Elderly Patients: Single Agent vs. Doublet Chemotherapy

Jared Weiss, MD
Thoracic Oncologist
UNC Lineberger Comp. Cancer Ctr.
Chapel Hill, North Carolina

TRANSCRIPT & FIGURES
I have the privilege of speaking to you today on the topic of therapeutic intensity for older lung cancer patients. My talk is entitled “How many drugs for elderly patients – 0, 1, or 2,” because that’s one of the major controversies that plays out in the real world.

The first point to be made in discussing the appropriate intensity of treatment for older patients is that older patients have a lot more life expectancy than many people think by common sense.

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The elderly: In the absence of severe comorbidity, life expectancy is likely driven by the lung cancer

SSA actuarial life table, cited in Weiss, 2013
A 70 year old man in good health has an average of 14 years of life expectancy – that number is 16 years for women, and so a lot of this therapeutic nihilism that comes from doctors that say, “well this person is old, they’re going to die soon anyway,” is really unfounded – there’s quite a bit of quality life to be had for many older lung cancer patients and therefore, appropriate treatment should be pursued.

“Traditional” View of Quality of Life

Chemo causes:
- Nausea
- Alopecia
- Fatigue
- Infections

Therefore, maximize quality of life by avoiding chemo.
The traditional view of quality of life in cancer is that chemotherapy causes all kinds of terrible side effects – lots of nausea, loss of hair, fatigue and infections. So the dominant world view to many, both patients and I think doctors even too, is that the kindest thing to do is to give no drugs to avoid these horrible side effects and that's the best way to maximize quality of life. It is certainly true that our drugs have very real side effects that cause very real suffering. The problem is that simplistic view of quality of life ignores the suffering that the cancer causes, and lung cancer is unfortunately one of the more brutal cancers.

![An Alternative View of Quality of Life](image)

Cancer growth causes:

* Pain
* Cough
* Shortness of breath
* Fatigue
* Organ Failure
* Thrombosis
* Hoarse voice
* Nausea
* Anorexia

Chemo can alleviate cancer suffering.

Better drugs and better supportive care means more tolerable anti-cancer therapy.
When lung cancer presses on a nerve, and there are nerves throughout the body, it causes pain. When it spreads within the lung, it can clip off airways, causing cough and shortness of breath. When it spreads anywhere in the body, the soluble factors it releases can cause fatigue, trouble eating, blood clots, and so on and so forth. Anywhere in the body you can imagine lung cancer spreading, it can cause suffering. So I actually view quality of life more as a balance where our considerations have to consider both the suffering caused by the side effects of our treatment, on the one hand, but also preventing the suffering that lung cancer causes. A good treatment is one that minimizes the side effects, but also minimizes the suffering from the cancer and looks globally at total quality of life.

ELVIS, beyond being the king of trials, at least in terms of trial naming, was also the first trial to show a real improvement in survival by treating older lung cancer patients. At the time of design of this study there was legitimate controversy as to whether we were doing good by treating older lung cancer patients at all.
So this trial, at that time, randomized fit older patients to single agent therapy with a drug called vinorelbine or to placebo. As you can see at the left, there was a small but significant survival advantage with the use of vinorelbine, and at least as importantly, at right, you can see there was also a quality of life advantage to the use of this treatment.

However, our standard of care for patients unselected by age is actually two drugs, not one. One of those drugs should be a platinum drug, and the other a partner drug like vinorelbine or many others.
CALGB 9730 was a randomized trial; patients were unselected by age – half got doublet therapy, two drugs, the other half got just one drug. So you can see at left, in younger patients, there is a survival advantage to the use of two drugs over one, and as you can see at the right, this survival advantage held for older patients.

After those results there was a lot of controversy still about whether to give two drugs or one. The camp that believed that one drug was better for older patients gave gemcitabine or vinorelbine. The camp the believed in two – a lot of us were very into this regimen of carboplatin with paclitaxel broken up
to be given weekly. What we liked about this regimen is that for the fit older patient who tolerates beautifully, you can plow straight ahead, maximize his or her benefit. For the older patient that starts to get into some trouble with side effects, you can dose modify or even completely bail — you’re not stuck with three or four weeks worth of drug in the patient.

So this was a very well designed French trial that took what those who believed in single agent were using for fit older patients, versus what those who believed in double agent were using for their patients, and randomized them one against the other.
As you can see here, there was an improvement in cancer control with two drugs versus one, and this did translate into a significant and meaningful improvement in survival.

But you might ask me, “are all older patients fit,” and of course they’re not. With aging comes more medical problems, more medicines, greater fatigue, loss of hearing, loss of kidney function, and a variety of other physiological changes, and so it’s important to talk not just about the fit elderly, but also about the less fit elderly. In oncology, fitness is measured in terms of performance status.
Performance status 2 are those borderline patients that we think of, how intensely should we treat and where there's great controversy.

There actually is a recent trial that looks specifically at these PS 2 or borderline-functional patients giving them single agent therapy with pemetrexed or double agent therapy with carboplatin and pemetrexed.
Overall this trial of patients with borderline-functional status showed an improvement in survival with two drugs versus one.
What about patient with limited performance status? Still 2 drugs!

A huge portion of the patients in this trial were elderly, and so when we look at our less fit elderly patients as a subgroup of this trial, you see here that there’s still an improvement in survival.

I should mention the two drugs versus one elderly study that I had mentioned earlier did have a subgroup analysis by those patients with borderline-functional status, and there was an improvement as well in that group.
Here’s toxicity when looking at two drugs versus one – you can see of course there are more side effects with two drugs versus one, but really nothing horrible. Carboplatin really added a small but real amount of toxicity, and for the survival advantage and improvement in suffering from cancer control provided, in my opinion it’s worth it for patients with good performance status, as well as perhaps those with somewhat borderline status.
So in summary, two is better that one, and I show here for your amusement my twins Betty and Dina that we're delighted to welcome to the family – two is better than one! I thank you for your kind attention.