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Lung Cancer

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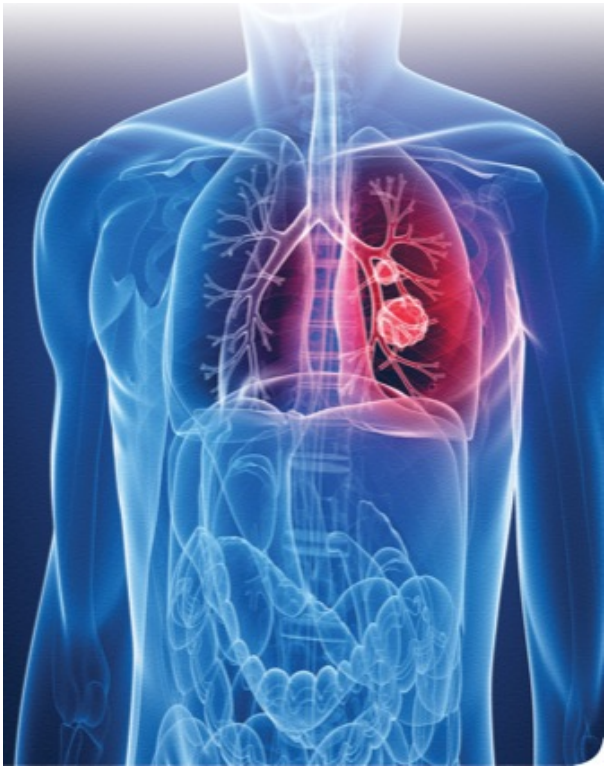
Research Biopsies Pose Barrier to Lung Trial Enrollment



Requiring participants in non-small cell lung cancer (NSCLC) clinical trials to provide tumor tissue samples is “a significant barrier” to enrollment, according to a team of investigators in Canada.

The investigators described the consequences of this increasingly common practice as “sobering,” for both the patients and investigators conducting clinical trials (*J Thorac Oncol* 2016;11[1]:79-84, PMID: 26762742).

“It’s a really interesting paper, because research biopsies are becoming more common in research trial design,” said Lecia Sequist, MD, MPH, a clinical researcher at Massachusetts General Hospital Cancer Center, in Boston, who was not involved in the study.

The investigators, led by Charles Lim, MD, reviewed the cases of patients with advanced NSCLC who were evaluated for clinical trials of systemic therapy at the Princess Margaret Cancer Centre, in Toronto, between January 2007 and March 2015. They identified 636 patient cases and 55 clinical trials, 54 of which were linked to investigational treatment. Tumor samples were required for participation in 38 trials. Six of the trials required repeat or trial-specific biopsies, whereas 32 permitted the use of archival tissue in lieu of a new biopsy.

In total, 60% of patients received study treatment, the investigators wrote. They found that patients in clinical trials that did not require tumor tissue samples were nearly 30% more likely to receive study treatment than those in trials that required samples (83% vs. 55%; *P*<0.0001) (Table). Moreover, the investigators wrote, patients considering trials without tumor tissue requirements had a shorter wait time between providing consent and beginning treatment (median, nine vs. 16 days; *P*=0.002). Similarly, when comparing patients considering enrolling in trials that mandated repeat or trial-specific biopsies with those considering trials that permitted the use of archival tissue, they found that the latter were both more likely to receive study treatment (59% vs. 38%; *P*=0.0007) and have a shorter time interval between initial consent and the start of treatment (median, 14 vs. 54 days; *P*<0.001).

Table. Trial Treatment and Time Points for Patients In Trials With and Without Required Research Biopsies

Characteristic	All Therapeutic Trials: 54 Trials, 549 Consents	Tissue Not Required: 17 Trials, 102 Consents	Mandatory Biopsy: 37 Trials, 447 Consents	Repeat Biopsy Optional: 31 Trials, 360 Consents	Mandatory Repeat Biopsy: 6 Trials, 87 Consents
Patients receiving study treatment, %	60	83	55	59	38
Time from consent to study treatment start					
n	329	85	244	211	33
Median, d	15	9	16	14	54
Interquartile range, d	6-28	6-20	7-33	6-25	46-49
Range, d	0-142	0-61	0-117	0-142	25-117
Time from consent to repeat biopsy					
n	128	1	127	59	68
Median, d	18	19	18	16	21
Interquartile range, d	11-27	NA	11-27	8-23	12-29
Range, d	0-213	NA	0-213	1-213	0-113

NA, not available Modified from Lim C, et al. *J Thorac Oncol*. 2016;11(1):79-84, PMID: 26762742.

With respect to the 220 patients (40%) who were not able to receive study treatment, the investigators found that the most common barrier to participation was the absence of a prespecified biomarker required for enrollment (34%), followed by withdrawal of consent (20%), disease progression or death after consent was given but before the beginning of treatment (17%), comorbid conditions or poor performance status (15%) and insufficient tissue for molecular analysis (10%).

The investigators highlighted the introduction of potential delays in delivering treatment resulting from collection, laboratory analysis and biomarker testing of tumor tissue samples as a particularly important consequence of mandatory tumor tissue requirements in NSCLC

clinical trials. While waiting for the completion of these procedures, “patients remain at risk for clinical deterioration from progression of their underlying lung cancer, thus making even small delays highly detrimental,” they noted.

The investigators proposed several potential solutions to the observed barriers to participation in clinical trials, including routinely banking tumor tissue at diagnosis, facilitating the use of available diagnostic samples for trials and developing peripheral blood assays. They also recommended finding ways to reduce central laboratory turnaround time, or else granting permission for testing at accredited local laboratories, which they noted is prohibited by many clinical trials, particularly industry-sponsored trials. Finally, they recommended that more resources be provided for timely acquisition of tissue for clinical trials.

Dr. Sequist said investigators designing future clinical trials should follow the study’s recommendations. “Other studies have focused on improvements in safety and on trials becoming faster; they spend a lot of time talking about the benefits, so it’s interesting to see a paper talking about the negatives,” she said. “It’s important to talk about how the speed of drugs coming to the market has increased—it’s much faster than it used to be,” Dr. Sequist added. “We should note the benefits, but it’s also important to talk about the caveats, as these authors have done.”

—Ajai Raj