Brachytherapy Boost in Locoregionally Advanced Nasopharyngeal Carcinoma. A Prospective Randomized Trial of the International Atomic Energy Agency

E. Rosenblatt[1], M. El-Gantiry[2], I. Elattar[3], M. Afiane[4], N. Benjafaar[5], S. Abubaker[6], Y. Chansilpa[7], B. Vikram[8], M. Abdel-Wahab[9,10], P. Levendag[11]

1International Atomic Energy Agency, Vienna, Austria, 2National Cancer Institute University of Cairo, Cairo, Egypt, 3National Cancer Institute University of Cairo, Cairo, Egypt, 4Department de Radiotherapie, Centre Pierre et Marie Curie, Centre Hospitalier Universitaire Mustafa (CHU), Alger, Algeria, 5Institut National d'Oncologie, Rabat, Morocco, 6Institute of Nuclear Medicine and Oncology, Pakistan Atomic Energy Commission (PAEC), Lahore, Pakistan, 7Siriraj Hospital, Faculty of Medicine. Mahidol University, Bangkok Thailand, 8National Cancer Institute, Bethesda, MD, 9Taussig Comprehensive Cancer Center, Cleveland Clinic, Cleveland, OH, 10International Atomic Energy Agency, Vienna, Austria, 11Erasmus University, Rotterdam, Netherlands

Purpose/Objective(s): To determine whether brachytherapy boost after standard external beam radiation and chemotherapy improves outcome in patients with locally advanced nasopharyngeal carcinoma.

Materials/Methods: Patients with nasopharyngeal carcinoma WHO Grades I to III and TNM Stages III or non-metastatic Stage IV were eligible for this Phase III randomized multi-institutional study. Patients were randomized centrally to either arm (A) induction chemotherapy, followed by external beam radiotherapy (EBRT) with concomitant cisplatin (n = 139) or arm (B), the same schedule plus a brachytherapy boost to the nasopharynx (n = 135). The EBRT doses given were 70 Gy to the primary tumor and positive lymph nodes and 46 Gy to the clinically negative neck. The additional nasopharyngeal brachytherapy boost in arm (B) was given by either low dose-rate (LDR) or high dose-rate (HDR) brachytherapy techniques using 11 Gy for LDR and 3 fractions of 3 Gy each for HDR. The primary endpoint was 3-year overall survival (OS) and secondary endpoints were: local control (local recurrence free survival or LRFS), regional control, distant metastasis and serious (Grade 3 – 4) adverse events.

Results: Two hundred seventy-five patients were randomized from five institutions between September 2004 and December 2008. The two arms were comparable with regard to age, gender, stage, and grade. Two hundred seventy-three patients completed the treatment. The median follow-up was 29 months (0.2 – 67 months). The effect of treatment arm, country, age (<40 vs. 40 or > years), gender, WHO pathology, stage (T3 – 4, N2 – 3 vs. other) and chemotherapy on OS, DFS, and LRFS was studied. Stage significantly affected OS ($p = 0.024$) and DFS ($p = 0.018$) while age significantly affected OS ($p = 0.014$). None of the other factors studied were significant for OS, DFS, or LRFS. The 3-year LRFS in the nasopharynx was 60.5% and 54.4% in arms A and B, respectively ($p = 0.647$). The 3-year regional control rate in the neck was 59.7% and 54.3%, respectively ($p = 0.7$). Distant metastasis developed in 59.7% of patients in arm A and 55.4% in arm B ($p = 0.377$). Patients with T1/T2 N+ had a 3 year LRFS of 51.8% in Arm A (62 patients) vs. 57.9% in Arm B (67 patients) ($p = 0.343$). The Grade 3 – 4 toxicity rate was 21.6% (30/139) and 24.4% (33/135), respectively ($p = 0.687$).

Conclusions: The addition of a brachytherapy boost to external beam radiation and chemotherapy did not improve outcome in locally advanced nasopharyngeal carcinoma.