723

CA 125 IS AN UNRELIABLE MARKER FOR MONITORING RESPONSE TO TAXOL THERAPY IN PATIENTS WITH RELAPSED OVARIAN CANCER. Van der Burg MEL, Myles JD, Hoskins PJ, Ten Bokkel Huinink WW, Eisenhauer E. Rotterdam Cancer Institute: Daniel den Hoed Kliniek, PO box 5201, 3008 AE Rotterdam, The Netherlands and the NCI Canada Clinical Trials Group.

In the treatment of ovarian cancer (OC) the serum marker CA 125 is generally accepted as a reliable marker for monitoring objective response (OR) and detection of early progression (PD). In a review of 12 published reports in the setting of first line cisplatin based therapy, a rise in CA 125 corresponded to PD in 97% of patients (pts), and a decrease in CA 125 to an OR in 87% of pts. (Neth J Med 40:36,1992). However, there is no standard definition of CA 125 response. In a large European-Canadian trial of Taxol in relapsed OC, 191 pts had serial CA 125 determinations and an elevated CA 125 at baseline. They were classified as having serologic response (SR): 2 consecutive decreases in CA 125, or serologic progression (SPD): 2 consecutive rises in CA 125. Of the 191 pts, 109 met criteria for SR, 61 for SPD and 21 met neither criterion. 27 Pts had SPD documented after initial SR. The objective tumour response (on the base of radiographic evaluation in 173 pts and physical examination in 18 pts) in each pt subsequent to SR or SPD is shown:

	Objective Response				
Serum CA 125	CR/PR	SD	PD	Total	Correctly Classified
SR	32	51	26	109	29%
SPD	11	12	38	61	62%
SPD after SR	1	12	14	27	52%

The correlation between serologic assessment of response and objective measurement of tumour volume was poor. There was substantial within pt variability of CA 125 levels, especially when the CA 125 was measured weekly. The cause of this fluctuating pattern, however, remains speculative.
Conclusion: In relapsed ovarian cancer, assessment of CA 125 response c.q. progression as defined here is of limited value in assisting assessment of objective tumour response to taxol.

724

THE VALUE OF SURGICAL TREATMENT FOR ILEUS IN OVARIAN CANCER

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In a retrospective study 60 patients, that experienced an ileus due to ovarian cancer during the years 1985-1991, were studied. In 17 of the 58 evaluable patients in a follow up time of 0-61 months a recurrence of ileus was observed after conservative or surgical treatment. Median follow up after treatment for ileus for 58 patients (41 without ileus recurrence) was 2 months (1 mo), 28 (17) with follow up of ≥ 3 mo, 16 (8) with f.u. of ≥ 6 mo and 6 (3) with f.u. of at least 12 months. A forward stepwise proportional hazard (Cox) regression analysis was used to identify prognostic factors and to test the difference between conservative and surgical treatment for ileus. Ultimately there was no evidence for a difference in prognosis between conservatively and surgically treated patients. From the multivariate analysis, the interval of last surgery to ileus and the presence of ascites emerged as the significant prognostic factors. Based on this finding, two prognostic groups were defined: GI Interval 0 months (ovarian cancer primarily presented with ileus) with or without ascites, or Interval ≥ 6 months without ascites and GII Interval 1-5 months with or without ascites or Interval ≥ 6 months with ascites. The median ileus free survival of these two groups differed significantly: 8 months for GI and 1 month for GII. At 6 months 56% of GI patients were still alive without ileus and 0 % of GII. At 12 months in the GI group 26 % was still alive without ileus and at 24 months 14 %. Although a clear tendency toward a longer ileus free survival was seen in the patients that were treated surgically for their ileus especially in the GI group, this observation was not statistically significant (p = 0.052)

725

CISPLATIN AND TREOSULFANE CHEMOTHERAPY IN THE TREATMENT OF METASTATIC OVARIAN CANCER

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At the Department of Obstetrics and Gynaecology, University Erlangen, 58 patients with metastatic ovarian cancer were treated with a combined chemotherapy of cisplatin and treosulfane.
After primary surgery with maximal tumordebulking patients received 4 cycles of 100mg/m^2 cisplatin and 5g/m^2 treosulfane in a monthly interval.
After this treatment 46 of the 58 patients underwent a second look operation. The remissionrate was 81 % and 52 % of the patients devellopped no recurrences or metastases.
The median follow up is 18 months with a variation of 3 - 55 months
There occured only a small number of serious side effects and mainly due to cisplatin.
Referring to this experiance the combination of cisplatin and treosulfane seems to be a promissing chemotherapy in the treatment of metastatic ovarian cancer.

726

CISPLATIN AND TREOSULFANE CHEMOTHERAPY IN THE TREATMENT OF METASTATIC OVARIAN CANCER - LOW VERSUS HIGH DOSE

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The combination of Cisplatin 100mg/m^2 and Treosulfane 5g/m^2 is a promising chemotherapy in the treatment of metastatic ovarian cancer. In order to minimalize the side effects of this chemotherapy without any loss of effectivness 92 patients were treated in a prospective randomised trial after maximal primary surgery either with Cisplatin 50mg/m^2 and Treosulfane 5g/m^2 (low dose) or Cisplatin 100mg/m^2 and Treosulfane 5g/m^2 (high dose) four times in monthly intervalls. 44 patients belonged to the low dose group, 48 patients to the high dose group. After this treatment 23 patients of the low dose group and 33 patients of the high dose group underwent a second look surgery. The remissionrate of the low dose group was 41% compared to the 50% remissionrate of the high dose group. 70% of the low dose group patients and 60% of the high dose group patients devellopped recurrences within a median disease free intervall of both 11 months. Side effects were more frequently regarded in the high dose group. Concerning remissionrate and recurrences high dose chemotherapy achieved better results. Survival and side effects did not show a significant difference between the two randomized groups.

727

VALUE OF SUPRARADICAL SURGERY IN ADVANCED OVARIAN CYSTADENOCARCINOMAS

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In advanced ovarian cystadenocarcinomas the main prognositc factor is the amount of residual disease after initial surgery. Since 1985, for resection to be as complete as possible, supraradical surgery was performed with more or less extended peritoneal and intestinal resections according to the extent of the disease.
Eighty-five patients with stage III or IV disease underwent surgery at the IGR from 1985 to 1991. The mean age was 52. Fifty-two recto-sigmoid colonectomies, 21 segmental and 11 total colonectomies have been performed.
The postoperative mortality and morbidity rates were 2.3 % and 34 % respectively. Surgery was followed by combination chemotherapies with cisplatin with a median number of 7 cycles.
Second look laparotomy was only performed in 25 patients (29 %), 14 of which were positive.
The 2-year overall survival rate is 65 %. A significant difference was found in survival at 2 years between patients (n=57) without residual tumor and patients (n=28) with residual tumor, after initial surgery : 87 % and 50 % respectively.
These results suggest that aggressive surgery seems to be efficient. However more patients and a longer follow up are required to confirm the value of this approach.

728

CATHEPSIN-D IN OVARIAN CANCER. CORRELATION WITH OESTROGEN RECEPTORS, PROGESTERON RECEPTORS AND EPIDERMAL GROWTH FACTOR RECEPTORS.

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In 88 primary ovarian tumours we mesaured cathepsin-D /CD/, using an immunoradiometric assay, epidermal growth factor receptors, first by using single point screen, then by full Scatchard analysis over a concentration range bettween 0.86-16.6 nM, and oestrogen receptors /ER/ and progesteron receptors /PR/ using EORTC method. Cut-off values for CD is taken as 20< pmol/mg.
The cathepsin-D /high or low is not correlated with ER and PR. Some correlation was found with EGFR /p 0.038/.
CD status not related to any patological parametar. Further studies are needed to evaluate whether CD could represent prognostic factor in ovarian cancer or not.

Keywords: ovarian cancer, cathepsin-D, EGFR.