National Lung Matrix Trial (NLMT): First Results from an Umbrella Phase II Trial in Advanced Non-Small Cell Lung Cancer (NSCLC)

Barcelona—The largest stratified medicine dataset of non-small cell lung cancer patients indicates further molecular stratifications could benefit from targeted therapies, according to research presented today at the IASLC 2019 World Conference on Lung Cancer, hosted by the International Association for the Study of Lung Cancer.

The National Lung Matrix Trial is the largest precision medicine trial in NSCLC patients globally, testing a wide range of therapies tailored specifically to target key genetic changes in cancer cells. Data from this trial was reported today by Dr. Gary Middleton from the University of Birmingham, United Kingdom.

Oncogene-addicted NSCLC can achieve substantial clinical benefit with single agent targeted therapy. Seeking to extend this paradigm to other more genetically complex NSCLC, Dr. Middleton today reported first results of NLMT, an umbrella phase II trial that stratifies NSCLC patients to rationally selected targeted therapies. In an umbrella clinical trial, patients are assigned to a particular treatment arm of the trial based on their type of cancer and the specific molecular makeup of their cancer.

NLMT screens eight targeted drugs for signals of activity using a Bayesian adaptive design in 22 molecularly defined cohorts. For single agents, clinically relevant outcomes are either median progression-free survival for more than three months or objective response rate and/or durable clinical benefit rate (DCBR) at 24 weeks greater than 30 percent. This novel approach provides insight into the drug-biomarker combinations that have the strongest potential for further research.

Middleton and his colleagues recruited 315 patients from a screened population of more than 4,000 patients. Results were as follows:

Of the six palbociclib cohorts, the Bayesian estimate of the true median progression free survival in KRAS mutation was 5.4 months, KRAS mutation with concomitant STK11 loss 2.71 months, CDKN2A loss squamous 4.46 months and CDKN2A loss non-squamous 3.19 months. Data for crizotinib show greater than 99% predicted probability of success in ROS1 gene fusions and MET exon 14 skipping mutation but less than 1% for Met amplification with regards to objective response rate.

Middleton reported that responses to selumetinib/docetaxel in NF1 mutation in adenocarcinoma warrant continuation. Recruitment to vistusertib was halted at interim for LKB1 single mutation: the
predicted probability of success for DCBR in those with KRAS mutation with concomitant STK11 loss is 32% with Bayesian estimate of the true DCBR of 27% and with no objective responses. Four cohorts received capivasertib including those with PIK3CA amplifications the Bayesian estimate for the true DCBR is less than 15% for all arms.

These first results from the largest stratified medicine dataset in NSCLC indicate further molecular stratifications could benefit from targeted therapies. Reporting interim outputs for all cohorts will allow reappraisal of the global stratified medicine strategy in cancer.

About the WCLC:

The WCLC is the world’s largest meeting dedicated to lung cancer and other thoracic malignancies, attracting more than 7,000 researchers, physicians and specialists from more than 100 countries. The goal is to increase awareness, collaboration and understanding of lung cancer, and to help participants implement the latest developments across the globe. The conference will cover a wide range of disciplines and unveil several research studies and clinical trial results. For more information, visit wclc2019.iaslc.org.

About the IASLC:

The International Association for the Study of Lung Cancer (IASLC) is the only global organization dedicated solely to the study of lung cancer and other thoracic malignancies. Founded in 1974, the association’s membership includes more than 7,500 lung cancer specialists across all disciplines in over 100 countries, forming a global network working together to conquer lung and thoracic cancers worldwide. The association also publishes the Journal of Thoracic Oncology, the primary educational and informational publication for topics relevant to the prevention, detection, diagnosis and treatment of all thoracic malignancies. Visit www.iaslc.org for more information.

# # #