Pharmatest Management NEWS

SPECIAL EDITION - CANCER

Cancer

Some important facts from Central and Eastern Europe and Central Asia.

Breast Cancer *Colon Cancer*
Bronchial Cancer *Prostata Cancer*
Ovarial Cancer *Lung Cancer*

Our Medical & Managing Director Dr. Alexander Siebel, introduces "S&P" Pharmatest Management GmbH, and considers the current situation of cancer in Eastern Europe.

Dr. Alexander Siebel
Medical and Managing Director
"S&P" Pharmatest Management

Dear colleagues,

Once again, "S&P" Pharmatest Management is proud to present you a new edition of our Medical Report. This time, we have prepared a special edition on the topic that almost all of us consider to be as one of the biggest challenges to modern medicine: cancer.
Each year, more than 3,5 million people die of cancer. With nearly 5 and a half million cancer patients in the world, that means two thirds of them do not survive the disease. And the rate is growing: almost 3 million new cases are reported every year.

Being specialized in Eastern Europe, we have prepared a few articles from the top specialists in those countries in order to get an accurate idea of the dimensions of cancer in the population, the different ways to fight it and the progresses made.
Eastern Europe is especially hit with cancer. Statistics report that over a million people die of cancer every year. Taking a closer look at some of them, we see that in the Ukraine, over 90.000 people suffer it and the death rate is as high as 70%. Poland does not look much better: with nearly 70.000 patients, a similar death rate is observed. In the Czech Republic 16.000 people die every year, and the total of patients is around 24.000. Another source of alarming figures is Russia, where over 240.000 people suffer from any type of cancer, from which the impressive figure of 170.000 deaths results, which over 140.000 reported new cases every year.

This death toll is moving many pharmaceutical companies to investigate cancer and the related life expectancy. Especially in the USA and Western Europe, great efforts are being made, but the saturation in their national centres retard the investigations.

Exactly that is the advantage of performing oncological studies in Eastern Europe: the amount of new cases is extremely large, and the typical centralization of the patients in large specialized centres makes it very good for reaching a vast number of patients in a short period of time. "S&P" Pharmatest Management has a very reliable network of audit-certified oncological centres ready to perform your study. We will be very glad to further help you with your special requests on this kind of studies.

Yours sincerely,

Dr. Alexander Siebel

"S&P" Pharmatest Management
Gneisenaustr. 67, 10961 Berlin, tel.: +4930 692 2425, fax: +4930 693 7500, E-mail: SP10961B@t-online.de

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Now, a selection of our centres in Lithuania, Czech Republic,Bulgaria, Poland, Russia, Ukraine and Uzbekistan will introduce themselves and discuss the situation in their respective countries.

Lithuania

Eugenijus Stratilatovas MD & Michailas Aizenas MD
Lithuanian Oncology Center

In the last year, 13.888 new cancer cases were registered in Lithuania. In comparison with the previous year, the number of new cases increased by 3,4%. The incidence was 374,9 per 100.000 inhabitants.
The most common cancer types in Lithuania are differenced by sex. While in males the most common types are lung, prostate, stomach, skin and bladder cancers, females suffer more from breast, skin, ovary, corpus uteri and cervix uteri cancers. These most common cancers made 76% of all new cases in 1999.
The number of cancer cases and incidence in Lithuania is rapidly increasing. Incomparison with 1990, the total number of all cancer cases increased by 44%, and the incidence increased 44%. By types, the biggest increase in the incidence was found in prostate, thyroid and skin cancers. Some cancers even had a small decrease in the incidence, for example stomach and larynx.
In Lithuania, the primary cancer diagnostic is usually performed at primary level by the family doctor or general practitioners and also in regional general hospitals or policlinics. Special cancer treatment is being performed in regional cancer hospitals, such as the Kaunas Cancer Hospital, Klaipda Hospital Oncology Dept or Siauliani Hospital. Patients with brain/CNS and eye malignant tumors are concentrated in the Kaunas Medical University Clinic's Department of Neurosurgery, Ophtalmology and Radiotherapy. Patients with leukaemias are treated in the Haematology Departmets at Vilnius and Kaunas Hospitals.
The largest cancer hospital in Lithuania is the Lithuanin Oncology Center (LOC), a state institution responsible for the organization and management of cancer care in the whole country, as well as a teaching and scientific institution for the Vilnius University.
Regarding the cancer treatment, three main methods are combined in Lithuania: surgery, radiotherapy and chemotherapy.
In the LOC, more than 5.500 surgical operations are performed per year, among them laryngectomies, pulmonectomies, gastroectomies, colonectomies, rectum extirpations, breats operations, hysterectomies and other curative and palliative operations due to malignant tumors.
About radiotherapy, most types are now available in Lithuania. Our center for example has a linear accelerator, gammatherapy machines and for intracavitary therapy. Also, open isotopes are used to treat some types of cancer.
Almost all modern chemotherapeutic agents are now available in Lithuania. Widest use is that of taxanes, platinum compounds, gemzar and campto. Monotherapy with one agent is rarely used, in more than 90% of the cases there is a use of a combination of anticancer drugs.
The LOC also uses photodynamic therapy (PDT) in the treatment of skin cancer and melanoma, as well as sometimes for lung, bladder and nasal sinuses cancer. The immunotherapy is mainly used for kidney cancer and skin melanoma, while hormonotherapy is widely used to treat hormone dependable malignancies.
Right now, our centre is investigating the use of PDT in solid tumors and the efficacy of new chemotherapy regimes and anticancer drugs.
Since 1998, a Cancer Control Programme was adopted by the Lithuanian Health Authorities in order to support investigations in the field of cancer prevention. All of these investigations are performed in accordance with the international standards and protocols. These is strenghtened by the co-operation with other clinical departments in Sweden, Norway, Germany, France and the USA.

Czech Republic

Jaroslav Sterba, MD, PhD
Head of the Pediatric Oncology Dept.
University Children's Hospital Brno

Specialized treatment for children with oncological diseases in the Czech Republic has a relatively short history. 1964, Prof. Josef Koutecky started the Prague Motol Pediatric Oncology Department. At present, they are treating over 150 new patients with solid tumors and lymphomas each year, covering the region of Bohemia and the whole country with bone marrow transplant programme.
The second pediatric oncology department is in Brno, which covers the Moravian region, with over 80 new cases of pediatric solid tumors and lymphomas annually.
The incidence of malignat diseases seems to be similar to that in other European countries.

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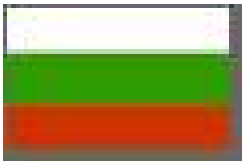
The most common diagnoses in this area are brain tumors, lymphomas, neuroblastomas, soft tissue sarcomas, Wilm's tumor and bone sarcomas. The figures for these cases do not differ much from the surrounding European countries or North America. In the last years, however, the incidence of pediatric oncology in the region is slightly increasing, similar to the developement in neighbouring countries.
In the Czech Republic, there is a national pediatric oncology working group, which provides the standards of care using cooperative group protocols from Europe and North America. Since 1985, the Czech Children's Leukaemia working group has been following the German Berlin-Frankfurt-Münster (BFM) protocols for patients with with acute lymphoblastic leukaemia (ALL) and acute myelogenous leukaemia (AML). The Motol Children's Haematology Hospital performs over 20 transplants a year. In order to follow new developements and recent international protocols, several new molecular biology and other specialized laboratories are available in Prague, Brno and Olomuc, which help determining the diagnosis and follow-up of the patients.
A very important area of of interest is dealing with the problem of individualized dosing schedules for certain chemotherapy drugs. It is remarkable, that even now, during molecular era, we are still dosing our toxic chemotherapy drugs based on body-surface are (BSA) to everybody, many of whom have significant toxicity. We believe that BSA-based dosing provides us with a false sense of accuracy. It is definitely precise, but not accurate. Particular attention should be paid to the young children and infants as they are exceptionally vulnerable to the acute complications associated with the the delivery of aggressive multimodal therapy and the potential long term sequels of antineoplastic therapy on growth and development. We are currently running several ICH-GCP studies in infants and young adults in the abovementioned indications.

Poland

Jaroslaw Kyczok MD
Warsaw

In Poland, the amount of new patients with cancer each year is of over 120.000. This figure embraces almost all kinds of cancer types, including palliation. Though, the most common sorts we are faced with are lung cancer, breast cancer, gynaecology tumors, rectum and large bowel cancer. Only lung, breast and gynaecological cancers are 50% of the total of cases.
Some of these types are increasing, while fortunately other are decreasing in number of new cases. Among the increasing ones we have lung, large bowel and breast cancer. Causes for the increase can be traced to smoking habits for lung, diet habits for large bowel, but they are still unknown causes for mamma cancer. The main decreasing types are stomach cancer and gynaecology, due to a better screening and prevention.
In Poland, the treatment of cancer is done with almost all kind of possible therapies. This includes the newest types of chemotherapy and combined treatments. Though, the most spread standard therapy are mainly surgery together with adjuvant radio-chemotherapy.
Other new therapies are as well being under investigation in Poland. In teletherapy for example, stereotactic treatment, multileaf collimators and dynamic collimators. In chemotherapy, all new drugs are being tested in phase I and II studies. Regarding brachytherapy we have stereotactic treatment and intraoperative brachytherapy.
All this scientific reasearch is mainly supported in Poland by the KBN, the Polish Committee of Sciences, depending from the Government. The Polish scientific reasearch does not differ from the international standards. All the projects are led together with international offices or with pharmaceutical companies according to ICH-GCP standards.
Our department is currently co-operating with a lot of other departments around the globe, mainly in the USA, Germany, France, UK, Austria, Canada, Israel and Japan, as well with other centres in Warsaw, Krakow, Poznan and Wroclaw, taking part in other ICH-GCP trials for Western sponsors.



Bulgaria

Prof. I. N. Chernosemsky
Director of the National Oncological Centre Sofia

The most common cancers in Bulgaria are lung, prostate, stomach and breast with the incidence rates; 2962, 1092, 1640 and 3053 respectively.
The anti-cancer movement in Bulgaria is particularly strong, in both the private and government sectors. Medication and treatment is provided free of charge by the government, and the centralised health system means that the whole population has access to these medications. The hospitals work closely with the Ministry of Health, collaborating and thus, maintaining a consistent and high level of care. Herbal and homeopathic specialists work parallel to and in close collaboration with traditional physicians completing the comprehensive network.

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The first systematic approach to tackling oncology in Bulgaria began with the establishment of a cancer centre in Sofia in 1950. The institute was created to act as the core of a specialised national network of 14 regional oncological centres throughout Bulgaria. The Cancer Hospital has 250 beds, an outpatient consultation unit, various diagnostic departments with certificates for quality assurance, a radiotherapy unit, seven in-patient wards (defined by cancer site), a medical oncology unit, psychosocial support and quality of life services. The main laboratories at the National Oncological Centre serve in- and out-patients 24 hours per day and are used successfully in the conduction of basic and clinical trials. It is especially interesting that the National Oncological Centre conducts in-vitro and in-vivo testing for antitumour activity, toxicity, genotoxicity and carcinogenecity. Specialised departments have also been established to combat oncology: The National Cancer Registry, Cancer Control and Epidemiology.

The National Oncological Centre boasts a large number of highly qualified specialists: 104 Professors, Associate Professors and Research Fellows, of whom 50 also have scientific degrees. The infrastructure of the centre allows for clinical trials of a diverse range of oncological indications to be undertaken successfully and to be approved by regular inspections and audits. The staff is completely familiar with the ICH-GCP standards and participate in trials accordingly. Multi-centre trials are also a possibility here using the beds and facilities of the centre.

Our work and activities are varied and cover a wide spectrum: We are involved in R&D projects with leading international and national programs, partnerships with pharmaceutical companies, other medical products and new medical technologies.

Russian Federation

Prof. V.F Semiglazov
Head of the Department of Surgery
N.N. Petrov Research Institute of Oncology, St. Petersburg

Cancer incidence in Russia has increased by 8% over the last 10 years. The absolute number of cancer patients has increased by 20% (thus, amounting to more than 400,000 people).

According to the St Petersburg Cancer Registry, the highest incidence rate for men is due to lung cancer and the highest incidence rate for women is due to breast cancer. The overall incidence of cancer is soaring due to the rapidly aging population in Russia, as is the case in most countries.

Cancer patients in Russia are concentrated in St. Petersburg and Moscow. Both cities have very high morbidity rates - in Moscow, more than 27,000 new cancer patients are diagnosed annually, in St. Petersburg, more than 17,000. The highest incidence rates of the most common cancers are also concentrated in the aforementioned cities here, the incidence rate of breast cancer is 48,4 per 100,000, of lung cancer 93,0 per 100,000, colon cancer 54,8 per 100,000, prostate cancer 23,5 per 100,000, corpus uteri 12,7 per 100,000.

There are six comprehensive cancer research centres in the Russian Federation: N.N. Blokhin Russian Oncological Centre of Academia of Medical Science (Moscow), N.N. Petrov Research Institute of Oncology Ministry of Health (St. Petersburg), P.A. Hercen Moscow Oncological Institute Ministry of Health, Research Institute of Oncology (Rostov-na-Donu), Research Institute of Oncology (Tomsk), Altay Oncological Centre (Barnaul). Additionally, each Russian region has an oncological dispenser and hospital with 300-400 beds.

The main activities of the cancer centres focus on the fundamental problems of carcinogenesis (particularly transplacental carcinogenesis), molecular genetics of tumours, primary prevention and experimental therapy and screening of the anti-tumour activity of new drugs. Moscow and St. Petersburg cancer centres cooperate with main international organizations and societies: UICC, WHO, EORTC, ESMO, ESSO, ASCO.

Phase I, II, III evaluation of new drugs are activated mostly in N.N. Blokhin and Herzen Oncological Centres in Moscow and N.N. Pertrov Research Institute of Oncology in St Petersburg. Over the past ten years, investigators from these centres have cooperated with large international pharmaceutical companies (Amgen, Bristol-Myers Squibb, Glaxo Wellcome, Novartis, Pharmacia&Upjohn, Hofmann-La Roche, Smith Kline Beecham, Zeneca, Asta Medica and Pfizer are among these companies) in the conduction of Phase I-III clinical trials. The cooperation between these oncological centres and the pharmaceutical companies is a testament to the quality of data and practical laboratory skills in all trials. Research workers and investigators are very familiar with international trial standards (GCP / ICH) and quality assurance programs. Given the importance of the quality of surgery, radiotherapy, chemotherapy and hormonotherapy in determining outcome, these programs are mandatory for cancer services and the conduction of trials.

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Ukraine

Ihor Kovalchuk MD
Director of the Lviv Medical University Oncological Clinic

In the Ukraine, there are more than 8.000 patients receiving chemotherapy in the various forms of oncology only in the Lviv region. There, the most frequent oncological cases are lung cancer, breast cancer, stomach cancer and skin cancer (but no melanoma). Except for the stomach cancer, which has decreased in the last years, all other forms have experienced a growth in the number of patients. For example, the Lviv region only has and incidence rate of more than 35 per 100.000 inhabitants ($^0/_{0000}$), breast cancer is 45 $^0/_{0000}$, skin cancer has 30 $^0/_{0000}$ and colorectal ca. 20 $^0/_{0000}$.
The most frequently used treatments in Ukraine are surgery, radiotherapy and currently also drug therapy, and the overall research does not really differ much from the scientific methods internationally used.
In the Ukrainian Research Institute of Oncology and Radiology in Kiev (the largest one in the country), is currently treating 8.000 patients, and over 3.000 surgical operations are performed in the centre.
The number of new patients is very large: nearly three quartes of a million people were registered by the oncology departments (incidence of 1463 $^0/_{0000}$). There were especial large increases in oral cavity cancer, some intestines, uterus, skin, breast, prostate gland, bladder and thyroid glad in the last years. Though, the cancer prevalence in Ukraine keeps a persistent tendency to increase. Our institute is currently participating in several ICH-GCP trials in various indications like non-small cell lung cancer, colon cancer, breast cancer (phase II-III).

Uzbekistan

F. K. Djuraeva, MD
National Oncological Scientific Center Tashkent
D.D. Yuldasheva MD
Oncological Dispenser Tashkent City

The oncological situation in the world remains difficult and requires the attention of theoretical and clinical medicine. At present, more than 9 million people in the world are ill with cancer and the mortality is over 5 million a year.
The etiopatogenesis study of malignant tumors indicates that cancer is the disease of all the organism. There are four basic aspects in the disease development: the genetic predisposition, environmental influence, radiotherapy and chemotherapy influence. In this article, we would like to analyse the oncological situation both in the whole Republic of Uzbekistan and especially in the city of Tashkent during the period between 1996-2000.
Nearly 18.000 new cancer patients were registered in 2000, while in 1996 there were only 15.000. This situation can be explained at first by the demographic growth, with a population increase of over half a million in 4 years.
A closer analysis of malignant tumors in Uzbekistan and Tashkent during the period 1996-2000 showed a stable character of the increase of major cancer types: breast, gastric, lung, skin (including melanoma), acute leukaemia and malignant lymphomas.
Breast cancer rate in the whole country increased from 5,9 to 6,2 $^0/_{0000}$, but only in Tashkent, this increase was more dramatic, rising from 16,7 up to 18,0 $^0/_{0000}$. Only the Sirdarya region registered a decrease of ca. 1,5 points.
The incidence of gastric cancer in Uzbekistan also decreased, but very slightly. Again, only the Tashkent region experienced an increase from 9,4 to 10,2 $^0/_{0000}$. The average lung cancer incidence decreased notably in the whole Republic during this four-year period.
Unfortunately, skin cancer and melanoma incidence suffered a considerable increase and the tendency is rising, the same happening with malignant lymphoma.
The diagnosis of malignant tumors in the Republic of Uzbekistan during the preventional examinations in the year 2000 equaled to 35,8% (increase of 5,3% since 1996). During the considered period, and due to improvement in the management of medical service on the early revealing and preventive examination of the population in the Republic of Uzbekistan, the number of patients with stage1-2 breast cancer increased up to 62,3%, lung cancer to 36% and gastric cancer up to 38,4%, all of which significantly improved the choice of a better treatment method of the malignant tumors and and increase in the patient survival.
In the year 2000, out of the 16.000 people who needed treatment, 86% of them completed a special anticancer therapy. The surgical method was used as monotherapy in 24% of them, and radiotherapy was also used as monotherapy in some of the regions of Uzbekistan, though clinical experience shows that the most effective treatment of malignant tumors is a combinated and complex therapy. At this point, our centre is carrying out phase II and III studies in breast, colon and non-small cell lung cancers.

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All these centres presented here are just a short selection of S&P's wide range of specialized clinics, hospitals, policlinics and university hospitals that we are working with. S&P Pharmatest is one of the first, most experienced and successful CROs to operate in Central and Eastern Europe, where the vast population and centralized Health Care System provide the ideal conditions for implementation of phase II-II trials. Our network of experienced centers give us the possibility of rapid recruitment in different trial conditions. Since 1995, S&P has recruited over 20,000 patients for ICH-GCP trials. All this being controlled by our local-based project management and monitoring teams which provide us with an outstanding data quality, continuously approved by external audits.
Interested? Just contact us to realize how much faster your clinical trial can be carried out with the best documentation quality demanded by the ICH-GCP guidelines!
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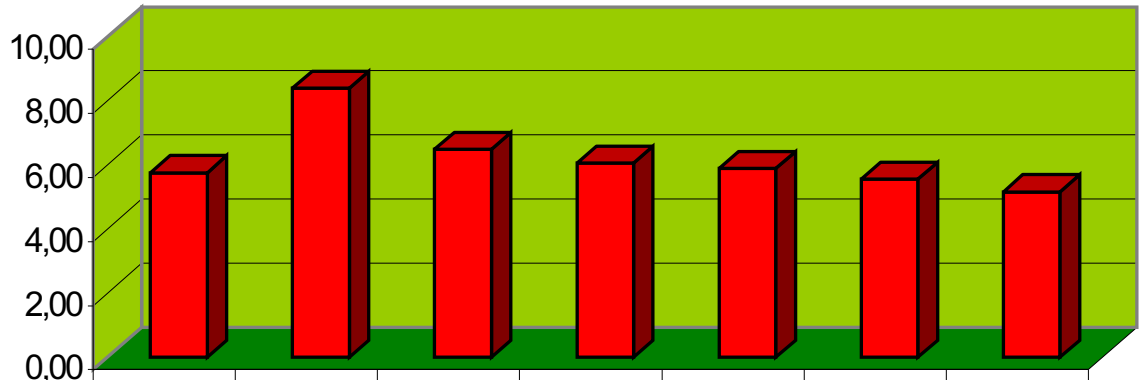
And get on the road to success!

Here are selected statistics from the World Health Organization's extensive cancer database regarding the situation in Central and Eastern Europe.

Incidence rate (per 1.000)



	Bulgaria	Czech	Poland	Russia	Ukraine	Lithuania	Romania
Incidence (per 1.000)	5,75	8,38	6,47	6,04	5,88	5,54	5,16

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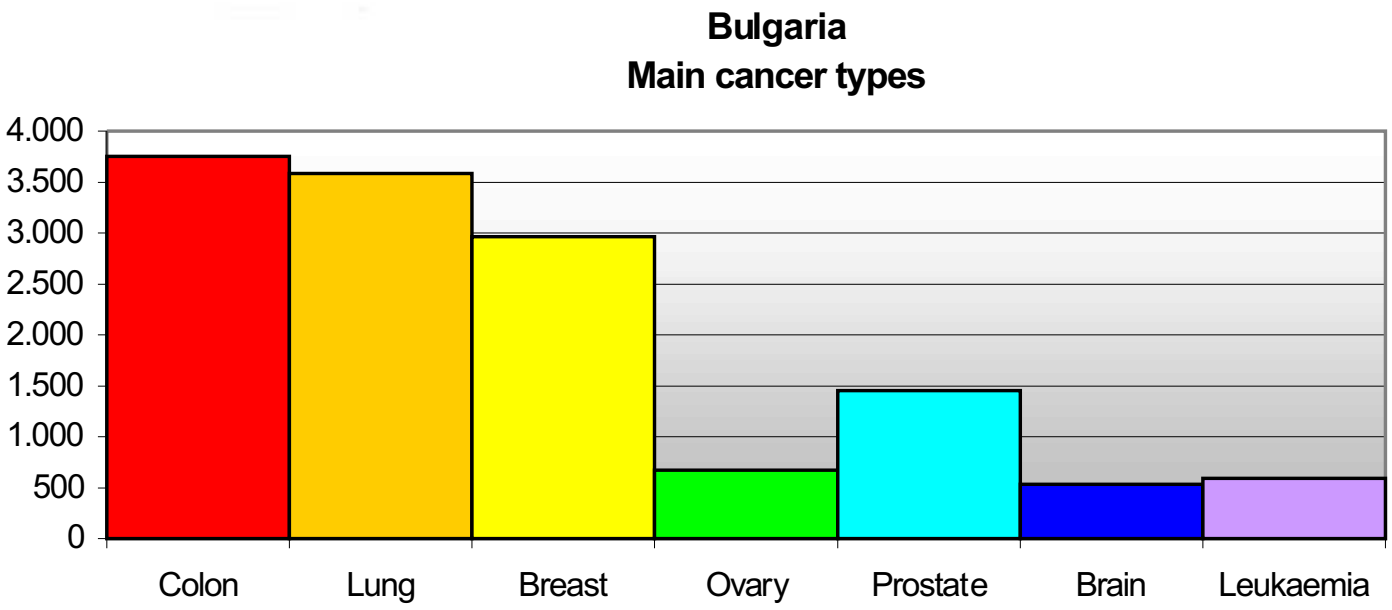

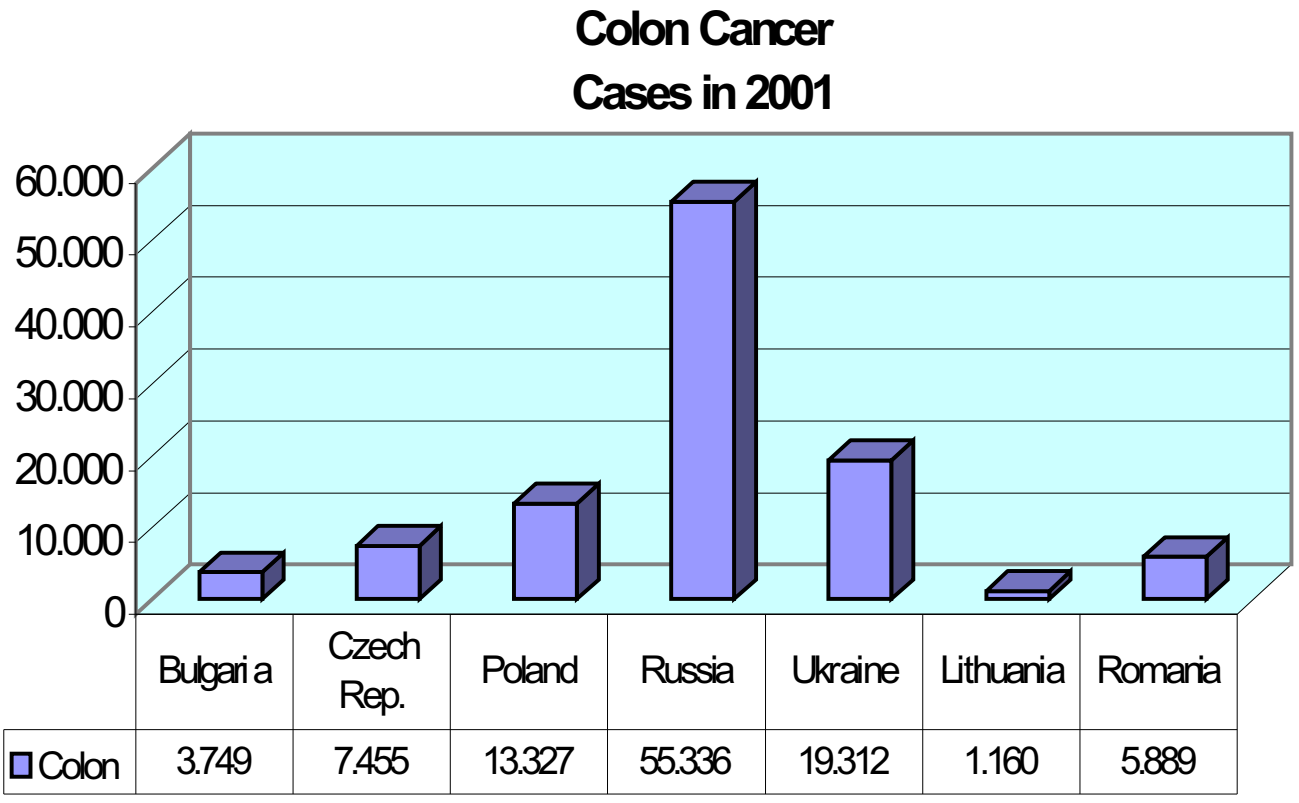

	Bulgaria	Czech Rep.	Poland	Russia	Ukraine	Lithuania	Romania
Colon	3.749	7.455	13.327	55.336	19.312	1.160	5.889

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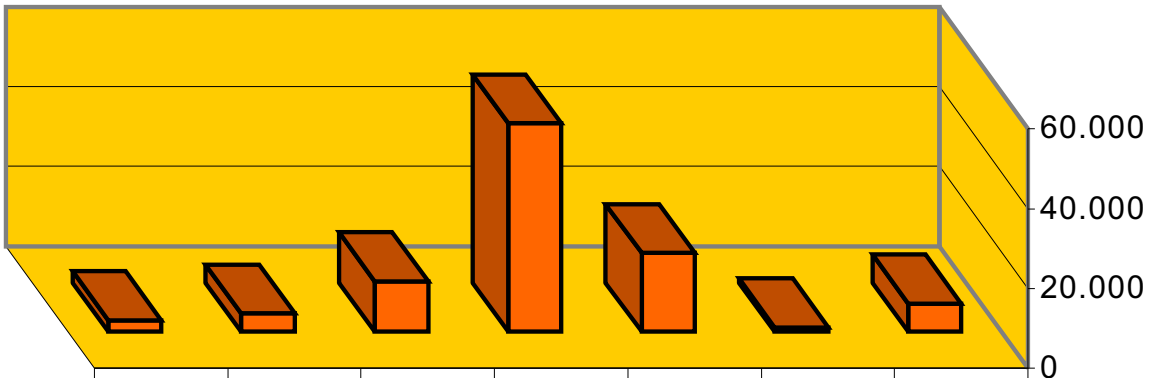
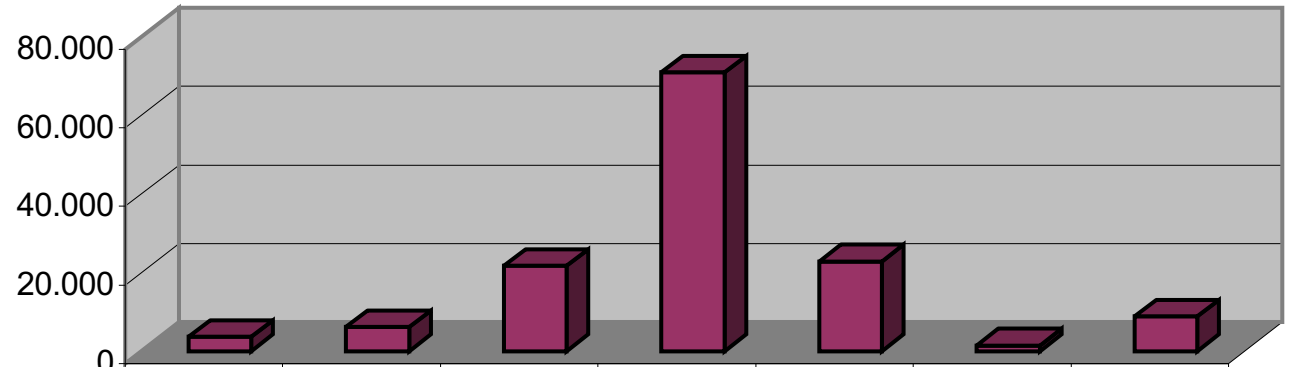
Breast Cancer
Cases in 2001



	Bulgaria	Czech Rep.	Poland	Russia	Ukraine	Lithuania	Romania
Breast	2.961	4.598	12.648	52.185	19.722	1.123	7.107

Lung Cancer
Cases in 2001



	Bulgaria	Czech Rep.	Poland	Russia	Ukraine	Lithuania	Romania
Lung	3.587	6.086	21.719	70.932	22.840	1.486	8.862

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