**Improvements Made in the Local Control of Advanced Non-Small Cell Lung Cancer**

A phase II trial involving 47 patients with inoperable, advanced non-small cell lung cancer indicated that combining radiation therapy and RSR13 (efaproxiral sodium) delays tumor progression and increases survival. Researchers from the Vanderbilt-Ingram Cancer Center in Nashville, TN, and international collaborators presented the study. RSR13 is known to increase the release of oxygen from hemoglobin, thereby enhancing the effectiveness of radiation therapy. The participants received two courses of paclitaxel (Taxol®, Bristol-Myers Squibb, New York, NY) and carboplatin (Paraplatin®, Bristol-Myers Squibb) chemotherapy followed by daily RSR13 over 30 minutes (75 mg/kg with possible adjustments to 50 mg/kg or 100 mg/kg) and 32 doses (at 2 Gv) of chest radiation therapy. The overall response rate was 89% (39 of 44 patients), and the median survival time was 20.6 months. The major side effects were RSR13-related hypoxemia and radiation-induced pneumonitis. Comparing patient time to progression inside the radiation portal (24.8 months) and outside (11.3 months) suggests that induction by paclitaxel and carboplatin followed by RSR13 plus radiation therapy offers significant benefit for patients with advanced non-small cell lung cancer.

**Chemotherapy Plus Radiation After Surgery May Increase Survival of Patients With Head and Neck Cancer**

The results of a six-year study (1994–2000) of radiation alone or radiation plus chemotherapy (CT) involving 334 patients who had surgery for head and neck cancer were presented by researchers from Ospedale San Giovanni, in Bellinzona, Switzerland, and colleagues. Patients were randomized into radiation therapy (RT) once a day (2 Gy up to 66 Gy in 33 fractions) or RT plus three courses of CT (cisplatin 100 mg/m²) groups. The estimated overall survival of the RT-CT arm was increased significantly over the RT-only arm (65% versus 49%; p = 0.0057). At 34 months, the three-year, disease-free survival rate was 59% for the RT-CT group and 41% for the RT-only group (p = 0.0096). The improved survival rates for the RT-CT arm occurred with no increase in morbidity. No significant differences between the two arms were observed for objective mucositis, granulocytopenia, or thrombocytopenia. This study suggested that radiation plus chemotherapy following surgery should be considered for patients with locally advanced head and neck cancer.

**Fludarabine Phosphate Shows Promise for Treatment of Patients With Non-Hodgkin's Lymphoma**

An international multicenter trial presented by researchers from the University Medical Center in Utrecht, Netherlands, demonstrated a superior response from fludarabine phosphate (Fludara®, Berlex Laboratories, Wayne, NJ) compared to cyclophosphamide, vincristine, and prednisone (CVP) for patients with non-Hodgkin’s lymphoma. Fludarabine is a nucleoside analog that, in vivo, is rapidly dephosphorylated to an active metabolite, fluoro-arabinofuranosyl-adenine. Between 1993 and 1997, 381 patients were enrolled in the study and randomized into groups to receive eight cycles of standard CVP every four weeks or a standard fludarabine treatment, 25 mg/m² daily for five days every four weeks. The overall response rates for those who remained in the study were 75% and 58% for the fludarabine and CVP arms (p = 0.001). The median times to progression, 21 months versus 15 months for the fludarabine and CVP treatments, were not statistically significant. Hematologic toxicities, thrombocytopenia and neutropenia, were significantly higher in the fludarabine arm (28% versus 12%, p = 0.001; and 8% versus 1%, p = 0.002). Withholding treatment until disease symptoms occurred did not alter the overall survival rate or response to treatment.

**Bexxar® Demonstrates Effectiveness in Patients With Non-Hodgkin’s Lymphoma**

Bexxar® (Corixa Corporation, Seattle, WA) is a combination agent that includes both an unlabeled monoclonal antibody

**Activity of Ontak™ in Patients With Cutaneous T Cell Lymphoma**

Ontak™ (denileukin diftitox, Ligand Pharmaceuticals, San Diego, CA), a fusion protein combining diptheria toxin and interleukin-2 (IL-2), is used to treat patients with cutaneous T cell lymphoma (CTCL) who have tumors with IL-receptors. It targets cells with IL-2 receptors that have the p55 (CD25), p75 (CD122), and p64 (CD132) subunits, including some normal lymphocytes, leading to cell death. About 60% of patients with CTCL have tumors bearing the IL-2 receptor. Targetin® (bexarotene, Ligand Pharmaceuticals) increases the levels of p55 and p75 subunits in the IL-2 receptor in vitro. A study from Tufts New England Medical Center in Boston, MA, of nine patients with CTCL evaluated whether in vivo IL-2 expression could be increased by Targetin and whether the combination of Targetin plus Ontak was tolerable. Targetin doses were 75, 150, 225, or 300 mg per day, and on day eight Ontak treatment was begun at 18 mg/kg per day three times every 21 days. The overall response rate with the combination therapy was 75%, and the p55 levels increased in six of the seven patients treated with Targetin 150 mg/day. The following side effects were found: grade 2 or 3 leukopenia (n = 4), grade 2–4 lymphopenia (n = 6), hypertriglyceridemia (n = 8), thyroid toxicity (n = 7), hypersensitivity to Ontak (n = 1), and vascular leak syndrome (n = 3). The overall assessment determined that the tolerability profile of the two agents was acceptable and phase II trials are planned.

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