INTERVIEW

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Tracks 1-8

Select Excerpts from the Interview

Tracks 1-2

CASE DISCUSSION: A 59-year-old Hispanic woman and smoker with Stage IIIA adenocarcinoma of the lung who undergoes treatment with chemoradiation therapy

DR SCHILLER: This patient had been in a relatively good state of health until presenting with a 3-month history of cough and a 2-week history of hemoptysis. Workup revealed a 4-cm mass in the right main stem bronchus, about 2 centimeters from the carina. She also had multiple enlarged right-sided mediastinal lymph nodes and was diagnosed with a T3N2 Stage IIIA adenocarcinoma of the lung.

She received weekly carboplatin/paclitaxel with concurrent TRT followed by 2 cycles of consolidation carboplatin/paclitaxel. She experienced some dysphasia while receiving TRT, but that cleared relatively quickly. She did not experience any weight loss but did note some fatigue. Overall, she tolerated treatment well.

DR LOVE: What type of molecular testing for mutational changes was performed?

DR SCHILLER: We did not test for some of the driver mutations, because such testing has not yet been proven to be applicable to patients with Stage III disease who would

be receiving chemoradiation therapy. Molecular testing is an active area of investigation in this setting.

Debate is ongoing in the field about when to test for mutations and whether this should be done routinely. We have 2 reasons for not performing routine testing in this setting. First, this patient may never need to be tested if she is cured by the treatment she receives. Second, in this situation in which we do not have a lot of tumor, who knows what other mutations we may need to test for a couple years down the line? The tumor tissue will be archived for such purposes. The point of recurrent disease would be a good time to test for mutational changes.

DR LOVE: We've heard debate about the use of consolidation therapy after radiation therapy. Why did you administer carboplatin/paclitaxel consolidation therapy in this patient's case?

DR SCHILLER: My treatment choice was based on the results of the randomized Phase II LAMP trial for patients with unresected Stage IIIA/B NSCLC. The trial had 3 arms. Patients received 2 cycles of induction paclitaxel/carboplatin followed by TRT or 2 cycles of induction paclitaxel/carboplatin followed by weekly paclitaxel with concurrent TRT or weekly paclitaxel/carboplatin/TRT followed by 2 cycles of paclitaxel/carboplatin. In this trial, concurrent weekly paclitaxel/carboplatin and TRT followed by consolidation was associated with the best outcome (Belani 2005).

We must differentiate between weekly carboplatin/paclitaxel and any other weekly chemotherapy regimen when administering it for radiation-sensitizing purposes. You are not administering it to clear micrometastatic disease. That's why I believe you need standard doses at some point of the chemotherapy.

DR LOVE: What are the other alternatives to induction paclitaxel/carboplatin when using TRT?

DR SCHILLER: Another option is cisplatin/etoposide, which is the typical SWOG regimen, administered concurrently without any consolidation therapy (Gandara 2003). Standard doses are administered concurrently with TRT, with the idea of using this regimen, both as a radiation sensitizer and systemic therapy. However, it can be a tougher regimen to administer. Although one cannot compare across studies, the data are generally similar with these 2 regimens.

Track 6

CASE DISCUSSION: A 69-year-old man and smoker with extensive-stage small cell lung cancer (SCLC)

DR SCHILLER: This patient presented with cough, hemoptysis, fatigue and a 5-lb weight loss, all of which had occurred relatively quickly over several weeks. He had a large, bulky, 8-cm left-side mass invading into the left main stem bronchus. He also had liver metastases but no bone or brain metastases. He was diagnosed with extensive-stage SCLC. After receiving 4 cycles of cisplatin/etoposide, he had a marked tumor reduction in his liver and lung.

We also elected to administer prophylactic cranial irradiation, based on studies that show that even patients with extensive-stage disease, if they achieve a very good partial response, might also experience a survival benefit.

DR LOVE: Have there been any interesting data presented over the past several years on the treatment of SCLC, particularly with regard to the use of immune checkpoint inhibitors?

DR SCHILLER: SCLC has been an orphan disease for a while. The equivalent of the Lung-MAP trial (NCT02154490) for patients with SCLC is planned. This will be a trial in which the patient's tumor is collected and sequenced. Based on the sequencing data, the patient will be assigned to the appropriate agent.

Immune checkpoint inhibitors represent another interesting area. Data presented at the 2015 ASCO meeting demonstrated a promising response rate with immune-directed therapies in patients with SCLC (3.1). I believe that we're going to see a lot more interest in this area. The data suggest that with the immune checkpoint inhibitors, responses are observed in tumor types such as lung cancer — particularly in smokers — with high mutational load. ■

3.1

Efficacy and Safety of Immune Checkpoint Inhibitors in Recurrent[1] or Extensive-Stage[2] Small Cell Lung Cancer

	CheckMate 032[1]		KEYNOTE-028[2]
Outcome	**Nivo** (n = 40)	**Nivo + ipi** (n = 46)	**Pembro** (n = 20)
ORR	18%	17%	35%
Complete response	0%	2.2%	0%
Partial response	18%	15%	35%
Stable disease	20%	37%	5%
Overall survival	4.4 mo	8.2 mo	NR
Grade ≥3 AEs	**Nivo** (n = 40)	**Nivo + ipi** (n = 47)	**Pembro** (n = 20)
Fatigue	2.5%	0%	NR
Diarrhea	0%	8.5%	NR
Rash	0%	4.3%	NR
Pneumonitis	0%	2.1%	0%
Asthenia	NR	NR	5%
Increased bilirubin	NR	NR	5%
Colitis (Grade 5)	NR	NR	5%

Nivo = nivolumab; ipi = ipilimumab; pembro = pembrolizumab; ORR = objective response rate; NR = not reported; AEs = adverse events

Conclusions:

- Clinical responses with nivo with or without ipi regardless of PD-L1 expression[1]
- Promising antitumor activity with pembro in pretreated PD-L1-positive small cell lung cancer[2]

[1] Antonia SJ et al. *Proc ASCO* 2015;**Abstract 7503**; [2] Ott PA et al. *Proc ASCO* 2015;**Abstract 7502**.

SELECT PUBLICATIONS

Belani CP et al. **Combined chemoradiotherapy regimens of paclitaxel and carboplatin for locally advanced non-small-cell lung cancer: A randomized phase II locally advanced multi-modality protocol.** *J Clin Oncol* 2005;23(25):5883-91.

Gandara DR et al. **Consolidation docetaxel after concurrent chemoradiotherapy in stage IIIB non-small-cell lung cancer: Phase II Southwest Oncology Group study S9504.** *J Clin Oncol* 2003;21(10):2004-10.