A Phase III Study on the Concurrent Use of Oral Pilocarpine to Reduce Hyposalivation and Mucositis Associated with Radiation Therapy in Head and Neck Cancer Patients. Final Results of RTOG 97-09

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Purpose:

Radiation therapy (RT) continues to play a major role in the management of head and neck (H&N) cancer. Two of the major treatment morbidities are acute mucositis and acute and chronic xerostomia. The former can affect tolerance and result in treatment breaks, while the latter is largely permanent and can significantly impact the quality of life (QOL) of many patients. Pilocarpine (P) is a cholinergic agonist that acts to stimulate the salivary glands. Pilocarpine is the only approved sialogogue for radiation induced xerostomia. The primary objective of this study is to determine whether the concomitant use of P is able to preserve salivary flow in H&N cancer patients receiving curative RT.

Methods and Materials included:

Selected patients were required to have at least 50% of the volume of the major salivary glands receive at least 50Gy. They agreed to provide stimulated and unstimulated samples of saliva (measured in ml/min) prior to, 3 mo and 6 mo after initiation of RT and complete the Univ. of Washington H&N QOL forms. Patients were randomized to receive P at 5 mg qid or placebo. 249 patients were registered of whom 244 were eligible for analysis. Following 3mo of drug/placebo patients were allowed to take open label P.

Results included:

Toxicities from P were mild. Mucositis scores were similar in both groups- 43% on both arms experienced ulceration. At 3 months following the initiation of RT, the average reduction in unstimulated salivary flow was statistically different in P group –1.1 ml/min vs. -1.7 placebo ($p < 0.047$). At 6mo, with over 50% of placebo patients switching to P, there was a difference in unstimulated flow, but not statistically significant ($p = .09$). More than 50% of P pts stopped P at 3mo and when compared to placebo that never received P, they had > 50% better salivary flow ($p=0.088$).

Conclusions:

The significant difference in unstimulated salivary flow advocates for the concomitant use of oral P to decrease radiation associated xerostomia. Oral P did not influence the onset or grade of mucositis. Patients could not distinguish xerostomia from mucositis and their affect on QOL, thus, having the latter (mucositis) results in no improvement in QOL.