

Answer 1:

Bibliographic Information

Progress of gene therapy for esophageal cancer in Japan. Matsubara, Hisahiro; Ochiai, Takenori. Dept. of Academic Surgery, Graduate School of Medicine, Chiba University, Japan. Gan to Kagaku Ryoho (2003), 30(7), 944-949. Publisher: Gan to Kagaku Ryohosha, CODEN: GTKRDX ISSN: 0385-0684. Journal; General Review written in Japanese. CAN 140:70020 AN 2003:643825 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A review. Retrovirally expressed interleukin-2 gene, granulocyte macrophage-colony stimulating factor gene, herpes simplex virus-thymidine kinase gene and p53 gene in human esophageal cancer cells showed antitumor effects in a nude mice xenotransplant model. We established a clin. protocol of gene therapy for advanced esophageal cancer using the wild type p53 gene with an adenovirus vector. In Dec. of 2000, we began the first tumor suppressor gene therapy trial. Now, this trial, which has 9 patients. There have been no serious adverse event excluding fever and local pain. The feasibility of this treatment appears fairly good in these 9 cases. Furthermore, we developed a new method for transducing genes without a virus vector since a virus vector has several potentially unwanted properties. In vivo electroporation is a useful strategy for cancer gene therapy. Moreover, elec. pulse to established solid tumors increases intracellular concns. of chemotherapeutic agents. Transduction of the wild-type p53 gene by electroporation decreased the amt. of nedaplatin required for tumor suppression. Electrochemo-gene therapy is a relatively simple method and can produce a better therapeutic effect.

Answer 2:

Bibliographic Information

Antitumor activity of new combination chemotherapy with irinotecan hydrochloride and nedaplatin against human cervical cancer cell lines. Yamamoto, Kaichiro; Iwahana, Michio; Kumazawa, Eiji; Kakihata, Koji; Abe, Kunio; Hirano, Fuyumi; Tohgo, Akiko; Hoshiai, Hiroshi; Noda, Kiichiro. Department of Obstetrics and Gynecology, Sakai Hospital, Kinki University School of Medicine, Sakai, Osaka, Japan. Oncology Reports (2003), 10(3), 593-598. Publisher: Oncology Reports, CODEN: OCRPEW ISSN: 1021-335X. Journal written in English. CAN 139:316809 AN 2003:347654 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Antitumor activity of combination chemotherapy with irinotecan hydrochloride (CPT-11) and nedaplatin was compared to that with CPT-11 and cisplatin. In vitro cytotoxicity of SN-38 (an active metabolite of CPT-11) in combination with nedaplatin or cisplatin was evaluated using three human cervical cancer cell lines (ME-180, CaSki and SiHa). IC50 values of nedaplatin against these three human cervical cancer cell lines were about 2-fold as high as those of cisplatin, indicating somewhat weak cytotoxic effects of nedaplatin. Interactions between two drugs in combination were investigated using a simultaneous-exposure schedule and analyzed by the IC50-based isobologram method. Simultaneous exposure to SN-38 with each platinum prepn. showed synergistic and additive effects against ME-180 and SiHa. In vivo antitumor effects of CPT-11 in the combination with each platinum were studied using SiHa xenografts. While CPT-11, nedaplatin and cisplatin alone hardly showed any antitumor effects even at the max. tolerated dose (MTD) levels, the combination chemotherapy with CPT-11 and nedaplatin or cisplatin resulted in significant antitumor effects even at three-quarter MTD of CPT-11 combined with two-third MTD of platinum. All treatments were tolerable for mice, indicating that the combinations did not cause significant enhancement in toxicity. In clin. application, nedaplatin causes a lower incidence of nephropathy and does not require the replacement of a large vol. of fluid, which is needed for cisplatin administration, facilitating treatment at the outpatient clinic. In addn., the incidences of digestive disorder, peripheral neuropathy and auditory disorder are lower. These findings suggest that the combination chemotherapy with CPT-11 and nedaplatin for squamous cell cancer of uterine cervix is very useful in clin. practice. A dose-finding study should be conducted.

Answer 3:

Bibliographic Information

Enhanced antitumor efficacy of nedaplatin with 5-fluorouracil against human squamous carcinoma xenografts. Takeda, Yukihiko; Kasai, Hisanori; Uchida, Naomi; Yoshida, Hiroshi; Maekawa, Ryuji; Sugita, Kenji; Yoshioka, Takayuki. Shionogi Research Laboratory, Shionogi and Co., Ltd., Osaka, Japan. *Anticancer Research* (1999), 19(5B), 4059-4064. Publisher: International Institute of Anticancer Research, CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 132:273853 AN 2000:4290 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor efficacy of a combination of nedaplatin (NDP) with 5-fluorouracil (5-FU) was evaluated in human squamous carcinomas *in vivo*. Because NDP was developed as a 2nd-generation platinum complex, the antitumor activity of NDP plus 5-FU was also compared with that of cisplatin (CDDP) plus 5-FU. 5-FU was injected daily for 5 days and either NDP or CDDP was injected once via the tail vein into mice implanted with KB3-1, OCC-1-JCK, LJC-1-JCK or Ma44 human squamous carcinomas. In some expts., continuous administration of 5-FU by an osmotic pump was utilized. The sequential administration of 5-FU prior to NDP or CDDP (FN or FC therapy, resp.) enhanced the inhibition of tumor growth in comparison with NDP, CDDP or 5-FU monotherapy against KB3-1, OCC-1-JCK and LJC-1-JCK squamous carcinomas. The FN combination treatment was synergistic and as effective as FC treatment. FN treatment involving continuous infusion of 5-FU with an osmotic pump also led to enhanced tumor growth inhibition and prolonged survival in mice bearing Ma44 squamous carcinoma. The results demonstrated the antitumor efficacy of NDP plus 5-FU against 4 human squamous carcinoma xenografts and suggested the clin. effectiveness of the combination FN treatment.

Answer 4:

Bibliographic Information

Alteration of sensitivity to cis-diamine(glycolate)-platinum(II) (254-S) in oral tumor xenografts following multiple applications. Sai, Shin-Ichi; Kumazawa, Hirobumi; Tachikawa, Takuya; Yamashita, Toshio; Kawamoto, Keiji. Department Otolaryngology, Kansai Medical University, Moriguchi, Japan. *International Journal of Oncology* (1996), 8(1), 57-63. Publisher: National Hellenic Research Foundation, CODEN: IJONES ISSN: 1019-6439. Journal written in English. CAN 124:193602 AN 1996:93024 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The emergence of resistance to platinum analogs is considered to be a major problem in the treatment of head and neck cancer. Therefore, it is important to clarify the mechanisms of resistance to these analogs and the mechanisms of the processes related to this resistance. The study of emergence of resistance in the solid tumors is particularly relevant. In the present study, the effect of a platinum analog (254-S), on the response of an oral carcinoma cell line grown as a xenograft in nude mice, was studied. The effect of a full dose administered as a single *i.p.* injection of 254-S (15 mg/kg \times 1) on tumor growth was not significantly different from the effect of repeated *i.p.* injections of 254-S, administered 3 times at 1/3 of this dose (5 mg/kg \times 3), or 5 times at 1/5 of this dose (3 mg/kg \times 5). However, when a single full-dose *i.p.* injection of 254-S (15 mg/kg \times 1) was administered to each group of mice again at the 9th and 12th weeks after the initial treatment, different effects on tumor growth were obsd. among each group. The groups which received repeated treatment with 254-S (5 mg/kg \times 3, or 3 mg/kg \times 5) showed a decrease in the inhibition of tumor growth, suggesting the emergence of resistance to 254-S. The study of platinum accumulation in the tumor tissues and a flow cytometric anal. of proliferating cell nuclear antigen (PCNA) supported the possibility that resistance to 254-S increases in tumor tissues treated repeatedly. These observations suggest that the potential use of this exptl. assay as a model, may provide further insights into the therapeutic mechanisms of resistance to antineoplastic agents in the treatment of solid cancerous head and neck tumors.

Answer 5:

Bibliographic Information

Pharmacokinetic correlation between experimental and clinical effects on human non-small-cell lung cancers of

cis-diammineglycolatoplatinum (254-S) and cis-diamminedichloroplatinum. Koenuma, Mitsuo; Kasai, Hisanori; Uchida, Naomi; Wada, Tooru; Hattori, Maki; Oguma, Takayoshi; Totani, Tetsushi; Inaba, Makoto. Shionogi Research Laboratories, Shionogi and Co., Ltd., Osaka, Japan. *Anticancer Research* (1995), 15(2), 417-21. Publisher: Anticancer Research, CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 123:74379 AN 1995:671092 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The in vitro and in vivo antitumor activities of 254-S, a novel Ptm complex, and cis-diamminedichloroplatinum (CDDP) against established cultured cell lines and xenografts of human non-small-cell lung cancer (NSCLC) were correlated with their clin. effects, based on the previous finding that the cytotoxicity of CDDP depends on the area under the plasma concn.-vs.-time curve (AUC). The IC50 of 254-S and CDDP for inhibiting the in vitro growth of 4 cultured NSCLC lines was 0.82-7.8 and 0.53-4.2 $\mu\text{g/mL}$, resp.. Of the 4 cell lines, only the most sensitive line, RERF-LC-AI, had an IC50 close to the specific concns. (0.50 for 254-S and 0.32 $\mu\text{g/mL}$ for CDDP) that reproduce in vitro the clin. AUCfree (24.8 and 5.34 $\mu\text{h/mL}$) of the resp. drugs. Six lines of human NSCLC xenografts implanted in nude mice were treated with 254-S and CDDP at a dose (13.2 and 3.7 mg/kg, resp.) equiv. to the clin. doses with respect to the plasma AUCfree. 254-S and CDDP exhibited significant antitumor effects on two and one, resp., of the 6 lines. These in vitro and in vivo findings were relatively well correlated with the reported clin. response rates of 15-19% for 254-S and 14-15% for CDDP.

Answer 6:

Bibliographic Information

In vivo screening models of cisplatin-resistant human lung cancer cell lines using SCID mice. Heike, Yuji; Takahashi, Minako; Ohira, Tatsuo; Arioka, Hitoshi; Funayama, Yasunori; Nishio, Kazuto; Ogasawara, Hayato; Saijo, Nagahiro. Pharmacology Division, National Cancer Center Research Institute, Tokyo, Japan. *Cancer Chemotherapy and Pharmacology* (1995), 35(3), 200-4. CODEN: CCPHDZ ISSN: 0344-5704. Journal written in English. CAN 122:305721 AN 1995:535837 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

In vivo screening models of a cisplatin (CDDP)-resistant human small-cell lung cancer cell (SCLC) line, H69/CDDP, and a non-small-cell lung cancer cell (NSCLC) line, PC-14/CDDP, were evaluated. The transplantability of the tumor xenografts to SCID mice was more than 90%. Tumor xenografts of H69/CDDP and PC-14/CDDP showed CDDP resistance during in vivo treatment. The novel anticancer agent 254-S showed only a partial effect on the growth of H69/CDDP and PC-14/CDDP while ormaplatin showed no cross resistance to CDDP. The in vivo results correlated well with the results of the in vitro MTT assay. In this in vivo sensitivity test, H69/CDDP and PC-14/CDDP were more sensitive to ormaplatin than its parental cell lines. In vivo sensitivity testing using SCID mice bearing transplanted CDDP-resistant tumors was shown to be useful for evaluating the effects of new anti-cancer drugs, esp. those that might overcome CDDP resistance.

Answer 7:

Bibliographic Information

Predictability of preclinical evaluation of anticancer drugs by human gastrointestinal cancer-nude mouse panel. Fujita, Masahide; Fujita, Fumiko; Sakamoto, Yasuo; Sugimoto, Takuji; Shimozuma, Kojiro; Taguchi, Tetsuo. Res. Inst. Microb. Dis., Osaka Univ., Suita, Japan. *Gan to Kagaku Ryoho* (1991), 18(9), 1429-37. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 115:269825 AN 1991:669825 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The predictability of clin. responses to anticancer agents was studied using a human cancer-nude mouse panel. The human cancer lines used were 12 gastric, 4 colorectal, 3 breast, 2 pancreatic cancers and 1 melanoma xenografted into BALB/c athymic nude mice.

Treatment was conducted daily 25 times for antimetabolites, and intermittently 5 times once or twice a week for other drugs. The dosage of each drug was the maximal tolerated dose predetd. for the treatment and schedule. Four weeks after the initiation of treatment, the therapeutic effect was evaluated by the tumor growth inhibition rate (IR) based on the mean tumor wt. When the IR was >58%, the drug was evaluated as effective. The clin. response rate of each drug was referred from the result of a phase II study. Direct comparison of antitumor effects on 16 tumor xenografts with responses to the corresponding clin. therapy of each donor patient revealed a fairly high accordance rate (94%). To elucidate the value of human cancer-nude mouse panel as a preclin. secondary screening, the response rates to 8 anticancer drugs used in 15 cancer xenografts were compared with the cumulative clin. data available for each drug. Generally, the response rates of the human cancer xenografts to the drugs showed fairly good correlations with the cumulative clin. response rates to the corresponding drugs in the same organs. Using this panel, preclin. examns. of 6 new agents under development, including 254-S and 2 cisplatin derivs., were performed in order to collect clin. data.

Answer 8:

Bibliographic Information

Studies on chemotherapy for adenocarcinoma of the uterine cervix using xenografts transplanted in nude mice.

Yamagishi, Masaji. Fac. Med., Toyama Med. Pharm. Univ., Toyama, Japan. Nippon Sanka Fujinka Gakkai Zasshi (1991), 43(2), 165-72. CODEN: NISFAY ISSN: 0300-9165. Journal written in Japanese. CAN 115:341 AN 1991:400341 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Adenocarcinoma of the human uterine cervix was successively transplanted into nude mice and the effects of chemotherapy on adenocarcinoma of uterine cervix were investigated in this transplanted tumor. First, it was confirmed that both the original tumor and the transplanted tumor were apparently histol. the same as adenocarcinoma of the uterine cervix (endocervical type). And the transplanted tumor was shown to have the features of adenocarcinoma by an electron microscope. The doubling time of the transplanted tumor was 9.2 days. For the chemotherapy study, first the therapeutic effects of 11 kinds of agents were screened by single-agent chemotherapy applied to the transplanted tumor. From the results of this series, 6 regimens for multi-agent chemotherapy were tried on the transplanted tumor. The effects of the chemotherapy were evaluated following Battelle Columbus Labs. Protocol and histopathol. The relative regression rates for the tumors treated with mitomycin C (MMC) + cyclophosphamide (CPM) and MMC + CPM + methotrexate (MTX) were 72.99 and 80.9% ($T_n/T_o = 0.84$), resp. The results suggest that the combinations of MMC + CPM or MMC + CPM + MTX are regimens that are possibly effective on the adenocarcinoma of human uterine cervix and are worth be trying clin.

Answer 9:

Bibliographic Information

Advantages in combination chemotherapy using cisplatin and its analogs for human testicular tumor xenografts. Hida, Shuichi; Okada, Kenichiro; Yoshida, Osamu. Fac. Med., Kyoto Univ., Kyoto, Japan. Japanese Journal of Cancer Research (1990), 81(4), 425-30. CODEN: JJCREP ISSN: 0910-5050. Journal written in English. CAN 113:70834 AN 1990:470834 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor effects and toxicities of combination chemotherapies using cisplatin (CDDPO) and its analogs were compared with those of single drug therapies. Congenitally athymic nude BALB/c (nu/nu) mice were used to est. antitumor activities of these compds. against human testicular tumor (Ht-14) xenografts and hetero-BALB/c (nu/+) mice were used to evaluate the toxic effects of the drugs. Combination therapy with half dosages of CDDP and carboplatin (JM8) (CDDP: 2, JM8: 20 mg/kg/day for 5 days), or of CDDP and (glycolato-O,O')-diammineplatinum (II) (254S) (CDDP: 2, 254S: 4 mg/kg/day for 5 days), resulted in significant tumor regression. The combination of CDDP and JM8 had the highest therapeutic efficacy, while the CDDP and 254S combination had a lower antitumor potency. In addn., the toxicities of the combination therapies were lower than what was produced by the highest dosage of CDDP (4

mg/kg/day for 4 days). These results demonstrated that the antitumor activities of these combination chemotherapies were equal or superior to the activity of CDDP or an analog alone, and that the toxicities produced by these combinations were more manageable than those produced by single drug therapies.

Answer 10:

Bibliographic Information

Preclinical evaluation of several cisplatin (CDDP) analogs against human esophageal carcinoma by subrenal capsule assay.

Terashima, Masanori; Ikeda, Kenichiroh; Kawamura, Shuji; Takagane, Akinori; Maesawa, Chihaya; Sudoh, Takayuki; Okamoto, Kazumi; Ishida, Kaoru; Satoh, Masao; Saito, Kazuyoshi. 1st. Dep. Surg., Iwate Med. Univ., Japan. Gan to Kagaku Ryoho (1990), 17(2), 269-73. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 113:168 AN 1990:400168 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor activities of CDDP analogs (CBDCA, NK-121, 254-S) were evaluated preclinically by subrenal capsule assay (SRCA) with cyclophosphamide pretreatment. The antitumor activities against serially transplanted human esophageal cancer xenograft (IMEs-1) were compared with s.c. transplantation assay in nude mice and SRCA. The antitumor activities in SRCA were similar to those of in nude mice assay system (CBDCA > CDDP > 254-S > NK-121). Thus SRCA was considered to be useful for the evaluation of the activities of these agents. The activities were also tested against 10 human esophageal tumors obtained clin. The sensitivity rate of these agents were 50% for CDDP, 30% for CBDCA, 30% for NK-121, and 30% for 254-S, resp. These analogs seemed to be less effective than CDDP. However, in two cases analogs were active though CDDP was inactive. The results suggest that these analogs are useful for the cases in which CDDP can not be given due to the toxicities and also for outpatient use.

Answer 11:

Bibliographic Information

Antitumor activity of cisplatin analogs against malignant ovarian tumor xenografts into nude mice. Hamaguchi, Kinya; Miyahara, Kenichi; Nishimura, Haruo; Tashiro, Masamichi; Kishi, Nobuhiro; Matsumura, Takashi; Yakushiji, Michiaki; Kato, Toshi. Sch. Med., Kurume Univ., Kurume, Japan. Nippon Sanka Fujinka Gakkai Zasshi (1988), 40(11), 1755-9. CODEN: NISFAY ISSN: 0300-9165. Journal written in English. CAN 110:128176 AN 1989:128176 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

When tested against the ovary tumor cell line OH-1 (serous cystadenocarcinoma) transplanted into nude mice, the platinum compds. 254-S and JM-8 were more potent than DWA2114R and the comparison compd. cisplatin, whereas when they were tested against the MP-1 (mucinous cysadenoma) cell line, JM-8 and cisplatin were the most potent agents. The platinum compds. temporarily decreased the body wt., but did not induce any death during treatment. The histol. effects of the platinum compds. on the tumor cell lines varied greatly.

Answer 12:

Bibliographic Information

Evaluation of combined nedaplatin and docetaxel therapy for human head and neck cancer in vivo. Erratum in: Anticancer Res. 2006 May-Jun;26(3a):2187 Yamada Hajime; Maki Hideo; Takeda Yukihiro; Orita Satoshi Shionogi Research Laboratories, Shionogi & Co. Ltd., Fukusima-Ku, Osaka, Japan Anticancer research (2006), 26(2A), 989-94. Journal code: 8102988. ISSN:0250-7005. Journal; Article; (JOURNAL ARTICLE) written in English. PubMed

ID 16619497 AN 2006213914 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

BACKGROUND: Nedaplatin (NDP) was developed as a second-generation platinum complex. The antitumor efficacy of the combination of NDP with docetaxel (TXT) was evaluated against human head and neck carcinoma. The antitumor activity of NDP plus TXT was compared with that of some other platinum compounds, cisplatin (CDDP) and carboplatin (CBDCA) plus TXT. **MATERIALS AND METHODS:** Mice implanted with HNC-3 or KB3-1, human head and neck carcinoma were administered i.v. NDP, CDDP or CBDCA plus TXT. **RESULTS:** The antitumor efficacy was enhanced significantly by the combination of NDP with TXT. Combined NDP plus TXT treatment exerted antitumor efficacy comparable to that of combined CDDP plus TXT treatment. Thrombocytopenia induced by NDP was not enhanced by the combination of NDP and TXT. **CONCLUSION:** The results suggest that combined NDP and TXT can alleviate thrombocytopenia caused by NDP and that this combination may have significant potential in clinical use.

Answer 13:

Bibliographic Information

Preclinical combination chemotherapy of nedaplatin with gemcitabine against gemcitabine-refractory human lung cancer. Takeda Yukihiko; Wada Tohru; Nishitani Yoshinori; Matsumoto Mitsunobu; Hojo Kanji; Maekawa Ryuji; Yoshioka Takayuki Shionogi Research Laboratories, Shionogi & Co., Ltd, 12-4 Sagisu, 5-Chome, Fukushima-ku, Osaka 553-0002, Japan Cancer letters (2002), 182(1), 61-8. Journal code: 7600053. ISSN:0304-3835. Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 12175524 AN 2002421493 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

The antitumor efficacy of the combination of nedaplatin (NDP) with gemcitabine (GEM) was evaluated against Ma44/GEM, a GEM-refractory subline of Ma44 human lung cancer, which was established by serial in vitro passage of Ma44 cells in the presence of GEM. Ma44/GEM showed less sensitivity to GEM and cytosine arabinoside with resistance factors of 7.7 and 8.3, respectively, but not to Taxol, Irinotecan, Mitomycin C and NDP. Flow cytometry analysis demonstrated that membrane transporter molecules such as multidrug-resistant, multidrug-resistant related protein or lung resistant protein were not induced in Ma44/GEM cells. In vivo experiments confirmed the less sensitivity of Ma44/GEM to GEM. The resistant factor of Ma44/GEM to GEM in vivo was estimated to be 6.7 in terms of ED(50). MA44/GEM-implanted athymic mice were treated with GEM i.v. once followed by i.v. injection of NDP at an interval of approximately 30 min. The mice were treated again with GEM after 3 or 4 days. The combined dosing of NDP with GEM resulted in synergistically enhanced inhibition of tumor growth against Ma44/GEM. The antitumor efficacy of the combination of NDP and GEM was superior to the best effect of either monotherapy. These results demonstrate the effectiveness of the combination of NDP with GEM against the GEM-refractory human lung cancer model.

Answer 14:

Bibliographic Information

Induction of p53-dependent apoptosis in vivo by nedaplatin and ionizing radiation. Nakamura Y; Hasegawa M; Hayakawa K; Matsuura M; Suzuki Y; Nasu S; Yamakawa M; Mitsunashi N; Niibe H Department of Radiology and Radiation Oncology, Gunma University School of Medicine, Maebashi, Gunma 371-8511, Japan Oncology reports (2000), 7(2), 261-5. Journal code: 9422756. ISSN:1021-335X. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 10671668 AN 2000138547 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

p53 protein expression, apoptosis and growth delay induced by nedaplatin, a novel platinum compound, were investigated in vivo, and compared with those induced by ionizing radiation. A human ependyoblastoma with wild-type p53 was transplanted subcutaneously to the thighs of nude mice. The incidences of p53 protein-positive cells and apoptosis in tumors increased following exposure to ionizing radiation. In tumors treated with nedaplatin, they also increased, but the incidences of p53 protein-positive cells and apoptosis induced by 32 mg/kg nedaplatin, 1/2 LD50, were lower than those induced by 1 Gy irradiation. However, growth-delay assay showed no significant difference between the efficacy of 32 mg/kg nedaplatin and that of 1 Gy irradiation. These results suggest that the main antineoplastic activity caused by nedaplatin may be mediated through different mechanisms than those of the p53-dependent early apoptosis.

Answer 15:

Bibliographic Information

Antitumor effect of CPT-11, a camptothecin derivative, on human testicular tumor xenografts in nude mice.

Miki T; Sawada M; Nonomura N; Kojima Y; Okuyama A; Maeda O; Saiki S; Kotake T Department of Urology, Osaka University Medical School, Japan European urology (1997), 31(1), 92-6. Journal code: 7512719. ISSN:0302-2838. Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 9032542 AN 97184772 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

OBJECTIVE: The antitumor effect of CPT-11, a camptothecin derivative, on two human testicular embryonal carcinomas (TTSC-2 and TTSC-3) heterotransplanted into-nude mice was studied. **MATERIALS AND METHODS:** Tumor-bearing nude mice were given daily intraperitoneal injections of the anticancer drugs in 0.1 ml saline 3 times at 3-day intervals. At the end of the experiments tumors were resected and subjected to light-microscopic observation. **RESULTS:** When 10, 30 and 50 mg/kg of CPT-11 was administered to tumor-bearing mice intraperitoneally, the antitumor effect of CPT-11 was observed dose-dependently in both TTSC-2 and TTSC-3. When 30 mg/kg of CPT-11 was administered in combination with CDDP, complete tumor regression was observed in both TTSC-2 and TTSC-3 tumors. Histological findings correlated well with the decrease in tumor volume of treated tumors. No mice died after treatment with CPT-11 in a single-agent and combination chemotherapy. **CONCLUSION:** Chemotherapy with CPT-11 was an effective and safe method against human testicular tumors heterotransplanted in nude mice.

Answer 16:

Bibliographic Information

Advantages in combination chemotherapy using the camptothecin analogue CPT-11 and cisplatin analogues for human testicular cancer xenografts.

Miki T; Kotake T Department of Urology, Osaka University Medical School Hinyokika kyo. Acta urologica Japonica (1993), 39(12), 1221-5. Journal code: 0421145. ISSN:0018-1994. (ENGLISH ABSTRACT); Journal; Article; (JOURNAL ARTICLE) written in Japanese. PubMed ID 8285173 AN 94113132 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

The antitumor effects of combination chemotherapies using CDDP and the camptothecin analogue CPT-11 were compared with those of vinca alkaloids or podophyllotoxins, and those of CPT-11 and cisplatin analogues were also estimated. Two human testicular cancer xenografts (TTSC -2 and TTSC-3) heterotransplanted in nude mice were used. Combination therapy with CPT-11 and CDDP resulted in significant tumor regression and was much more effective than that of CDDP and vinca alkaloids or podophyllotoxin. The combination of CPT-11 and either CDDP or 254-S was significantly more effective than that of CPT-11 and either carboplatin or DWA2114R. Four evaluable refractory testicular cancers were treated with combination chemotherapy with CPT-11 and CDDP or 254-S as third line chemotherapy. Two patients remain alive and disease free and two patients died of disease. We concluded that the

present combination is active in refractory testicular cancer.

Answer 17:

Bibliographic Information

Comparative studies of the antitumor activities of CDDP and the analogs--using gynecological carcinomas transplanted into nude mice. Suzumori K; Yasui Y; Suzumori K; Yagami Y Dept. of Obstetrics and Gynecology, Nagoya City University Gan to kagaku ryoho. Cancer & chemotherapy (1989), 16(3 Pt 1), 387-91. Journal code: 7810034. ISSN:0385-0684. (COMPARATIVE STUDY); (ENGLISH ABSTRACT); Journal; Article; (JOURNAL ARTICLE) written in Japanese. PubMed ID 2649007 AN 89192418 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

In the present study, comparison of the therapeutic effects of CDDP and the analogues (CBDCA, 254S, DWA2114R and NK121) on human gynecological carcinomas transplanted into nude mice (uterine cervical cancer; UZ-1-N, endometrial cancer; UE-1-N, ovarian cancer; OCI-1-N, OS-4-N and OS-8-N) was made. CDDP (5 mg/kg), CBDCA (50 mg/kg), 254S (25 mg/kg), DWA (50 mg/kg) and NK121 (18 mg/kg) were administered intraperitoneally every four days at three doses. Simultaneously the tumor size and the body weight were measured and the peripheral WBC and BUN were examined. The results were as follows: 1) The administration of 254S caused a marked inhibition of the tumor growth against all xenografts into nude mice. 2) CDDP and CDDP analogues except 254S were not effective against UE-1-N, but in this xenograft antitumor activity of 254S was remarkable. 3) With 254S, there were a decrease in body weight and the peripheral leukopenia and the elevation of BUN level were more severe. Although 254S has severe side effects, 254S is seemed to be recommendable for the treatment of gynecological malignancies.