Does Age Matter? Treating Older Patients with Advanced NSCLC

We know far too little about the best way to treat older patients with NSCLC, that lung cancer, like many other cancers, is a disease highly related to advanced age. First, how do we define an older, or elderly, population in cancer treatment terms? Beyond the joke that it increases as the person answering gets older, in the US it’s usually around 70, occasionally defined as 65, generally outside of the US. Despite the fact that the average age for patients newly diagnosed with lung cancer is in the late 60s, trials done in lung cancer far disproportionately enroll younger patients. It’s only been in the last few years that trials have been done specifically looking at older patients, or including them in large enough numbers in broader trials to ask meaningful questions about whether they should be treated identically or differently than younger patients.

Before assessing whether older patients might be good candidates for the same standard therapies as younger patients, the early studies tested whether single-drug chemotherapy was better than no treatment at all. By far the most influential of these was the Elderly Lung Cancer Vinorelbine Italian Study, affectionately known as ELVIS (you have to give the Italians credit for developing such a great acronym, when English isn’t even their first language!). The ELVIS trial randomized 191 patients 70 years or older to receive either vinorelbine, also known as Navelbine, as a single agent for 2 weeks in a row and then a week off, along with supportive care, or “best supportive care” alone. At that time, it wasn’t clear whether giving chemotherapy to older patients was helpful or potentially harmful, so having half of the patients receive no chemo was considered ethical. The trial clearly demonstrated that older patients demonstrated from this chemo, and the proportion of patients alive one year after enrolling on the trial was more than double in the chemo-treated arm. At the time time, quality of life measurements also favored the patients getting treated, so it wasn’t as if patients had to trade off longer survival for feeling worse during that time. The highlights of the trial are shown below.

After that, some trials tested whether giving two “non-platinum” drugs, usually gemcitabine with navelbine, was better then navelbine alone. Those trials showed mixed results, so it remained unclear whether it was better to just choose one drug or two. At the same time, several small trials showed that other single agent regimens, including gemcitabine, or either of the commonly used taxanes (taxol or taxotere) all appeared to be feasible in elderly and or poor performance status (low acticity level) patients, so any of these choices was widely
considered appropriate, and navelbine was probably chosen a bit more often because it often has a pretty mild side effect profile and had the ELVIS trial demonstrating the survival benefit.

Despite the general perception that all of the single-agents being used for elderly or poor performance status patients produce essentially the same results, one trial that actually showed a difference has recently been reported by Kudoh and colleagues (abstract here). In this trial, 180 Japanese patients, age 70 or older, with previously untreated advanced NSCLC received either navelbine as a single-agent (2 weeks on treatment, one week off), or taxotere one day every 3 weeks. Of note, the dose used in Japan was 60 mg/m2, 20% less than we generally use in the US, although the lower dose is standardly used in Japan. The elderly patients receiving taxotere had a response rate that was more than double that seen with navelbine, the median survival was more than 4 months longer and one year survival 22% higher in the recipients of taxotere. The trial design and highlights of the results are shown here:

![Comparison of Two Single-Agent Approaches in Elderly Patients](image)

(click to enlarge)

While results in Japan and the US are not always the same, potentially due to differences in side effects and activity against the cancer in different genetic populations, but the differences are striking enough that I might now consider there to actually be meaningful differences that would favor me selecting taxotere over another option as a single-agent.

But the question of whether older and/or sicker patients should receive doublet chemo still remained. Differences based on age were reviewed in one very large trial by the Eastern Cooperative Oncology Group (ECOG 1594 trial, abstract here) that showed that any of the commonly used platinum-based doublets produced comparable results was reviewed by patient age. This review, by Dr. Corey Langer in Philadelphia, showed that patients over 70 did every bit as well as the younger patients, whether looking at response rate or survival measures, although they did have a tendency to experience more toxicities, including lower blood counts and occasional neurologic side effects. The highlights are shown here:

![Results <70 vs ≥70 Years](image)

(click to enlarge)
Although there were only a few patients in their 80s enrolled on the trial, the exploratory analysis of these patients suggested that they did considerably worse than other patients, so although patients in their 70s seemed to benefit quite a bit, there may still be an age issue in the higher range.

Another trial that has been very important in interpreting whether elderly patients are candidates for doublet therapy has been the CALGB 9730 study by Rogerio Lilenbaum, from Miami. This trial enrolled 561 patients, not restricted by age, to carboplatin/taxol every three weeks or just the taxol, directly asking whether a platinum-based doublet gave better results than a modern single agent. Most of us in the field were not surprised that the overall population did better with a two-drug combination, but it was notable that elderly patients also clearly did better, in terms of response rate and survival, with the carbo/taxol doublet compared to taxol alone:

![CALGB 9730 Results by Age](image)

(click to enlarge)

Overall, the studies with older patients pretty consistently show that “functional age” and how active a person tends to be is much more important in predicting how a patient can tolerate treatment than “chronologic age” (like they say: “you’re only as old as you feel”). It’s only when you get toward and beyond 80 that we really become unsure about the wisdom of full-bore chemo (even a very fit 85 year-old has an 85 year-old liver and kidneys). But importantly, more and more of our trials in lung cancer are now including older patients and asking specific questions about how this very significant subpopulation of the cancer community is best treated.