Gynecologic Oncology Group Study 229C: Personal Reflection

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I heard the statistician say, "The drug does not have sufficient activity to study further in this population." It was my co-investigator on GOG study 229C, *Gefitinib in the Treatment of Advanced and Recurrent Endometrial Cancer* (see related extended abstract in this issue*), calling from Roswell Park in Buffalo. He had just completed the analysis of data from 26 women treated on our study – a study which had been five years in the making from concept to clinical trial.

These are the most damning words a clinical investigator can hear. I thought back to the beginning, when our preclinical studies indicated a new molecular agent, gefitinib, a member of a class of small molecules which blocks the epidermal growth factor receptor, could kill cancer cells in the laboratory. I sold the idea to use the drug for patients with endometrial cancer to the NIH and the pharmaceutical company based upon this rosy picture of activity. I thought about the seed money we used to initiate the trial, which had come from the family of a patient who had died of the disease, Barbara Beach. The family had so hoped that gefitinib would do for others what previous treatments failed

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Please cite this paper as: Leslie KK. Gynecologic Oncology Group Study 229C: Personal Reflection. Proc Obstet Gynecol. 2013;3(3 Suppl):Article 2 [2 p.]. Available from: http://ir.uiowa.edu/pog/. Free full text article.

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to do for their mother. They donated $250,000.00 in her honor to support this trial!

Then I thought about the patients – 26 women who had failed all other therapies and hoped against hope to find a cure in gefitinib. After all, hadn't we shown them the laboratory data? Hadn't we believed ourselves that we had found a breakthrough agent? As the lead investigator, I was blinded to their names and their clinical outcomes until the very end of the study….I knew them only as numbers, like G17982, etc. I knew them only as the blocks of tumor tissues sent to my laboratory to study. The assays had appeared promising on the tissues – why didn't it work in the patients??

I said to my colleague, "I can't believe that gefitinib didn't help anyone – it just doesn't seem possible given our preliminary data." He replied, "What I meant to say is that the drug does not have more activity than standard chemotherapy. That doesn't necessarily mean that no one benefited. Let me see…..oh yes, I meant to mention that patient G55394 had a complete response."

"You said a complete response? You mean she is cured? What does that really mean if the drug is not active?"

"She had a recurrent tumor nodule which has now disappeared," he said in a matter of fact statistical tone. "But that doesn't guarantee that it was as a result of the drug, you know."

I often think of Mrs. G55394 and hope she enjoyed the years she lived after taking gefitinib – I hope she enjoyed her family and all of the important things in life. I will never know her personally, but she is a big part of my life even now. Cancer will never be cured by a single drug; I know that now as does everybody in the field. Nevertheless, some agents work very well for unique tumors, and it is now our goal to understand why.

**See "A phase II evaluation of gefitinib in the treatment of persistent or recurrent endometrial cancer: A Gynecologic Oncology Group study. Proceedings in Obstetrics and Gynecology, 2013; 3(3 Suppl):5." An abstract of Leslie KK, Sill MW, Fischer E, Darcy KM, Mannel RS, Tewari KS, Hanjani P, Wilken JA, Baron AT, Godwin AK, Schilder RJ, Singh M, Maihle NJ. A phase II evaluation of gefitinib in the treatment of persistent or recurrent endometrial cancer: a Gynecologic Oncology Group study. Gynecol Oncol. 2013 Jun;129(3):486-94. doi: 10.1016/j.ygyno.2013.02.019. Epub 2013 Feb 21. PubMed PMID: 23438670*