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Phase I study of novel anti-cancer drug uses tumor mRNA expression to identify responders

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The first-in-human dose escalation study of the pan-FGFR (fibroblast growth factor receptor) inhibitor BAY 1163877 in patients with treatment-refractory locally advanced or metastatic solid tumours were reported today at the ESMO 2016 Congress in Copenhagen. The novel compound uses messenger RNA (mRNA) in tumours to identify patients who will respond.

"Most studies of FGFR inhibitors have looked at FGFR abnormalities in tumours with limited success," said lead author Dr Markus Joerger, attending medical oncologist, St Gallen Cancer Centre, Switzerland. "This study used an innovative biomarker approach of tumour FGFR mRNA expression."

This multicentre phase I study was conducted in six countries. The dose-escalation study was followed by expansion cohorts in patients with high tumour FGFR mRNA levels. A total of 80 patients were enrolled and treated, including 23 patients in the dose-escalation phase and 57 patients in the expansion cohorts in bladder cancer, head and neck cancer, lung cancer, and all comers.

The dose escalation study tested five doses ranging from 50-800 mg BID (twice daily). BAY 1163877 has a half-life of about 12 hours and revealed less than dose-proportional increase in exposure at doses above 200 mg. A maximum tolerated dose was not defined because there were

no dose-limiting toxicities. Based on the results of preclinical studies, the effect on serum phosphate levels and clinical analyses, 800 mg BID was recommended for future study.

Regarding toxicities, most patients developed low-grade hyperphosphatemia, which occurs with all FGFR inhibitors. These patients were given a phosphate binder and the dose of BAY 1163877 could be reduced to avoid further increases of phosphate levels in the blood.

In the expansion cohorts, the highest activity of BAY 1163877 was seen in bladder cancer, with three partial remissions out of eight patients. Partial remissions were also seen in individual patients with squamous cell lung cancer, squamous cell carcinoma of the head and neck and adenoid cystic carcinoma, the latter response lasting more than one year.

Joerger said: "BAY 1163877 is a well-tolerated compound with an innovative biomarker approach that effectively identifies patients who have a good chance to benefit. Further studies should be conducted, particularly in bladder cancer where about 35% of patients are FGFR mRNA positive."

Commenting on the results, Prof Giuseppe Curigliano, Chair of the Division of Early Drug Development Therapeutics, European Institute of Oncology in Milan, Italy said: "FGFR inhibitors may provide a therapeutic opportunity to patients with rare tumours. In this patient population there were some patients with adenoid cystic carcinoma with long term control of the disease. In the context of molecular screening programmes we may offer a chance to patients with FGFR mRNA expression."

"The toxicity profile of BAY 1163877 is better than other FGFR inhibitors under development," he continued. "More studies are needed

to identify which patients will benefit from FGFR inhibitors - in this study, tumour FGFR mRNA expression was the best predictor of response. The next step will be to validate these results in future clinical trials."

Provided by European Society for Medical Oncology

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