1208 POSTER

Long-term survival in a phase III randomised study of topotecan (T) vs paclitaxel (P) in advanced epithelial ovarian carcinoma

G. Ross[1], S. Lane[2], G. Dane[1]. *For the International Topotecan Study Group; [1] GlaxoSmithKline, Harlow, Essex, UK; [2] GlaxoSmithKline, Collegeville, PA, USA*

Purpose: We have continued to monitor the survival of patients randomised in a previously reported multicentre, randomised phase III study of topotecan vs paclitaxel in patients with advanced epithelial ovarian carcinoma who had failed one prior platinum-based regime (1, 2).

Methods: Patients with bidimensionally measurable disease were randomised to topotecan (1.5 mg/m2/day dx5) or paclitaxel (175 mg/m2/day as a 3-hour infusion) q 21 days. Patients were eligible for treatment with the alternate therapy at third line and these results have recently been published (3).

Results: A total of 226 patients were evaluable for response. As previously reported, the demographic characteristics were similar in both treatment groups. The EORTC QOL-C30 questionnaire was also used to measure eight symptoms at baseline and during each course (pain, anorexia, diarrhoea, fatigue, N/V, dyspnea, constipation, and insomnia); the results were similar. Time-to-progression was 18.9 wks in the topotecan group (range <1-92.6+ wks; 25% censored) and 14.7 in the paclitaxel group (range <1-137.3+ wks; 12.3% censored) (P=0.076). Survival was 63.0 wks in the topotecan group (range <1-238.4+ wks; 20.5% censored) and 53.0 wks in the paclitaxel group (range: <1-226.3+ wks; 12.3% censored) (P=0.438). Both treatment arms continue to provide long-term survival benefit. While the median survival remains constant, 20% of topotecan patients and 12% of paclitaxel patients remain alive at least 4 years after randomisation. The survival curves for topotecan and paclitaxel will be presented at the meeting.

Conclusion: Topotecan continues to demonstrate comparable efficacy and survival to paclitaxel with manageable and noncumulative hematologic toxicity. Non-haematological toxicity was generally mild for both groups. The long-term survival rate indicates substantial therapeutic benefit for this group of patients receiving therapy at relapse of ovarian carcinoma. (Supported by SmithKline Beecham)

References

[1] ten Bokkel Huinink W et al. J Clin Oncol. 1997; 15: 2183-2193;
[2] Gordon A, et al. Proc Am Soc Clin Oncol. 1998; 17 (Abstract 1374);
[3] Gore M et al. J Clin Oncol. 2001; 19: 1893-1900.

Other gynaecological tumours

1209 POSTER

Influence of anemia on tumor growth and tumor control- an investigation on advanced cervical cancers

G. Haensgen[1], U. Krause[2], S. Pigorsch[3], J. Dunst[4].
[1] Martin-Luther-University, Radiotherapy, Halle, Germany;
[2] Martin-Luther-University, Pathology, Halle, Germany;
[3] Martin-Luther-University, Radiotherapy, Halle, Germany;
[4] Martin-Luther-University, Radiotherapy, Halle, Germany

Background: The relationship between pre-treatment hemoglobin level and outcome is well-known in tumor patients. We investigated the correlation between pre-treatment hemoglobin, microvessel density (MVD) and the proliferation index on local response in advanced cervical cancer.

Material and Methods: The prospective study between 1995 - 1999 comprises of 87 patients with advanced cervical cancer with FIGO stage IIB (19), IIIB (59) and IVA (9), who were treated by definitive radiotherapy (external beam and HDR-Afterloading) in curative intention. The tumorspecific 3-year-survival was analyzed dependend on tumorstage and pre-treatment hemoglobin as well as the hemoglobin level at 20 Gy. Prior to therapy biopsies were taken in 46 pts. and stained by immunohistochemistry with anti-CD31 for microvessel density. From the same biopsy investigations by flowcytometry were performed for S-phase-determination as an marker for proliferation. For data analysis SPSS 9.0 was used. Results: Stage IVA (FIGO) in comparison to stages IIB and IIIB (p=0.0012) and pre-treatment hemoglobin at a cut-off level of 11g/dl (p=0.0018) were revealed as independent significant prognostic factors. Concerning the microvessel density we found a worse 3-year-survival for patients with tumors with high microvessel density (median 128/10 HPF) 41+ 24% (n=24) in comparison to a low microvessel density 69 + 11% (n=22). The correlation for MVD was not significant p = 0.12. For hemoglobin level and microvessel density we could confirm a trend with p=0.08.In an multifactorial analysis a survival benefit (p<0.05) for non-anemic patients neither pre-treatment nor at 20 Gy (Hb>11g/dl) compared to patients with decreasing hemoglobin level over radiotherapy was found. Local tumor progression was seen frequently in patients with stage IVA (relative frequency 0.67) and in anemic patients (0.38 Hb< 11g/dl vs. 0.20 Hb> 11g/dl). Anemic patients showed a higher prolifaration rate with 25 + 16% versus 17 + 10% of cells in S-phase (p=0.059).

Conclusion: Tumor anemia worsens prognosis on local response in patients with advanced cervical cancer. Tumors with high proliferation rate are more common in anemic patients. The treatment of anemia may improve local response but does not promote aggressiveness of tumors.

1210 POSTER

Transperineal low dose rate interstitial brachytherapy in the treatment of carcinoma of the uterine cervix. Long term results

A.A. Puthawala[1], A.M.N. Syed[1], P. Disaia[2], M. Berman[2], N.N. Abd-Elaziz[1], A. Londrc[1]. *[1] Long Beach Memorial Medical Center, Radiation Oncology, Long Beach, USA; [2] UCI Medical Center, GYN Oncology, Orange, USA*

Purpose: To evaluate the long term results of transperineal interstitial brachytherapy in the treatment of locoregionally advanced carcinoma of the uterine cervix.

Materials and Methods: Between 1977 and 1997, a total of 185 women with biopsy-confirmed carcinoma of the uterine cervix underwent definitive radiation therapy. All patients were staged using FIGO system. Stage IB (barrel) 21 (11%), stage IIA 9 (5%), IIB 68 (37%), IIIA 13 (7%), IIIB 64 (35%), IVA 8 (4%), and IVB 2 (1%). Majority of these patients were unsuitable for conventional intracavitary brachytherapy due to bulky disease, distorted anatomy, tumor extension to lower vagina or to pelvic wall with fixation. All patients were treated with a combination of external beam irradiation to the pelvis to a dose of 5040 cGy over 5* weeks time. A lower midline block was used after 3960 cGy. Two separate interstitial implants were performed at two week intervals delivering 20 to 25 Gy dose with each implant. The dose was typically prescribed to the entire implant volume with dose rate of 60 to 80 cGy per hour with MEAN implant dose to Point "A" of 25 Gy.

Results: The MEAN follow-up period for the entire group is 51 months (range 3 to 223 months). An initial local tumor control was achieved in 152/185 (82%) of patients. A sustained locoregional control was maintained in 73% (136/185) until the time of last follow-up or death. The five-year overall survival rate was 45% while five-year disease-free survival for the entire group was 58%. This has been broken down according to the FIGO stage 65%, 67%, 49%, and 17% for stage I, II, III and IV, respectively. Isolated distal metastasis developed in 28/185 (15%) of patients and 49 patients who failed locoregionally, 16 (33%) also developed distal metastatic disease. RTOG grade 1 & 2 GU and GI toxicity was self-limited to all patients and grade 3 acute toxicity was experienced by 32% of patients. The late grade 3 and 4 GU and GI complications occurred in 17/185 (9%) of patients requiring surgical intervention.

Conclusion: Transperineal interstitial brachytherapy is efficacious and safe for the patients with bulky and advanced cervical cancer who are not ideal candidates for conventional intracavitary brachytherapy.

1211 POSTER

Tumor growth inhibition by antisense DNA methyltransferase oligonucleotide in cervical cancer

C.L. Chen, Sin-Ming Ip, Hextan Y.S. Ngan. *The University of Hong Kong, Obstetrics and Gynecology, Hong Kong, Hong Kong*

Cervical cancer is one of the most common female cancers worldwide. Apart from the involvement of HPV infection, many genetic and epigenetic changes are also play important roles in this cancer. DNA methylation (methylation in the CpG island of promoter site resulting in inactivation of tumor suppressor genes) and genomic imprinting (preferentially expression one of the parental original allele) are two important epigenetic events involved in many human cancers. So far, DNA methyltransferase (DNMT1)which has both maintainance and de novo methylation function is considered the important enzyme in these two epigenetic events. However, the role of DNMT1 in cervical cancer is not quite clear.

In this study, we first studied the imprinting status for two imprinting genes: IGF2, H19 genes as well as the methylation status of several tumor