Patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) region are generally incurable. The goals of treatment are more limited, and include prolongation of overall survival or progression-free survival and palliation of existing symptoms. Response rates to methotrexate as high as 77% have been reported in patients with no prior treatment. The most widely studied and used dosing is weekly intravenous administration of 40 to 60 mg/m². Response rates to bleomycin are in the 15% to 20% range. As early as 1977, cisplatin was found to induce rapid responses in 30% of patients who had been heavily pretreated with surgery, radiation, and chemotherapy. Higher response rates were seen in patients without prior treatment.

The combination of cisplatin/5-fluorouracil emerged as a favored treatment regimen in the 1980s and 1990s. This was based initially on phase II trials published in the mid-1980s testing induction chemotherapy, in which response rates of 67% and 70% with complete response rates of 19% and 27% were seen.1

Other new agents were tested in patients with advanced SCCHN. Both docetaxel and paclitaxel stood out as having high single-agent response rates (21% to 42%). In cancers responsive to taxanes, docetaxel and paclitaxel are active on both the weekly and every-21-day schedules. Docetaxel administered every 3 weeks is probably more active and associated with more adverse events than when administered on a weekly schedule, whereas weekly paclitaxel may be better tolerated and more efficacious than when administered every 21 days.2

Examples of new agents (response rates) in the same class as historically active agents in SCCHN include ifosfamide (26%), pemetrexed (26%), oxaliplatin (10%), capecitabine (8%) and vinorelbine (6%).7 Active agents with novel mechanisms of action or targets include irinotecan (14%), cetuximab (13%), gefitinib (11%), and erlotinib (4%).7 In a large randomized phase III study (TAX 324) comparing cisplatin/docetaxel/fluorouracil (TPF) to cisplatin/fluorouracil (PF), TPF was superior to PF in patients with locally advanced head and neck cancer.1 Unfortunately, it is unclear to what extent the use of these agents has brought about meaningful improvement in clinically relevant outcomes in this setting. No one agent or regimen is known to significantly increase survival compared to other agents. Individualized decisions in these circumstances should
focus on benefits of palliation versus the risks of treatment toxicity.

CASE
A 61-year-old male patient was initially diagnosed with poorly differentiated squamous cell carcinoma (T3N1M0) of the larynx with glottic and infraglottic extension and with a right cervical lymph node metastasis of 2 cm. He received initial treatment with radiation therapy (6400 cGy) and concurrent chemotherapy with weekly cisplatin for seven weeks in May 2009, with a 90% partial response. PET-CT was performed in August 2009 with a persistent post-chemoradiotherapy tumor without the patient accepting a salvage laryngectomy, so treatment was attempted with a second line chemotherapy regimen with 5FU-cisplatin-docetaxel and cetuximab as described by Haddad for 4 cycles with partial response of 80% by PET-CT.4

In January 2010 a new laryngoscopy showed edema in the right half of the larynx with suspected submucosal tumor activity and with a right 2×2 cm cervical lymph node, which increased in volume and consistency, suggesting tumor activity. A rescue total laryngectomy and right radical neck dissection was performed in February 2010. Pathology reported a poorly differentiated squamous cell carcinoma extensively affecting the right glottis, subglottis, thyroid cartilage, thyroid gland and soft tissue with one level II node metastasis with capsular rupture and nine nodes without metastasis. HPV was not tested. HIV was negative. The patient received 4 cycles of postoperative chemotherapy with 5-FU/cisplatin. In July 2010, the patient presented again with tumor activity in the area of the laryngectomy and bilateral neck lymphadenopathy, right axillary adenopathy. A new PET-CT scan showed bilateral tumor activity in the neck, right axillary adenopathy, left paratracheal node and left pulmonary parenchymal metastatic nodule (Figure 1).

A third-line chemotherapy scheme was given with paclitaxel 80 mg/m² and nimotuzumab 50 mg/m² IV each week for 7 weeks as induction.5,6 Therapy continued alternating with the same drugs every 15 days and methotrexate 25 mg/m² IM every 15 days as maintenance, receiving a total of 30 cycles.

The response was complete and maintained at 16 months (December 2011) on the basis of physical examination and imaging studies according to new PET-CT with disappearance of the tumor necrosis area, the axillary and cervical lymphadenopathy, as well as pulmonary metastases (Figure 2). The toxicity was very mild, only neutropenia grade I and peripheral neuropathy grade I-II. There was no evidence of skin rash. The patient was asymptomatic with excellent general condition and without any tumor activity on physical examination.
DISCUSSION

Recurrent and/or metastatic HNSCC has a poor prognosis, with an overall survival (OS) ranging from 3 to 4 months when untreated and to 6 to 9 months when treated with platinum-based therapy. This patient was treated with one of the best combination of drugs (5FU-cisplatin-docetaxel and cetuximab) without complete response. This regimen TPF plus cetuximab had a 100% response rate and 80% complete response rate in a phase I trial.

Nimotuzumab (CIMAher, Center of Molecular Immunology, Havana, Cuba) is a humanized monoclonal antibody used to treat squamous cell carcinoma of the head and neck. Like cetuximab, nimotuzumab binds to the epidermal growth factor receptor (EGFR), a signaling protein that normally controls cell division. This third-line chemotherapy combination with paclitaxel-nimotuzumab-methotrexate seems to be an active combination and needs further clinical trials to validate its use in heavily treated patients.

Author contributions
Conception and design: Leonardo Verduzco; Provision of study patient: Elizabeth Haydee Aguirre; Collection and manuscript writing: Haydee Cristina Verduzco.

REFERENCES