

Interview with Dr. Toni Wozniak, MD on Small Cell Lung Cancer
By Howard (Jack) West, MD
March, 2009

Dr. West: Hello, I'm Dr. Jack West, medical oncologist at Swedish Cancer Institute in Seattle, Washington and President and CEO of GRACE, the Global Resource for Advancing Cancer Education. I'm fortunate to have the opportunity to speak today with Dr. Antoinette Wozniak, known as Toni to friends. She is a medical oncologist, Professor of Medicine and lung cancer expert at the Barbara A. Karmanos Cancer Center at Wayne State University in Detroit, Michigan. Thanks so much for taking the time.

Dr. Wozniak: Thanks Jack.

Dr. West: Copies of the transcript as well as a PDF file of figures from the program are available at the website www.cancerGRACE.org/GRACEcasts. Let's start today with a discussion of small cell lung cancer, a field for which our progress has been slow over the last couple of decades. What do you consider to be the standard treatment for patients now with limited stage small cell lung cancer?

Dr. Wozniak: The standard of care really hasn't changed very much. The standard of care for someone with a good performance status would be concurrent chemotherapy and radiation and the chemotherapy would be platinum-based with etoposide usually two courses given with radiation and two courses following radiation. The radiation, if possible, should be hyperfractionated, given twice a day.

Dr. West: So you'd mentioned the twice daily schedule and yet that is not something that is employed that often for something that has some survival data associated with that. What do you think are the limitations in its uptake in broad practice?

Dr. Wozniak: Well, it's actually you're right Jack, it's not used broadly. We happen to work with the radiation therapist who wrote the study that was published in the New England Journal (of Medicine), and it was a study in which chemotherapy was given concurrent with radiation and patients were randomized to get single fraction standard radiation to 45 Gray versus BID to 45 Gray. And I think there are several reasons it hasn't become the standard of care even though the BID radiation are more superior. It's inconvenient. I think that's one of the big things. Patients have to get the radiation twice a day with some time in between and it's an all day affair. Also, there is some question as to whether 45 Gray given BID is really the same as given a single fraction; I think that's been the

issue. So, currently there is a trial that's ongoing, an inter-group trial, looking at whether single fraction higher dose radiation is just as good as 45 Gray given BID. So, hopefully we'll answer that question relatively soon.

Dr. West: Do you routinely send your patients for prophylactic cranial irradiation after completing chemo and radiation for limited stage?

Dr. Wozniak: Yes I do. I explain it to them and I offer it to them. If I have a very elderly patient I might reconsider that, it depends; but for the most part, I think most people do get prophylactic cranial radiation, even now with extensive disease that's responded to treatment.

Dr. West: What do you tell people about the risk versus benefit if they express a concern particularly about cognitive problems afterwards?

Dr. Wozniak: Well, unfortunately, the information with cognitive problems is not really well defined. And to the most part, most people do tolerate it quite well. I tell them that there is that possibility, although it's a little unclear as to the risk, the nature of the risk and the amount of risk in taking the radiation. In my opinion, I think that the development of brain metastasis is worse than the potential risk of neurocognitive problems.

Dr. West: What about your approach for patients with extensive small cell lung cancer?

Dr. Wozniak: Well, obviously, we haven't made a lot of progress in this disease. There have been trials looking at new agents, but nothing is out there in terms of improving treatment. So, off trial, I generally use carboplatinum and etoposide as my standard treatment and we do have a maintenance trial with Sutent and we're trying to accrue patients to that.

Dr. West: You had mentioned this trial of maintenance therapy probably compared to a placebo. What is the background and what is the current status of maintenance therapy as a concept to improve survival in small cell lung cancer?

Dr. Wozniak: Unfortunately, many of the trials of maintenance therapy are all negative. So there is no proof that maintenance therapy is of value in this disease. But we keep trying and, actually, I think one of the ways to try is to investigate some of these new agents in that particular manner.

Dr. West: You'd mentioned the concept of giving prophylactic cranial irradiation not only for patients with limited stage small cell, but also potentially for patients with extensive disease. We have seen data come out of Europe with that that suggests a survival benefit. You would say then

that that data is enough to potentially change our standard and recommend that approach for responding patients with extensive small cell?

Dr. Wozniak: Yes I would. I think we were all surprised with that data when it was reported a couple of years ago at our national meeting. But the data is the data and it appears that it does improve survival, so I reserve it for patients who have had a good response to upfront treatment and who have maintained their performance status. And I think probably the improvement survival comes from the fact that they have a reduction in the development of brain metastases which can be quite difficult to manage.

Dr. West: What is your approach for patients who have relapsed small cell lung cancer and do you make a distinction between the patient who has evidence of recurrent progressing disease six weeks versus six months after their last chemotherapy?

Dr. Wozniak: I think that someone who has a long progression-free interval might be someone who's still sensitive to the original chemotherapy. So if someone has a progression-free interval of six months, I tend to go back to the original treatment. In terms of second-line, otherwise, again, we are interested in new agents and we hope for, we don't have any studies open now, but we are trying to open a study for a second-line chemotherapy with a novel agent. Now, outside a study, I think you have various options. I generally don't use combination chemotherapy, I tend to use single agent. I think some of the options are taxine, particularly Taxol, I've had some, just--this is anecdotal, I've had some luck with that. It's actually an active agent. I used irinotecan second-line or etoposide on some occasions. There are some reports that that works with a different schedule and giving it orally. But, in general, the results with second-line therapy have been pretty disappointing.

Dr. West: You had mentioned that the progress has been slow and we're still using therapies that have been around for more than a decade. Are there agents being tested now, out on the horizon, that you might be hopeful could be integrated as new tools in small cell?

Dr. Wozniak: Well, many of the new targeted agents that we are evaluating in non-small cell are also being look at in small cell. The angiogenesis inhibitors, the tyrosine kinase inhibitors, nothing has come as yet in terms of being useful, but that doesn't mean we don't keep trying. We're also looking at agents that may attack certain targets that are present in small cell like BCL-2. There is an anthracycline, like Amrubicin, that was evaluated initially in Japan and is being evaluated as possibly a better anthracycline, an anthracycline-based treatment

was what we used to do in the past. I think we sort of abandoned that because it is a bit more myelosuppressive and the other thing is that it's hard to combine with radiation. But, still, anthracyclines are active in this disease. So that'll be interesting. So I think that are some new cytotoxics as well as these targeted agents that are being evaluated and hopefully we'll come up with something that is useful in this disease. I think what we have to do is overcome resistance, because, in my opinion, the diseases are very sensitive to chemotherapy initially. I think that it develops resistance. So I think the key is try to keep that from happening, which isn't so easy.

Dr. West: Toni, thank you so much for taking the time today. I really appreciate it.