage determination should be based on a review of the assay specific data rather than a determination that there is insufficient evidence to justify coverage of CTC assays.

We thank you for the opportunity to submit these comments.

Sincerely,

A handwritten signature in black ink, appearing to read 'JoAnne Glisson', with a stylized flourish at the end.

JoAnne Glisson
Senior Vice President

¹ For a recent review of the evidence supporting CTC markers, see, *e.g.*, Dotan E, et al. Circulating tumor cells: evolving evidence and future challenges. *The Oncologist*. 2009. 14(11):1070-82.