

### **Use of medicines in the last six days of life and their financial evaluation**

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Palliative care offers numerous benefits to the incurably ill patients. In the last days before death, patients may experience 5 most frequent symptoms (pain, nausea and vomiting, restlessness and confusion, dyspnea, increased secretion from the respiratory tract), which are alleviated by medicines prescribed in advance. The purpose of the retrospective research was to determine the differences in the use of medicines in the last 6 days of life among patients in palliative care who were managed by the palliative care team and patients managed at other departments of the Institute of Oncology without the help of the palliative care team (control group). Each group consisted of 25 patients; the groups were comparable with regard to the primary tumour site and age of the patients. We have established that the

majority of patients in both groups received strong opioids, while more patients in palliative care also received other medicines for the relief of symptoms (haloperidol, midazolam, dexamethasone, butylscopolamine, metoclopramide). On average, the patients in palliative care were given 10 different active substances, and the control group received 14. The cost of medicines in the palliative care group of patients was 15 € per patient per day, which was 2.7 times lower than in the control group, where the cost of medicines amounted to 42 € per patient per day. The difference in the costs was primarily a result of the unnecessary prescribing of low-molecular heparins, systemic antibiotics and antimycotics, and parenteral nutrition.

### **Progressive multifocal leukoencephalopathy following rituximab therapy in a patient with a relapsed mantle cell lymphoma in complete remission**

Tanja Roš, Matej Horvat, Mara Popović, Barbara Jezeršek Novaković

Progressive multifocal leukoencephalopathy (PML) is a rare and usually fatal demyelinating disease of the brain that is developed almost exclusively in patients with immunodeficiency and is a result of a latent infection with the JC polyomavirus. In recent years, several cases of PML have been reported following rituximab therapy. We present our first confirmed case of PML in a 55-year-old HIV-negative patient with a relapsed mantle cell lymphoma who was treated successfully with chemotherapy, rituximab and autologous transplantation of

peripheral haematopoietic stem cells (PHSC). By reporting this case we wish to draw attention to the importance of PML in differential diagnosis of patients with a progressing neurological symptoms and immunodeficiency following lymphoma treatment with rituximab and stress the importance of early detection of this disease with evidence of JC virus infection in the cerebrospinal fluid or stereotactic brain biopsy sample.

### **Plant cells in urine of patients with bricker ileal conduit**

Tanja Planinšek, Aleš Kladnik, Živa Pohar Marinšek, Margareta Strojjan Fležar

Cytology samples occasionally reveal different contaminants, such as talc, crystals and cotton wool strings. The routine examination of cytology urine samples to confirm malignancy occasionally showed contamination with plant cell. We have established that they were present only in patients with a Bricker ileal conduit. Urine preparations for the routine cytopathological examination were prepared with membrane filtration, fixed in Delaunay solution and stained according to Papanicolaou. They were examined using the light microscope. We also prepared adhesives preparations made by the companies Coloplast and ConvaTec, which are used by the ostomist to attach the bag on the urostomy. Plant cells were found only in the Coloplast adhesives. Morphologically, they were equal

to the plant cells found in the urine of patients with a Bricker ileal conduit. To continue, we also provided preparations from different substances, namely adhesives components. Plant cells were present only in the preparations of guar gum, which is produced from *Cyamopsis Tetragonoloba* seeds. The size, shape and colour of plant cells differed from those of epithelial intestinal cells. The latter are present in the urine of patients with a Bricker ileal conduit, thus even an inexperienced cytotechnologist would have difficulty confusing them with dysplastic human cells. Nevertheless, it is important to take knowledge of all elements found in cell samples and to provide an explanation for sample contamination in the event of unusual findings, such as plant cells.

## **Clinical trials of new types of treatment in oncology - demand more!**

Boštjan Šeruga

In phase III randomised clinical trials (RCT), which are more and more often sponsored by profit-oriented pharmaceutical companies, the researchers compare the new anti-cancer treatments with the standard ones. If the new treatment proves to be more effective in the RCT, it is usually approved for use in daily clinical practice. As health care professionals, we are obliged to provide critical evaluations of new treatments and demand transparency of their benefits.

The transparency of the indicated benefits of new anti-cancer treatments can be additionally improved by providing access to clinical research protocols, based on which the new treatments are approved for use, and impartial reports on their adverse effects. The researchers and sponsors should conduct updated and secondary analyses of RCT more often, as they might be a source of additional significant findings.

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## **Chronic myelogenous leukemia**

Urška Bokal and Tanja Južnič Šetina

Chronic myelogenous leukemia (CML) is a rare myeloproliferative disease with an incidence of approximately 1-2/100,000 population per year. It is a clonal disease of a pluripotent stem cell committed to granulopoiesis. Most patients are diagnosed in the chronic phase when the blood count typically shows leukocytosis with predominance of mature neutrophil granulocytes and there are evident signs of increased metabolism, such as fatigue, weight loss and perspiration, and splenomegaly. Through the accelerated phase, the chronic phase progresses to a blast crisis resembling acute leukemia. The diagnosis is based on the discovery of the Philadelphia chromosome

arising as a consequence of chromosomal translocation t(9;22), BCR-ABL gene or its product, BCR-ABL tyrosine kinase, in the peripheral blood or bone marrow cells. Significant progress in the treatment of CML was accomplished by the discovery of the BCR-ABL tyrosine kinase inhibitors, which provide long-term disease control, namely with imatinib as the first choice of treatment in the chronic phase of CML. The other two possible treatments are the allogeneic transplantation of haematopoietic stem cells and palliative treatment with chemotherapeutics.

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## **Recovery itself is not enough - a case report**

Olga Blatnik, Jurij Miloš Borovšak, Berta Jereb

Advances in the treatment of malignancies in children have improved their survival rates. However, the recovery may eventually be followed by the development of adverse late effects of treatment. These changes, which are often asymptomatic, may be detected on time only if the patients are monitored regularly even after they have com-

pleted their treatment. The article presents a case of a patient who was irradiated in childhood and treated with chemotherapy, dying at a young age with signs of cardiac dysfunction, which was most likely a result of cancer treatment. Cardiac changes were diagnosed only at autopsy.

## VMAT - Volumetric Modulated Arc Therapy

Primož Peterlin, Emir Kuduzović, Primož Strojjan

Volumetric Modulated Arc Therapy (VMAT) Volumetric Modulated Arc Therapy (VMAT) is one of the most advanced radiation therapy techniques, which has been used by the Division of Radiation Oncology at the Institute of Oncology in Ljubljana since March 2011. The fundamental characteristic of VMAT is that the linear accelerator delivers the photon beam for the entire duration of the treatment head's rotation around the patient's body. While doing so, it simultaneously changes 3 parameters: the shape of the radiation field, the treatment head's rotation speed and the dose speed of the delivered photon beam. On the contrary, the Intensity Modulated Radiotherapy (IMRT) utilises static radiation fields and delivers the dose

at a constant speed. Compared to IMRT, the most important strengths of VMAT are shorter irradiation time, which makes it less likely that the patient (or target - the tumour) will move on the table of the irradiation device, and a lower dose burden to healthy tissues around the target so that the conformity of the dose distribution in the target region and the level of protection of the healthy organs and tissues surrounding it are comparable to those provided by IMRT or, in some cases (irradiation of the pelvic region), even more improved. The article presents VMAT: its features, course of treatment, indications for the selection and the hazards associated with such an accurate radiation therapy.

## Clinical pathways for cancer genetic counselling and testing at the Institute of Oncology in Ljubljana

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Four clinical pathways for patient management have been prepared within the scope of the Cancer Genetic Counselling and Testing Clinic. In the preparation of clinical pathways, we focused on the patient as the basic guideline for the establishment of the management algorithm. The objectives of clinical pathways for cancer genetic counselling and testing do not differ from clinical pathways in other areas. They represent the basis for equal management of patients, the basis for improving continuously the quality of management, and they also enable the measurement of management effectiveness. The health care system considers the safe and quality treatment of each patient to be the highest value and priority of all providers of health services. The manner in which the health services are provided

is of utmost importance: the approach to patient management must be based on scientific evidence and uniform within each single health organisation. Such approach is enabled by the use of clinical pathways. Patient management has been changing continuously, depending on the management doctrine. Within the framework of multi-disciplinary meetings, it is also subject to constant amendments and improvements. The clinical pathways for cancer genetic counselling are being improved continuously, thus they are not a static document but a live substance constructed daily to improve the quality of patient management.

## Overdiagnosis

Nebojša Glumac

In this article we will describe a phenomenon in cancer medicine known as overdiagnosis. As there is still no official Slovenian translation for this term, a Slovenian term "prediagnosticiranje" is used in the article, specifying cancer that does not cause symptoms or death if undiagnosed. This requires two conditions: an existence of a larger sub-clinical cancer base and active detection of this base, screening. Randomised studies have provided estimates of overdiagnosis in screening, being: 25% for breast cancer, 50% for lung cancer, and

more than 60% for prostate cancer. Restrospective studies and population statistics show overdiagnosis of neuroblastoma, thyroid cancer, kidney cancer and melanoma. Therefore, the patients must be informed of the size of the problem and the possible negative effects of treatment of this disease, which might otherwise never have affected them at all. Thus, it would be necessary to provide better estimates of overdiagnosis frequency and discover the methods to minimise this problem.

### **Merkel cell carcinoma**

Darja Eržen

The Merkel Cell Carcinoma (MCC) is a rare, aggressive and often deadly neuroendocrine skin carcinoma. Recently, there has been a growing interest in this type of cancer due to its increasing incidence and possible viral connection. The article presents the clinical picture,

staging system, treatment and experience of the Institute of Oncology Ljubljana (IOL). Also included is a review of 40 patients treated at the IOL from 1994 to 2011.

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### **Biological markers p16 and Ki-67 for defining cervical intraepithelial neoplasia in biopsy samples of the cervix**

Margareta Strojan Fležar, Helena Gutnik

The biological markers p16 and Ki-67 are indirect indicators of high-risk human papillomavirus infections (HR-HPV) connected to the formation of precancerous changes in the cervix. In diagnostically more challenging cases, they can be used to distinguish between cervical intraepithelial neoplasia and morphologically similar non-neoplastic changes. They can be determined using standard immunohistochemical methods on tissue slices from cervical biopsy

samples. In the daily histopathological evaluation of the cervical biopsy samples with additional immunohistochemical staining for p16 and Ki-67, a high-grade cervical intraepithelial neoplasia (CIN2 and CIN3) is usually ruled out, which prevents excessive treatment of changes in the cervix. Such diagnostic approach can also be used in the histopathological evaluation of intraepithelial neoplastic changes of the endocervical glandular epithelium.

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### **Surgical treatment of endometrial carcinoma unresolved issues**

Sonja Bebar

Endometrial carcinoma is the most common type of gynaecological cancer in the developed world. The selected treatment is surgery, complemented by radiotherapy in the event of a more advanced disease, and increasingly also by chemotherapy. The scope of a

surgical treatment is still to be determined, which requires adoption of new doctrines. New approaches to treatment are being developed, but it is necessary to consider also the specificity of the treatment of younger patients.