TRENDS-in-MEDICINE

BULLETIN:

AMERICAN SOCIETY OF CLINICAL ONCOLOGY (ASCO) – PREVIEW

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by Lynne Peterson

In a web and teleconference with reporters, ASCO highlighted six studies. ASCO abstracts – other than late breakers – are now off embargo, and these are the ones ASCO chose to present to the media. This is a brief write-up mostly to provide a sense of the tone and focus of those choices and the webcast. About 39,000 attendees are expected at ASCO in Chicago June 1-5, 2018, and there will be ~5,000 abstracts. The theme this year: Delivering, Discovering, and Expanding the Reach of Precision Medicine.

Breast cancer: ROCHE's Herceptin (trastuzumab)

The government-funded, Phase III, 4,088-patient, U.K. study, PERSEPHONE, found that 6 months of Herceptin is non-inferior to 12 months in women with HER2+ early-stage breast cancer, but 6 months had less cardiotoxicity. At 4 years, disease-free survival was 89.4% with 6 months of Herceptin vs. 89.8% with 12 months. The percentage of patients who stopped Herceptin for cardiotoxicity was 8% with 12 months vs. 4% with 6 months of Herceptin.

From 12%-15% of women diagnosed with early breast cancer have HER2+ breast cancer, so these findings potentially will affect a lot of women. The principal investigator, Helena Earl, MD, an oncologist from the University of Cambridge, said, "We are convinced this will mark the first steps to a reduction in Herceptin treatment."

However, experts, including Dr. Earl, said they do not expect any *immediate* shift to a 6-month course. ASCO president Bruce Johnson, MD, said, "By reducing [duration of therapy by half, they cut down on the number of people who had to stop the treatment by half. And certainly we anticipate this will have an effect on cost as well."

Other comments included:

- *Dr. Earl:* "We will present the results on June 4th, and then there will be a peer reviewed publication, which is in hand, and then it needs to be rigorously scrutinized…I think what we are saying at the moment is we need to have a very detailed look at this group of patients. The headline result is that 6 months is as good as 12 months. This is a real-world result, but we need to be very careful and cautious about coming out at this point and saying 6 months is enough."
- *ASCO chief medical officer Richard Schilsky, MD:* "We don't have the data yet on overall survival. That will come with time…I think we need time for the data to mature…When we see results from a trial, we are looking at average results, and undoubtedly there well may be some women who don't do as well with only 6 months of treatment…We need to look for biomarkers. Personally, I find the results quite compelling, and I think it is likely it will signal a shift even in the U.S. oncology community toward shorter duration of adjuvant Herceptin therapy."
- *ASCO president Dr. Johnson:* "Fewer than 10% of patients have died, so this is a group of patients who are very effectively treated…and only 12% relapsed. The benefit in terms of cardiotoxicity is pretty clear…We have to be circumspect on how long to wait and how much data are needed. It may be too early to make a definite change in practice."

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In 2012, a study found that 2 years of Herceptin was not better than 1 year, but 6 months of Herceptin has never been studied before. Asked if this trial will change payor coverage of Herceptin in the U.K. or the U.S.:

- *Dr. Earl:* "I think we have to wait for longer follow-up and take a real close look at the data, but what we hope is that this will become, for many women, standard of care…In changing treatment from established 12 months, that is always going to be a very complex and challenging thing to do."
- *Dr. Schilsky:* "In the U.S. I think it is unlikely that payors will mandate a shift to 6 months until and unless either the label for Herceptin is changed in a supplemental new drug application submission to the FDA based on data…or recommendations begin to appear in accepted clinical practice guidelines. Until one of those things occurs, there is not a rationale for payors to mandate a physician undertake course of [just 6 months]."
- *Dr. Johnson:* "In my opinion, the efficacy drives most of the therapeutic decision-making…Five-year follow-up is a reasonable initial step, but for being certain of the efficacy, you probably need a bit more time."

T-cell malignancy: GLAXOSMITHKLINE's Arranon/Atriance (nelarabine)

T-cell acute lymphocytic leukemia/lymphoma (T-ALL/T-LLy) affect 1 of every 6 children diagnosed with ALL, but 20% of those children do not survive even with best available treatment. The federally-funded, Phase III COG-AALL0434 trial in 1,545 patients found that adding nelarabine improved 4-year disease-free survival to 91%, an increase of nearly 10%, in T-ALL patients (but not T-LLy patients). In T-ALL patients who didn't achieve induction remission, nelarabine more than doubled the survival rate to 54%.

Principal investigator Kimberly Dunsmore, MD, a pediatric hematologist from the Carilion Clinic in Roanoke VA, said, "These are the best-ever survival data [in this cancer]." And she said the benefits were obtained without an increase in toxicity. However, nelarabine does have toxicity, with 8% of patients having Grade 3/4 neurotoxicity – motor and sensory neuropathy.

Non-small cell lung cancer (NSCLC): Genetic testing

A study, led by Nathan Pennell, MD, PhD, a medical oncologist at the Cleveland Clinic, compared the cost-effectiveness of next-generation sequencing (NGS) testing vs. different approaches to sequential gene tests of NSCLC patients in a hypothetical health plan with 1 million members. The study made some assumptions: that after a single gene test, 50% of patients would undergo further testing (e.g., for clinical trial entry), that 8% of patients would need a re-biopsy (with only 30% of those patients actually getting one).

The conclusions:

- Upfront NGS testing would save that imaginary health plan $1.4 million-$2.1 million.
- NGS and a Hotspot panel (multiple single-gene tests done at the same time) results in appropriate therapy being initiated 2.7-2.8 weeks faster than sequential or exclusionary testing.
- NGS identified a higher percentage of patients with targetable alterations than other strategies.
- The current genomic alterations with FDA-approved therapies are EGFR, ALK, ROS1, and BRAF, but NGS testing will also identify other alternatives likely to get FDA-approved therapies in the future, including MET, HER2, RET, and NTRK1.
- Increasing the percentage of patients tested by NGS leads to consistent decreases in costs to payors.

ASCO's Dr. Johnson, a lung cancer specialist, said, "NGS panels are 50-400 genes, so you have a lot more information at a cost that is competitive or less…So, this will be welcome news for people who take care of ordering these gene panels."

Lung cancer – screening

A study found that an amazingly low percentage of patients at high risk of lung cancer are getting screened for the disease. In 2013 the U.S. Preventive Services Task Force recommended annual low-dose CT (LDCT) screening for smokers at high risk of lung cancer – those age 55-80 who smoked 30 pack-years and who currently smoke or have quit within the past 15 years. In 2015 the Centers for Medicare and Medicaid Services (CMS) agreed to cover LDCT.

However, a study, using data from the American College of Radiology's Lung Cancer Screening Registry, which includes 1,796 sites, found that only 1.9% of eligible smokers are getting screened – 141,260 out of the estimated 7,612,975 who were eligible for LDCT.

The principal investigator, Danh Pham, MD, a hematologist from the James Graham Brown Cancer Center at the University of Louisville, said, "This is a call to action to increase the much-needed screening." ASCO's Dr. Johnson added, "It is very disappointing how uncommon this [screening] is…There is a certain segment of people who think it [lung cancer] is a sort of self-punishment. We hope the message will get out…and people will get in and get screened for lung cancer."

Asked how the lung cancer screening rate can be increased, Dr. Pham said, "The most radical thing we can suggest is making lung cancer screening a national quality health measure, the way CMS made breast cancer screening and colonoscopies a national area of improvement in 2008." ASCO's Dr. Schilsky said, "I agree that could be an effective strategy…Screening of high-risk patients is mostly by primary care doctors, not oncologists, so we need to be sure primary care doctors are well aware of the screening data and are referring the appropriate patients for screening and are aware of the screening centers in their community." ASCO's Dr. Johnson added, "ASCO is working with the American College of Physicians and other primary care groups to get the message out and to educate our patients who have been treated successfully."

Head and neck cancer: Mobile monitoring of dehydration

Head and neck cancer (HNC) patients who undergo radiation therapy have a high symptom burden and an increased risk for dehydration. A study by MD Anderson Cancer Center researchers found that using mobile and sensor technology can assist in early detection of both symptoms and dehydration risk in outpatient care. They remotely collected and analyzed weekday weight and blood pressure using Bluetooth-enabled devices and patient-reported outcomes with a mobile app. Clinicians reviewed the data daily.

The study found that the remote monitoring lowered the severity of both general and HNC-specific symptoms vs. usual care. There was good patient adherence to the monitoring. There was no data on quality of life, but the researchers speculated that the monitoring might improve both quality of life and health outcomes.

Cancer-related insomnia: CBT vs. acupuncture

According to ASCO's Dr. Johnson, 60% of cancer patients have trouble sleeping. The usual treatment is sleeping pills, but there are two other options: cognitive behavioral therapy (CBT) and acupuncture. Perhaps surprisingly, 73% of U.S. cancer centers offer acupuncture.

Researchers, led by Jun Mao, MD, an integrative medicine specialist at Memorial Sloan Kettering Cancer Center, set out to figure which of those 2 non-drug therapies was better. The answer was:

- At 8 weeks, both treatments produced clinically meaningful benefits (>8-point reduction in the insomnia index score).
- After 8 weeks of therapy, the benefit is maintained for another 12 weeks.
- In mild insomnia, CBT is more effective than acupuncture.
- In severe insomnia, there is no significant difference between the two therapies.