6LB Late Breaking

Randomized study of the importance of Novel Erythropoiesis Stimulating Protein (Aranesp®) for the effect of radiotherapy in patients with primary squamous cell carcinoma of the head and neck (HNSCC) – the Danish Head and Neck Cancer Group DAHANCA 10 randomized trial

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Aim: The primary objective of the trial was to evaluate, in an open randomized trial, if the correction of low haemoglobin (Hb) levels by means of darbepoetin alpha (Aranesp®) during radiotherapy improves outcome of curative radiation treatment in patients with HNSCC. Following the outcome of a planned interim analysis which showed inferiority of the experimental treatment the trial was stopped on November 28, 2006, and subjected to the following analysis which was performed per July 1, 2007.

Patients and Methods: Pts with HNSCC eligible for primary radiotherapy alone (except those with T1 glottic cancers) and with with Hb values below 9.0 mmol/l (14.0 g/dl) were randomized to receive Aranesp® together with accelerated (6 weekly fractions) fractionated radiotherapy (66–68 Gy in 33 to 34 fx). In addition, patients were also treated with the hypoxic radiosensitizer Nimorazole. Aranesp® was given subcutaneously in a dose of 150 micrograms. The first dose was administrated the week prior to start of radiotherapy and continued once a week until completion of radiotherapy, or stopped earlier if the Hb exceeded 9.6 mmol/l (15.5 g/dl). Patients were recruited from all Danish oncological centers and from the Norwegian Radium Hospital in Oslo.

Results: In total, 522 patients had been randomized at the time of the interim analysis (of a planned intake of 600) with a median follow-up time since randomization of 37 months (range 8–60). Of these 515 were eligible for analysis (255 pts treated with Aranesp® and 260 pts in the control group). Among these, 167 have experienced a loco-regional failure (the primary study endpoint). There have been 218 deaths of which 163 are known to be of the cancer in question. Overall, the patients were evenly distributed according to the stratification parameters (gender, T and N staging, tumor site, institution) which, except the latter, were also found to significantly discriminate prognosis within the material. Aranesp® resulted in the expected increase in Hb with more than 91% of the patients obtaining the planned increase. The compliance to Aranesp® was good without excess incidence of major serious adverse events. Overall, the results showed a poorer outcome in 5-year actuarial loco-regional control (56% vs. 69% ($p = 0.02$, RR: 1.44 [1.06–1.96]) for the Aranesp® vs. control arm. This was also seen for the endpoint of disease-free survival (48% vs. 63% for Aranesp® vs. control, $p = 0.004$, RR: 1.49 [1.13–1.97]). The difference in tumor control resulted in a similar difference in 5-year disease-specific survival (51% vs. 67% for Aranesp® vs. control, $p = 0.05$, RR: 1.38 [1.01–1.88]), whereas there was no significant difference in overall survival (38% vs. 51% for Aranesp® and control respectively, $p = 0.08$, RR: 1.28 [0.98–1.68]). There was no difference in the risk of developing distant metastases or in non-cancer related deaths, neither was there any enhanced risk of cardio-vascular events observed in the experimental arm. There were no apparent differences in acute or late radiation related morbidity. All univariate analyses were confirmed in a multivariate setting.

Conclusion: Correction of the Hb level with Aranesp® in patients with HNSCC resulted in a significantly poorer tumor control after radiotherapy. The treatment principle was abandoned and the difference in outcome is currently being subjected to further examination.

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