Top Five Highlights in Lung Cancer, 2014

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5) Genomic Testing Goes Mainstream

- Broad “multiplex” testing of a multitude of genes in one panel hasn’t yet delivered on its great promise, since there aren’t yet enough “actionable” mutations to help most patients, but 2014 was the year when genomic testing broke out from limited academic centers to the rest of the cancer care world.

- We are entering a new era of both understanding and treatments matched to the cancer. It will also lead to a new classification of cancer based more on the mutation(s) seen in the cancer than the anatomic definition of a cancer based on its tissue of origin.
4) Building Further Momentum for Immune Checkpoint Inhibitors

• Though the FDA hasn’t approved a PD-1 or PD-L1 inhibitor for lung cancer yet, these agents have all shown profound activity in a minority of patients, about 20-25%, who can demonstrate a dramatic and sustained response.

• Multiple immune checkpoint inhibitors are being studied in every clinical setting, alone and in combination with every other treatment for lung cancer.

• These agents are approaching escape velocity for lung cancer. They are poised to change practice profoundly, and soon.
3) Small Benefits for Large NSCLC Populations

- In Europe, Vargatef (nintedanib), an oral antiangiogenic cancer agent, was approved to be administered with Taxotere for patients with advanced lung adenocarcinoma, based on an approximately 2 month improvement in median survival with this combination in the phase III LUME Lung-1 trial.

- The improvement in median overall survival seen with the addition of anti-angiogenic antibody Cyramza (ramucirumab) to Taxotere was a mere 1.5 months, but any improvement for broad populations of previously treated patients with advanced NSCLC is welcome.

- This is especially true when this approach includes the oft-excluded patients with squamous NSCLC. The study led to the approval of Cyramza in lung cancer by the FDA just in the last few weeks.

Overall survival curves from REVEL trial (Garon, Lancet Oncol 2014)
2) Breaking the Impasse Against EGFR & ALK-Positive NSCLC Acquired Resistance

- 2014 saw FDA approval of Zykadia (ceritinib) for XALKORI-refractory ALK-positive NSCLC, though it has greater activity in ALK inhibitor-naive patients. Unlike XALKORI, it and a bevy of other very active additional second generation ALK inhibitors also have impressive activity against CNS disease.

- This year, both AZD9291 and CO-1686 (rociletinib) broke out as 3rd generation EGFR inhibitors with great activity (response rates ~50-60% for both) in patients with T790M mutation as the mechanism of acquired resistance. Trials are rolling out around the world.

“Waterfall plot” of responses to AZD9291, T790M+ NSCLC (Janne, ASCO 2014)
1) CMS Approves Low Dose Chest CT (LDCT) Screening for Lung Cancer in High Risk Patients

- In November, the Center for Medicare and Medicaid Services (CMS) finally voted to approve LDCT screening for the specific population studied in the large National Lung Cancer Screening Trial (NLST) that demonstrated a 20% survival benefit from screening higher risk patients (age 55-74, 30 “pack-year” smoking history).

- The approval, however, was accompanied by unprecedented restrictions, including strict mandates about which patients were eligible, requirements for detailed counseling about the high potential for ambiguous lung nodules and the need for smoking cessation counseling, and a requirement that screening only be done at experienced centers.

- We should see a significant shift in stage of presenting with lung cancer and an improvement in survival if LDCT is broadly implemented.
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