

Libelule: a randomized phase 3 study to evaluate the clinical relevance of early liquid biopsy in patients with suspicious metastatic lung cancer

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Abstract

Background Genomic profiling is a major component for first-line treatment decisions in patients with non-small cell lung cancer (NSCLC) and the timeliness of biomarker testing is essential to improve time to treatment initiation (TTI) or avoid inappropriate treatment.

Objective We aimed to demonstrate the feasibility and clinical relevance of early liquid biopsy (LB) at the time of advanced lung cancer suspicion to accelerate TTI.

Methods The phase III LIBELULE trial included patients with radiological suspicion of advanced lung cancer. They were randomized (1:1), the control arm receiving diagnostic procedures according to each center's practice and the LB arm with additional testing performed at the first visit using the InVisionFirst -Lung assay. When LB results were informative, treatment was initiated on the basis of: InVisionFirst -Lung alone for patients with EGFR, BRAFV600E mutation, ALK, ROS1 rearrangement; InVisionFirst -Lung and pathological results for patients with ERBB2, MET exon 14, KRAS, BRAF nonV600 and/or LKB1 mutations, RET, NTRK rearrangement. Patients were enrolled in cancer centers, university or general hospitals and private practice centers, to reflect the diversity of practices. Treatment initiation and type were defined according to ESMO guidelines. Primary endpoint was the time from randomization to initiation of appropriate treatment based on informative genomic and pathological results in the intention-to-treat population.

Results 319 patients were enrolled (LB: 161; control: 158). Median age was 68 years, 28.8% were non-smokers, 18.1% had PS 2 and 56.7% had adenocarcinoma. In LB arm, 81% of patients had circulating tumor DNA findings. The mean TTI was not significantly reduced (LB: 29.0 days (d); control 34d (p=0.26)). Sensitivity analyses showed a shorter TTI in patients from the LB arm who received systemic treatment (LB: 29.1d; control: 38.9d, p=0.01), in patients with advanced non-squamous NSCLC (LB: 29.5d; control: 40.3d, p=0.01), and in patients with first-line targetable alterations (LB: 21d; control 37.4d) (p=0.004). Time to contributory genomic results was significantly reduced (LB: 17.9d; control 25.6d, p<0.001).

Conclusion Early liquid biopsy testing did not significantly shorten the TTI in unselected patients referred for suspected advanced lung cancer. Nevertheless, it could reduce the TTI in patients eligible for systemic treatment, particularly for those with actionable alterations.

Do you have any conflicts of interest?

Yes, I have a conflict of interest.

Amgen, Astrazeneca, Boehringer Ingelheim, Janssen, Lilly, MSD, Pfizer, Roche, Takeda, BMS, Daiichi Sankyo Inc, Sanofi