PCI was well tolerated and had no adverse effects on the quality of life. Headache was the most common side effect. The only grade 3 adverse event was headache, which occurred in 4% of patients. Late radiation effects were rare. Grade 3 late effects (severe headache or severe central nervous system dysfunction) developed in approximately 2% of patients.

Dr. Slotman concluded, "Patients with extensive disease-small cell lung cancer who respond to chemotherapy should now routinely be offered PCI."

Final Results of the EORTC Intergroup Randomized Phase 3 Study 40983 Evaluating the Benefit of Perioperative FOLFOX4 Chemotherapy for Patients with Potentially Resectable Colorectal Cancer Liver Metastases

Perioperative chemotherapy provided benefit for patients with colorectal cancer who were treated with surgery for potentially resectable liver metastases. Bernard Nordlinger, MD, Ambroise Paré Hôpital, France, reported this finding on behalf of the European Organisation for Research and Treatment of Cancer.

Dr. Nordlinger noted that liver metastases recur in approximately two-thirds of patients who are treated with surgery alone. He explained that the addition of preoperative chemotherapy would help to reduce the size of liver metastases before surgery. The addition of postoperative chemotherapy would help to kill dormant cancer cells in the remaining portion of the liver. The chemotherapy regimen (6 cycles of FOLFOX4) was chosen because of its response rates of more than 50% among patients with metastatic colorectal cancer.

The study included 364 patients with potentially resectable liver metastases demonstrated on computerized tomography (CT). The patients were randomly assigned to the perioperative chemotherapy and surgery arm (182 patients) or to the surgery alone arm (182 patients). Resection of the liver was actually done in 151 patients in the perioperative chemotherapy arm and in 152 patients in the surgery alone arm. The primary endpoint of the study was progression-free survival (PFS).

Preoperative chemotherapy led to a 29.5% decrease in the size of the liver lesion (from a median of 45 mm to 30 mm). A complete response was achieved in 3.8% of patients and a partial response in 40.1% of patients after preoperative chemotherapy. Disease remained stable in 35.2% of patients. Disease progressed in 6.6%.

At interim analysis, the Independent Data Monitoring Committee authorized an early release of the final data. Perioperative chemotherapy was associated with better PFS for the total patient population (Table 1). Subgroup analysis demonstrated that better PFS was associated with perioperative chemotherapy for the eligible patient population, or the 171 patients in each arm who had evidence of resectable metastases on CT (Figure 1A). The PFS rate also favored perioperative chemotherapy among the patients who had liver resection (Figure 1B).

Table 1. Results.

	n pts CT	n pts Surgery	% absolute difference in 3-year PFS	Hazard Ratio (Confidence Interval)	p-value
All patients	**182**	**182**	**+7.2%** (28.1% to 35.4%)	**0.79** (0.62-1.02)	**p=0.058**
All eligible patients	**171**	**171**	**+8.1%** (28.1% to 36.2%)	**0.77** (0.60-1.00)	**p=0.041**
All resected patients	**151**	**152**	**+9.2%** (33.2% to 42.4%)	**0.73** (0.55-0.97)	**p=0.025**

Figure 1A. PFS in Eligible Patients.

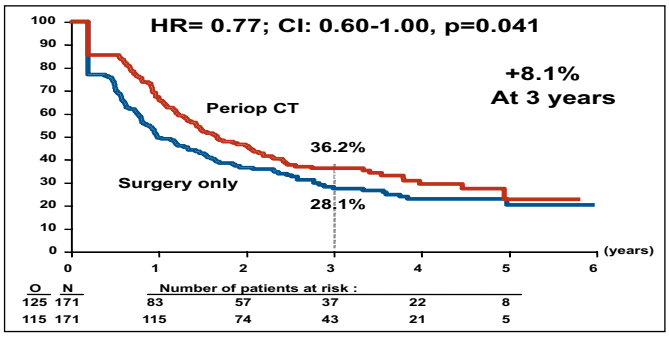
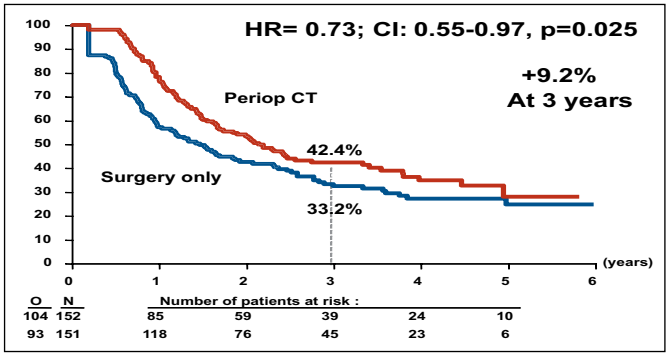


Figure 1B. PFS in Resected Patients.



Preoperative chemotherapy was associated with grade 3 neutropenia (18.1%), diarrhea (8.2%), nausea (3.5%), and sensory neuropathy (2.3%). There was one case of grade 4 febrile neutropenia. Postoperative chemotherapy was also associated with a high incidence of grade 3 sensory neuropathy (9.6%), grade 3 or 4 leukopenia (12.2%), and grade 3 or 4 neutropenia (34.8%). The frequency of postoperative complications was significantly higher for patients who received perioperative chemotherapy (25.2% vs 15.9% for surgery alone; p=0.04). There were higher incidences of biliary fistula, hepatic failure, intra-abdominal infection, and re-operation among patients who received perioperative chemotherapy.

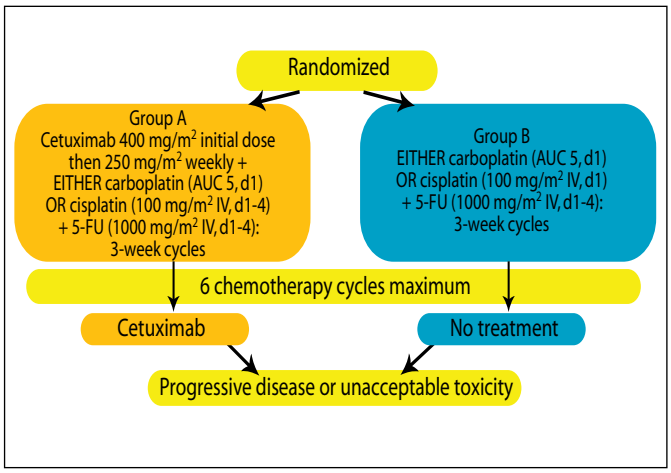
Results of the EXTREME Study

Overall survival for patients with head and neck cancers is significantly prolonged with the addition of cetuximab to platinum-based chemotherapy, according to results of the phase 3 EXTREME study. In addition, stated investigator Jan Baptist Vermorken, MD, PhD, University Hospital Antwerp, Edegem, Belgium, "Adding cetuximab did not increase toxicities above those characteristic of platinum-based therapy".

Epidermal growth factor receptor (EGFR) is highly expressed in squamous cell carcinoma of the head and neck (SCCHN), and is an independent prognostic factor for unfavorable local control rates, disease-free survival and overall survival. Cetuximab is an IgG1 monoclonal antibody that specifically targets EGFR and induces antibody-dependent cell-mediated cytotoxicity. Both pre-clinical [Fan Z et al. *Cancer Res* 1993] and clinical research has shown synergy between cetuximab and platinum-based chemotherapy (cisplatin or carboplatin) with 5-FU (fluorouracil) [Burtness B et al. *J Clin Oncol* 2005; Bourhis J et al. *J Clin Oncol* 2006].

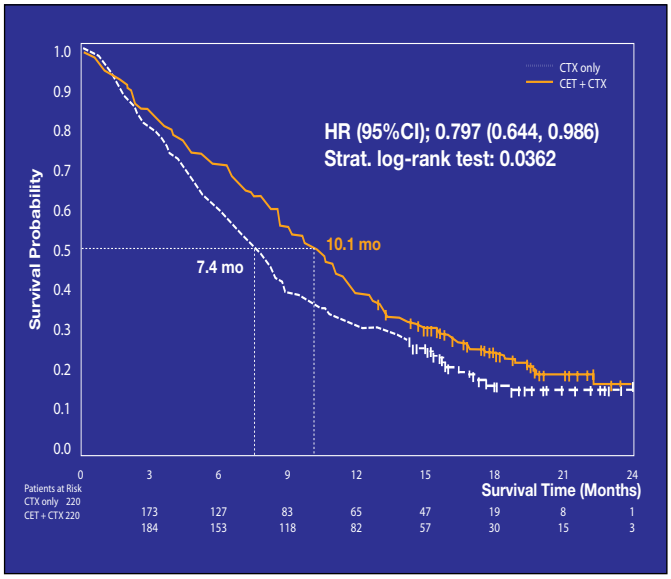
EXTREME was a randomized, phase 3 multicenter study comprised of 442 patients (median age ~56.5 years; ~90.5% men) with recurrent or metastatic SCCHN unsuitable for local therapy. Patients were randomly assigned to treatment with cetuximab + platinum (carboplatin or cisplatin) + 5-FU (n=222) or platinum (carboplatin or cisplatin) + 5-FU (n=220) for a maximum of 6 chemotherapy cycles. Patients receiving cetuximab continued on maintenance cetuximab until disease progression or unacceptable toxicity (Figure 1). The primary endpoint was overall survival (OS).

Figure 1. Study Design.



Median OS was significantly longer in the cetuximab plus chemotherapy group (10.1 months vs 7.4 months, respectively; p=0.036; Figure 2).

Figure 2. Overall Survival.



Overall adverse event rates were similar for the two study arms; although acne-like rash and infusion reactions occurred (~5%) only in the cetuximab group and vomiting (~5%) and diarrhea (~5%) were higher with cetuximab-containing therapy. Anemia, neutropenia and thrombocytopenia were higher with platinum-based therapy alone.

Dr. Vermorken concluded, "This is the first systemic treatment in 25 years to show a survival benefit over platinum-based chemotherapy in recurrent/metastatic SCCHN."