

National Population Based Breast Cancer Screening Program - Dora has Been Launched

Mateja Krajc, Maja Primic Žakelj, Kristijana Hertl and Maksimiljan Kadivec

National population based breast cancer screening program – Dora has been launched. At the end of March 2008, first women from the Ljubljana municipality received an invitation letter sent by Dora invitation office to attend screening mammography. First screening mammographies will be taken at the screening unit at the Institute of Oncology Ljubljana. The program will slowly be expanding and, by establishing new screening units, it will cover the target population of the whole Slovenia. High-quality of the organization of screening program is of essential importance in early detection of breast cancer and reduction of mortality due to this disease. The key elements of a high-quality screening program include the appropriate education and professional qualification of the personnel, primarily radiologists

and radiological engineers, and also of other personnel participating in further diagnostics and treatment, double reading of mammograms, interdisciplinary cooperation, appropriate technical quality of mammography machines, appropriate information system, and monitoring and evaluation of program quality indicators. Furthermore, the selection of the target population of women for screening mammography has to be made in an organized and systematic way. An appropriate response in this population must be achieved through the use of personal invitations and health education campaigns. The Program Dora meets all the requirements of the European guidelines concerning quality control and treatment.

Targeted Treatment of Metastatic Gastrointestinal Stromal Tumors in Slovenia.

Ajša Repar, Erika Matos and Branko Zakotnik

Gastrointestinal stromal tumors (GIST) are rare mesenchymal neoplasms. They express the cell-surface transmembrane receptor KIT, a product of the c-kit proto-oncogene. Frequent mutations of KIT result in the constitutive activation of KIT signaling, which leads to uncontrolled cell proliferation and resistance to apoptosis. Until recently, surgery was the only successful treatment for localized GIST, while there was no effective treatment for metastatic disease. With the discovery of imatinib mesylate and sunitinib, selective inhibitors of certain protein tyrosine kinases, the prognosis of unresectable or

metastatic GIST has substantially improved from a median survival of 6 months to almost 5 years. From 2001, we have successfully treated 51 patients with GIST at the Institute of Oncology Ljubljana. Median survival of our patients is 66 months. This treatment success can be attributed to the fact that all Slovenian metastatic GIST patients were treated by the multidisciplinary sarcoma team at our institution, which is, for a small country as Slovenia, a rational approach to the management of a rare disease.

Rituximab for Non-Hodgkin's Lymphoma.

Barbara Jezeršek Novaković and Ana Benigar

The introduction of rituximab into the treatment of patients with Non-Hodgkin's lymphomas has changed the long term prognosis of patients with CD20 positive B-cell lymphomas, especially follicular and diffuse large B-cell lymphomas. The NCCN guidelines recommend the application of rituximab also for the treatment of patients with other types of lymphomas, such as marginal cell lymphomas, mantle cell lymphomas and chronic lymphocytic leukemia. The addition of rituximab to chemotherapy improves the overall response rate, prolongs the response duration and the overall survival both in the patients with follicular and other indolent CD20 positive lymphomas and diffuse large B-cell lymphomas. Maintenance treatment with rituximab in the patients with indolent lymphomas further prolongs the remission and some of the studies have also shown the survival benefit. However, the maintenance therapy in aggressive lymphomas most probably gives no further improvement in the patients who received rituximab already in the induction treatment. Rituximab has been used at the Institute of Oncology Ljubljana since 1998. In the period from 2004 to 2006, we have treated 340 patients with rituximab either as a single agent (minority of patients) or in combination with chemotherapy. Our treatment group included 46.8% of patients with diffuse large B-cell lymphomas and 19.4%

with follicular lymphomas; 67.4% of patients were treated with R-CHOP combination, while the others received different rituximab-chemotherapy combinations. The overall response rate regardless of the histological type of lymphoma was 78.8% (62.4% complete responses, 2.6% unconfirmed complete responses, 13.8% partial responses) and the highest response rate was achieved in the patients with aggressive follicular lymphomas (91.7%). In 75% of patients, regardless of the histological type of lymphoma, the response lasted more than 12 months, the median response duration has not been reached yet. The longest disease-free survival was observed in the patients with diffuse large B-cell lymphomas. The overall survival rate of all patients, regardless of the type of lymphoma, was 75% 26 months after the beginning of treatment and the median overall survival has not been reached yet. The longest overall survival was observed in the patients with indolent follicular lymphomas. The treatment results with rituximab obtained at the Institute of Oncology Ljubljana are comparable to the results of larger randomized trials. According to the beneficial influence of rituximab on the long term prognosis of patients with CD20 positive lymphomas, it became the standard of treatment in these patients.

Late Sequels of Combined Treatment of Rectal Cancer.

Vaneja Velenik, Franc Anderluh, Irena Oblak and Barbara Šegedin

Preoperative radiochemotherapy followed by TME surgery has gained acceptance in multimodality treatment of locally advanced rectal cancer. The potential benefits of this treatment must be balanced against the risk of increased morbidity when determining the appropriate treatment for individual patients. Effects of combined modality

treatment on rectal, voiding and sexual function are quantified by various scoring methods. Speaking a common language in reporting the results is warranted.

High rate of rectal and urogenital complications has prompted us to incorporate this information in the preoperative counseling.

Some data from the Report on National Cervical Cancer Screening Program in the years 2006 and 2007.

Maja Primic Žakelj, Ana Pogačnik and Marjetka Uršič Vrščaj

The national cervical cancer screening program (with the name ZORA after Slovenian initials for organized cervical cancer screening program) has the goal to decrease cervical cancer incidence and mortality in Slovenia. As in the nineties, despite regular smear taking activity in gynecological practice (opportunistic screening), the cervical cancer incidence started to increase. In 2003, after the initial pilot study, an organized screening program was established. Each woman aged between 20 and 64 years should be invited to a preventive gynecological examination, including PAP smear once in every three years (after two negative smears) - either by her "personal" gynecologist with whom she has already been registered or by the Screening Center in case she has not been registered yet. All smear reports (in electronic form) from all cytological laboratories are gathered in the central database of the Screening Registry that is linked to the central Population Registry. The Screening Registry enables also sending invitations to the women whose smear has not been registered for four years. National guidelines for quality assurance and control of all procedures involved in cervical cancer screening and treatment of intraepithelial lesions and of cervical cancer were prepared. In the Screening Registry at the Institute of Oncology Ljubljana, all smear and pathology reports are registered. These data serve to

monitor coverage and compliance with screening together with other screening performance indicators. The condition for establishing such an information system was a uniform smear report and standardization of work in cytopathology laboratories. Four years after the start of the program, 70% of women in the target age group (20–64 years) had at least one smear registered in the Screening Registry. The percentage is about 80% till the age of 45 and smaller among older women. In 2006, 245.416 smears were registered from 220.820 women; 176.633 women attended the screening (80%), in others, smears were taken as follow-up or because of clinical indications. Screening smears were less adequate or inadequate in 5.9% of cases, and in 7.2%, any cell abnormality was found. In Cervical Pathology Registry, 8.620 histological reports were registered, more than half of them were from diagnostic biopsies. In 2006, 160 new cervical cancer patients were registered. The linkage of their data with the Screening registry enables us to review their screening history; nearly three quarters of these patients did not attend regular screening. According to the data from the Cancer Registry of Slovenia, the incidence rate of cervical cancer started to decrease, especially in the age group of 35 to 49 years.

Suppressive and Substitution Therapy with Thyroid Hormones.

Nikola Bešič

A patient with papillary or follicular thyroid carcinoma and unfavorable prognostic factors should have low serum TSH level in order to diminish the risk of recurrence. However, in order to prevent side effects on target organs (heart, bones), the levels of thyroid hormones should be inside the normal reference range. Whenever the thyroid doesn't produce enough hormones in a patient with a benign thyroid

disease, the patient should be treated with a hormone replacement therapy. The aim of the substitution therapy is that TSH, free T4 and free T3 are inside the normal reference ranges. Bioequivalence of different generic drugs with thyroxin may differ from 12.5 to 25%. Therefore, if one thyroxine drug is changed with another one, a laboratory test of TSH level has to be performed after six weeks.

Influence of Preanalytical Variables on the Quality of Laboratory Test Results.

Barbara Možina

The process leading to clinical laboratory result involves an examination and assessment process that is composed of the preanalytical, analytical and postanalytical phases. Preanalytical phase is an important component of laboratory medicine and of quality of total laboratory work. The preanalytical phase consists of the preparation of patients, technical aspects of specimen collection, sample transport, storage of sample, specimen preparation prior to analysis and

several biological variables and interference factors which influence test results.

Laboratory scientists, doctors, nurses and everyone involved in the chain of events in the preanalytical phase, have become increasingly aware of the important influence of preanalytical variables on the test results of patients.

Quality Control in Locoregional Treatment of Breast Carcinoma.

Marko Novak and Janez Žgajnar

The prognosis of the breast cancer patients is dependent on the biological properties of the cancer, but cosmesis, morbidity and locoregional control are the result of a surgical act. The outcome of different surgical procedures can be measured. In breast cancer

patients, optimal care starts with a proper surgical act, based on optimal imaging and diagnosis. The right type of operation should be indicated and performed by an experienced surgeon.

Adverse Effects of Treatment with EGFR Inhibitor – Cetuximab.

Janja Ocvirk

Cetuximab is a chimeric human-murine monoclonal antibody against the epidermal growth factor receptor (EGFR). It has shown activities against multiple malignancies in clinical trials. EGFR-inhibitors often cause skin toxicity, most frequently acneiform eruption. Xerosis, eczema, fissures, telangiectasias, nail changes and paronychia can be seen in some cases, rarely hyperpigmentation. Management of the

skin toxicity helps patients to overcome cetuximab-associated skin toxicity and is of great importance for patients' compliance. It is generally manageable with standard topical or systemic antibiotics and anti-inflammatory agents. Education of patients prior to beginning the therapy and proactive intervention at the first signs of skin toxicity are keys to successful management

MRI-based 3D Brachytherapy for Cervical Cancer.

Primož Petrič, Robert Hudej and Maja Mušič

Brachytherapy, in combination with external beam radiotherapy and chemotherapy, plays an essential role in radical treatment of locally advanced cervical cancer. Implementation of MRI based treatment planning and individual optimization of dwell-times and dwell-positions of ¹⁹²Ir pulsed- and high-dose rate stepping sources enables dose escalation in the target volume while respecting normal tissue tolerance. Development of novel combined intracavitary/interstitial

applicators allows for an accurate, reproducible and individualized insertion of a low number of needles into the parametria to achieve an adequate target coverage in tumors with unfavorable topography. When compared to standard, Manchester point »A« based method, these innovative approaches result in improved local control without increasing side effects rates.

Launching FDG PET-CT Imaging at the Institute of Oncology Ljubljana.

Barbara Vidergar – Kralj

PET/CT using 18F-fluorodeoxyglucose (FDG-PET/CT) is performed at the Institute of Oncology Ljubljana. PET/CT combines Positron Emission Tomography, which shows metabolism and function of the cells, with Computed Tomography, which shows detailed anatomy. FDG –PET/CT plays a major part in diagnostic evaluation of patients with suspected malignant tumors, in staging of malignancies and in

therapy monitoring. Correct preparation of patients for the PET is important to ensure maximum diagnostic yield. The most important steps to be taken are control of glucose level, minimizing effects of physiological activity, and timing of scan performance. Due to a number of causes yielding false negative or false positive results, several interpretation criteria should be used to evaluate images.

Update on Adjuvant Treatment of HER2-Positive Breast Cancer.

Erika Matos

Although trastuzumab-based regimens have improved both systemic control and overall survival in the patients with HER2-positive breast cancer, in some of these patients, tumor progression occurs despite trastuzumab treatment. New target therapies are searched for these patients. The most promising and, in terms of clinical use, the most developed is lapatinib, a small molecule, tyrosine-kinase inhibitor that targets not only HER2- but also HER1-receptor. It is already

used for treating the HER2-positive metastatic breast cancer patients after failure of trastuzumab therapy, but its effectiveness in adjuvant therapy has not been proven yet. ALTTO (Adjuvant Lapatinib and/or Trastuzumab Treatment Optimization) is a randomized phase-three multi-center study of adjuvant lapatinib, trastuzumab, their sequence and their combination in the patients with HER2 positive primary breast cancer.

Manifest Hypothyroidism Diagnosed prior to an Extensive Surgery.

Katja Kogovšek, Patricija Ečimovič, Nada Rotovnik Kozjek and Nikola Bešič

Overt hypothyroidism is a rare condition that can result in severe intraoperative and postoperative complications. Preoperative detection and management is essential for safe anesthesia. If possible, surgery should be postponed until thyroid function tests normalize.

We present a patient with severe untreated hypothyroidism that was detected only on preoperative anesthetic evaluation. Key diagnostic features of hypothyroidism as well as optimal preoperative management are described.