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ASCO SPECIAL ARTICLE

American Society of Clinical Oncology Provisional Clinical Opinion: Epidermal Growth Factor Receptor (*EGFR*) Mutation Testing for Patients With Advanced Non–Small-Cell Lung Cancer Considering First-Line EGFR Tyrosine Kinase Inhibitor Therapy

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ABSTRACT

Purpose

An American Society of Clinical Oncology (ASCO) provisional clinical opinion (PCO) offers timely clinical direction to ASCO's membership following publication or presentation of potentially practice-changing data from major studies. This PCO addresses the clinical utility of using epidermal growth factor receptor (*EGFR*) mutation testing for patients with advanced non–small-cell lung cancer (NSCLC) to predict the benefit of taking a first-line EGFR tyrosine kinase inhibitor (TKI).

Clinical Context

Patients with *EGFR*-mutated NSCLC have a significantly higher rate of partial responses to the EGFR TKIs gefitinib and erlotinib. In the United States, approximately 15% of patients with adenocarcinoma of the lung harbor activating *EGFR* mutations. *EGFR* mutation testing is widespread at academic medical centers and in some locales in community practice. As of yet, there is no evidence of an overall survival (OS) benefit from selecting treatment based on performing this testing.

Recent Data

One large phase III trial (the Iressa Pan-Asia Study [IPASS] trial), three smaller phase III randomized controlled trials using progression-free survival as the primary end point, and one small phase III trial with OS as the primary end point, all involving first-line EGFR TKIs and chemotherapy doublets, form the basis of this PCO.

Provisional Clinical Opinion

On the basis of the results of five phase III randomized controlled trials, patients with NSCLC who are being considered for first-line therapy with an EGFR TKI (patients who have not previously received chemotherapy or an EGFR TKI) should have their tumor tested for EGFR mutations to determine whether an EGFR TKI or chemotherapy is the appropriate first-line therapy.

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INTRODUCTION

The American Society of Clinical Oncology (ASCO) has established a rigorous, evidence-based approach—the provisional clinical opinion (PCO)—to offer a rapid response to emerging data in clinical oncology. The PCO is intended to offer timely clinical direction to ASCO's oncologists after publication or presentation of potentially practice-changing data from major studies (Appendix, online only).

This PCO addresses the clinical utility of epidermal growth factor receptor (*EGFR*) mutation testing for patients with advanced non–small-cell lung cancer (NSCLC) to predict response to first-line therapy with EGFR tyrosine kinase inhibitors (TKIs; erlotinib or gefitinib).

STATEMENT OF THE CLINICAL ISSUE

In the United States, approximately 15% of patients with adenocarcinoma of the lung harbor activating *EGFR* mutations. The majority of these mutations are in exons 19 and 21 of the *EGFR* gene. Phase III randomized controlled trials (RCTs) of EGFR TKIs in the first-line setting have shown a benefit in response and progression-free survival (PFS), but not overall survival (OS), for patients with *EGFR*-mutated NSCLC who received an EGFR TKI in first-line treatment. Greater than 90% of patients included in the majority of these trials had adenocarcinoma of the lung. Currently, neither erlotinib nor gefitinib has been approved for first-line therapy of lung cancer by the US Food and Drug Administration.

ASCO'S PROVISIONAL CLINICAL OPINION

On the basis of the results of five phase III RCTs, patients with advanced NSCLC of the lung who are being considered for first-line therapy with an EGFR TKI (patients who have not previously received chemotherapy or an EGFR TKI) should have their tumor tested for EGFR *mutations to determine whether an EGFR TKI or chemotherapy is the appropriate first-line therapy.*

LITERATURE REVIEW AND ANALYSIS

This PCO addresses using *EGFR* mutation testing in the context of first-line treatment of NSCLC based on trials comparing an EGFR TKI to a platinum-based chemotherapy doublet. Studies considered were limited to those comparing an EGFR TKI with chemotherapy, because the latter has been the standard of care for first-line treatment. The PCO addresses the role of *EGFR* mutation testing in selecting first-line treatment. The ASCO 2009 Guideline Update on stage IV NSCLC addresses the use of EGFR TKIs in the second- and third-line settings.[1]

The major impetus for the PCO was the publication by Mok et al[2] that reported the results of the Iressa Pan-Asia Study (IPASS). ASCO asked the National Cancer Institute's Physician Data Query (PDQ) Adult Cancer Editorial Board to conduct an assessment of this trial to inform the PCO. This assessment is summarized in this article. Results from other relevant trials are also reviewed.

Overview of IPASS

IPASS was a phase III, multicenter, randomized, open-label, parallel-group study comparing gefitinib with carboplatin plus pacli-taxel as first-line treatment for patients in East Asia who had advanced adenocarcinoma of the lung and were nonsmokers or former light smokers with other specific clinical characteristics. The primary outcome of interest was PFS, and the trial was designed to show noninferiority.[2] Table 1 lists further details and outcomes.

In IPASS, participants were not randomly assigned by marker status, although the marker analysis was preplanned. The study used the amplification refractory mutation system and *EGFR* 29-mutation detection testing. Of patients whose tissue was evaluable, almost 60% tested positive for the mutation (primarily exon 21 L858R mutations and exon 19 deletions). Data were available for those with known and unknown marker status (Table 1). In addition to efficacy outcomes, the original publication of IPASS presented data on the correlation of quality of life and mutation status.

National Cancer Institute PDQ Editorial Review Assessment

On request from ASCO, the National Cancer Institute's PDQ Editorial Board provided a written assessment of the IPASS data.[9] This assessment reported that the IPASS study met its primary objective of demonstrating noninferiority and showed the superiority of gefitinib compared with carboplatin/paclitaxel for PFS. The study demonstrated that gefitinib is superior to carboplatin/paclitaxel as an initial treatment for adenocarcinoma of the lung among nonsmokers or former light smokers in East Asia, based on the PFS findings. The hazard ratio (HR) for progression or death for all participants regardless of mutation status was 0.74 (95% CI, 0.65 to 0.85; $P < .001$); for patients who tested positive for *EGFR* activating mutations, the HR was 0.48 (95% CI, 0.36 to 0.64; $P < .001$); and for patients who tested negative for *EGFR* activating mutations, the HR was 2.85 (95% CI, 2.05 to 3.98; $P < .001$). Therefore, patients who tested positive had longer PFS with gefitinib, and patients who tested negative had shorter PFS with gefitinib (according to the tests listed earlier). The result of the treatment $\times$ *EGFR* status interaction test was $P < .001$ in the original report by Mok et al.[2]

At the time of the IPASS initial publication, an analysis of OS according to mutation status was also performed, although this analysis included only 81 deaths in the mutation-positive subgroup and 94 deaths in the mutation-negative subgroup. The HRs with gefitinib were 0.78 (95% CI, 0.50 to 1.20) in the subgroup that tested positive and 1.38 (95% CI, 0.92 to 2.09) in the subgroup that tested negative. The PDQ assessment also noted that although the OS results were not mature, they were concerning because they suggest that patients with adenocarcinoma of the lung who test negative may have inferior survival if their initial treatment is with an EGFR inhibitor rather than combination chemotherapy. Since the PDQ assessment, investigators have presented mature survival results of IPASS. The HRs with gefitinib were 1.00 (95% CI, 0.76 to 1.33) for patients who tested positive for mutation and 1.18 (95% CI, 0.86 to 1.63) for patients who tested negative for mutation (treatment $\times$ biomarker status interaction test, $P = .48$).[3]

The assessment highlighted some substantive points for the PCO ad hoc panel's consideration, as follows. First, the participants in IPASS were people from China, Japan, Korea, Thailand, and Taiwan. Therefore, the applicability of these results to non-Asian populations with similar clinical or mutational features is uncertain because there may be additional environmental or genotypic factors between populations that may alter sensitivity to therapy. Second, the magnitude of

Table 1. Trials of EGFR TKIs in Lung Cancer

Study	Trial Characteristics	Treatments by Arm*	Population and Variable	All Patients		*EGFR* Mutation Positive		*EGFR* Mutation Negative		*EGFR* Mutation Status Unknown	
				EGFR TKI Arm	Control Arm	EGFR TKI Arm	Control Arm	EGFR TKI Arm	Control Arm	EGFR TKI Arm	Control Arm
			RCTs With Clinically Selected Patients								
IPASS[2-4]	Primary end point: PFS; 100% adenocarcinoma; PS: 0-2	Gefitinib (n = 609) *v* carboplatin/paclitaxel (n = 608)	Total No. of patients	1,217		261		176		780	
			No. of patients per arm	609	608	132	129	91	85	386	394
			Response rate, %	43	32.2	71.2	47.3	1.1	23.5	43.3	29.2
			P	< .001		.0001		.0013		< .001	
			Median PFS, months	5.7	5.8	9.5†	6.3†	1.5†	5.5†	6.6†	5.8†
			HR	0.74‡		0.48		2.85		0.68‡	
			95% CI	0.65 to 0.85‡		0.36 to 0.64		2.05 to 3.98		0.58 to 0.81‡	
			P	< .001		< .001		< .001		< .001	
			Treatment × biomarker status interaction test, P			< .001§					
			Median OS, months (final results)[3]	18.8	17.4	21.6	21.9	11.2	12.7	18.9	17.2
			HR	0.90		1.00		1.18		0.82	
			95% CI	0.79 to 1.02		0.76 to 1.33		0.86 to 1.63		0.70 to 0.96	
			P	NS		NS		NS		.015	
			Treatment × biomarker status interaction test, P			.48§					
First-SIGNAL; Lee et al,[5] optional exploratory analysis	Primary end point: OS; 100% adenocarcinoma; PS: 0-2	Gefitinib (n = 159) *v* gemcitabine/cisplatin (n = 154)	No. of patients	159	150	26	16	27	27	NA	NA
			Response rate, %	53.5	45.3	84.6	37.5	25.9	51.9		
			P	.1533		.002		.051			
			Median PFS, months	6.1	6.6	8.4	6.7	2.1	6.4		
			HR	0.813‡		0.613		1.517			
			95% CI	0.641 to 1.031‡		0.308 to 1.221		0.88 to 2.615			
			P	.044		.084		.071			
			Median OS, months	21.3	23.3	30.6	26.5	18.4	23.3		
			HR	1.003		0.823		1.199			
			95% CI	0.749 to 1.343		0.352 to 1.922		0.57 to 2.52			
			P	.428		.648		.632			
			RCTs With Patients With Tumors Harboring *EGFR* Exon 19 or 21 Sensitizing Mutations									
Maemondo et al[6]	Primary end point: PFS; > 90% adenocarcinoma; PS: 0-2	Gefitinib (n = 114) *v* carboplatin/paclitaxel (n = 114)	No. of patients	NA	NA	114	110	NA	NA	NA	NA
			Response rate, %			73.7	30.7				
			P			< .001					
			Median PFS, months			10.8	5.4				
			HR			0.30					
			95% CI			0.22 to 0.41					
			P			< .001					
			Median OS, months			30.5	23.6				
			P			.31					
			(continued on following page)									

				All Patients		EGFR Mutation Positive		EGFR Mutation Negative		EGFR Mutation Status Unknown	
Study	Trial Characteristics	Treatments by Arm*	Population and Variable	EGFR TKI Arm	Control Arm	EGFR TKI Arm	Control Arm	EGFR TKI Arm	Control Arm	EGFR TKI Arm	Control Arm
Mitsudomi et al[7]	Primary end point: correlation of marker with PFS; ≥ 93% adenocarcinoma; PS: 0-1	Gefitinib (n = 88) v cisplatin/docetaxel (n = 89)	No. of patients	NA	NA	86	86	NA	NA	NA	NA
			Response rate, %			62.1‖	32.2‖				
			P			< .001					
			Median PFS, months			9.2	6.3				
			HR			0.489					
			95% CI			0.336 to 0.71					
			P			< .001					
			Median OS, months			30.9¶	Not reached¶				
			HR			1.638					
			95% CI			0.75 to 3.58					
			P			.211					
OPTIMAL; Zhou et al[8]	Primary end point: PFS; ≥ 86% adenocarcinoma; PS: 0-2	Erlotinib (n = 82) v gemcitabine/carboplatin (n = 72)	No. of patients	NA	NA	82	72	NA	NA	NA	NA
			Response rate, %			83	36				
			P			< .001					
			Median PFS, months			13.1	4.6				
			HR			0.16					
			95% CI			0.10 to 0.26					
			P			< .001					

Table 1. Trials of EGFR TKIs in Lung Cancer (continued)

Abbreviations: EGFR, epidermal growth factor receptor; TKI, tyrosine kinase inhibitor; IPASS, Iressa Pan-Asia Study; PFS, progression-free survival; PS, performance status; OS, overall survival; NS, not significant; First-SIGNAL, First-Line Single Agent Iressa Versus Gemcitabine and Cisplatin Trial in Never-Smokers with Adenocarcinoma of the Lung; NA, not available.
*Numbers in parentheses indicate intent-to-treat population.
†Data from the 45th Annual Meeting of the American Society of Clinical Oncology (ASCO), Orlando, FL, May 29-June 2, 2009 (oral presentation); slides available through ASCO Virtual Meeting.
‡Although these values were reported in the original publications, a single HR is not readily interpretable because the survival curves cross, suggesting a violation of the proportional hazards assumption.
§P value for EGFR Mutation Test Positive and EGFR Mutation Test Negative.
‖Response rates for patients with measurable disease (gefitinib, n = 58; cisplatin/docetaxel, n = 59).
¶OS results not mature at the time of publication (observed deaths at analysis, n = 17 for gefitinib and n = 10 for chemotherapy).

benefit from erlotinib versus chemotherapy obtained in clinical trials testing gefitinib is not currently known when using erlotinib (the only EGFR TKI now approved in the United States). Extrapolations from other analyses suggest possible comparability.

Other Relevant Clinical Trials

To supplement the PDQ assessment, the ad hoc panel reviewed several additional relevant RCTs that addressed the predictive utility of EGFR mutation testing. Studies were included if they were phase III RCTs that investigated response to first-line EGFR TKIs compared with chemotherapy among patients with advanced NSCLC with respect to EGFR mutational status. Some study inclusion criteria, the agent in the control arm, and whether or not the marker status was known at the time of study entry and random assignment differed among studies. Two of the five studies have been published in peer-reviewed publications at the time of production of this PCO.[6,7] The other three sets of data are from meeting presentations, including the IPASS marker analysis,[4,5,8] and IPASS survival results.[3]

The four additional trials (other than IPASS) are described briefly here. Table 1 lists further details and outcomes of these studies. In one of the studies, participants were selected by clinical characteristics, as they were in IPASS. In the other three trials, presence of an EGFR activating mutation was an eligibility requirement.

Participants selected by clinical characteristics. The trial in which participants were selected by clinical characteristics, an exploratory analysis of an RCT, was presented by Lee et al.[5] All participants had adenocarcinoma and were never smokers, and more than 88% were women. The test used in the study was not reported. A positive mutation test result was not a requirement for participation. The treatment arms involved gefitinib versus gemcitabine, and OS was the primary end point. This trial found a greater response rate with gefitinib for patients who tested positive for a mutation. PFS was also longer but was not statistically significant.

Participants selected by EGFR mutation status. In the first of the other three trials, published by Maemondo et al,[6] more than 90% of the participants had adenocarcinoma, 63% or more were women, and all had tested positive for activating EGFR mutations with peptide

nucleic acid–locked nucleic acid (PNA-LNA) polymerase chain reaction clamp method testing. The treatment arms involved gefitinib versus a platinum/taxane doublet, and PFS was the primary end point. The study found a statistically significant benefit in PFS and response rate for patients who received gefitinib compared with patients who received chemotherapy. In the second study, published by Mistudomi et al,[7] 93% or more of participants had adenocarcinoma, approximately 60% were women, and all tested positive with tests for specific activating *EGFR* mutations, confirmed by direct sequencing. The treatment arms also involved gefitinib versus a platinum/taxane doublet, and PFS was the primary end point. In both studies, participants represented all smoking statuses. The second trial also found a statistically significant benefit in PFS and response rate for patients who received gefitinib compared with patients who received chemotherapy. In the third study, the OPTIMAL trial (in abstract form), more than 86% of the participants had adenocarcinoma, 58% or more were women, 69% or more were never smokers, and all tested positive for activating *EGFR* mutations by polymerase chain reaction.[8,10] The trial compared erlotinib with gemcitabine/carboplatin. In this trial, the response rate with erlotinib was more than twice that with chemotherapy, and PFS was 13.1 months versus 4.6 months, respectively (HR, 0.16; 95% CI, 0.1 to 0.26; $P < .001$).

Integrative Discussion and Analysis

The results of these four other studies, taken together, support the findings of the IPASS analysis—prolonged PFS and higher response rates for patients who tested positive for *EGFR* activating mutation(s) and received an EGFR TKI. Primarily on the basis of IPASS, there was a higher response rate and longer PFS from chemotherapy for patients who tested negative for *EGFR* mutation. Survival data were recently presented showing an apparent lack of survival advantage with gefitinib for patients with either mutation status.[3] This may be the result of cross-over treatment.

Because the IPASS study demonstrated markedly improved PFS from chemotherapy for patients who tested negative for *EGFR* mutations, this result would suggest that these patients should not receive first-line EGFR TKI therapy and will receive greater benefits with chemotherapy. Similarly, a randomized, phase III, European study of 670 unselected patients evaluating erlotinib versus placebo as first-line therapy in patients who were not felt to be candidates for chemotherapy failed to show an OS benefit with erlotinib (HR, 0.98; $P = .77$). Again, this suggests that a first-line EGFR TKI is not beneficial in patients who do not test positive for *EGFR* mutations.[11]

Because all of the patients in the primary trial supporting this PCO, IPASS, had adenocarcinoma, as well as ≥ 86% to 100% of the patients in the other studies, the PCO recommendation applies mainly, but not exclusively, to patients with adenocarcinoma.

As mentioned earlier, additional important issues exist for which there is, as of now, no direct evidence. The first concerns differences and similarities between the North American populations and the Japanese, Chinese, Korean, Thai, and Taiwanese populations involved in these trials. It seems that there are no significant differences in the types and locations of *EGFR* mutations between the NSCLCs of Asians and non-Asians. All *EGFR* mutations are in the same loci of the DNA of NSCLC tumors (exons 18 to 21).[12] In addition, this seems to be true for the secondary mutation T790M, which confers resistance to EGFR TKIs,[13,14] and for the *MET* gene amplification resistance mechanism between people of different ethnicities.[15,16] In addition, the presence

of *EGFR* mutations is both a predictive and prognostic factor. The prognosis among patients who tested positive for an *EGFR* activating mutation, have not received an EGFR TKI, and have had resections is better than for patients who tested negative by univariate, but not multivariate, analysis. This finding is similar in both Japanese and US patients.[17] There are now many published reports of using EGFR TKIs for patients with tumors with mutated *EGFR*, and the studies have similar overall response rates and OS rates despite different geographical locations and despite which EGFR TKI was used. The response rates generally range from 62% to 83%, and OS times range from 23 to 39 months.[2,5,7,15,18-20]

Second, the majority of these trials used gefitinib; however, gefitinib is not available to most people with advanced NSCLC in the United States, unlike in Japan and Western Europe. In the United States, availability is currently limited to erlotinib. Initial analyses of outcome by *EGFR* mutation status for erlotinib in a phase III trial from China (OPTIMAL) showed similar results to IPASS. There have been no completed phase III head-to-head clinical trials comparing first-line erlotinib and gefitinib. In addition to the OPTIMAL analyses of *EGFR* mutation testing and erlotinib, it may be possible to extrapolate results indirectly from prospective-retrospective analyses of two studies—one of second- or third-line erlotinib and the other of maintenance erlotinib. The study of second- or third-line erlotinib showed higher response rates with erlotinib for patients who tested positive for mutations than for patients who tested negative.[21] The study of maintenance erlotinib showed a statistically significant difference in PFS for patients who tested positive for a mutation(s) receiving erlotinib versus placebo during maintenance treatment and whose disease had not progressed after four cycles of platinum-based chemotherapy.[22] This study also showed a PFS and OS benefit for patients whose NSCLC tested negative for mutations. In the patients who tested positive, the PFS benefit was greater than the OS benefit, perhaps as a result of the poststudy use of EGFR TKIs in patients receiving placebo. The PFS benefit seen in the population who tested positive provides support for the potentially comparable benefit of erlotinib versus gefitinib in this patient population.

Third, an additional issue of importance is the use of PFS as a primary end point in IPASS and three of the additional trials. There has been debate about the utility of this end point; traditionally, OS has been the primary end point in such trials. The choice of PFS as an end point may have been guided by the fact that it is difficult to disaggregate the effect of frequent use of second- and third-line poststudy EGFR TKIs on OS outcomes.

Finally, the ad hoc panel commented that there is often a limited amount of tissue for mutation testing and, therefore, endorses a relevant recommendation in ASCO's stage IV NSCLC guideline update: "In order to obtain tissue for more accurate histologic classification or for investigational purposes, the Update Committee supports reasonable efforts to obtain more tissue than what is contained in a routine cytology specimen."[1] Properly fixed material from cytology cell block preparations is generally required for analysis, as opposed to cytology smear preparations. Development of more sensitive mutation analysis techniques may help in case of limited tumor material availability.

This PCO is limited to mutation testing. On the basis of available evidence thus far, mutation analysis has proven to be the most reliable methodology to evaluate for EGFR alterations that correlate with response to TKI inhibitor sensitivity or PFS. Please note that the trials

discussed in the PCO searched only for activating mutations. Mutations conferring resistance to EGFR TKIs also exist (eg, T790M) and may be identified by direct sequencing. At the time of publication of this PCO, there was no US Food and Drug Administration–cleared test for the *EGFR* mutation. Fluorescent in situ hybridization and immunohistochemistry testing for EGFR at the present time are not recommended for the purposes of treatment decisions because they do not reproducibly predict outcome. Testing issues are additionally discussed in a *Journal of Oncology Practice* companion publication.

RESEARCH PRIORITIES

OS results from ongoing trials are needed. A head-to-head comparison of erlotinib versus gefitinib could provide more information about the similarities and differences between these agents and confirm whether IPASS results are applicable to patients receiving erlotinib. A trial similar to IPASS in North America would inform the question of whether or not the results of IPASS were specific to the regions from where the participants were drawn or are indeed generalizable.

An ongoing European phase III trial (European Randomized Trial of Tarceva Versus Chemotherapy [EURTAC]) is randomly assigning patients with known *EGFR* activating mutations to erlotinib versus first-line chemotherapy (platinum doublet) with a study-specified cross over to the opposite therapy at the time of progression. PFS is the primary end point (ClinicalTrials.gov identifier: NCT00446225). The results of this study may be available later in 2011, may be more generalizable to the North American population, and will add information about erlotinib in this role.

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Acknowledgment

Appendix

Overview of the Provisional Clinical Opinion Development Process

Provisional clinical opinion (PCO) topic selection. The American Society of Clinical Oncology (ASCO) Clinical Practice Guidelines Committee (CPGC) leadership is responsible for accepting, reviewing, and approving proposed PCO topics on behalf of the ASCO Board of Directors. The selection of this PCO topic was guided by the Topic Selection Algorithm that is used by the CPGC to guide selection of topics for ASCO's clinical practice guidelines (www.asco.org/guidelines/manual).

PCO Evidentiary Basis

PCOs are informed by expeditious methodologic assessments of the data in question. To this end, ASCO has established a relationship with the National Cancer Institute's Physician Data Query (PDQ) Editorial Boards. The PDQ's Editorial Boards are comprised of content experts in oncology and related specialties. On request from ASCO, the relevant PDQ Editorial Board provided a written assessment of the new data from the Iressa Pan-Asia Study (IPASS).

Ad Hoc PCO Panel

The ASCO PDQ Editorial Board's assessment was forwarded to an ad hoc panel that was selected and charged by the CPGC to draft the PCO. The ad hoc panel includes seven content experts and a patient representative. The membership of the ad hoc panel was chosen in accordance with ASCO's Conflicts of Interest Management Procedures for Clinical Practice Guidelines (www.asco.org/guidelinescoi). The Conflict of Interest Procedures call for the majority of ad hoc panel members to have no relationships with companies potentially affected by the PCO and generally require ad hoc panel co-chairs to be free from relationships with affected companies.

PCO Review and Approval

The PCO was approved by a unanimous vote of the ad hoc panel members; the CPGC leadership (Past-Chair, Chair, Chair-Elect, and Board liaison) and selected content experts drawn from the CPGC membership; and a subset of the ASCO Board (Past-President, President, and President-Elect) and selected content experts drawn from the Board membership and appointed at the discretion of the President.

Table A1. Ad Hoc Panel Membership

Participant	Institution
Giuseppe Giaccone, MD, PhD, Co-chair	National Cancer Institute
Vicki Leigh Keedy, MD, Co-chair	Vanderbilt University Medical Center
Mary Beth Beasley, MD, FACP	Mount Sinai Medical Center
David H. Johnson, MD, FACP	University of Texas, Southwestern Medical Center
Lisa M. McShane, PhD	National Cancer Institute
Daniel T. Milton, MD	Hematology/Oncology of Indiana, PC
John R. Strawn, MD	Patient Representative
Heather A. Wakelee, MD	Stanford University