20 AN UPDATE OF THE DUTCH MULTICENTER PVB-STUDY IN DISSEMINATED TESTICULAR NON-SEMINOMAS

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Since 1976, 71 patients with disseminated testicular non-seminomas have been treated with combination chemotherapy comprising Cis-platinum, Vinblastine and Bleomycin, according to Einhorn[1], usually comprising 4 cycles. This series includes 40 patients previously reported[2]. Forty-one of 71 patients (58%) achieved a complete remission.

Table 1
Results of the chemotherapy according to the histology

Histology+	patients	CR	PR	Toxic Death	Progres
TD	1	-	1	-	-
MTI	13	8	5	-	-
MTU	48	29	14	4	1
MTT	9	4	4	-	1
Total	71	41 (58%)	24 (34%)	4	2

+TD = Teratoma differentiated;
MTI = Malignant teratoma intermediate;
MTU = Malignant teratoma undifferentiated;
MTT = Malignant teratoma trophoblastic.

One patient achieved a complete remission during the year of maintenance chemotherapy. Four patients were rendered free of disease by surgery after the completion of the remission induction therapy. Thus, a total of 46 patients (65%) has become free of tumor. Of the 41 patients who achieved a complete remission by induction chemotherapy alone, 2 patients subsequently relapsed after a period of 7 and 13 months, respectively.

A.T. van Oosterom et al. (eds.), Therapeutic Progress in Ovarian Cancer, Testicular Cancer and the Sarcomas, pp. 247-252.

The latter patient developed brain metastases. A third patient died of a non-therapy related myocardial infarction after a complete remission duration of 6 months. Thus, 38 of 41 complete responders are still free of disease after a follow up period of 2-40 months (average 16 months, median 18 months).
Twenty-two complete responders are off therapy for a duration of 3-21 months, an average duration of 8 months and a median duration of 7 months. Twenty-four patients (34%) achieved a partial remission. Seventeen out of 24 had progression after 3-8 months while 7 are still in partial remission for $2\text{-}12^{+}$ months. Four of 71 patients (6%) died of toxicity; two of Bleomycin induced pneumonitis, one of agranulocytic sepsis and one of myocardial infarction during hemodialysis for renal failure due to Cis-platinum. Two of 71 patients showed progression of the disease after an initial response.
In 29 patients the response to treatment has been histologically verified. It was striking to find necrosis and fibrosis in 11 of these cases. More mature differentiation of the malignant tumor was found in eleven patients. The differentiation into teratoma differentiated did not lead to inclusion in the complete remission status.

Table 2
Histologically verified response to chemotherapy

Type of Surgery	Patients	Normal Architecture	Necrosis	Fibrosis	More mature hist.	progr.
Supraclav.	1	-	-	1	-	-
Thoracotomy	4	1	-	-	3	-
Laparotomy	24	4	4	6	8	2
Total	29	5	4	7	11	2

The side effects of the chemotherapy were markedly more severe in those patients who had previously been treated with radiotherapy (table 3).

Table 3
Side effects of the chemother. according to previous ther

	pretreatment		no pretreatment
	radio ± chemo	chemo	
side effects	18	11	42
Granulocytopenia 500/mm^3, 5 days	13 (72%)	4 (36%)	12 (30%)
Thrombocytopenia 50.000/mm^3, 5 days	10 (56%)	-	5 (12%)
Sepsis	8 (44%)	4 (36%)	2 (5%)
Renal failure	9 (50%)	4 (36%)	5 (12%)

In the non-pretreated patients the response to chemotherapy was better as compared to that in pretreated patients.

Table 4
Relationship between previous treatment and complete remission rate

	Patients	CR (%)
No pretreatment	42	26 (62%)
Chemotherapy	11	6 (55%)
Radiotherapy ± chemotherapy	18	9 (50%)

Patients with advanced abdominal disease- according to Samuels' criteria[3]- responded less well.
Advanced abdominal disease combined with pulmonary disease was even more resistant to PVB chemotherapy (table 5). This observation has also been reported by Peckham[4].

Table 5
Results of the chemotherapy according to the extent of the disease

	patients	CR (%)
Minimal pulmonary tumor	6	5 (83%)
Advanced pulmonary tumor	17	12 (70%)
Advanced abdominal tumor	21	13 (62%)
Minim. abd. + pulm. tumor	10	9 (90%)
Advanced abd. + pulm. tumor	16	1 (6%)
B-HCG as the sole parameter	1	1

It is of interest to note that two out of four patients who had previously been treated with Samuels' regimen[5] including Vinblastine and Bleomycin yet achieved a complete remission by PVB chemotherapy. They are both free of disease for a period of 22^{+} months and off maintenance therapy for a period of 13 months. The other two patients achieved a partial remission of 3 months duration.
In conclusion it appears that the described chemotherapeutic regimen is highly effective even though our patient population contains a high proportion of pretreated patients. Also in patients who have previously been treated with VB, the PVB combination may be curative.
We feel that most of the patients achieving a complete remission, verified by surgery after the chemotherapy, will actually be cured.

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