

Metformin plus EGFR TKIs for lung adenocarcinoma

The results of an open-label, randomised, phase 2 clinical trial have shown that patients with EGFR-mutated advanced lung adenocarcinoma given EGFR tyrosine kinase inhibitors (TKIs) plus metformin have improved progression-free survival compared with individuals given the TKIs alone.

139 adult patients with histologically confirmed stage IIIB–IV lung adenocarcinoma with an activating EGFR mutation who had never been previously treated with EGFR TKIs were assigned in a 1:1 ratio to one of two treatment groups. The first group (n=70) received an EGFR TKI (erlotinib, afatinib, or gefitinib) at a standard dosage and the second group (n=69) received the same treatment with EGFR TKIs plus 500 mg of metformin twice per day. The primary outcome was progression-free survival in the intention-to-treat population, and

secondary outcomes included overall survival, objective responses, and safety.

Median progression-free survival was significantly longer in the metformin plus EGFR TKI group than in the EGFR TKI alone group (13.1 months [95% CI 9.8–16.3] vs 9.9 months [7.5–12.2]; hazard ratio [HR] 0.60, 95% CI 0.40–0.94; p=0.03). Median overall survival was also significantly longer in the metformin plus EGFR TKI group than in the EGFR TKI alone group (31.7 months [95% CI 20.5–42.8] vs 17.5 months [11.4–23.7]; HR 0.50, 95% CI 0.28–0.90; p=0.02). Objective responses were achieved by 49 (71%) of 69 patients in the metformin group versus 38 (54%) of 70 in the EGFR TKI group (HR 0.48, 95% CI 0.24–0.97; p=0.04). Grade 3–4 adverse events included diarrhoea, rash, nausea, and mucositis and occurred at a similar frequency in both groups.

Study author Oscar Arrieta (Instituto Nacional de Cancerología, Mexico City, Mexico) said, “Studies which seek a wider array of treatment options for lung cancer patients are particularly important, and we as a scientific community should acknowledge the fact that not all patients have access to next-generation drugs. Studying agents for drug repurposing could offer new combinations which can improve outcomes while also circumventing the financial toxicity which can be associated with other schemes. There is a fair amount of evidence for repurposing of drugs for oncologic purposes and it is important that we consider performing clinical research focused on these agents which are widely used and come with a known safety profile from years of mass use.”

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