

Metronomic chemotherapy option for advanced oral cancer



Triple oral metronomic chemotherapy with erlotinib, methotrexate, and celecoxib is active and is a promising treatment option for patients with platinum-refractory oral cavity cancer and poor prognosis, according to a new study.

In the phase 1–2 trial, Vijay Patil and colleagues (Tata Memorial Centre, Mumbai, India) enrolled 91 patients with platinum-resistant squamous cell carcinoma of the oral cavity or disease that had progressed soon after previous treatment. Patients received erlotinib 150 mg once per day, celecoxib 200 mg twice per day, and methotrexate once per week. 15 patients were included in phase 1, in which the primary endpoint was to establish the optimal biological dose of methotrexate. An expansion cohort of 76 patients was included in phase 2, for which the primary endpoint was 3-month

progression-free survival. Safety was a secondary outcome.

Median follow-up was 6·8 months (range 0–16·8). In phase 1, 9 mg/m² was established as the optimal biological dose of methotrexate. In phase 2, 3-month progression-free survival was 71·1% (95% CI 60·5–79·3). 6-month overall survival was 61·2% (95% CI 49·2–67·8), and the proportion of patients who achieved a response was 42·9% (95% CI 33·2–53·1). The most common grade 3–4 adverse events were hyponatraemia (13 [15%] of 88 patients) and increased alanine aminotransferase concentration (five [6%]).

Coauthor Kumar Prabhaskar (Tata Memorial Centre, Mumbai, India) said, “This study provides [an] innovative Bayesian approach to drug development for combination therapy. We are currently running a randomised

study with this combination in patients with very poor prognosis to confirm this finding.”

“This is a very interesting trial,” commented Nicolas André (Assistance Publique—Hôpitaux de Marseille, Marseille, France). “The results are quite good both in terms of response and safety. I guess this is what global oncology [should] aim at: the same inexpensive, non-toxic, active treatment available and doable for patients living in both high and low-income countries.

“Everett Vokes (University of Chicago, Chicago, IL, USA) added, “The early response data appear promising. Additional studies will be required to establish the mechanistic interactions of erlotinib and celecoxib with methotrexate and broader applicability of the regimen.”

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