Ocean View Hematology/Oncology Medical Group (OVHOMG)

NEWSLETTER

Lung Cancer and Other News

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EVOLVING TREATMENT PARADIGMS IN NSCLC

CUSTOMIZATION OF NSCLC TREATMENT : evaluating the roles of histology, maintenance therapy, and testing for mutations in EGFR

HISTOLOGY MATTERS. In 2007, a retrospective analysis using subset histology data from a Phase III study of patients with previously treated advanced NSCLC identified a statistically significant improvement in OS for non-squamous patients treated with pemetrexed, compared with those treated with docetaxel. A Phase III prospective study confirmed survival differences based on histology when it showed a significantly superior OS for cisplatin-pemetrexed versus cisplatin-gemcitabine in patients with adenocarcinoma(12.6 vs 10.9 months) and large cell carcinoma histology(10.4 vs 6.7 months). In contrast, in patients with squamous cell histology, there was a significant improvement in survival with cisplatin-gemcitabine compared with cisplatine-pemetrexed(10.8 vs 9.4 months). Pemetrexed is a thymidylate synthase(TS)-inhibiting agent. In NSCLC.\, baseline TS levels are higher in squamous cell carcinoma compared with adenocarcinoma.

NEW TARGETED THERAPIES: EGFR, KRAS, ELM4-ALK mutations and IGF-1 receptor as new targets.

EGFR (epidermal growth factor receptor) mutations are associated with sensitivity to the TKIs gefitinib and erlotinib.

The seminal IPASS study(First-line Iressa versus carboplatin/paclitaxel in Asia) demonstrated moderate efficacy for gefitinib(Iressa) in advanced non-small-cell lung cancer patients, most

notably in patients with predictive factors, including adenocarcinoma histology, no history of smoking, and Asian ethnicity(N Engl J Med 361, 2009).
In the NEJ002 study, researchers from Japan has shown that gefitinib, as a single agent, significantly delayed disease progression in patients with EGFR mutations, making it a reasonable choice as first-line treatment for advanced NSCLC. This is the first Phase-III study for advanced NSCLC patients selected prospectively by sensitive EGFR mutations, and demonstrates superiority of gefitinib against carboplatin/paclitaxel in terms of PFS(10.4 months with gefitinib vs 5.5 with chemotherapy) in the first line.
Based on this data, many oncologists are recommending routine testing of EGFR mutation status, and gefitinibe as standard Rx in NSCLC patients with EGFR mutation.
A new therapy–ALK inhibitors. EML4-ALK is a novel fusion oncogene in NSCLC. ALK mutations are particularly frequent in light or never smokers. Unlike EGFR mutations, they are found more often in males (61% vs 30%). They occur almost exclusively in adenocarcinomas, and doesn't seem to be any variation by ethnicity. ALK rearrangements in NSCLC are relatively rare, 3% to 5% in an unselected NSCLC population. PF02341066, an oral ALK inhibitor developed by Pfizer, has demonstrated efficacy in ALK-positive patients (response has been observed in 65% of the patients enrolled), allowing early development of a Phase III trial of an ALK inhibitor with docetaxel as second-line therapy.

MAINTENANCE THERAPY: Debate continues about delayed (second- or third-line) versus immediate(maintenance) chemotherapy in patients who have already received first-line therapy.
The large Phase III SATURN trial tested erlotinib maintenance versus placebo after platinum-based doublet chemotherapy in stage IIIB/IV NSCLC. Results showed significantly increased PFS with erlotinib in all patients, as well as improved OS(12 vs 11 months).
Another large Phase III trial evaluated pemetrexed as maintenance therapy for patients with advanced NSCLC who did not progressed on an initial platinum-based doublet. Pemetrexed

maintenance resulted in significantly better OS than placebo.(13.4 vs 10.6). and increased PFS. In July 2009, FDA approved pemetrexate(Alimta) for maintenance treatment of patients with locally advanced or metastatic nonsquamous NSCLC.
The Phase III ATLAS trial compared bevacizumab (Avastin) therapy with or without erlotinib, after completion of chemotherapy with bevacizumab for first-line treatment of advanced NSCLC. The ATLAS study, the first to evaluate combination versus single-agent maintenance therapy options, showed significant improvement in PFS in the group receiving combination therapy(4.8 vs 3.7 months).

SBRT (Stereotactic body radiation therapy) may soon become the standard of care for inoperable NSCLC. According to the results of a Phase II trial presented at the American Society for Radiation Oncology(ASTRO) 51 st Annual Meeting, SBRT provided a very high rate of local control(98%) and overall survival of 56% at 3 years in patients with inoperable early-stage lung cancer. This compares favorably with historic results with conventional radiation. I addition to being more effective then conventional radiation, SBRT is administered much quicker, taking place in 3 outpatient sessions, in only 1 week.

ISSUES IN CANCER SCREENING AND PREVENTION

NCCN Guidelines for prostate cancer recently updated to stress careful consideration of active surveillance, also referred to as ”watchful waiting” for men with low-risk prostate cancer, who have a life expectancy of less than 10 years.
NEW CERVICAL CANCER SCREENING GUIDELINES -The new ACOG evidence-based guidelines released in Nov.2009 state that women should have their first cervical cancer screening-standard Pap or liquid-based cytology- at age 21, and be screened every two years instead of annually. Women age 30 and older who have had three consecutive negative test results may be

screen once every three years. Women with certain risk factors may need more frequent screening.
Results from a retrospective study published in the Journal of Clinical Oncology, Nov. 10, 2009 provided evidence that higher 25-hydroxyvitamin D3 levels, at diagnosis, are associated with both thinner tumors and better survival from melanoma, independent of Breslow thickness. Patients with melanoma, and those at risk of melanoma, should seek to ensure vitamin D sufficiency. Additional studies are needed to establish optimal serum levels for these patients.

High levels of vitamin D in the blood appears to be linked to lower risks of colorectal cancer, although it's not clear if higher intake of vitamin actually prevents the disease. It is not known whether supplements are necessary if people reach certain levels through a healthy diet, exercise and moderate exposure to sunlight. The research, published online Jan. 21 in BMJ, is based on a study of more than 520,000 people from 10 countries in Western Europe.

NEW THERAPIES-NEW HOPE

PROVENGE (SIPULEUCEL-T) – On April 29, 2010, the U.S Food and Drug Administration approved sipuleucel-T, an autologus cellular immunotherapy for the treatment of asymptomatic or minimally symptomatic metastatic, castrate resistant(hormone refractory) prostate cancer. Patients treated with sipuleucel-T had an improvement in median OS(25.8 months versus 21.7 months). Sipuleucel-T consists of autologus peripheral blood mononuclear cells, obtained by leukapheresis and cultured(activated) with a recombinant human protein(PAP-GM-CSF).

AFINITOR (EVEROLIMUS) –proven 2 nd line therapy in advanced RCC, after VEGEFR-TKI failure (sunitinib, or sorafenib). Afinitor is a mTOR inhibitor, and targets both tumor cells and blood vessel cells. Afinitor has immunosuppressive properties, and may predispose patients to systemic

bacterial and fungal infections. May also cause non-infectious pneumonitis.

ADVANCES IN PERSONALIZED THERAPY

Oncotype DX colon cancer test: Genomic Health Inc. recently announced commercial availability of its Oncotype DX cancer test, a 12-gene expression test developed for the assessment of risk of recurrence in patients with stage II disease after surgery. Clinical studies provided support for the use of the Oncotype DX colon cancer Recurrence Score as an independent predictor of recurrence risk in stage II colon cancer patients, I addition to the number of nodes examined.

Myriad Genetisc, Inc. will soon launch Prolaris, a 46-gene prognostic test that quantitatively determines the risk of recurrence in patients who have undergone prostatectomy. Prolaris is a molecular diagnostic assay that offers urologists, and oncologists a more accurate way of determining a prostate cancer patient's risk of recurrence, and therefore guiding adjuvant therapy decisions.

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