

Answer 1:

Bibliographic Information

Development of a panel of 15 human ovarian cancer xenografts for drug screening and determination of the role of the glutathione detoxification system. Kolschoten, Geertruida M.; Pinedo, Herbert M.; Scheffer, Peter G.; Schluper, Hennie M. M.; Erkelens, Caroline A. M.; Boven, Epie. Department of Medical Oncology, University Hospital Vrije Universiteit, Amsterdam, Neth. *Gynecologic Oncology* (2000), 76(3), 362-368. Publisher: Academic Press, CODEN: GYNOA3 ISSN: 0090-8258. Journal written in English. CAN 133:83805 AN 2000:126284 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The authors have established a panel of 15 human ovarian cancer xenografts grown s.c. in the flank of the nude mouse. Similar to the clinic, the xenografts show differences in histol. subtype and vol. doubling time. The authors detd. whether the panel is useful for drug screening by testing the sensitivity to 6 conventional anticancer agents. In addn., the authors investigated whether the glutathione detoxification system affects sensitivity to cisplatin and cyclophosphamide, major drugs in the treatment of ovarian cancer. Mice bearing well-established tumors were treated at max. tolerated doses as defined by a reversible wt. loss $\leq 15\%$ of their initial wt.: cisplatin 5 mg/kg i.v. weekly $\times 2$, cyclophosphamide 150 mg/kg i.p. 2-weekly $\times 2$, doxorubicin 8 mg/kg i.v. weekly $\times 2$, hexamethylmelamine i.p. 150 mg/kg every other day $\times 4$, methotrexate i.p. 150 mg/kg weekly $\times 2$, and 5-fluorouracil 60 mg/kg i.p. weekly $\times 4$. Glutathione levels and the activities of 3 different glutathione-dependent enzymes were measured in untreated xenograft tissues. Growth inhibition $>75\%$ was reached for cisplatin in 40%, for cyclophosphamide in 27%, and for doxorubicin in 20% of the xenografts. Methotrexate and 5-fluorouracil did not induce growth inhibition of importance. Hexamethylmelamine showed $>75\%$ growth inhibition in 53% of the xenografts, which may be caused by the favorable metab. of the drug in mice when compared with that in patients. Glutathione levels varied 3.6-fold in the xenografts and did not show a relation with sensitivity to cisplatin, cyclophosphamide, or doxorubicin. No relation was found between the activities of glutathione S-transferase and glutathione peroxidase and the sensitivities to the 3 anticancer agents. Glutathione reductase activity, however, showed a weak, inverse relation with the efficacy of cisplatin and cyclophosphamide (r values of -0.55 and -0.58, resp.).

The sensitivity to the 6 anticancer agents of the authors panel of 15 human ovarian cancer xenografts reflects the response rates known for similar drugs in ovarian cancer patients. In that respect, the panel may be useful for drug screening as well as studies on the relevance of drug resistance features in vivo. The various components of the glutathione detoxification system did not predict for primary drug resistance which confirms clin. data in ovarian cancer. (c) 2000 Academic Press.

Answer 2:

Bibliographic Information

Antitumor effect of trimelamol against human breast carcinoma xenografts in nude mice. Koh, Jun-Ichi; Kubota, Tetsuro; Hoshiya, Yasunori; Asanuma, Fumiki; Yamada, Yoshinori; Kitajima, Masaki; Coley, Helen M.; Judson, Jan R. Department Surgery, Social Insurance Saitama Chuo Hospital, Urawa, Japan. *Oncology Reports* (1996), 3(4), 613-617. Publisher: Oncology Reports, CODEN: OCRPEW ISSN: 1021-335X. Journal written in English. CAN 125:104547 AN 1996:438416 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor effect of trimelamol, a synthetic analog of hexamethylmelamine, was investigated in human breast carcinoma xenografts in nude mice. Four tumor lines studied, T-61, Br-10, R-27 and MCF-7, were estrogen receptor (ER)-pos. and their growth was estradiol-dependent. The MX-1 line was ER-neg. and grew estradiol-independently. Trimelamol (60 mg/kg) was administered i.p., 5 days a wk, for 3 wk. Trimelamol had potent, dose-dependent antitumor activity on T-61 and MX-1, with a marginal effect on Br-10, while R-27 and MCF-7 were insensitive to this agent. This antitumor spectrum on human breast carcinoma xenografts is similar to that previously reported for hexamethylmelamine on the same xenograft models. Trimelamol is water-sol. and does not require the metabolic activation needed for hexamethylmelamine. These advantages allow the parenteral administration of trimelamol and warrant the further investigation of this drug for breast carcinomas.

Answer 3:

Bibliographic Information

In vivo antitumor activity of hexamethylmelamine against human breast, stomach and colon carcinoma xenografts. Tanino, Hirokazu; Kubota, Tetsuro; Yamada, Yoshinori; Koh, Jun-ichi; Kase, Suguru; Furukawa, Toshiharu; Kuo, Tsong-Hong; Saikawa, Yoshiro; Kitajima, Masaki; Naito, Yasuaki. Dep. Thoracic Cardiovascular Surgery, Wakayama Medical College, Wakayama, Japan. Japanese Journal of Cancer Research (1995), 86(8), 770-5. Publisher: Japanese Cancer Association, CODEN: JJCREP ISSN: 0910-5050. Journal written in English. CAN 123:275342 AN 1995:820122 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

We have evaluated the antitumor activity of Altretamine (hexamethylmelamine, HMM) on human carcinoma xenografts serially transplanted in nude mice. Five human breast carcinoma xenografts, MX-1, T-61, MCF-7, R-27 and Br-10, were inoculated s.c. into female nude mice. Two human stomach carcinoma xenografts, SC-1-NU and St-4, and three human colon carcinoma xenografts, Co-3, Co-4 and Co-6, were inoculated s.c. into male nude mice. One pellet of 17 β -estradiol (0.1 mg/mouse) was inoculated s.c. in the mice transplanted with MCF-7 when the tumors were inoculated. HMM was administered per os daily for 4 wk. MX-1 and T-61 tumors regressed completely after treatment with HMM at a dose of 75 mg/kg (the max. tolerated dose: MTD) for MX-1 and 25 mg/kg for T-61. Br-10 was sensitive, whereas MCF-7 and R-27 were resistant to HMM at its MTD. HMM exerted the most potent antitumor effect against T-61. Against MX-1, it exerted an antitumor effect equiv. to that of cisplatin or cyclophosphamide. In addn., this agent was effective against all stomach and colon carcinoma xenografts, in particular St-4 (T/C% = 10.7: the mean tumor wt. of treated group/the mean tumor wt. of control group) and Co-3 (T/C% = 31.5%) which are insensitive to presently available agents. HMM seems worthy of further clin. investigation as a candidate agent to treat breast, stomach, colon and other carcinomas.

Answer 4:

Bibliographic Information

Antitumor activity of hexamethylmelamine on human tumor xenografts serially transplanted in nude mice. Kubota, Tetsuro; Tanino, Hirokazu; Watanabe, Masahiko; Kitajima, Masaki. School Medicine, Keio University, Shinjuku, Japan. Anticancer Research (1994), 14(6B), 2521-4. CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 122:305980 AN 1995:533057 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor activity of hexamethylmelamine (HMM) was evaluated using four human tumor xenografts serially transplanted in nude mice. HMM was dissolved in 0.2 mL of 1% hydroxypropyl cellulose per mouse and administered perorally daily, except on Sunday, for 4 wk, giving an estd. max. tolerated dose (MTD) of HMM of 75 mg/kg. The MX-1 cell line showed dose-dependent sensitivity to HMM and was completely eradicated by treatment at the MTD. The min. ED of HMM against MX-1 was calcd. to be 22.1 mg HMM/kg, resulting in the chemotherapeutic index of 3.4. The demethylated derivs. of HMM, pentamethylmelamine and tetramethylmelamine, were also effective against MX-1, whereas trimethylmelamine was ineffective. The effect of HMM was more marked when the drug was administered on day 1 after tumor inoculation, compared with administration during the exponential growth phase. HMM is thought to be a promising agent for the treatment of several types of human carcinoma, producing active metabolites in vivo after peroral administration.

Answer 5:

Bibliographic Information

Antitumor activity of hexamethylmelamine on human breast carcinoma xenografts in nude mice. Tanino, Hirokazu; Kubota, Tetsuro; Naito, Yasuaki; Sakurai, Takeo. Dep. Thorac., Wakayama Med. Coll., Wakayama, Japan. Wakayama Igaku (1992), 43(4), 623-6. CODEN: WKMIAO ISSN: 0043-0013. Journal written in Japanese. CAN 119:173744 AN 1993:573744 CAPLUS

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Abstract

Oral administration of hexamethylmelamine (25 and 75 mg/kg/day for 4 wk) caused regression of human breast carcinoma implants in nude mice. The max. tolerated dose of the drug was 75 mg/kg.

Answer 6:

Bibliographic Information

Use of heterotransplants in diffusion chambers for determining the individual drug sensitivity of human ovarian cancer to chemotherapeutic drugs. Sobol, I. L.; Marenich, A. F. Cancer Res. Cent., Moscow, USSR. Byulleten Eksperimental'noi Biologii i Meditsiny (1979), 88(8), 243-5. CODEN: BEBMAE ISSN: 0365-9615. Journal written in Russian. CAN 91:150972 AN 1979:550972 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The sensitivity of 10 ovarian tumor heterotransplants in diffusion chambers in mice to hexamethylmelamine [645-05-6], cyclophosphane [50-18-0], 5-fluorouracil [51-21-8], methotrexate [59-05-2], dactinomycin [50-76-0], 17-hydroxyprogesterone caproate [630-56-8], and thiotepa [52-24-4] was variable. E.g., hexamethylmelamine, cyclophosphane, 5-fluorouracil, and methotrexate had a brief inhibiting effect in growth of a solid glandular cancer, inhibited growth of a glandular papillary cancer, and had no effect on growth of a papillary adenocarcinoma. In 4 of 5 cases where results of these expts. were compared with results of expts. obtained in the treatment of patients with the same drugs, exptl. results correlated with clin. findings.