Ukrain

Drugs Exp Clin Res. 1996;22(3-5):243-5. Related Articles, Links

Ukrain therapy of recurrent breast cancer with lung metastases (case report).

Kadan P, Korsh OB, Melnyk A.

Ukrainian Anti-Cancer Institute, Vienna, Austria.

A recurrent breast cancer with lung metastases was treated with the new anticancer drug Ukrain. The first two courses led to subjective improvement of the general condition as well as work capability; appetite improved and shortness of breath disappeared. After the sixth course of Ukrain therapy objective improvement was found clinically on X-ray, in haematological and biochemical data and improved tumour markers. Lymph nodes and lung metastases disappeared. The patient showed a full clinical remission.

Publication Types:

· Case Reports

PMID: 8899340 [PubMed - indexed for MEDLINE]

Langenbecks Arch Surg. 2002 Jun;387(2):84-9. Epub 2002 Jun 19. Related Articles, Links

Efficacy of ukrain in the treatment of pancreatic cancer.

Zemskov V, Prokopchuk O, Susak Y, Zemskov S, Tkachenko O, Hodysh Y, Nowicky W.

Department of General Surgery, National Medical University, prosp. Holosiivsky, 59B, 03039 Kyiv, Ukraine.

BACKGROUND: This monocentric study evaluated the effect of ukrain in the treatment of pancreatic cancer. MATERIAL AND METHODS: Between January 1996 and December 1999 we treated 21 patients with 10 mg ukrain every second day x10. The control group received supportive treatment only. RESULTS: Ukrain treatment was well tolerated. Mean values on pain measure and Karnofsky index were significantly better in the ukrain group than in controls (P<0.05). One-year survival was 76% in the ukrain group, compared to 9.5% in the control group. Median survival after treatment with ukrain was 574 days, compared to 197 days in the control group. CONCLUSIONS: Our data demonstrate that ukrain improves quality of life in patients suffering from advanced pancreatic cancer and significantly prolongs survival time in these patients.

Int J Radiat Biol. 2002 Jan;78(1):17-27. Related Articles, Links

Ukrain, an alkaloid thiophosphoric acid derivative of Chelidonium majus L. protects human fibroblasts but not human tumour cells in vitro against ionizing radiation.

Cordes N, Plasswilm L, Bamberg M, Rodemann HP.

Section of Radiobiology and Molecular Environmental Research, Eberhard-Karls-University Tuebingen, Hoppe-Seyler-Strasse 3, 72076 Tubingen, Germany.

PURPOSE: Ukrain, an alkaloid thiophosphoric acid derivative of Chelidonium majus L., has demonstrated a promising impact on chemotherapy in a variety of malignancies. The effects of the drug on cell survival, alteration of the cell cycle and induction of apoptosis were examined without and in combination with ionizing radiation (IR). The TP53 status of the cell lines used was also investigated. MATERIALS AND METHODS: Exponentially growing human tumour cell lines MDA-MB-231 (breast), PA-TU-8902 (pancreas), CCL-221 (colorectal), U-138MG (glioblastoma), and human skin and lung fibroblastic cells, HSF1, HSF2 and CCD32-LU were studied by colony assay, flow cytometry (cell-cycle, annexin-V staining for apoptosis) and Western blotting. Ukrain was used in concentrations from 0.1 to 50 microg ml(-1) for 1, 3 and 24 h and radiation as single doses of 1-10Gy. Combined drug-radiation exposure employed 1 microg ml(-1) Ukrain for 24h plus 2-8 Gy. RESULTS: Ukrain cytotoxicity was time- and dose-dependent. The combination of Ukrain plus IR gave enhanced toxicity in CCL-221 and U-138MG cells, but not in MDA-MB-231 and PA-TU-8902 cells. Most strikingly, a radioprotective effect was found in normal human skin and lung fibroblasts. Flow-cytometry analyses supported the differential and cell line-specific cytotoxicity of Ukrain. CCL-221 and U-138MG cells accumulated in G2 after 24-h Ukrain treatment, whereas no alterations were detected in the other tumour cells and normal fibroblasts tested. Western blotting of TP53 demonstrated non-functional overexpression in all tumour cell lines without affecting p21. HSF1 presented wild-type TP53 and a p21 response after IR. Flowcytometric analyses of annexin-V staining showed no induction of apoptosis after Ukrain treatment in comparison with untreated controls. CONCLUSIONS: Differential effects of Ukrain in modulating radiation toxicity of human cancer cell lines and its protective effect in normal human fibroblasts suggest that this alkaloid may have potential properties for clinical radiochemotherapy.

Drugs Exp Clin Res. 2000;26(5-6):341-56. Related Articles, Links

Ukrain: a novel antitumor drug.

Uglyanitsa KN, Nefyodov LI, Doroshenko YM, Nowicky JW, Volchek IV, Brzosko WJ, Hodysh YJ.

Medical Institute of Grodno, ul Gorkogo 80, 230015 Grodno, Belarus.

A review of the recent literature on the new anticancer drug Ukrain is provided herein. We review Ukrain, a thiophosphate derivative of alkaloids from Chelidonium majus L., its capacity to exert selective cytotoxic and cytostatic effects on tumor cells, simultaneously acting as an immune response modifier, its good tolerance and lack of side effects even after long-term application, perspectives of the application of this drug in oncology.

Cancer Lett. 2000 Nov 28;160(2):149-57. Related Articles, Links

Ukrain(TM), a semisynthetic Chelidonium majus alkaloid derivative, acts by inhibition of tubulin polymerization in normal and malignant cell lines.

Panzer A, Hamel E, Joubert AM, Bianchi PC, Seegers JC.

Department of Physiology, University of Pretoria, P.O. Box 2034, 0001, Pretoria, South Africa.

Ukrain(TM) has been described as a semisynthetic Chelidonium majus alkaloid derivative, which exhibits selective toxicity towards malignant cells only. Its mechanism of action has hitherto been uncertain. We found that Ukrain(TM) inhibits tubulin polymerization, leading to impaired microtubule dynamics. This results in activation of the spindle checkpoint and thus a metaphase block. The effects of Ukrain(TM) on the growth, cell cycle progression and morphology of two normal, two transformed and two malignant cell lines did not differ. We could thus find no evidence for the selective cytotoxicity previously reported for Ukrain(TM).

Drugs Exp Clin Res. 1992;18 Suppl:51-4. Related Articles, Links

Ukrain both as an anti cancer and immunoregulatory agent.

Nowicky JW, Manolakis G, Meijer D, Vatanasapt V, Brzosko WJ.

Ukrain Anti-Cancer Institute, Vienna, Austria.

Thirty six stage III cancer patients were treated with Ukrain, a semisynthetic drug derived from Chelidonium majus L. alkaloids conjugated with thiophosphoric acid. The drug was injected intravenously every second day in a dose of 10 mg per injection. Each patient received 300 mg of the drug (30 injections). The cytostatic effect of Ukrain was monitored clinically and by ultrasonography (USG) and computer tomography (CT), as well as by determination of CEA and CA-125 in the sera of patients with rectal and ovarian cancers, respectively. The influence of Ukrain on immune parameters was

evaluated by monoclonal antibodies (MAb) to CD2, CD4, CD8 and CD22. The influence of Ukrain on immune parameters in cancer patients was matched with its effect on these parameters in 20 healthy volunteer controls. The results obtained indicate that Ukrain, in a concentration not cytostatic in normal cells, is cytostatic for malignant ones, and may suppress the growth of cancer. The compound also has immunoregulatory properties, regulating the T lymphocyte subsets.

Drugs Exp Clin Res. 1998;24(5-6):213-9. Related Articles, Links

Ukrain (NSC-631570) in experimental and clinical studies: a review.

Jagiello-Wojtowicz E, Kleinrok Z, Urbanska EM.

Department of Pharmacology and Toxicology, Medical University School, Lublin, Poland.

The need to find a safe and highly effective cure for neoplastic disease remains a major challenge for modern pharmacology. This paper reviews the available literature on Ukrain (NSC631570), a novel semisynthetic drug obtained from Chelidonium majus L. alkaloids. Ukrain has been demonstrated to possess antineoplastic and immunomodulatory properties. Inhibition of the growth of cancer cell lines in vitro, tumor mass reductions in vivo, and partial and complete remissions in oncological patients, occur as a result of Ukrain application. The drug may interfere directly with the metabolism of cancer cells and it also improves the functioning of the host immune system. Diminished synthesis of DNA, RNA and proteins, the inhibition of cellular oxygen consumption, and the induction of programmed cell death in malignant cells have been described following Ukrain administration. The drug can also modify the immunological response via an increase in the number of total T-cells and a normalization of the T-helper/T-suppressor lymphocyte ratio. Ukrain therapy produces neither toxic consequences nor allergic reactions towards the drug. Several case reports and clinical trial data indicate that Ukrain may ameliorate effectively the progress of neoplastic disease and/or induce a total cure.

Drugs Exp Clin Res. 1992;18 Suppl:73-7. Related Articles, Links

Chelidonium majus L. (Ukrain) in the treatment of cancer patients.

Lohninger A, Hamler F.

2nd Dept. of Obstetrics and Gynaecology, Vienna Medical School, Austria.

Ukrain, a semi-synthetic thiophosphoric acid compound of alkaloid chelidonine isolated from Chelidonium Majus L., Tris(2-([5bS-(5ba,6b,12ba)]-5b,6,7,12b,13,14- Hexahydro-13-methyl][1,3]-benzodioxolo[5,6-c]-1,3-dioxolo[4, 5- i]phenanthridinium-6-ol]-Ethaneaminyl) Phosphinesulfide 6HCl, causes a regression of tumours and metastases in many oncological patients. More than 400 documented patients with various carcinomas in different stages of development have been treated with Ukrain. The authors report on only three different cases treated with preparation Ukrain. Ukrain can be helpful in improving the general condition and prolonging life by reduction of the tumour progression and its immunomodulating effect on the organism.

Drugs Exp Clin Res. 1992;18 Suppl:13-6. Related Articles, Links

Studies concerning the effect of Ukrain in vivo and in vitro.

Bruller W.

Bundesstaatliche Anstalt fur Experimentall-Pharmakologische und Balneologische Untersuchungen, Vienna, Austria.

Ukrain, a reaction product of different alkaloids of Chelidonium majus L. (celandine) with Thio tepa has been investigated for possible use as an anticancer agent. A possible tumour inhibiting effect on the Ehrlich mouse ascites tumour is now tested in vivo. Moreover, possible changes in the oxygen consumption of mouse ascites tumour cells and a guinea pig liver homogenate are to be determined after the administration of Ukrain in vitro with the aid of an oxygen electrode.

Cancer Lett. 2000 Mar 13;150(1):85-92. Related Articles, Links

The antimitotic effects of Ukrain, a Chelidonium majus alkaloid derivative, are reversible in vitro.

Panzer A, Joubert AM, Bianchi PC, Seegers JC.

Department of Physiology, University of Pretoria, South Africa. apanzer@medic.up.ac.za

Ukrain is alleged to be an effective chemotherapeutic drug which causes minimal side-effects as a result of selective toxicity towards malignant cells only. We previously failed to confirm this claim and found Ukrain to be equally toxic to normal, transformed and malignant cell lines by causing a metaphase arrest. In this study we have found the antimitotic actions of Ukrain to be reversible in low doses in vitro, as shown by flow cytometry and concurrent haematoxylin and eosin stains. We hypothesize that the lack of side-effects found in vivo may be due to the lack of therapeutically effective dosages being administered, therefore enabling cells to overcome the metaphase arrest and survive.

Drugs Exp Clin Res. 2000;26(5-6):267-73. Related Articles, Links

Effects of Ukrain on the activities of DNA-nicking enzymes.

Votrin II, Voltchek IV, Kurochkin SN, Kolobkov SL.

Institute of Biological and Medical Chemistry, Russian Academy of Medical Sciences, Moscow, Russia.

We studied the effects of Ukrain, a novel antitumor drug, on the activities of calcium, magnesium-dependent endonuclease (CME) and manganese-dependent endonuclease (MnDE) in rat liver nuclei, the activity of topoisomerase I assessed by pUC19 plasmid relaxation and CME activity in the nuclei of lymphocytes from colon cancer patients. Ukrain was found to exert a dose-dependent inhibiting effect on both CME and MnDE, similar to that exerted by erythropoietin, which was used as a reference preparation. Both Ukrain and erythropoietin also caused dose-dependent inhibition of topoisomerase

I activity. The influence of Ukrain on CME activity in the nuclei of the lymphocytes of colon cancer patients was differential, depending on treatment efficacy. The results suggest that DNA-nicking enzymes may be a target of Ukrain and may mediate its antitumor effects.

Drugs Exp Clin Res. 1992;18 Suppl:5-11. Related Articles, Links

Enhancement of macrophage tumouricidal activity by the alkaloid derivative Ukrain. In vitro and in vivo studies.

Sotomayor EM, Rao K, Lopez DM, Liepins A.

Department of Microbiology and Immunology, University of Miami School of Medicine, Florida.

Ukrain is a semisynthetic drug with immunomodulatory properties, derived from Chelidonium majus L. alkaloids and thiophosphoric acid. The effect of this compound on the growth of Balb/c syngenic mammary adenocarcinoma was assessed. Intravenous, but not subcutaneous or intraperitoneal, administration of this drug was found to be effective in delaying tumour growth in an actual therapeutic protocol initiated five days after tumour implantation. No untoward side-effects were observed using these in vivo treatment modalities. The role of macrophages in the observed retardation of tumour development was investigated using peritoneal exudate macrophages (PEM) in cytotoxicity assays. In previous studies, the authors have found that PEM of mammary tumour bearing mice lose their capacity to kill a variety of tumour target cells including the in vitro cultured homologous tumour cells (DA-3). Pretreatment of PEM from normal mice with 2.5 microM Ukrain for 24 h followed by stimulation with either IFN-gamma or with LPS+IFN-gamma enhanced their cytotoxic activity. Treatment of PEM from tumour bearing mice with 2.5 microM Ukrain and LPS results in a reversal of their defective cytotoxic response against the DA-3 target cells. Furthermore, Ukrain alone, in the absence of a secondary signal, induced the activation of tumouricidal function of PEM from tumour bearing but not from normal mice. These data indicate that Ukrain's in vivo effects against the development of mammary tumours may be due, at least in part, to its ability to restore macrophage cytolytic function.

Drugs Exp Clin Res. 2000;26(5-6):163-70. Related Articles, Links

A method for determination of Ukrain in blood plasma for monitoring and pharmacokinetic study.

Doroshenko YM, Hodysh YY, Uglyanitsa KN, Nefyodov LI.

Institute of Biochemistry, National Academy of Sciences, Grodno, Belarus. nef@biochem.belpak.grodno.by

We developed a method using high-performance liquid chromatography for the determination of the main fluorescent component of Ukrain, a novel antitumor and immune-stimulating drug. Our method was based on ion-pair separation of Ukrain from perchloric acid extracts using reversed-phase column, buffer with high molarity (0.5 M potassium phosphate, pH 2.65), high concentration of ion-pair reagent in the mobile phase (10 mM octylsulfonic acid), controlled temperature of the separation (45 degrees C) and detection by fluorescence (360/455 nm). Under the above conditions a peak of

the main Ukrain compound was resolved from fluorescent peaks of the sum of alkaloids of Chelidonium majus L. although several peaks of alkaloids were retained in Ukrain as traces. The height of this main peak was nearly constant, while the alkaloid peaks varied depending on the series of the preparation; chelidonine and thio-triethylenephosphoramide gave no peaks. Analytical recovery for Ukrain from human plasma was 98.0 +/- 4.5%. Therefore, Ukrain possesses neither significant stable binding to plasma proteins nor adsorption in blood cells.

Drugs Exp Clin Res. 2000;26(5-6):149-56. Related Articles, Links

Bcl-2 overexpression protects human keratinocyte cells from Ukrain-induced apoptosis but not from G2/M arrest.

Roublevskaia IN, Haake AR, Polevoda BV.

Department of Dermatology, University of Rochester School of Medicine and Dentistry, Rochester, New York, USA.

Exposure of ME180 and A431 carcinoma cells to Ukrain (NSC-631570), a semisynthetic compound consisting of alkaloids isolated from Chelidonium majus L. (Papaveracea), results in cell cycle arrest at the G2/M phase. Ukrain selectively inhibits growth of ME180 and A431 cells at a concentration range from 3.5 microM to 7.0 microM and induces apoptosis. In contrast, normal human keratinocytes showed no difference in the kinetics of progression through the cell cycle in response to this compound. We found that at a concentration of 7.0 microM of this drug Bcl-2 protein overexpression protected HaCaT cell line keratinocytes against apoptosis induced by Ukrain but did not prevent G2/M arrest. Following exposure of normal keratinocytes to Ukrain, we detected an increase in Bcl-2 protein levels and a significant change in protein modification as suggested by observation of its different isoform with shifted electrophoretic mobility. Bcl-2 protein expression and its isoform distribution did not change substantially in ME180 and A431 carcinoma cells. We also suggest that drug-induced mitotic arrest and apoptosis represent dual Ukrain action on cell cycle progression machinery and Bcl-2-involved program cell death in the cell.

Drugs Exp Clin Res. 1992;18 Suppl:63-7. Related Articles, Links

Lymphocyte subsets in patients with lung cancer treated with thiophosphoric acid alkaloid derivatives from Chelidonium majus L. (Ukrain).

Staniszewski A, Slesak B, Kolodziej J, Harlozinska-Szmyrka A, Nowicky JW.

Department of Thoracic Surgery, Wroclaw Medical School, Poland.

Lymphocyte subsets were evaluated in nine men (aged 42-68 years, mean 57 years) with histologically proven lung cancer, previously untreated. Lymphocyte subpopulations were quantified by immunofluorescence using monoclonal antibodies against total T-cells, T-helper and T-suppressor cells. In addition, the percentage of NK cells and the helper/suppressor (H/S) ratio were evaluated. The number of B-cells was determined by surface immunoglobulin immunofluorescence. Chelidonium majus L. (preparation Ukrain) was applied as an intravenous injection every three days. One

course consisted of 10 applications of 10 mg each. All immunological tests were performed before and after drug administration. The treatment was generally well tolerated. The results showed an increase in the proportion of total T-cells, and a significant decrease in the percentage of T-suppressor cells. The normalization of the H/S ratio was also noted. However, there were no signs of activation of NK, T-helper and B-cells. The restoration of cellular immunity was accompanied by an improvement in the clinical course of the disease. This effect was particularly pronounced in patients who responded to further chemotherapy. Objective tumour regression (CR+PR) was seen in 44.4% of treated patients. Four out of nine patients (44.4%) died of progressive disease during the course of this study. It is concluded that Ukrain can be immunologically effective in lung cancer patients and can improve human cellular response.

Drugs Exp Clin Res. 2000;26(5-6):279-83. Related Articles, Links

Chitotriosidase as a new marker of macrophage stimulation in a tumor model treated with cyclophosphamide and Ukrain.

Korolenko TA, Djanayeva SJ, Falameyeva OV, Wevers RA, Filjushina EE, Buzueva II, Kaledin VI, Sandula J, Nowicky J.

Institute of Physiology, Siberian Branch, Russian Academy of Medical Sciences, Novosibirsk, Russia.

Ukrain has previously been demonstrated to exert a malignotoxic effect in vivo. This antitumor drug has been effective in the treatment of some malignancies in experimental animals as a result of immunostimulation (macrophage stimulation). In the present study, serum chitotriosidase activity was measured as a biochemical marker of macrophage stimulation in several murine and rat models of macrophage stimulation. It was shown that zymosan, carboxymethylated glucan and Triton WR 1339 administration to CBA mice or Wistar rats was followed by a considerable increase in serum chitotriosidase activity. Murine LS lymphosarcoma development decreased serum chitotriosidase activity. Antitumor treatment by Ukrain or cyclophosphamide did not restore this index to the normal value.

Drugs Exp Clin Res. 2000;26(5-6):249-52. Related Articles, Links

Retrospective study of Ukrain treatment in 203 patients with advanced-stage tumors.

Aschhoff B.

Villa Medica Clinic, Edenkoben, Germany.

A total of 203 advanced-stage cancer patients suffering from different types of cancer who had exhausted all conventional forms of therapy were treated with the novel antitumor drug Ukrain over a period of 2.5 years at the Villa Medica Clinic in Germany. Seventy-six patients (37.4%) were simultaneously treated with regional deep hyperthermia in which tumor tissue was heated to > 42.5 degrees C. Patients also received complementary oncological treatment with selen, cimetidine, thyme extract

and vitamin A. In view of the advanced stage of the disease, the results of therapy were surprising. Forty-one patients (20.2%) achieved total remission, 122 (60.1%) partial remission and only 40 (19.7%) did not respond to treatment. The highest response rates were in patients with seminoma (three out of four patients had total remission and one had partial remission) and in prostate cancer [14 out of 20 patients (70%) achieved total remissions and five achieved partial remission].

Drugs Exp Clin Res. 1992;18 Suppl:1-4. Related Articles, Links

Selective inhibition of in vitro cell growth by the anti-tumour drug Ukrain.

Hohenwarter O, Strutzenberger K, Katinger H, Liepins A, Nowicky JW.

Institute of Applied Microbiology, University of Agriculture, Vienna, Austria.

The inhibitory effect of Ukrain on malignant cells and on normal cells, in vitro, has been compared. To obtain a 50% inhibition of cell growth, a tenfold concentration had to be used with normal endothelial cells compared to a human osteosarcoma cell line. Hybrids of the two cell types showed nearly the same sensitivity as normal cells. A laser scanning microscope showed a high uptake of Ukrain in malignant cells, while the content in normal cells under the same experimental conditions was substantially lower.

Drugs Exp Clin Res. 2000;26(5-6):239-47. Related Articles, Links

Clinical aspects of cancer treatment and new biochemical mechanisms of the drug Ukrain.

Uglyanitsa KN, Nefyodov LI, Karayedova LM, Nowicky JW, Brzosko W.

Oncology Department of Grodno Higher Medical School, Grodno, Belarus.

A random group of 50 patients in tumor stages T1-3N0-2M0 was selected from breast cancer patients and given Ukrain therapy by intravenous injection. Twenty-five patients received a total dose of 50 mg Ukrain (5 mg every second day, 10 injections altogether). Twenty-five patients received a total dose of 100 mg Ukrain (10 mg every second day, 10 injections altogether).

Drugs Exp Clin Res. 2000;26(5-6):195-9. Related Articles, Links

New biochemical mechanisms of the anticancer effect of Ukrain in the treatment of cancer of the urinary bladder.

Nefyodov LI, Uglyanitsa KN, Nechiporenko NA, Smirnov VY, Brzosko W, Karavay NL.

Analytical Biochemistry Laboratory, Institute of Biochemistry, Belarus National Academy of Sciences, Grodno, Belorussia.

The aim of this study was to elucidate the mechanisms of the anticancer effect of Ukrain

by comparing the processes of formation of the pool of free amino acids and their derivatives in the blood plasma and tumor biopsy specimens and unchanged bladder tissue in 28 patients with T1N0M0 bladder cancer. The examination was carried out before and after Ukrain treatment (10 mg i.v./day, for 20 days), which was combined with systemic chemotherapy for bladder cancer. Twenty-eight patients served as controls and received systemic chemotherapy only. Compared with healthy donors, the blood plasma of patients with urinary bladder cancer showed decreased concentrations of thiol-containing free amino acids and glutamine (Gln) and increased levels of nonessential (glutamic acid, proline, alanine) and aromatic (phenylalanine) free amino acids. In contrast to conventional chemotherapy, treatment with Ukrain eliminated the blood plasma amino acid imbalance in patients with bladder cancer, concomitantly enriching the pool of free amino acids and their derivatives in unchanged urinary bladder tissue and decreasing concentrations of Gln and leucine (Leu), regulators of malignant cell proliferation and differentiation, by 30-50%. In this situation, the concentrations of Gln and Leu in tumor tissue and the surrounding healthy urinary bladder tissue correlated highly significantly and negatively (r = -0.95). In conclusion, Ukrain prevents active free amino acid transport into urinary bladder tumor tissue, inhibiting the activities of protein biosynthesis, gluconeogenesis and energy production. The combined decrease in Gln and Leu levels in urinary bladder tumor tissue is a specific sign of the antitumor effect of Ukrain and a mechanism of its cancerostatic action by controlling the processes of amino acid pool formation in the tumor.

Pharmacol Ther. 1991 Oct;52(1):35-84. Related Articles, Links

The clinical pharmacology and use of antimicrotubule agents in cancer chemotherapeutics.

Rowinsky EK, Donehower RC.

Division of Pharmacology and Experimental Therapeutics, Johns Hopkins Oncology Center, Baltimore, Maryland 21205.

Although there has been a rapid expansion of the number of classes of compounds with antineoplastic activity, few have played a more vital role in the curative and palliative treatment of cancers than the antimicrotubule agents. Although the vinca alkaloids have been the only subclass of antimicrotubule agents that have had broad experimental and clinical applications in oncologic therapeutics over the last several decades, the taxanes, led by the prototypic agent taxol, are emerging as another very active class of antimicrotubule agents. After briefly reviewing the mechanisms of antineoplastic action and resistance, this article comprehensively reviews the clinical pharmacology, therapeutic applications, and clinical toxicities of selected antimicrotubule agents.

Drugs Exp Clin Res. 1991;17(2):139-43. Related Articles, Links

Evaluation of thiophosphoric acid alkaloid derivatives from Chelidonium majus L. ("Ukrain") as an immunostimulant in patients with various carcinomas.

Nowicky JW, Staniszewski A, Zbroja-Sontag W, Slesak B, Nowicky W, Hiesmayr W.

Ukrainian Anti-Cancer Institute, Vienna, Austria.

This paper summarizes the preliminary results of two independent clinical trials conducted with the preparation "Ukrain", containing thiophosphoric acid alkaloid derivatives from the plant Chelidonium majus L. (greater celandine), in order to investigate whether it has immunopotentiating properties in cancer patients. A total of twenty-seven patients with various malignancies were treated with "Ukrain" given intravenously in a dose of 10 mg every three days. In all patients the cellular and humoral immune response was studied. There was an increase in both total T-cells and T-helper lymphocytes, a decrease in T-suppressor cells, and normalization of the helper/suppressor (HIS) ratio. A significant increase in erythrocyte-rosette-forming T-cells and NK cells was also demonstrated. Serum immunoglobulin levels, complement components (C3 and C4), and acute phase proteins were not significantly enhanced. Restoration of cellular immunity was accompanied by an improvement in the patients' performance status and in the clinical course of the disease. The treatment was generally well tolerated. The present study shows that some therapeutic benefit from the use of Chelidonium majus ("Ukrain") as an immunostimulant in cancer patients can be achieved.

Drugs Exp Clin Res. 2000;26(5-6):191-3. Related Articles, Links

Results of Ukrain monotherapy of prostate cancer.

Uglyanitsa KN, Nechiporenko NA, Nefyodov LI, Doroshenko YM, Brzosko W, Nowicky W.

Oncology Department, Higher Medical School, ul Gorkogo 80, 230015 Grodno, Belarus.

This study included 15 patients with newly diagnosed prostate cancer with an average age of 71 years (62-85 years). The patients received Ukrain at a total dose of 100 mg (10 mg intravenously every second day, 10 injections altogether). After two to three injections of Ukrain, all the patients noted considerable subjective improvements in their state. Ukrain increased the amount of total T-lymphocytes, including "active" T-lymphocytes, decreased the content of T-suppressors and increased that of T helpers, correspondingly raising the T helper/T-suppressor ratio. Our results undoubtedly indicate the efficacy of Ukrain in the treatment of prostate cancer.

Drugs Exp Clin Res. 1996;22(3-5):193-4. Related Articles, Links

Synergic influence of Ukrain and protoporphyrin amino acid conjugates on human malignant cell lines.

Brzosko WJ, Graczyk A, Konarski J, Nowicky JW.

Roch Brzosko Memorial Centre for Natural Medicine, Warsaw, Poland.

Simultaneous cytotoxicity of Ukrain and protoporphyrin amino-acid derivatives was tested on four malignant cell lines and the cytotoxic effect after laser irradiation was compared with cytotoxicity of Ukrain and protoporphyrin amino-acid derivatives applied on similar cell lines separately. It was found that Ukrain and protoporphyrin amino-acid derivatives act synergistically as cytotoxic substances on the malignant cell lines.

Drugs Exp Clin Res. 1996;22(3-5):103-13. Related Articles, Links

Modulation of immune effector cell cytolytic activity and tumour growth inhibition in vivo by Ukrain (NSC 631570).

Liepins A, Nowicky JW.

Faculty of Medicine, Memorial University, St. John's, Newfoundland, Canada.

Ukrain is a semisynthetic compound consisting of alkaloids from Chelidonium majus L. conjugated to thiophosphoric acid, with immunomodulatory and therapeutic properties in cancer patients. The present in vitro studies demonstrate that Ukrain is an effective biological response modifier augmenting, by up to 48-fold, the lytic activity of splenic lymphocytes obtained from alloimmunized mice. The lytic activities of interleukin-2 (IL-2) treated spleen cells and peritoneal exudate lymphocytes were also significantly increased by the addition of Ukrain to the cell mediated lysis (CML) assay medium. The highest Ukrain-induced enhancement of splenic lymphocytolytic activity in vitro was found to occur at day 18 after alloimmunization was dose-dependent and specific for the immunizing P815 tumour cells. Since Ukrain was present only during the CML assays, its mode of action is thought to be via direct activation of the effector cells' lytic mechanism(s). The effect of Ukrain on the growth of Balb/c syngenic mammary adenocarcinoma was also evaluated. Intravenous, but not subcutaneous or intraperitoneal, administration of this drug was found to be effective in delaying tumour growth in an actual therapeutic protocol initiated five days after tumour implantation. No deleterious side-effects were observed using these in vivo treatment modalities. The role of macrophages in the observed retardation of tumour development was investigated, using peritoneal exudate macrophages (PEM) in cytotoxicity assays. Previous studies showed that PEM of mammary tumour-bearing mice lose their capacity to kill a variety of tumour target cells including the in vitro cultured homologous tumour cells (DA-3). Pretreatment of PEM from normal mice with 2.5 microM Ukrain for 24 h, followed by stimulation with either IFN-gamma or with lipopolysaccharide (LPS) plus IFN-gamma enhanced their cytotoxic activity. Treatment of PEM from tumour-bearing mice with 2.5 microM Ukrain and LPS results in a reversal of their defective cytotoxic response against DA-3 target cells. Furthermore, Ukrain alone, in the absence of a secondary signal, induced the activation of tumouricidal function of PEM from tumour-bearing, but not from normal, mice. These data indicate that Ukrain's in vivo effects against the development of mammary tumours may be due, at least in part, to its ability to restore macrophage cytolytic function.

Drugs Exp Clin Res. 2000;26(5-6):223-30. Related Articles, Links

Comparative evaluation of the efficiency of various Ukrain doses in the combined treatment of breast cancer. Report 1. Clinical aspects of Ukrain application.

Uglyanitsa KN, Nefyodov LI, Brzosko V.

Oncology Department, Grodno Higher Medical School, Grodno, Belarus.

This study was carried out in 75 patients with histologically confirmed breast cancer. Patients were divided into three groups of 25. The control group received symptomatic

corrective therapy prior to mastectomy. The two other groups were given neoadjuvant therapy with Ukrain injections. The first group received a total course dose of 50 mg Ukrain at single doses of 5 mg injected every second day (a total of 10 injections) and the second group received a total Ukrain dose of 100 mg but with single doses of 10 mg. Five to seven days after the last injection patients from all groups were subjected to mastectomy according to Halsted, Patey or Madden. No allergic reactions or adverse effects were observed after the first course of injections or the whole course of Ukrain therapy, regardless of the dose. After five to six injections some patients noticed slight burning sensations and insignificant morbidity in the tumor area, which, according to a number of authors, testifies to the therapeutic activity of the preparation. Practically all patients who were administered Ukrain noticed remarkable positive changes in the second half of treatment: improvement in appetite, normalization of sleep, disappearance of general weakness and the appearance of confidence in recovery. After the course of treatment with Ukrain, the contours of the tumorous node became more clearly defined, which facilitated mastectomy. Changes in the tumor tissue were one-sided in their qualitative differences in comparison to the control group and were not dose-dependent. Qualitative and quantitative reactions to Ukrain by both intact lymphatic nodes and those affected by the metastatic process contribute to more quantitative and radical performance of the most important stage of mastectomy--removal of the regional cellulose together with the lymphatic nodes. The results of this study showed the efficiency of both doses (50 and 100 mg) of Ukrain with neither performing significantly better than the other.

Drugs Exp Clin Res. 1992;18 Suppl:55-62. Related Articles, Links

Preliminary studies on the effect of Ukrain (Tris(2-([5bS-(5ba,6b,12ba)]- 5b,6,7,12b,13,14-hexahydro-13-methyl[1,3] benzodioxolo[5,6-v]-1-3- dioxolo[4,5-i]phenanthridinium-6-ol]-Ethaneaminyl)Phosphinesulfide.6HCl) on the immunological response in patients with malignant tumours.

Danilos J, Zbroja-Sontag W, Baran E, Kurylcio L, Kondratowicz L, Jusiak L.

Hospital for Obstetrics and Gynaecology, Lublin, Poland.

Preliminary clinical observations and studies on immunological response-indicators were made in eight patients with malignant tumours, who had been administered parenteral injections of Ukrain. The results suggest that the preparation is a non-toxic immunostimulator inducing production of thymodependent T lymphocytes. The preparation improves general health of patients, has anti-allergic action, and sedative and anti-inflammatory effects. It can inhibit growth of malignant tumours.

Drugs Exp Clin Res. 1998;24(5-6):253-60. Related Articles, Links

Macrophage stimulation and antitumor effect of Ukrain.

Korolenko TA, Svechnikova IG, Filjushina EE, Kaledin VI, Vakulin GM, Usynin

IF, Tsyrendordjiev DD.

Institute of Physiology, Siberian Branch of Russian Academy of Medical Sciences, Novosibirsk, Russia.

It has previously been demonstrated that Ukrain administration (0.5 mg in mice of 20 g, five times) to A/Sn mice results in retardation of HA-1 tumor growth in the liver and a prolongation of lifespan compared with untreated controls. In the present study Ukrain was tested as a macrophage stimulator in intact mice and animals with HA-1 hepatoma. There were no changes to the carbon particles phagocytosis rate in the case of a single administration of Ukrain to intact mice. Significant secretion of procathepsin B into ascitic fluid was shown in tumor mice as well as marker enzyme of macrophages beta-hexosaminidase activity, suggesting an influx of macrophages into ascites. Single Ukrain administration increased this index, and repeated drug injections were followed by a tendency to normalization of secretion. The cytolytic effect of Ukrain against tumor cells (as a result of macrophage stimulation) is the most probable mechanism of its antitumor action, but this suggestion needs further experimental evidence with special attention paid to the balance of proteinases and endogenous proteinase inhibitors.

Drugs Exp Clin Res. 2000;26(5-6):249-52. Related Articles, Links

Retrospective study of Ukrain treatment in 203 patients with advanced-stage tumors.

Aschhoff B.

Villa Medica Clinic, Edenkoben, Germany.

A total of 203 advanced-stage cancer patients suffering from different types of cancer who had exhausted all conventional forms of therapy were treated with the novel antitumor drug Ukrain over a period of 2.5 years at the Villa Medica Clinic in Germany. Seventy-six patients (37.4%) were simultaneously treated with regional deep hyperthermia in which tumor tissue was heated to > 42.5 degrees C. Patients also received complementary oncological treatment with selen, cimetidine, thyme extract and vitamin A. In view of the advanced stage of the disease, the results of therapy were surprising. Forty-one patients (20.2%) achieved total remission, 122 (60.1%) partial remission and only 40 (19.7%) did not respond to treatment. The highest response rates were in patients with seminoma (three out of four patients had total remission and one had partial remission) and in prostate cancer [14 out of 20 patients (70%) achieved total remissions and five achieved partial remission].