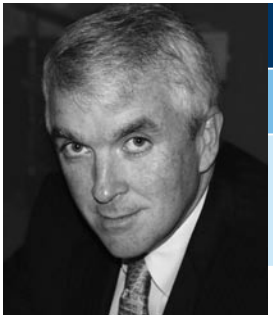

INTERVIEW

Thomas J Lynch Jr, MD

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Tracks 1-17

Track 1 Early palliative care for patients with metastatic non-small cell lung cancer (NSCLC)

Track 2 ARIES: An observational cohort study of bevacizumab-based treatment in advanced NSCLC

Track 3 Rates of severe pulmonary hemorrhage in patients receiving bevacizumab on the ARIES trial

Track 4 In vivo assessment of the effects of bevacizumab in advanced NSCLC

Track 5 Results of a Phase III Gyneco-logic Oncology Group study in advanced ovarian cancer: Role of maintenance bevacizumab after carboplatin/paclitaxel/ bevacizumab

Track 6 CAN-NCIC-BR19: Results of a Phase III study of adjuvant gefitinib in Stage IB to IIIA NSCLC

Track 7 Effect of EGFR and K-ras mutations on clinical outcomes in previously untreated NSCLC

Track 8 Activity of the irreversible EGFR tyrosine kinase inhibitor (TKI) afatinib (BIBW 2992) in patients with advanced NSCLC progressing on erlotinib or gefitinib

Track 9 Clinical features and outcomes of patients with NSCLC who harbor EML4-ALK and clinical activity of the oral ALK inhibitor crizotinib (PF-02341066)

Track 10 Phase III study of second-line crizotinib versus pemetrexed or docetaxel for patients with advanced NSCLC and a specific gene profile involving ALK

Track 11 Phase II trial of ipilimumab and paclitaxel/carboplatin as first-line therapy for Stage IIIB to IV NSCLC

Track 12 Results of a Phase III trial of nanoparticle albumin-bound (*nab*) paclitaxel/carboplatin compared to Cremophor®-based paclitaxel/ carboplatin as first-line therapy for advanced NSCLC

Track 13 Perspective on the role of immune-based therapy in NSCLC and other solid tumors

Track 14 **Case discussion:** A 68-year-old never smoker is diagnosed with NSCLC and an exon 19 mutation while receiving active treatment for chronic myelogenous leukemia

Track 15 **Case discussion:** A 55-year-old woman who received treatment five years ago for BRCA-mutant breast cancer presents with adenocarcinoma of the lung

Track 16 ECOG-E5508: A Phase III study of maintenance therapy with bevacizumab, pemetrexed or both after carboplatin/paclitaxel/ bevacizumab for advanced-stage nonsquamous NSCLC

Track 17 Clinical decision-making regarding the use of maintenance therapy in advanced NSCLC

Select Excerpts from the Interview

Track 1

DR LOVE: Would you comment on the paper you coauthored on early palliative care for patients with metastatic non-small cell lung cancer (NSCLC)?

DR LYNCH: Patients randomly assigned to the early palliative care arm received outstanding palliative care from a team of palliative care doctors, social workers and nurse practitioners. Patients met with the palliative care team once a month. I believe it was the psychosocial support that made the patients on the early palliative care arm stronger. We expected to find that early palliative care improves quality of life and also helps with depression and anxiety, which was demonstrated, but the most shocking finding was that a survival benefit emerged with early palliative care (Temel 2010; [1.1]).

Although some people could argue that survival was not the primary endpoint, I believe we could easily conclude that early palliative care did not adversely affect survival and that patients fare well when early palliative care is integrated. Perhaps with better control of depression and anxiety, patients make better decisions and are therefore benefitting from other therapies. It is important to remember that this was a single-center study and to consider what will happen when we do this across several centers with different palliative care units. The other issue will be whether this approach is applicable to other cancer types.

1.1

Phase III Study Investigating Early Palliative Care in Metastatic Non-Small Cell Lung Cancer

	Standard care (n = 74)	Early palliative care (n = 77)	*p*-value
Depressive symptoms	38%	16%	0.01
Aggressive end-of-life care	54%	33%	0.05
Median survival	8.9 months	11.6 months	0.02

Temel JS et al. *N Engl J Med* 2010;363(8):733-42.

Tracks 2-3

DR LOVE: Would you comment on the ARIES study you reported, which is examining bevacizumab use in advanced NSCLC in the community setting?

DR LYNCH: ARIES is a prospective observational cohort study evaluating the efficacy and safety of bevacizumab in the real-world setting and has enrolled approximately 2,000 patients so far. To enroll in the ARIES study, a patient

must be receiving a bevacizumab-containing regimen for the initial management of nonsquamous NSCLC.

The goal of the ARIES study is to evaluate how bevacizumab is performing in the real world as opposed to in clinical trials. In clinical trials, many patients, such as those with brain metastases, those receiving anticoagulation, those older than age 70 and those with a performance status of 2, are either not represented or are under-represented. Real concern exists about how bevacizumab will perform for these subpopulations.

Results from the ARIES study show that bevacizumab can be safely used for all of these subpopulations and that community oncologists are good at using bevacizumab and selecting appropriate patients (Wozniak 2010; [1.2]). The incidence of pulmonary hemorrhage is also small, which is fantastic, and might suggest that the location of the primary tumor might not be driving the rate of pulmonary hemorrhage (Kumar 2010). I am impressed that the toxicity profile of bevacizumab in the ARIES study is better than it was in the pivotal ECOG-E4599 study.

1.2

ARIES: Observational Cohort Study of Bevacizumab for Nonsquamous Non-Small Cell Lung Cancer in the Community Setting

	All patients (n = 1,970)	Age ≥70 (n = 650)	PS ≥2 (n = 182)	CNS metastasis (n = 150)
Progression-free survival (median)	6.7 months	6.8 months	5.8 months	6.0 months
Overall survival (median)	13.6 months	12.6 months	8.1 months	11.7 months
Severe pulmonary hemorrhage (PH)	0.8%	0.3%	1.0%	—
Grade 3 to 5 bleeding (excluding PH)	3%	3%	4%	—
Arterial thromboembolism	2%	3%	3%	—
Grade 3 to 5 CNS bleeding	0.1%	0%	0.5%	0%

These results suggest that advanced age, poor performance status and CNS metastasis are not necessarily contraindications for bevacizumab therapy.

Wozniak AJ et al. *Proc ASCO* 2010;**Abstract 7618**.

Tracks 9-10

DR LOVE: Would you summarize the EML4-ALK story in lung cancer?

DR LYNCH: I believe this is probably the most important development in lung cancer this year — or even during the past five years. When we learned about the EML4-ALK translocation, we started screening patients for this mutation

with a homegrown FISH assay that could reliably identify it. We found that, overall, approximately five percent of patients with NSCLC harbor the EML4-ALK translocation. It also appears in nonsmokers, but unlike the EGFR mutation, it is a little more common in men than in women. Also, patients with this translocation appear to be a bit younger than the patients who have EGFR mutations.

The Phase I study of crizotinib presented at ASCO 2010 featured one of the most incredible waterfall plots I have ever seen in lung cancer, with response rates in excess of 60 to 65 percent and good progression-free survival (PFS) (Bang 2010; [1.3]). I believe the story of EML4-ALK will be similar to the story of EGFR mutations — after 18 to 24 months, we will begin to see emergence of resistance to therapy.

From the perspective of the practicing oncologist, I believe that for now screening for the EML4-ALK oncogene in never smokers or former smokers makes sense, although one can make a valid argument for screening all patients. An ongoing Phase III trial is open and is randomly assigning patients to crizotinib or chemotherapy in the second-line setting (NCT00932893). The issue will be that inevitably some patients will receive chemotherapy and will not receive the ALK inhibitor in the subsequent line, and I believe one could make a strong argument for approving the drug based on the data that we have right now. ■

1.3

Activity of Crizotinib in a Phase I Study for Patients with ALK Fusion-Positive Non-Small Cell Lung Cancer (N = 82)

Parameter	Outcome
Objective response rate	57%
Disease control rate (DCR)* at eight weeks	87%
Six-month progression-free survival probability	72%

Toxicity: The most frequent adverse events were mild and moderate gastrointestinal events, including nausea (54%) and vomiting (44%), and mild visual disturbances (42%).

* DCR = complete responses + partial responses + stable disease

Bang Y et al. *Proc ASCO* 2010;**Abstract 3**.

SELECT PUBLICATIONS

Bang Y et al. **Clinical activity of the oral ALK inhibitor PF-02341066 in ALK-positive patients with non-small cell lung cancer (NSCLC).** *Proc ASCO* 2010;**Abstract 3**.

Kumar P et al. **Baseline (BL) radiographic characteristics and severe pulmonary hemorrhage (SPH) in bevacizumab (BV)-treated non-small cell lung cancer (NSCLC) patients (pt): Results from ARIES, an observational cohort study (OCS).** *Proc ASCO* 2010;**Abstract 7619**.

Temel JS et al. **Early palliative care for patients with metastatic non-small cell lung cancer.** *N Engl J Med* 2010;363(8):733-42.

Wozniak AJ et al. **Clinical outcomes (CO) for special populations of patients (pts) with advanced non-small cell lung cancer (NSCLC): Results from ARIES, a bevacizumab (BV) observational cohort study (OCS).** *Proc ASCO* 2010;**Abstract 7618**.