

Temozolomide and thalidomide effective in treating metastatic neuroendocrine tumors

Although medical treatments for hormone-secreting neuroendocrine tumors can help normalize hormone levels, they rarely reduce tumor size. Dacarbazine has shown some promise but is associated with marked adverse effects. Kulke *et al.*, therefore, assessed the efficacy and safety of a combination therapy comprising temozolomide and thalidomide.

This phase II trial evaluated 29 patients with histologically confirmed metastatic tumors. Thalidomide was given daily at a dose of 50–400 mg, whereas 150 mg/m² temozolomide was administered for 7 days, every other week. Doses of both agents were adjusted in response to adverse effects and the median treatment duration was 7.3 months. Overall, 16 patients discontinued therapy because of toxicity (median time to withdrawal 8.4 months). Serious treatment-related effects included neuropathy, thrombocytopenia, lymphopenia, and opportunistic infections. The radiologic response rate (complete or partial tumor regression) was 25%, with the regimen being most effective against pancreatic neuroendocrine tumors (5 out of 11 patients). The median response duration was 13.5 months. The biologic response rate, assessed by serum CHROMOGRANIN A levels, was 40%. Follow-up was for a median of 26 months. Only four patients experienced progressive disease and the 1-year and 2-year survival rates were 79% and 61%, respectively.

This small trial demonstrates that temozolomide and thalidomide combination therapy could be effective for treating neuroendocrine tumors; nevertheless, larger trials will be necessary to assess the efficacy and safety of this regimen fully.

Vicky Heath

Original article Kulke MH *et al.* (2006) Phase II study of temozolomide and thalidomide in patients with metastatic neuroendocrine tumors. *J Clin Oncol* 24: 401–406

Absorption of inhaled insulin is higher in smokers than in nonsmokers

Smoking has been shown to increase pulmonary permeability, and thereby to increase the absorption of inhaled insulin. To determine

the effect of cessation and resumption of smoking on the time course of inhaled insulin absorption, researchers in Germany conducted a case-control study that enrolled 20 nondiabetic male smokers and 10 matched nonsmokers. They compared the pharmacokinetics of inhaled and subcutaneously injected insulin before smoking cessation, after smoking cessation, and after resumption.

Baseline systemic insulin exposure and maximum insulin concentration were substantially higher in smokers than in nonsmokers after inhalation of insulin, and the time required to reach maximum insulin concentration was considerably reduced in smokers. By contrast, smoking had no effect on the pharmacokinetics of subcutaneously administered insulin. Although cessation of smoking initially led to an increase in inhaled insulin absorption, after 7 days without smoking, absorption of inhaled insulin fell to levels approaching those for nonsmokers. Resumption of smoking restored insulin exposure and maximum concentration to baseline levels within 3 days, completely reversing the effect of smoking cessation. Importantly, two hypoglycemic episodes were reported among the smokers.

This is the first study to show the immediate effects of both smoking and smoking cessation on absorption of inhaled insulin. The authors recommend that smokers with diabetes should not be prescribed inhaled insulin, because of the increased risk of hypoglycemia associated with its absorption profile.

Jim Casey

Original article Becker RHA *et al.* (2006) The effect of smoking cessation and subsequent resumption on absorption of inhaled insulin. *Diabetes Care* 29: 277–282

Proinsulin as a predictor of development of type 2 diabetes in obese children

A high serum proinsulin level and a low insulin-like-growth-factor-binding protein 1 (IGFBP-1) level are predictors of cardiovascular disease and diabetes in obese adults, but little evidence exists of the influence of these factors on children. The relationship between serum proinsulin and IGFBP-1 levels in obese children has been investigated by researchers in Japan, where the incidence of childhood obesity and the incidence of type 2 diabetes have greatly

GLOSSARY

CHROMOGRANIN A

A protein stored in and released from secretory vesicles of neuroendocrine cells; used as a marker of neuropeptide secretion