therapy and in 13% of patients who received interferon alone ($p < 0.0001$). The median PFS was 10.2 months for the combination therapy and 5.4 months for interferon alone.

Dr. Escudier explained that PFS was also evaluated in patient subgroups stratified according to Motzer score. For patients who had a favorable or intermediate Motzer score, the PFS was significantly better for interferon plus bevacizumab than for interferon alone. However, for patients with a poor score, there was no significant difference between the two treatment groups (Table 1).

Table 1. Progression-Free Survival for Subgroups Stratified According to Motzer Risk Score.

	Progression-Free Survival (Mos.)		
	Bevacizumab + Interferon	Interferon + Placebo	Hazard Ratio, P Value
Overall	10.2	5.4	0.63, <0.0001
Subgroups			
Favorable	12.9	7.6	0.60, 0.004
Intermediate	10.2	4.5	0.55, <0.0001
Poor	2.2	2.1	0.81, 0.457

At the time of interim analysis of overall survival, 251 of 450 scheduled events had occurred. The median overall survival had not been reached for the interferon plus bevacizumab arm and was 19.8 months for the interferon alone arm.

Interferon plus bevacizumab was well tolerated. The rate of grade 3 or 4 adverse events was 60% for the combination therapy arm and 45% for the interferon alone arm. The most common grade 3 or 4 adverse event was fatigue/asthenia/malaise, which occurred more frequently among patients who received interferon plus bevacizumab (23% vs 15%).

Prophylactic Cranial Irradiation in Extensive Disease Small Cell Lung Cancer

Percutaneous cranial irradiation (PCI) has had benefit for patients with limited disease small cell lung cancer (SCLC). The findings of a study now indicate that PCI also has benefit in the setting of extensive disease (ED)-SCLC, where the risk of brain metastases is high.

Ben Slotman, MD, PhD, VU University Medical Center, Amsterdam, the Netherlands, reported the findings of a study in which PCI led to a significant reduction in the risk of symptomatic brain metastases and a significant prolongation of survival.

The trial involved 286 patients with ED-SCLC who had a response to standard chemotherapy. The patients were randomly assigned to the PCI group (143 patients) or to the control group (143 patients). Persistent primary disease was present in approximately 75% of the patients in each group. Approximately 70% of patients had persistent metastases to lymph nodes, bone, lung, or other sites after completion of chemotherapy. Radiotherapy was usually given as 20 Gy in 5 fractions. Other radiotherapy schemes included 24-30 Gy in 8-12 fractions and 30 Gy in 10 fractions.

Dr. Slotman said that symptomatic brain metastases was defined as the radiographic evidence of brain metastases and the presence of one or more key symptoms. These symptoms included signs of increased intracranial pressure, headache, nausea and/or vomiting, cognitive and/or affective disturbances, seizures, or focal symptoms.

At 1 year, the rate of symptomatic brain metastases was significantly lower for patients in the PCI group than for patients in the control group (Table 1). One-year overall survival was also significantly better for patients treated with PCI. Dr. Slotman reported that PCI had no significant effect on extracranial disease progression. However, the treatment extended failure-free survival (Table 1). Symptomatic brain metastases was the first event in 9% of patients in the PCI group compared with 35% of patients in the control group.

Table 1. Comparison of Outcomes for PCI Group and Control Group.

	PCI Group (N = 143)	Control Group (N = 143)	Hazard Ratio, P Value
Rate of symptomatic brain metastases (%)	14.6	40.4	0.27 (0.16-0.44), <0.001
One-year overall survival rate (%)	27.1	13.3	0.68 (0.52-0.88), 0.003
One-year failure-free survival rate (%)	23.4	15.5	0.76 (0.59-0.96), 0.02

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.

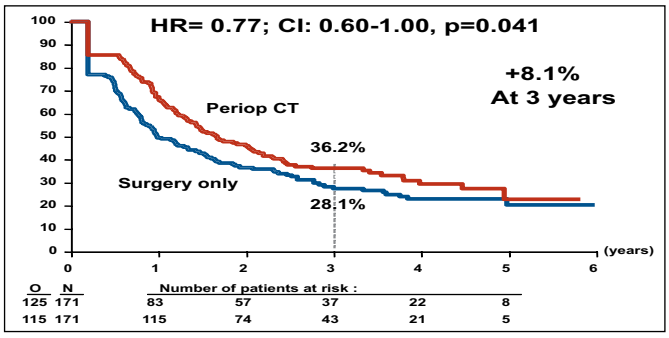

Figure 1B. PFS in Resected Patients.