INTERVIEW

Alex A Adjei, MD, PhD

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Tracks 1-10

Select Excerpts from the Interview

Tracks 1-2

CASE DISCUSSION: A 60-year-old man and former smoker with Stage IIB adenocarcinoma of the lung treated with cisplatin/pemetrexed

DR ADJEI: The appropriate adjuvant therapy in this setting is somewhat controversial, but the evidence-based treatment is vinorelbine/cisplatin. This regimen has the most robust data in terms of benefit (Sève 2007). However, sometimes one needs to extrapolate a bit. An active chemotherapy regimen in the metastatic setting in most situations will be active in the adjuvant setting. In my practice, we tend to administer cisplatin/pemetrexed to patients with adenocarcinoma of the lung. This is based on our experience indicating that it is probably the best regimen for patients with metastatic adenocarcinoma of the lung.

DR LOVE: What is the probability that a patient with early-stage adenocarcinoma of the lung would complete the standard cycles of cisplatin/pemetrexed versus cisplatin/vinorelbine?

DR ADJEI: Patients may not be particularly fit after surgery, so it is appropriate to use an adjuvant chemotherapy regimen that is well tolerated and can be administered on

schedule to increase the feasibility that all necessary cycles will be received. The Phase II TREAT trial investigated adjuvant cisplatin in combination with pemetrexed or vinorelbine in early-stage NSCLC (Kreuter 2013; [4.1]). Cisplatin/vinorelbine can be immunosuppressive, so in some cases patients may be unable to receive treatment on schedule. Cisplatin/pemetrexed is better tolerated.

Most oncologists believe that chemotherapy doublets administered in the metastatic setting will elicit equivalent results as adjuvant therapy. The Phase III ECOG-E1505 (NCT00324805) trial is ongoing but closed to accrual. This study is evaluating adjuvant chemotherapy with or without bevacizumab for patients with completely resected Stage IB (≥4 cm) to Stage IIIA NSCLC.

It incorporates several chemotherapy regimens, including doublets that are thought to produce similar results in the metastatic setting, such as cisplatin/pemetrexed and cisplatin/gemcitabine. Results from this trial will shed more light on the effectiveness and safety of the different adjuvant chemotherapy regimens.

4.1

TREAT: Results of a Phase II Trial of Adjuvant Chemotherapy with Cisplatin/Pemetrexed (CPx) versus Cisplatin/Vinorelbine (CVb) in Early-Stage Non-Small Cell Lung Cancer

Key endpoints	**CPx** (n = 67)	**CVb** (n = 65)
Feasibility rate*	95.5%	75.4%
Deaths	1 (1.5%)	2 (3.1%)
Withdrawal of consent	0	4 (6.2%)
Dose-limiting toxicities	2 (3%)	10 (15.4%)
Select adverse events (Grade 3-4)	**CPx** (n = 67)	**CVb** (n = 65)
Anemia	0%	1.5%
Thrombocytopenia	0%	0%
Neutropenia	9%	69%
Nausea/vomiting	7.5%	5%
Fatigue	6%	5.5%
Renal impairment	3%	0%
Febrile neutropenia	1.5%	7.7%
Constipation	1.5%	0%
Thromboembolic events	1.5%	0%

*$p = 0.001$

Kreuter M et al. *Ann Oncol* 2013;24(4):986-92.

Tracks 4, 6-7

CASE DISCUSSION: A 50-year-old woman and never smoker with EGFR wild-type adenocarcinoma of the lung receives carboplatin/pemetrexed → pemetrexed maintenance

DR ADJEI: This patient presented in 2009 with a pleural effusion, a lung mass and a solitary vertebral metastasis. At that time the only molecular testing being performed

was for EGFR mutation, and her disease harbored the wild-type form of EGFR. Based on today's technology, we can't classify her disease as pan-wild-type. She received 4 cycles of carboplatin/pemetrexed and achieved a near-complete response. She then received maintenance pemetrexed. She also received zoledronic acid for the solitary bone metastasis, but this had to be discontinued because of some dental issues.

Her disease was responsive to treatment until early this year, when she started experiencing back pain. Upon MRI scanning, we discovered more bony disease. She received radiation therapy, went back on pemetrexed and is now faring well. It has been 6 years, and she's still receiving maintenance pemetrexed.

DR LOVE: Have you considered performing multiplex molecular testing for ALK or ROS1 rearrangement for this patient?

DR ADJEI: No, we do not have any archived tissue to test. Because of the significant shortness of breath at presentation, we had to rapidly perform a chest tube drainage of the pleural fluids by pleurodesis. The DNA sample used for EFGR molecular testing was from the collected effusion cell pellets. Also, because she's fared so well on treatment, we haven't performed other molecular tests.

DR LOVE: Why did you not switch treatment after discovering more bony metastases?

DR ADJEI: The MRI scans revealed the involvement of about 3 vertebrae. A suggestion of epidural disease was observed, but that wasn't clear. Because she had no other evidence of disease, we radiated the spine and continued with pemetrexed instead of switching to another type of treatment. Our plan is to keep her on pemetrexed until disease progression, after which we'll perform a biopsy and multiplex testing.

DR LOVE: What is your rationale for initially administering carboplatin/pemetrexed without bevacizumab? How do you currently approach bevacizumab therapy?

DR ADJEI: My experience through the years has been that the addition of bevacizumab to carboplatin/pemetrexed produces more toxic effects. Patients experience more fatigue, and after receiving 4 cycles of induction therapy the question arises whether to administer pemetrexed, bevacizumab or both as maintenance therapy. In some instances I have used both, but I find that when I do this, it is impossible for the patient to continue maintenance pemetrexed/bevacizumab for a long time. Because of the significant fatigue, maintenance therapy must be discontinued.

The Phase III PRONOUNCE trial reported no significant survival benefit between induction carboplatin/pemetrexed and paclitaxel/carboplatin/bevacizumab in patients with advanced nonsquamous NSCLC (Zinner 2015). This demonstrates that carboplatin/pemetrexed produces good results in patients with adenocarcinoma of the lung and the addition of bevacizumab does not add significant benefit. As such, in my practice I use carboplatin/pemetrexed. Generally, I use bevacizumab if I decide to treat with paclitaxel/carboplatin. ■

SELECT PUBLICATIONS

Sève P et al. **Class III beta-tubulin expression and benefit from adjuvant cisplatin/vinorelbine chemotherapy in operable non-small cell lung cancer: Analysis of NCIC JBR.10.** *Clin Cancer Res* 2007;13(3):994-9.

Zinner RG et al. **PRONOUNCE: Randomized, open-label, phase III study of first-line pemetrexed + carboplatin followed by maintenance pemetrexed versus paclitaxel + carboplatin + bevacizumab followed by maintenance bevacizumab in patients with advanced nonsquamous non-small-cell lung cancer.** *J Thorac Oncol* 2015;10(1):134-42.