5 Minute JournalClub

Key ASCO Presentations
Issue 7, 2010

Effect of Early Palliative Care on End-of-Life Care Outcomes among Patients with Metastatic NSCLC

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CME INFORMATION

OVERVIEW OF ACTIVITY

Each year, thousands of clinicians and basic scientists sojourn to the American Society of Clinical Oncology (ASCO) Annual Meeting to learn about recent clinical advances that yield alterations in state-of-the-art management for all tumor types. Attracting tens of thousands of attendees from every corner of the globe to both unveil and digest the latest research, ASCO is unmatched in attendance and clinical relevance. Results presented from ongoing trials lead to the emergence of new therapeutic agents and changes in the indications for existing treatments across all cancer medicine. Despite the importance of the conference, the demands of routine practice often limit the amount of time oncology clinicians can realistically dedicate to travel and learning. To bridge the gap between research and patient care, this CME activity will deliver a serial review of the key presentations from the ASCO Annual Meeting and expert perspectives on how these new evidence-based concepts can be applied to routine clinical care. This activity will assist medical oncologists and other cancer clinicians in the formulation of optimal clinical management strategies for patients with diverse forms of cancer.

LEARNING OBJECTIVE

- Identify end-of-life outcomes significantly affected by early palliative care for patients with Stage IV NSCLC.

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This CME activity contains slides. To receive credit, the participant should review the slide presentation and complete the Educational Assessment and Credit Form located at CME.ResearchToPractice.com.

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Corey J Langer, MD
Professor of Medicine
University of Pennsylvania
Vice Chair, Radiation Therapy Oncology Group
Philadelphia, Pennsylvania

Advisory Committee: Abbott Laboratories, Abraxis BioScience, Amgen Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Biodesix, Bristol-Myers Squibb Company, Caris Diagnostics Inc, Clarient Inc, Genentech BioOncology, ImClone Systems Incorporated, Lilly USA LLC, Morphotek Inc, Novartis Pharmaceuticals Corporation, Onyx Pharmaceuticals Inc, Pfizer Inc, Sanofi-Aventis; Paid Research: Bristol-Myers Squibb Company, Genentech BioOncology, ImClone Systems Incorporated, Lilly USA LLC, OSI Oncology, Pfizer Inc; Speakers Bureau: Bristol-Myers Squibb Company, Genentech BioOncology, ImClone Systems Incorporated, Lilly USA LLC, OSI Oncology.

Lecia V Sequist, MD, MPH
Assistant Professor of Medicine, Harvard Medical School
Center for Thoracic Cancers, Massachusetts General Hospital Cancer Center
Boston, Massachusetts

Advisory Committee: Bristol-Myers Squibb Company; Consulting Agreement: Telik Inc.

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To go directly to the slides and commentary, **click here**.

Last Friday we hosted our annual daylong lung cancer Think Tank with seven renowned investigators, co-chaired by Tom Lynch (be on the lookout for the highlights audio program). One of the main objectives of this closed "recording session" was to review data sets from Chicago, and this dizzying scientific chat included discussion of the following work profiled in the enclosed slide sets:

1. **Crizotinib in patients with EML4-ALK mutations**
An update of the stunning Phase I-II data first presented at ASCO '09 included impressive waterfall plots in which almost all patients had reduced tumor sizes with this not-yet available agent. Approximately four to five percent of patients harbor this newly described translocation that fits the classic oncogene addiction model, and at the Think Tank Dr Lynch described one such individual from his practice who entered this study with substantial symptomatic tumor burden and is still in response two years later. All in attendance agreed on the urgency of making this agent available and of standardizing and disseminating the assay technology, but the faculty was unsure how long this will actually take.

2. **EGFR TKIs versus chemotherapy for patients with EGFR mutations**
A CALGB trial in first-line *metastatic* disease reinforced recent study results clearly demonstrating that a TKI without chemo is preferred for these patients. In contrast, the confusing and incomplete **BR19 trial** suggested the possibility that in the *adjuvant* setting, not only would EGFR TKIs not be beneficial, but for very much unknown reasons they could also be detrimental. Specifically because of this and one prior Stage III data set, there was a strong sentiment among the Think Tank investigators not to use these agents as adjuvant therapy outside a protocol setting.

By the end of this amazing day, it was apparent that a new tissue-based algorithm for systemic treatment of advanced non-small cell lung cancer was on the table. Specifically, the faculty endorsed the baseline evaluation for patients with adequate tumor specimens for EGFR and EML4-ALK mutations and maybe K-ras, which might be predictive of benefit with sorafenib. For patients with needle biopsies without the necessary tumor quantity to conduct these assays, the decision regarding rebiopsy must be individualized based on smoking history, site of disease and performance status. Ed Kim, who first reported his landmark "BATTLE" trial at AACR — followed by

more data from Roy Herbst at ASCO — cautioned that core biopsies by interventional radiology are much more likely to yield adequate tissue than those obtained by bronchoscopy. After hearing MD Anderson coinvestigator John Heymach comment on the unprecedented translational data in BATTLE, it was clear this was the future paradigm of lung cancer research.

3. **Palliative (supportive) care extends survival in the advanced disease setting**
In what some view as the biggest surprise of ASCO, a Harvard randomized trial demonstrated marked OS increases for patients who visited a palliative care specialist about once a month. Dr Lynch had a number of patients in this study and believes the benefits were primarily the result of better management of depression, anxiety and "existential angst." All agreed that "If this was a drug, we'd use it." How to get this advance to patients is unclear.

4. **Older patients may benefit from doublet chemotherapy in first-line advanced disease**
This **plenary presentation** confirmed an emerging theme within oncology: Older patients who can safely tolerate standard therapy derive the same benefits as younger patients.

Next up on our final ASCO issue of 5-Minute Journal Club: GI cancers and a provocative study in pancreatic cancer.

Neil Love, MD
Research To Practice
Miami, Florida

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This program is supported by educational grants from Bristol-Myers Squibb Company, Celgene Corporation, Genentech BioOncology and Millennium Pharmaceuticals Inc.

Research To Practice
One Biscayne Tower
2 South Biscayne Boulevard, Suite 3600
Miami, FL 33131

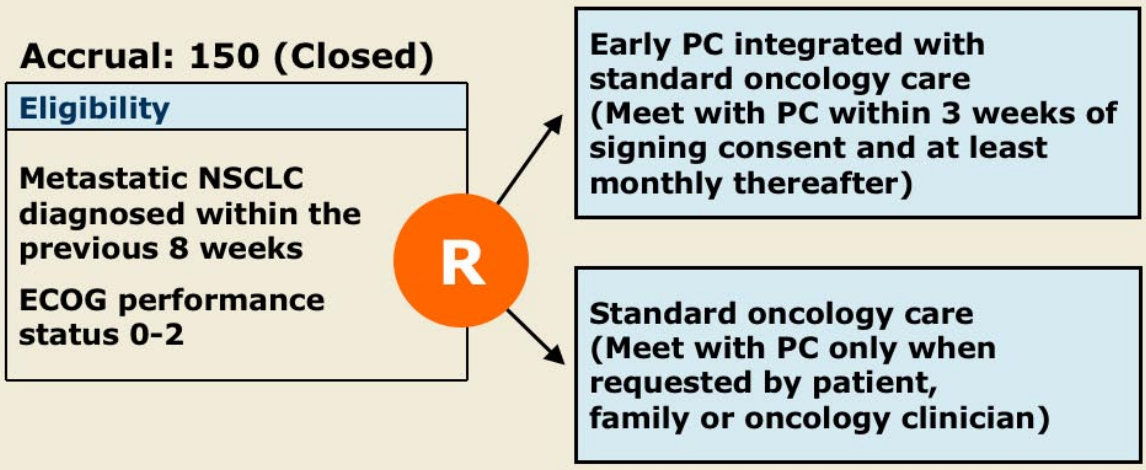
Effect of Early Palliative Care on End-of-Life Care Outcomes among Patients with Metastatic NSCLC

Presentation discussed in this issue

Temel JS et al. **Effect of early palliative care (PC) on quality of life (QOL), aggressive care at the end-of-life (EOL), and survival in stage IV NSCLC patients: Results of a Phase III randomized trial.** *Proc ASCO* 2010;**Abstract 7509**.

Slides from a presentation at ASCO 2010 and transcribed comments from recent interviews with Corey J Langer, MD (7/2/10) and Lecia V Sequist, MD, MPH (6/18/10)

Trial Schema



Prior to randomization, patients completed baseline measures of QOL (FACT-Lung) and mood (HADS and PHQ-9).

Temel JS et al. *Proc ASCO* 2010;Abstract 7509.

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Quality of Life (QOL) Measures at 12 Weeks

	Standard care Mean score	Early PC Mean score	*p*-value
FACT-Lung*	91.5	98.0	0.03
Lung Cancer Symptoms (LCS)*	19.3	21.0	0.04
Trial Outcome Index (TOI)*	53.0	59.0	0.009
Change in QOL from baseline to week 12	**Standard care Mean change**	**Early PC Mean change**	***p*-value**
FACT-Lung	-0.4	+4.2	0.09
FACT-Lung TOI	-2.3	+2.3	0.04

* Lower scores indicative of greater symptom burden

Temel JS et al. *Proc ASCO* 2010;Abstract 7509.

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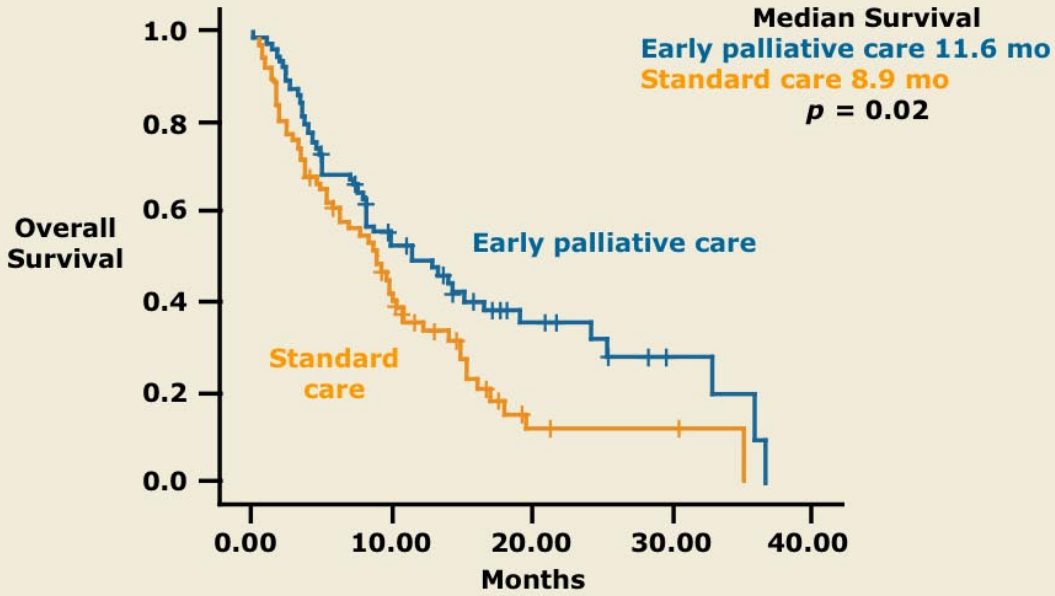
Survival Analysis



Controlling for age, gender and PS, adjusted HR = 0.59 (0.40-0.88), $p = 0.01$

With permission from Temel JS et al. *Proc ASCO* 2010;Abstract 7509.

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ASCO Quality Measures

Measure	Standard care - Median	Early PC - Median	*p*-value
Aggressive EOL care	54%	33%	0.05
No hospice	39%	31%	
Hospice <3 days	15%	3%	
Chemo within 14 days of death	24%	18%	
Documented resuscitation preferences	28%	53%	0.05

Temel JS et al. *Proc ASCO* 2010;Abstract 7509.

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Conclusions

- Compared to standard oncology care, integrated PC led to:
  1) Improvement in QOL
     - May be due to improved symptom management
  2) Lower rates of depression
     - May be due to improved symptom management and illness acceptance
  3) Less aggressive care at EOL
  4) Greater documentation of resuscitation preferences
  5) Higher survival rates. Survival was not a pre-specified study endpoint. Prolonged survival possibly related to:
     - Earlier recognition and management of medical issues; improved QOL and mood; less chemotherapy at the EOL; longer hospice admissions

Temel JS et al. *Proc ASCO* 2010;Abstract 7509.

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Investigator comment on the results of a study evaluating the effects of early palliative care on quality of life, aggressive care at the end of life and survival

This was a "sleeper abstract," and in the long run this study may change how we approach lung cancer. The trial met every endpoint: Quality of life, pain and depression scores were all improved. The patients who received early palliative care had fewer days in the hospital at the end of life and were more likely to be enrolled in hospice. Despite this and perhaps surprisingly, median survival was improved by 2.7 months, which is the outcome we seek with newer targeted agents. This is a very important paper and certainly merited its placement in the lung plenary session.

This study underscores the need to intervene early with palliative care issues. We tend to take a "go-stop" approach. We go full force with chemotherapy or various other interventions while we still think it's worthwhile. Then patients enroll in hospice and we shut the door and suddenly our whole approach shifts. We focus on managing symptoms. The emphasis here is that we have to do both in tandem and intervene early with palliative care. We have to discuss all the prognostic implications of the diagnosis and what long-range plans to implement.

Interview with Corey J Langer, MD, July 2, 2010

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Investigator comment on the results of a study evaluating the effects of early palliative care on quality of life, aggressive care at the end of life and survival

Dr Temel hypothesized that integrating palliative care when patients begin receiving chemotherapy for advanced NSCLC might improve quality of life for patients with metastatic lung cancer, which was indeed shown in this study. However, the real "buzz" at ASCO was the improvement in survival, despite the fact that patients in both arms received an equal number of chemotherapy regimens and the palliative care patients received less aggressive care at the end of life. The Kaplan-Meier curves looked very similar to what was observed in the ECOG study E4599, which evaluated carboplatin/paclitaxel with or without bevacizumab.

A couple of factors may have contributed to the improvement in survival, including better treatment of depression, which we know occurs at a very high rate in lung cancer and is associated with shorter survival. Additionally, better symptom control and faster recognition and treatment of problems may have played a role. In the end, we can't say definitively what contributed to the survival improvement, but Dr Temel is planning a larger, more definitive study to determine whether these results can be replicated in a multicenter fashion.

Interview with Lecia V Sequist, MD, MPH, June 18, 2010