

ITMIG 2017 – Prof. Patrick Loehrer: conduct more clinical trials to get more helpful information and benefits patients

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Expert's introduction

Patrick Loehrer, MD

Dr. Loehrer is Director of the Indiana University Melvin and Bren Simon Cancer Center and the H. H. Gregg Professor of Oncology and Associate Dean for cancer research at the Indiana University School of Medicine.

He is a specialist of a variety of cancers, including cancers of the testis, bladder, colon, pancreas and, most notably, the thymus gland. His research related to thymic cancer has been recognized with the Exceptional Service Award of the Foundation for Thymic Research. He is a founder of the Hoosier Cancer Research Network (formerly known as the Hoosier Oncology Group) and served as its chairman for two decades. He has also served as chairman of the Genitourinary Committee for the Eastern Cooperative Oncology Group (ECOG) and served as the director of the gastrointestinal research program at the IU Simon Cancer Center. Dr. Loehrer has received numerous awards, including the Flick Family Fund Award, the American Cancer Society Fellowship, etc. In 2010, he received the Special Recognition Award from the American Society of Clinical Oncology (ASCO).

Editor's note

On September 23th, the 8th International Thymic Malignancy Interest Group Annual Meeting (ITMIG 2017) was held in Torino, Italy, successfully ended after a dense 3-day agenda blending a superb scientific and educational program, with over 150 participants in the field from more than 20 countries or regions. During the meeting, Prof. Patrick Loehrer from the Indiana University Melvin and Bren Simon Cancer Center presented his perspectives at a panel discussion on the topic “How do we Choose our Therapies and Future Trial Designs in TET?” as an invited speaker (*Figure 1*). After the session, we were honored to conduct an interview with Prof. Loehrer (*Figure 2*).

In the interview, Prof. Loehrer shared his valuable



Figure 1 Snapshot of Prof. Loehrer's presentation.



Figure 2 Meeting with Prof. Loehrer.

experiences in clinical researches and important findings of his team. He suggested that more clinical trials should be conducted for more helpful information, which would bring more hope to patients. When asked about why he chose the career of medicine, Prof. Loehrer said, “*It was the disease that found me rather than I seeking it out. Fate chose me to be an oncologist and I chose to find out new treatments to change the fate of patients.*”

As below is an overview of the interview. More details please refer to the interview video (*Figure 3*, link to the

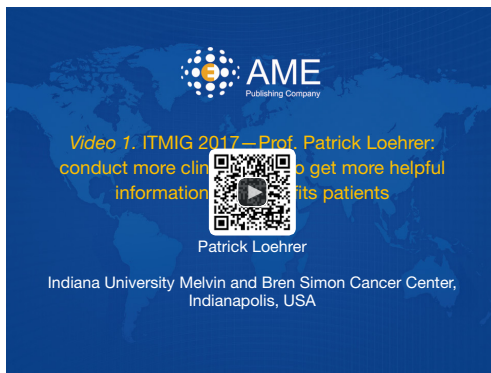


Figure 3 ITMIG 2017—Prof. Patrick Loehrer: conduct more clinical trials to get more helpful information and benefits patients (1). Available online: <http://www.asvide.com/articles/1850>

interview video: <https://youtu.be/1YFksEWDP-8>).

Interview questions & responses

AME: *Would you like to briefly introduce yourself, including your affiliation and interests?*

Prof. Loehrer: My name is Patrick Loehrer. I am a medical oncologist and Director of the Indiana University Melvin and Bren Simon Cancer Center in the United States. I've been involved with the thymoma research since the early 1980s, since I was a fellow, and I continue to do this to present day.

AME: *For chemotherapy regimens, which do you prefer for unresectable thymoma, CAP, ADOC, or TC?*

Prof. Loehrer: It will be a complicated question, so I try to dissect it. So in patients with advanced disease, the National Cancer Institute Guideline suggests CAP (cisplatin, doxorubicin and cyclophosphamide). For patients who are elderly and who may have a bad heart, we do not want to use anthracycline, then we will use carboplatin plus paclitaxel. Unfortunately, whether in stage four thymoma or stage four thymic carcinoma, chemotherapy alone is not curative. We can get greater response rates with anthracycline-based regimens, but it won't cure them. So we have to balance the side effects versus the benefits when we meet each individual patient. I typically don't use the ADOC regimen, which I think increases the risk of neuropathy without enhancing the tumor response.

AME: *Do you suggest I.O. treatment for thymoma and thymic carcinoma as the first line therapy based on the data available now? Which do you prefer for the second line therapy for thymoma?*

Prof. Loehrer: For patients with early stage diseases, whether thymoma or thymic carcinoma, we recommend surgical resection to remove it completely. If preoperatively, the surgeon finds it's unlikely to remove it completely, we will use chemotherapy to downsize the tumor and then do surgery. For patients who have completely resected disease, we do not use adjuvant chemotherapy. We may give radiation therapy for those patients who have positive margins. In patients with more advanced disease (i.e., stage four disease), we typically use CAP, such kind of combination chemotherapy. For patients who have a recurrence, there are a number of drugs that have single interactivity, including paclitaxel, pemetrexed, 5FU plus leukovorin (or capecitabine), gemcitabine, everolimus and octreotide plus prednisone (if octreotide scan is positive). All of those can be used as single agents. I think the best second line therapy would either be paclitaxel or pemetrexed. As patients are likely to get many different drugs in their lifetime, the order probably doesn't matter for the most part. I don't usually use combination therapy in second line therapy, because I think it adds side effects and difficulties to find out which drug works.

AME: *As it would be much easier to carry out international collaborations nowadays, do you think it is necessary to design a new larger clinical trial about carboplatin and paclitaxel in the treatment of TET?*

Prof. Loehrer: As it is a very rare tumor, we are only getting information through these prospective clinical trials. The problem I think it's more difficult today than it was when we conducted the trial. When I was a young man, we could do a clinical trial on average of 500–1,000 dollars per patient. Today the average cost per patient on a clinical trial is closer to 10,000 dollars, which has gone up dramatically. It is much more expensive to do clinical trials today than before. Most institutions may have one or two patients with thymoma a year. The institution doesn't want to go through the efforts of getting a clinical trial opened when they may or may not ever see a patient with that disease. So it's much harder to do that as works before. But I do think internationally we can do some work together, which will be very important.

AME: Nowadays, chemotherapy still plays important role in the treatment of TET. Can you give us a prospective suggestion on clinical trial design about chemotherapy of TET?

Prof. Loehrer: It is a very good question. When we look at chemotherapy in brand new patients, we are going to expect to have 70–80 percent of patients getting remission with CAP. When we look at the best targeted therapy, we only getting about 20 percent chance to get shrinkage of the tumors. So targeted therapy by and large is not being successful as we like it to be. Why? Probably in large part is that we don't have a right target. We need to do more analyses on what causes thymoma and what are the driver mutations we can stop. There are a couple of examples in which targeted therapy may work. But all the other data we have looked at are largely unsuccessful. More recently, we've done a trial in our university based on work with a human cell line we have established which demonstrated the important potential role of using a PI3 Kinase inhibitor. We did see most patients with major or minor activity with this drug. However, the company saw some side effects in other trials, so they decided not to pursue the drug anymore. We are now doing a trial on second line therapy with paclitaxel and a potential STAT3 inhibitor. We've actually been very excited with regressions seen in the majority of patients with previously treated thymic carcinoma in second line therapy. We've just had a discussion at this meeting about getting more information about molecular characterization of the tumors. We have a large data base called TCGA or The Cancer Genome Atlas project, from which we have got information from over a hundred patients with stage thymic tumors. Those patients are genetically different from those with white blood disease. By understanding this population, we may be able to come up better targeted therapies than we currently have. TCGA is sponsored by National Cancer Institute of the United States. It had 117 patients with thymic tumors, collected internationally. With TCGA we've looked at genomic information, mutation analysis and epigenomic, putting a host of different kind of factors, and then tying them to the clinical outcomes. We have achieved some success that some patients have had curative surgical resection without any part of radiation or chemotherapy.

AME: Can you briefly introduce some important findings of molecular research on TET from your team, as well as some ongoing research about TET?

Prof. Loehrer: There is one thing that cannot be under

empathized. There are patients with thymoma, even with advanced stage of thymoma, who can live 10, 20, and 30 years. So by logically, these patients have a slow growing tumor. And there are other patients only living a few months with it. And I think this happens despite therapies, and it really asks us to do more tumor programs. We ought to do a deep dive into the understanding of mutations in the genomic information that allows us to understand the behavioral differences of different kind of tumor types. Our institution is the leading institution of TCGA. I think one of the important factors that we have found out is that by using molecular diagnosis, we can come up with categories that are as good, if not better than the WHO histologic classification. This allows us to categorize patients with different subtypes. There is a unique marker we see genomic mutation in type A thymoma and AB thymoma. Yet, as we only found that patients with this marker would do well after surgery, targeting this marker is not really helpful. We do need to come up with marker that will help us differentiate those react poorly. And we also need to do analyses on patients with white blood disease, which has not been done before. Several years ago we came up with a gene signature that was able to segregate patients who did very well and did poorly after surgical resection. I think this type of analysis will be helpful in the future, because genomic analysis can help us get more helpful information and minimize the toxicity of chemotherapy or radiotherapy for patients.

AME: What encouraged you to be an oncologist?

Prof. Loehrer: When I was a young resident, I knew I wanted to pursue a career in oncology. One of the staff physicians had some patients he had treated so I wrote a paper about these three patients with thymoma. When I prepared the paper, I realized there was no prospective study ever conducted in thymoma. So when I went to Indiana University, I conducted a study on thymoma. It took about eight years to get the study completed because of the rarity of the tumor, but it was still the first study done with combination chemotherapy in this tumor. Once that study was done, more physicians and patients called me up, so I did a series of trials over the past 35 years. The patients looked well after treatments so I felt obligated to find more new treatments. It was the disease that found me rather than I seeking it out. I am very thrilled to work with ITMIG organization and investigators around the world to focus on this rare disease. There are a lot of specialist looking at

this disease from different angles, which gives patients great hope.

AME: What career would you choose besides an oncologist?

Prof. Loehrer: I think I would love to be a movie actor, a poet or a writer, which will be of fun. Actually, before entering a medical school, I majored in mechanical engineering. Engineering has played into my knowledgebase. And this made me look at medicine differently than those who majored in biology.

AME: Thank you very much for your sharing!

Prof. Loehrer: Thank you!

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