[News * Analysis * Commentary * Controversy]

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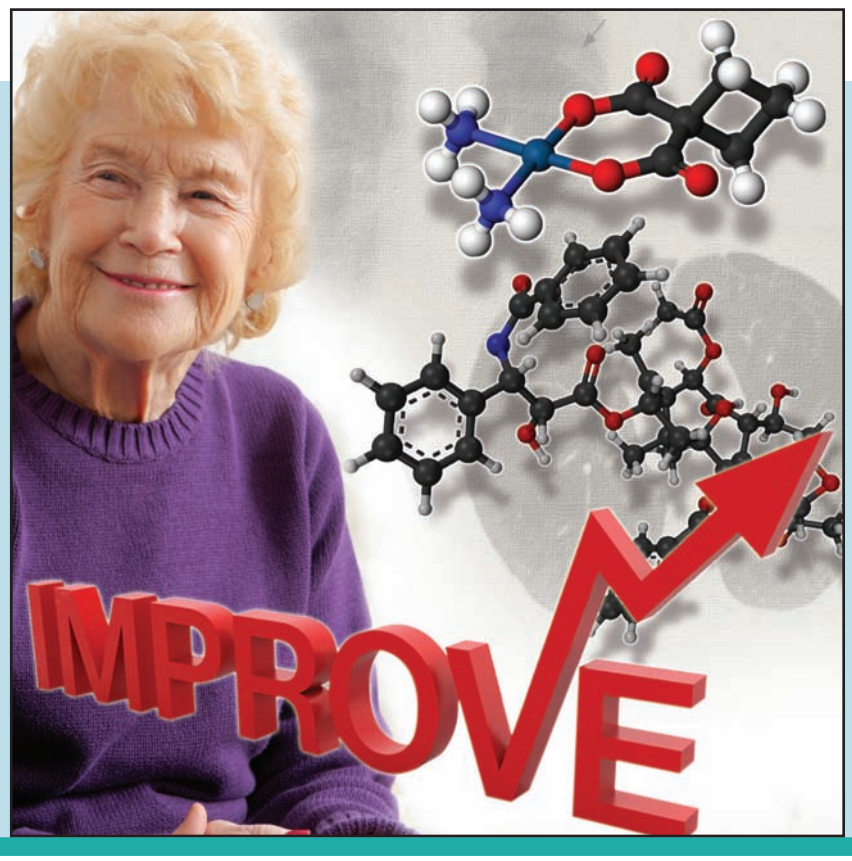

NSCLC: Doublet Therapy Shown as OK for Fit Older Patients

BY KURT SAMSON

For years, younger patients with advanced non-small-cell lung cancer have benefited from combined chemotherapy using platinum-based doublet chemotherapy, but the treatment was usually not given to older patients due to concerns about potential toxicity. A new study, though, shows that many patients over age 70 can also have increased survival without prohibitive toxicity. "At the end of the day," one expert told us, "age is just a chronological number, and performance status always trumps age. This Phase III trial validates what some of us have already been doing with carefully selected and monitored elderly NSCLC patients. These new results are not just positive, but significantly so."

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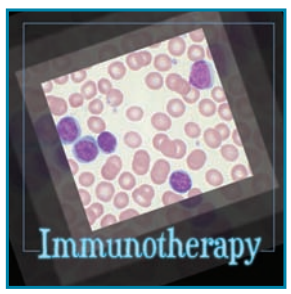

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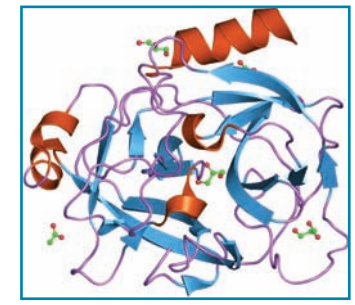
[ALSO]

PERIODICALS

Three Low PSA Scores Between Ages 40 and 60 Associated with Very Low Risk of Metastatic Prostate Cancer



BY RABIYA S. TUMA, PHD

PSA testing is known to be associated with a high rate of false positives and with being unable to distinguish between indolent and aggressive disease, and research continues on trying to find ways to improve on the problems. In one such effort, reported at the ASCO Annual Meeting, researchers found that men who had low scores on three sequential PSA tests between the ages of 40 and 60 had a very low risk of developing metastatic prostate cancer and, thus, could avoid future or more intensive screening (*Abstract 4512*).

"We can say that early PSA testing can discriminate many men at low risk from fewer men at highly elevated risk of death from prostate cancer many years later," said lead author Hans Lilja, MD, PhD, Attending Research Clinical Chemist at Memorial Sloan-Kettering Cancer Center, who presented the work.

"However, a single PSA test between ages 45 to 49 or 51 to 55 is not sufficient to rule out long-term risk of metastases from prostate cancer. But three tests between 40 and 60 would identify men at very low risk of disease, who can skip further tests — and thus would change the risk-benefit equation of PSA testing."

Rebuttal from Discussant

Not everyone is convinced that this scheme would improve the situation, though. In his discussion of the abstract, Joel B. Nelson, MD, the Frederic N. Schwentker Professor and Chair of the Department of Urology at the University of Pittsburgh School of Medicine, said that the data don't really help distinguish men who need follow-up and treatment from those who don't: "We need to ask is whether this will change how we screen.

"Low PSA is not a clinical problem," he said. "In the world of urology, it is the [men with] higher PSAs who fill our clinics…The ones who I am trying to figure out if they have prostate cancer are in the highest quartile."

Follow-up in Large Unscreened Population

To find ways to optimize PSA screening, Dr. Lilja and colleagues have been studying a cohort of 21,277 men in Sweden who provided blood samples between 1974 and 1986 and did not undergo regular PSA screening. The men were age 33 to 50 when they donated blood, and a subset of 4,999 men provided a second sample six years later.

With a follow-up of 27 years, 1,369 men were diagnosed with prostate cancer, 241 developed metastatic disease, and 163 died from prostate cancer.

Using the blood samples and follow-up data, Dr. Lilja and colleagues found that men whose PSA score was in the top 10% (1.6 ng/ml or higher) at age 45-49 accounted for 44% of the cancer-specific deaths. However, about 30% of the cases of metastatic disease occurred in men whose PSA was at or below the median (0.7 ng/ml).

There were similar results with a single test between the ages of 51 and 55. Specifically, 45% of the deaths occurred in

"A single PSA test between age 45-49 or 51-55 is not sufficient to rule out long-term risk of metastases from prostate cancer. But three tests between 40 and 60 would identify men at very low risk of disease, who can skip further tests—and thus would change the risk-benefit equation of PSA testing."

men in the top 10% of PSA scores, but 18% of the metastatic cases arose in men whose PSA was at or below the median.

"We cannot identify a tentative cut-point where men should have no further PSA testing," Dr. Lilja said. "A single PSA test at 45 to 49 or 51 to 55 is not sufficient to rule out subsequent risk of metastasis up to 30 years."

However, looking at the cumulative incidence, the team concludes that men whose PSA is at or below the median at both age 45 to 49 and at 51 to 55 have a very low risk (approximately 0.2%) of developing metastatic prostate cancer or dying from the disease during the next 15 years.

"Based on the current findings – and the data reported in *BMJ* in September 2010 [which correlated the risk of death with PSA at age 60] – we conclude that about half of all men may not benefit, importantly, from more frequent or intense screening than three PSA tests during their life-time," Dr. Lilja said. "We, instead, should focus the more frequent and elaborate screening efforts on the men at increased risk — for example, men with PSA levels above the median at age 45-49, 51-55, or at age 60."

Dr. Lilja disclosed that he holds patents on PSA assays and free PSA testing.

Time for a Consensus

In addition to questioning whether the newly reported data would really help sort out which patients need follow-up and treatment, Dr. Nelson emphasized that PSA testing and long-term prediction of prostate cancer risk seem to be without clear biological underpinnings. "I am always somewhat amused by the mechanism – or lack of mechanistic explanation," he said. "How does a single PSA test predict an event that will happen 30 years later? It is really quite remarkable."

"It is time that we take all of these data and make a consensus, rather than having people present these data and be provocative and make these sorts of claims. If we are going to change the way we screen, it should be evidence-based, on the totality of the data that we have."

—Study Discussant Joel B. Nelson, MD

He also questioned the need for further screening recommendations. In 1997 Ballentine H. Carter, MD, recommended that the field move to an every-other-year screening schedule for men whose PSA was less than 2 ng/ml. Since then there have been no less than four alternate screening schedules proposed, including every other year for all men, testing every five or eight years, and stopping all testing in men whose PSA at age 60 was less than 1 ng/ml (The last recommendation was from Dr. Lilja and colleague's 2010 *BMJ* paper.)

"I think it is time that we take all of these data and make a consensus, rather than having people present these data and be provocative and make these sorts of claims," Dr. Nelson said. "If we are going to change the way we screen, it should be evidence-based, on the totality of the data that we have."