Nature Reviews Clinical Oncology published online 13 December 2011; doi:10.1038/nrclinonc.2011.114-c2

AUTHOR'S REPLY

Use of discard pleural fluid in molecular research

Erin M. Olson, Nancy U. Lin, Ian E. Krop and Eric P. Winer

We thank Grannis for his comments and interest in our article—The ethical use of mandatory research biopsies. *Nat. Rev. Clin. Oncol.* **8**, 620–625[1] (Use of discard pleural fluid in molecular research. *Nat. Rev. Clin. Oncol.* doi:10.138/nrclinonc.2011.114-c1).[2] We agree that when research biopsies are included in clinical trials involving patients with metastatic cancer, the most accessible location of the disease is the preferred site of tissue collection. In patients with lung and breast cancers, malignant pleural effusions are common, and cytologically positive cancer cells can be readily collected from these effusions and analyzed in translational studies. Genomic, transcriptomic, methylation and proteomic studies can be performed on both fresh specimens and formalin-fixed paraffin-embedded (FFPE) blocks prepared with the cells collected from these effusions.[3–4] Importantly, molecular analyses of lung adenocarcinoma cells from pleural fluid have been used to predict response to targeted agents.[6,7] Investigations about the biological aspects of metastatic cells in the pleural fluid can be incorporated into the clinical trial protocols, and via serial pleural throacenteses, the molecular characteristics of these cells and potential mechanisms of acquired resistance to investigational agents can be analyzed.

The internal review boards will likely approve the protocols in which pleural fluid—that would have otherwise been discarded—is collected for scientific analysis. This approach adds minimal additional risk for the patients undergoing a clinically indicated thoracentesis. However, safety issues will arise if a protocol proposes serial or a single thoracentesis for only research purposes. Iatrogenic pneumothorax is more likely to occur after therapeutic thoracentesis and frequently requires insertion of a chest tube.[8] Nevertheless, as outlined by Grannis, in patients with indwelling pleural catheters there is a unique opportunity to regularly collect tumor cells without the need for repeated biopsies.

*Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, The Ohio State University College of Medicine, 300 West 10th Avenue, Columbus, OH 43210, USA (**E. M. Olson**). Dana-Farber Cancer Institute, Harvard Medical School, 450 Brookline Avenue, Boston, MA 02215, USA (**N. U. Lin**, **I. E. Krop**, **E. P. Winer**).*

Correspondence to: E. P. Winer
ewiner@partners.org

Competing interests
All authors declare that they receive grant support from Genentech.

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