ciated with diminished insulin sensitivity, whereas letrozole either has no effect or may even increase insulin sensitivity. This difference might be attributed to the steroidal vs the non-steroidal structure of each compound, respectively. Possibly, the androgenic structure of exemestane [7] may be directly responsible for the diabetes-promoting action (independent from its effect on aromatase and estrogen levels), as demonstrated for other androgens. The elucidation of this phenomenon warrants further research.

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Selective internal radiation therapy in patients with carcinoid liver metastases

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To the Editor

Most midgut carcinoids are malignant with metastases, most frequently to the regional lymph nodes and the liver. Metastatic midgut carcinoids may, due to secretion of serotonin, give rise to the carcinoid syndrome. Amelioration of the carcinoid syndrome can be achieved by medical treatment with alpha-interferon and somatostatin analogs or by debulking of liver metastases. Methods for such debulking include surgery, hepatic arterial embolization using occluding particles with or without cytotoxic drugs, and radiofrequency ablation. A new method for reduction of liver metastases, not accessible to surgery, is Selective Internal Radiation Therapy (SIRT), which means hepatic arterial embolization with ^{90}Yttrium-labelled microspheres either made of resin (SIR-Spheres™) or glass (Theraspheres™) [1].

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These particles are about 30–35 microns in diameter and are captured in the tumour vasculature, with a local radiation effect. SIRT, alone or in combination with chemotherapy, has shown promising effect in patients with metastatic colorectal cancer and primary hepatocellular cancer [2–4]. We have treated three female patients with progressing metastatic midgut carcinoid tumours with SIRT. A selective angiography of the celiac and superior mesenteric arteries was performed before treatment to clarify the vascular anatomy and for injection of ^{99m}Tc-macroalbumin in the hepatic artery selected for embolization. The patient was then moved to a gamma camera for a scan to be able to assess the uptake in the tumour, the lungs and in the intestine. In all three patients high uptake in the metastases and low shunting to the lungs could be demonstrated. Two weeks later embolization was performed with SIR-Spheres™ of the right liver lobe. All three patients received omeprazole for one month as ulcer protection and premedication with bethamethasone 8 mg intravenously (i.v.) and tropisetron 5 mg i.v. An infusion of octreotide 50 μg/h was started directly after the embolization and continued for 1 night. The dose of ^{90}Y varied between 1.0 and 1.3 GBq. For dosimetry, the surface method was applied [1]. The embolization was well tolerated, without serious adverse effects. All patients have been tired for several months after the embolization, two required antibiotics and one received a blood transfusion. None of them had any symptoms of ulcer or gastritis.

All three patients noted a partial radiological response (Figure 1), and 5′HIAA decreased in two of the patients. A decrease in size of the embolized lobe has been noted in all three patients, first detectable after 4 months, and also a compensatory increase in size of the non-embolized lobe. Two of the patients have been followed for 22 months and the third patient for 12 months, all still showing a partial radiological response in the embolized lobe.

This brief report demonstrates the possibility of using Selective Internal Radiation Therapy (SIRT) for debulking of liver metastases in patients with neuroendocine tumours. The treatment was well tolerated by all three patients. Embolization with particles, such as gelatine sponge or Embosphere™ has lead to objective responses in 40–80% [5,6] while chemoembolization with various drugs has yielded objective responses in 25–50% [6–8] of patients with carcinoids. In this small series, all three patients experienced a radiological response, which seems to be long lasting. In addition, two of our patients had a biochemical response and two experienced relief of their carcinoid syndrome. Necrosis was noted in the embolized metastases in all patients, indicating that assessment of treatment response after liver embolization by conventional radiological methods, such as RECIST or WHO measurements on CT scan, is inadequate after liver embolization. Instead, assessment of the viable tumour burden, for example by positron emission tomography with appropriate tracers, should be considered.

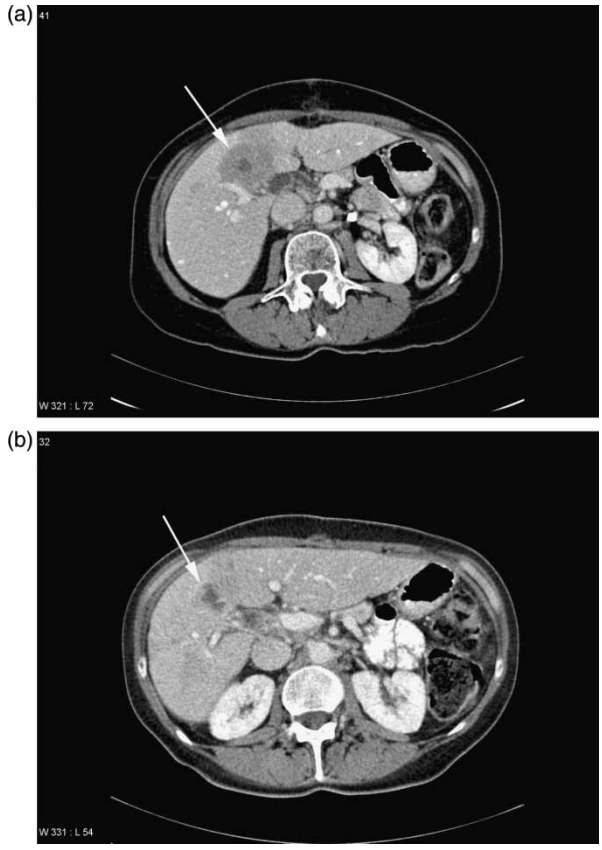

Figure 1. A. Liver metastases (arrow) before embolization of the right liver lobe with SIR-Spheres™. B. Decrease in size of liver metastases 4 months after embolization of the right liver lobe with SIR-Spheres™. The indicated metastasis is clearly smaller and contains a central necrosis (arrow). The right liver lobe has begun to decrease, while a hypertrophy is seen of the left liver lobe.

Hepatic arterial embolization with particles or chemoembolization can be repeated for several times, although the effect is often most prominent after the first one. In patients with primary hepatocellular carcinomas and metastatic colorectal cancer, SIRT has also been repeated in the same liver lobe. We noted shrinkage of the embolized lobe in all patients, possibly due to a radiation damage to the normal liver cells, and as well a compensatory increase in size of the non-embolized lobe. This may limit the number of treatments with SIRT in the same lobe. Although none of the patients experienced a permanent decrease in the liver function, treatment with SIRT of the other lobe in case of progressive metastases may be doubtful. Cell death from radiolabelled drugs may come after a long time, and more comprehensive studies with longer

follow-up are necessary to assess the long-term effects. The radiation dose to the healthy liver is hard to estimate for a single patient, since only beta-images are available after treatment with ^{90}Y, and the pretherapeutic scans have limitations due to particle size and the short half-life of ^{99}Tc.

In summary, hepatic arterial embolization with SIR-Spheres™ of patients with midgut carcinoids harbouring liver metastases seems promising, and may lead to long lasting radiological responses and symptomatic relief. The treatment is usually well tolerated.

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Irreversible ototoxicity associated with the use of erlotinib in a patient with pancreatic cancer

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To the Editor

Erlotinib hydrochloride (Tarceva) is an orally administered, reversible inhibitor of human epidermal growth factor receptor (EGFR) tyrosine kinase. So far the toxicity profile of the agent is considered acceptable. The main drug-related adverse-effects are cutaneous toxicity (acne-like rash) and diarrhea [1]. Auditory side-effects have not been reported as a consequence of therapy with erlotinib.

A 66-year-old woman underwent surgical resection of a pancreatic adenocarcinoma in December 2004. Apart from hypertension, her past medical history was unremarkable. In November 2006 she presented with local disease reccurence, confirmed cytologically by endoscopic ultrasound-guided fine-needle aspiration. She was treated with palliative gemcitabine chemotherapy from November 2006 until May 2007. Following the completion of

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