PS12 Late breaking

A randomized trial with 908 patients evaluating the importance of accelerated versus conventional fractionated radiotherapy in squamous cell carcinoma of the head and neck. First results of the IAEA–ACC Study Group

J. Overgaard, B.K. Mohanti, S. Bhasker, N. Begum, R. Ali, J.P. Agerwal, M. Kuddu, M.R. Baeza, A. Al-Amro, C. Stannard, F. Geara, B. Vikram, C. Crau

The IAEA–ACC Trial Center, Dept. of Experimental Clinical Oncology, Aarhus University Hospital, Denmark

Background: Several large randomized studies have shown that accelerated fractionation may be beneficial in the radiotherapy treatment of squamous cell carcinoma of the head and neck. These studies have been performed in Western Europe and USA, and it is unclear to which extend such treatment principle can be generalized to radiotherapy practice in the developing world where the therapeutic resources are less and the patients have a more heavy tumor burden. In order to test the applicability of these results in a global setting, the International Atomic Energy Agency (IAEA) initiated a two-armed randomised multicentre trial. The aim of the study was to examine whether reduction of the overall treatment time by increasing the number of weekly radiotherapy fractions from 5 to 6 (and maintaining same total dose and fraction number) would improve the tumor response, and were acceptable with regard to early and late morbidity, as well as being a suitable therapeutic principle in all therapeutic environments.

Patients and methods: Patients with squamous cell carcinoma of the larynx, pharynx and oral cavity eligible for primary curative intended radiotherapy alone were randomized between 5 or 6 weekly fractions of radiotherapy (66–70 Gy in 33 to 35 fx). Nine centres from Asia (*New Delhi, Mumbai, Peshawar, Islamabad*), Europe (*Tallinn*), Middle East (*Riyadh, Beirut*), Africa (*Cape Town*) and South America (*Santiago*) entered a total of 908 patients in the trial from 1999 to 2004. Patients had Stage I (n = 28), Stage II (n = 229) stage III (n = 337) or stage IV (n = 314) squamous cell carcinoma of the oral cavity (n = 212), oropharynx (n = 318), hypopharynx (n = 162) or larynx (n = 216). Prognostic factors like age, gender, site and stage were well balanced between the two arms.

Results: Of the 908 patients randomized 885 eligible and evaluable patients were included in the analysis. More than 92% received the planned total dose. The median treatment times were 47 and 40 days in the 5 and 6 fx/wk arm, respectively.

Overall, the results showed a benefit in 3-year loco-regional control (47% vs 36% ($p = 0.005$, RR: 0.68 [0.52–0.89]) for the 6 vs 5 fx/wk arm, respectively. The effect of overall treatment time appears to occur in the T-site (52% vs 42% for 6 vs 5 fx/wk respectively, $p = 0.007$, RR: 0.70 [0.53–0.91]), whereas the response in the neck nodes was not significant different. The benefit in tumor control resulted in a significant better disease-specific survival (54% vs 48% for 6 vs 5 fx/wk respectively. $p = 0.02$, RR: 0.73 [0.56–0.96]), whereas there was no significant difference in overall survival. Acute morbidity in the form of severe mucositis was significantly more frequent in the 6 fx/wk group, but there were no difference in late radiation side effects.

Conclusion: The accelerated schedule was considered superior to conventional fractionation, and since it does not require additional resources may it be a suitable new standard baseline treatment for primary radiotherapy of larynx, pharynx and oral cavity carcinoma which is applicable worldwide.

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