

THE DUCTH DEEP HYPERTHERMIA TRIAL: UPDATED RESULTS IN CERVIX CANCER

Franckena M.^{1*}, Stalpers L.J.A.², Koper P.C.M.³, Wiggenraad R.G.J.⁴, Hoogenraad W.J.⁵, Warlam C.C.⁶, van Dijk J.D.P.², Jobsen J.J.⁷, Van Rhoon G.C.^{1*} and van der Zee J.^{1*}

¹ *Daniel den Hoed Cancer Center, Erasmus Medical Center Rotterdam*

² *Academic Medical Center Amsterdam,*

³ *HagaZiekenhuis, Den Haag,*

⁴ *Medisch Centrum Haaglanden, Den Haag,*

⁵ *University Medical Center Sint Radboud, Nijmegen,*

⁶ *University Medical Center Utrecht,*

⁷ *Medisch Spectrum Twente, Enschede*

Background: The local failure rate in patients with locoregionally advanced cervical cancer is 41-72 % following radiotherapy alone (RT). Local control is a prerequisite for cure. The Dutch Hyperthermia Trial showed that combining radiotherapy with hyperthermia (RT+HT) improves local control at 3 years from 41 to 61 %^{1,2}. However, the follow-up in the early report was relatively short with a median of 43 months.

Purpose: To evaluate long-term results of a randomized phase III trial comparing RT with RT+HT after 12 years follow-up

Material and Methods: Eleven radiotherapy institutes participated in the study. One hundred and fourteen patients were randomized (n = 56 RT, n = 58 RT+HT) between 1990 and 1996. Prognostic factors were equally distributed over both groups. RT was given in 23-28 daily fractions of 1.8-2 Gy and brachytherapy (2 HDR applications of 17 Gy or 20-30 Gy LDR). HT was given 5-6 times, once weekly. The primary endpoint was local control; secondary endpoints were overall survival and toxicity.

Results: At 12 years follow-up, local control remains better in the RT+HT group (36% vs 56%, p = 0.02). The advantage of combined RT+HT was also reflected in a persistently better overall survival after 12 years from 20% (RT) to 37% (RT+HT). In a univariate Cox regression analysis, FIGO stage and WHO performance status (WHO-PS) were significant prognostic factors both for local control and survival. The benefit of HT remained significant after correction for these factors. In patients with continuing pelvic control, 30 % developed distant metastasis in the RT-group compared to 25 % in the RT+HT group (p = 0.4). The incidence of EORTC grade 3-5 radiation-induced toxicity was comparable in both groups.

Conclusions: Adding hyperthermia to radiotherapy in inoperable cervical cancer results in long-term major improvement of local control and survival, without an increase in toxicity.

References:

1 Van der Zee J, Gonzalez Gonzalez D, van Rhoon GC, van Dijk JD, van Putten WL, Hart AA. Comparison of radiotherapy alone with radiotherapy plus hyperthermia in locally advanced pelvic tumours: a prospective randomized, multicentre trial. *Lancet* 2000; 355: 1119-1125

2 Van der Zee J, Gonzalez Gonzalez D. The Dutch Deep Hyperthermia Trial: results in cervical cancer. *Int J Hyperthermia* 2002; 18: 1-12