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A randomised trial of the combination of lomeguatrib and temozolomide and temozolomide alone in patients with advanced melanoma

M Middleton¹, M Ranson², P Hersey³, J Beith⁴, D Thompson⁵, P Mortimer⁶, G Margison⁷

¹Cancer Research UK MOU, Oxford, United Kingdom; ²Christie Hospital, Manchester, United Kingdom; ³Melanoma Unit, Newcastle, NSW, Australia; ⁴Melanoma Unit, Sydney, Australia; ⁵Princess Alexandra Hosp., Brisbane, Australia; ⁶Kudos Pharmaceuticals, Cambridge, United Kingdom; ⁷Paterson Institute, Manchester, United Kingdom

We evaluated a combination of lomeguatrib (LM), a potent O⁶-methylguanine DNA-methyltransferase (MGMT) inactivator, and temozolomide (TMZ) in patients with advanced melanoma.

Trial Design: Patients with unresectable Stage III or IV cutaneous melanoma were randomised to receive either 40-80mg LM and 125mg/m² TMZ (LM/TMZ) or 200 mg/m² TMZ on days 1-5 of each 28-day treatment cycle. All treatments were administered by mouth. Patients on TMZ alone were offered LM/TMZ at progression, if they were fit enough to receive treatment.

Results: 104 patients were enrolled in the study, 52 in each arm. Twenty-seven TMZ-treated patients went on to receive LM/TMZ. Tumour response rates were 13.5% with LM/TMZ and 17.3% with TMZ alone. No TMZ progressor responded to LM/TMZ. All treatment arms were well tolerated, although more haematological adverse events were observed in the LM/TMZ combination arm. Tumour biopsies showed rapid recovery of MGMT after LM/TMZ with 40mg/day LM. Doses of LM were therefore escalated to 60 then 80mg/day.

Conclusions: The efficacy of LM and TMZ in this dosing schedule is similar to that of TMZ alone. Dosing of LM needs to be continued beyond that of TMZ to maintain MGMT depletion in tumour.