Table 1. Tumour types and responses to rIL-2/verapamil combination therapy

rIL-2 (IMU/m²/day)	Tumour type	Sites of disease	Clinical response
1.2	Renal cell carcinoma	Liver, nodes	PD
1.2	Melanoma	Liver, bone	NC
1.2	Melanoma	Skin, nodes	NC
2.4	Colon carcinoma	Liver, lung	NC
2.4	Melanoma	Liver, breast	NC
2.4	Melanoma	Liver, spleen, bone, lung	NC
4.8	Melanoma	Nodes	PD
4.8	Melanoma	Pleura, lung, liver, nodes Uterus	PD
4.8	Renal cell carcinoma	Mediastinal nodes	CR
9	Melanoma	Adrenal gland, nodes	MR
9	Renal cell carcinoma	Lung	MR
9	Melanoma	Liver	PR
9	Renal cell carcinoma	Lung	MR
9	Melanoma	Nodes	NC
9	Renal cell carcinoma	Lung, nodes	PD
18	Melanoma	Lung, skin, nodes	PD
18	Renal cell carcinoma	Lung, bone	MR
18	Renal cell carcinoma	Lung	PR

CR, complete remission; PR, partial remission; MR, minimal response; NC, no change; PD, progression of disease.

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Activity of Gemcitabine in Platinum-resistant Ovarian Germ Cell Cancer

K. Maas, T. Daikeler, L. Kanz and C. Bokemeyer

Eberhard Karls University, Department of Internal Medicine II, Otfried-Müller-Str. 10, 72076 Tübingen, Germany

OVARIAN GERM cell cancer (OGCT) is a rare disease accounting for less than 5% of all ovarian carcinomas. The importance of the disease is due to its relatively high incidence among children and young adults and the potential for cure by the use of platinum-containing chemotherapy [1]. The current recommendation of the Gynecologic Oncology Group (U.S.A.) for the treatment of advanced OGCT consists of cytoreductive surgery followed by three to six cycles of chemotherapy with bleomycin, etoposide and cisplatin (BEP) resulting in a 75% cure rate for advanced stage disease [1]. However, treatment of platinum-refractory OGCT remains difficult [2]. Paclitaxel is among the few drugs that have shown activity in platinum-resistant ovarian and testicular germ cell cancer [3, 4]. We report here the case of a patient with

Correspondence to K. Maas.
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an extensively pretreated platinum- and paclitaxel-refractory OGCT who achieved a partial response which has, thus far, lasted more than 5 months after treatment with the novel pyrimidine antimetabolite, 2′-2′-difluorodeoxycytidine (gemcitabine).

In June 1994, the previously healthy 37-year-old female was admitted to her local hospital with a rapidly growing abdominal mass. Laparotomy and histological work revealed a FIGO stage IIIc germ cell tumour of the right ovary consisting of choriocarcinoma, dysgerminoma, endodermal sinus tumour and embryonal carcinoma elements. Serum α-fetoprotein (AFP; 1850 kU/l), human chorionic gonadotrophin (hCG; 24 U/l) and CA 125 (183 U/ml) were markedly elevated.

The omentum, uterus and ovaries were surgically resected leaving minimal residual disease (tumour nodules of less than 5 mm in diameter). Postoperative chemotherapy with cisplatin and etoposide (PE) resulted in a peak of serum AFP at 10000 kU/l while both hCG and CA 125 levels returned to normal. After three cycles of PE, hepatic and retroperitoneal lymph node metastases were newly detected and chemotherapy was therefore changed to the PVB-regimen (cisplatin, vinblastine, bleomycin). Following an initial short-term response, progression occurred again after five cycles of PVB. Treatment was continued with one course of etoposide, cisplatin and ifosfamide (VIP) followed by a combination therapy of vinblastine, actinomycin D, cyclophosphamide, bleomycin and cisplatin (VAB-6). However, the disease progressed and salvage surgery revealed persistent germ cell cancer in the retroperitoneal lymph nodes. The following chemotherapy with paclitaxel (175 mg/m^2 d1) and ifosfamide (4000 mg/m^2 d1) (TI) resulted in a decrease of serum AFP, but levels remained elevated. Repeated surgery, after a single course of high-dose salvage chemotherapy with the VIC-regimen (etoposide 1000 mg/m^2, ifosfamide 2000/m^2, carboplatin 1000 mg/m^2 d1–3) followed by re-infusion of previously harvested haematopoietic progenitor cells, still showed vital malignant cells concordant with dysgerminoma and embryonal carcinoma. A second course of high-dose chemotherapy with paclitaxel (250 mg/m^2 d1), ifosfamide (2000 mg/m^2) and carboplatin (1000 mg/m^2 d2–4) supported by haematopoietic progenitor cell retransfusion again did not achieve a consistent response. The patient was therefore started on a palliative daily oral regimen with etoposide. However, rapid disease progression occurred following one month of oral therapy.

In a final attempt to slow disease progression in the relatively young patient i.v. bolus therapy with the novel pyrimidine antimetabolite gemcitabine was started. Pretherapeutic staging showed two hepatic metastases approximately 5 × 5 × 3 cm^3 in size as well as enlarged abdominal and retroperitoneal lymph nodes.

Between October 1995 and March 1996, the patient received five courses of gemcitabine (1000 mg/m^2 d1, 8, 15 every 28 d). Treatment had to be delayed several times because of neutropenia and prolonged thrombocytopenia (nadir values of 19.000/μl) in the heavily pretreated patient, but serious side-effects of gemcitabine therapy were not observed. After three courses, the size of the hepatic lesions had decreased more than 50% (residual size 1.1 and 2.0 cm in diameter) while the abdominal and retroperitoneal lymph nodes remained unchanged. Serum AFP values were subsequently reduced from 1780 kU/l (pretherapeutic level) to 460 kU/l. Gemcitabine therapy is currently continued and the patient has remained in stable partial response for over 5 months.

The novel pyrimidine antimetabolite gemcitabine has been shown to be active in a variety of malignant tumours including ovarian and non-small cell lung cancer [5, 6]. So far no activity in germ cell tumours has been reported and, to our knowledge, the effect of antimetabolites on germ cell cancer has not been investigated. Considering that our patient failed to achieve even short-term remissions following several aggressive chemotherapeutic regimens including high-dose salvage therapy with paclitaxel, ifosfamide and carboplatin, the observed response to gemcitabine appears impressive. Our observation indicates at least some activity of gemcitabine in platinum-resistant germ cell cancer warranting further studies to explore the role of antimetabolites in the treatment of germ cell tumours.

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