Provisional Clinical Opinion

By Daniel G. Haller, MD, and John V. Cox, DO, MBA

On January 13, 2009, ASCO released its first provisional clinical opinion (PCO). The subject of the PCO is *KRAS* testing in patients with metastatic colon cancer who are eligible for anti-EGFR antibody therapy. The PCO was prompted by cumulative data from many retrospective studies showing that patients with metastatic colon cancer with tumoral mutations in *KRAS* do not respond to these agents. The purpose of PCOs is to provide ASCO members direction on issues that have been informed by recent data that should affect clinical practice, such as *KRAS* testing. The need for timely opinion from ASCO is apparent as science becomes ever more complex and the pace of change increases. In addition, the demands of clinical practice make it difficult for oncologists to stay abreast of many of these changes. ASCO President Richard L. Schilsky, MD, recently commented that the goal of the PCO is to answer a member's query after hearing new data, "Does this change my practice?"

The process of identifying areas that justify a PCO and the mechanisms to vet the opinion are outlined in the appendices to the statement. The board and leadership of ASCO in the Health Services Committee oversee the process. Because of the nature of these bodies and the relative rarity of practice-changing data, it is not anticipated that PCOs will be released on a frequent basis; however, the Society does strive to be timely with information that will benefit members and cancer patients.

Many questions are raised by implementing this process. Inherent in choosing to take a position in a PCO is the expression of many judgments. What is the trigger that initiates the process? With the pressures of the marketplace, how will the process be protected from conflicts of interest? Will there be defined criteria that should automatically provide ASCO review? In an effort to better understand and develop criteria, the Health Services committee is retrospectively looking at recent ASCO annual meetings to review featured abstracts with the purpose of identifying data that would trigger a PCO. Obviously, this review is retrospective and is affected by the wisdom of time in clarifying what issues were practice-changing. However, it is hoped that this theoretical exercise can inform the committee of pitfalls in their process and hone the triggering criteria.

After a subject is defined as a candidate for a PCO, ASCO works with the National Cancer Institute's Physician Data Query (PDQ) editorial board to provide a timely, yet thorough, review of the data, in which new information is weighed against the standards in practice. The goals of this cooperative review are the assurance of providing an objective and scientifically rigorous assessment and underlining practice

relevance. Though there will certainly be pressures for prompt release of PCOs, the review process will take time, likely several weeks. Although speed and timeliness are important, the time lag required for the Physician Data Query editorial board to write a technical assessment and for the ASCO leadership to write the PCO is a strength of the process.

Possibly a more important role for PCOs will be to comment when data are too limited to make a change in practice. Producing a PCO that acknowledges that practice is changing too fast in response to immature science would be an important refinement of the process. In an era when oncologists have many agents to draw on and where there are many publications of early trials of multiple combinations of these agents, rushing to fill in clinical gaps before the science is clear and consensus develops is tempting. Clearly, some direction from experts on the basis of rigorous review of emerging data to resist this temptation would provide a valuable service, but it will require complex judgment and will likely not lend itself to strict criteria.

Not addressed in the PCO process is the need for ASCO to review these statements periodically. The very nature of our science is that evolving insights will force revision or withdrawal of a clinical opinion. The moniker "provisional" acknowledges this. It is possible that future data will require the prompt withdrawal of a PCO, and such a process should be anticipated. Also, consideration of a formal process of regular review and renewal of existing PCOs should be implemented. A mandated review of all of the opinions on a regular basis would assure continued relevance and validity to the statements. As ASCO guidelines are produced that incorporate the information outlined in a PCO, the PCO should be withdrawn and should yield to the more vigorous oversight process required of clinical guideline development.

When provisional clinical opinions are released, they will be published online at <http://www.asco.org> and ahead of print on the *Journal of Clinical Oncology* Web site, with commentary to appear in *Journal of Oncology Practice*. The full opinion will also be published in print in *JCO* as soon as practical. *JOP* will draw on the ASCO committees involved in the production of the opinion to publish comment on the practical implications of the opinion to oncology practice. We look forward to providing editorial comment and feedback on this process.

Daniel G. Haller, MD, and John V. Cox, DO, MBA, are the Editors-in-Chief of *Journal of Clinical Oncology* and *Journal of Oncology Practice*, respectively. This editorial will also be published in the April 20 issue of *JCO*.

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