INTERVIEW

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Tracks 1-10

Track 1	Incidence and pathogenesis of malignant pleural mesothelioma
Track 2	Efficacy of and quality of life after video-assisted thoracoscopic partial pleurectomy versus talc pleurodesis in patients with malignant pleural mesothelioma
Track 3	Overview of surgical approaches with curative intent for mesothelioma
Track 4	Evaluation of immune checkpoint blockade in mesothelioma
Track 5	**Case discussion:** A 40-year-old Asian never smoker who initially received erlotinib for Stage IV EGFR-mutant adenocarcinoma develops small cell lung cancer transformation
Track 6	Management of patients with acquired resistance to EGFR TKI therapy
Track 7	Choice of erlotinib versus afatinib as initial therapy for EGFR-mutant NSCLC
Track 8	Efficacy and tolerability of rociletinib, an irreversible, highly selective TKI of EGFR-activating and T790M mutations
Track 9	**Case discussion:** A 45-year-old patient with EML4-ALK-positive Stage IV adenocarcinoma of the lung with brain metastases
Track 10	Efficacy and toxicity profiles of crizotinib versus second- and third-generation ALK inhibitors

Select Excerpts from the Interview

Tracks 2-4

DR LOVE: How do you think through initial treatment options for patients with mesothelioma, particularly the issue of surgery?

DR TSAO: We typically offer 2 types of surgery. The first is an extrapleural pneumonectomy. This is a massive procedure for which probably 20 out of 100 patients are candidates, but it is undertaken with curative intent. Our surgeons remove the visceral and parietal pleura. They take out the affected lung and part of the diaphragm and pericardium, and then they reconstruct everything. They also perform a mediastinal nodal dissection. In general we do not use this approach for patients with sarcomatoid mesothelioma or for patients with mediastinal involvement of mesothelioma because outcomes for those patients after the surgery tend to be poor.

Typically, after recovering from an extrapleural pneumonectomy patients receive hemithoracic radiation therapy with either external beam or intensity-modulated radiation therapy. About 4 to 6 weeks after that we administer adjuvant cisplatin/pemetrexed if the patient did not receive any neoadjuvant chemotherapy. We use the same principle as in lung cancer, for which we recommend cisplatin instead of carboplatin for definitive intent.

The second procedure performed in the United States with definitive intent is the pleurectomy decortication. This is not considered an R0 resection because microscopic disease is left behind. With this technique, we leave the lung intact but peel off the tumor in the pleura throughout the chest. We may or may not perform a mediastinal nodal dissection.

In the past, because you couldn't radiate the intact lung after this procedure, it was often considered a purely palliative technique, but now innovative radiation therapy techniques allow us to radiate only the high-risk areas where tumor involvement was significant. We have documented cases with this procedure in which patients are disease free and experience long-term survival outcomes.

DR LOVE: How would you approach pleural effusion secondary to malignant mesothelioma?

DR TSAO: A recent article published by Rintoul and colleagues in *The Lancet* evaluated the use of video-assisted thoracoscopic partial pleurectomy (VAT-PP) versus talc pleurodesis for patients with malignant pleural mesothelioma. The authors reported no OS benefit with the use of VAT-PP in this patient population (Rintoul 2014). Even though quality of life appeared to be better at certain months with VAT-PP, my sense is that patients get a good palliative benefit from talc pleurodesis and if you can control their disease with systemic agents, they generally fare well overall.

Partial pleurectomy in this setting doesn't make a lot of sense to me because the recovery time is considerable. You can achieve a similar benefit with a talc pleurodesis and systemic chemotherapy.

DR LOVE: During the next 5 to 10 years, what do you believe will be the most successful approaches to systemic therapy for mesothelioma?

DR TSAO: I believe that the immunotherapeutic agents are critical in mesothelioma because it's an immunogenic disease. We know that PD-L1 is overexpressed, so trials evaluating the incorporation of the PD-L1 inhibitors into therapy are critical. Evidence of responses to immune checkpoint inhibitors in mesothelioma is mostly anecdotal because we don't have any trials open yet for these patients.

We are currently in the process of developing a SWOG study in the neoadjuvant setting for patients with mesothelioma to evaluate an anti-PD-L1 inhibitor in combination with chemotherapy followed by maintenance immunotherapy. These agents will also be evaluated in the metastatic setting in combination with chemotherapy.

Track 7

DR LOVE: Let's talk about NSCLC. What is your approach to first-line therapy for patients with EGFR-mutant disease? How do you choose between afatinib and erlotinib in this setting?

DR TSAO: Some data were presented at ASCO 2014 suggesting that afatinib seems to work in patients with deletion exon 19 and not so well in those with the L858R mutation (Yang 2014; [3.1]). So that's food for thought when deciding which of those 2 agents to administer in the front-line setting.

Of course, quality of life is always important. Afatinib does tend to cause a little bit more diarrhea as well as a bit more rash, but it is an irreversible inhibitor, so the

thought is that it might be more potent for those patients with EGFR deletion exon 19, which is the patient population for whom I have used afatinib up front thus far. ■

3.1

LUX-Lung 3 and LUX-Lung 6: Combined Overall Survival Analysis of Phase III Studies of Afatinib versus Chemotherapy as Up-Front Therapy for Patients with Advanced Non-Small Cell Lung Cancer Harboring Common EGFR Mutations

Patient group	Afatinib (n = 419)	Chemotherapy (n = 212)
Common mutations: del(19)/L858R Median OS	27.3 mo	24.3 mo
Hazard ratio (*p*-value)	0.81 (0.0374)	
	(n = 236)	(n = 119)
Del(19) subgroup Median OS	31.7 mo	20.7 mo
Hazard ratio (*p*-value)	0.59 (0.0001)	
	(n = 183)	(n = 93)
L858R subgroup Median OS	22.1 mo	26.9 mo
Hazard ratio (*p*-value)	1.25 (0.1600)	

OS = overall survival

Conclusion: This pooled analysis reveals that first-line afatinib significantly improves OS in patients with advanced non-small cell lung cancer harboring common EGFR mutations — del(19)/L858R — compared to chemotherapy.

Yang JCH et al. *Proc ASCO* 2014;**Abstract 8004**.

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