

Scientific Session-6

Radiosynovectomy & Bone Pain Palliation

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048

Radionuclide therapy for bleeding joints in hemophilia- A review

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The efficacy of radiosynovectomy has been proven by several studies and work in the past, including my experience. It can preserve function in hemophilic arthroses. This review will include the prevalence and incidence of hemophilia worldwide taking into account our potential patients for radiosynovectomy. The World Hemophilia Foundation has predicted 25% of all hemophilics will have hemarthroses. It will also discuss several studies done considering the various indications and contraindications, ideal radiopharmaceutical to be used, advantages and disadvantages as well as success rate of the procedure among hemophilics. Radiosynovectomy (RSV) or radiosynoviorthesis is the intraarticular injection of radioactive colloids to create fibrosis of the hypertrophic and highly vascularized synovium. It is a locally acting treatment for hemophilic arthropathy (HA). The accepted biological mechanism by which the radionuclides function involves the absorption by superficial cells of the synovium. Beta radiation leads to coagulation necrosis and sloughing of the cells, destroying diseased pannus and inflamed synovium. With the direct irradiation, it is expected that the regenerating synovium, after destruction, will be free of the disease. Hemophilia is a congenital blood disease, sex-linked trait that cause coagulation defects because of lack of Factor VIII (Hemophilia A) and Factor IX (Hemophilia B). Abnormal bleeding is usually at the musculoskeletal level. Hemarthroses or intraarticular hemorrhage is the most common musculoskeletal manifestation of hemophilics. They arise from the subsynovial venous plexus where a lack of thromboplastic activity has been demonstrated. Treatment options include transfusion of antihemophilic factor (AHF), which is quite expensive and temporary; surgical, which is bloody, and chemical synovectomy, which is done repeatedly, and quite painful and irritating.

Radiosynovectomy has to be considered as the initial procedure of choice for the treatment of patients with repeated hemarthroses in hemophilics since they are at poor risk for surgery. This will likewise prevent sequelae of several major bleeds thereby preventing deformity in the joints. Likewise, there is less need for future Factor VIII replacement if not at all. The other advantage is that RS allows agents that can have a systemic effect to act in a localized manner thereby preventing systemic effects.

Radiation synoviorthesis is a very effective procedure that decreases both the frequency and the intensity of recurrent bleeds related to synovitis. The procedure should be

performed as soon as possible to minimize the degree of articular cartilage damage. It can also be used in patients with inhibitors with minimal risk of complications. On the average, the efficacy of the procedure ranges from 76% to 80%, and can be performed at any age. The procedure slows the cartilaginous damage which intra-articular blood tends to produce in the long term. After 30 years of using radiation synovectomy worldwide, no damage has been reported in relation to the radioactive materials. Primary prophylaxis and radioactive synoviorthesis are the best ways that we have today of protecting against haemophilic synovitis and arthropathy of the joint.

It is apparent that from this review together with my personal experience that radiosynovectomy has an important role to play in providing effective treatment for hemophilic arthroses of over 3 episodes of bleeds in a six-month period. It is also the procedure of choice in patients for whom surgery is contraindicated because of the presence of clotting factor inhibitors. The indication for a synoviorthesis is then chronic haemophilic synovitis causing recurrent hemarthroses, unresponsive to haematological treatment. Radiosynovectomy is an established and efficacious therapy for the treatment of bleeding joints in hemophilia.

049

Radiosynoviorthesis (RSO): influencing factors and therapy monitoring

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Abstract not available

050

Treating bone metastases: Use of radionuclides in combination with other therapies

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A range of radiopharmaceuticals have been used to treat bone pain including P-32, Sr-89 as pure beta emitters, Sm-153 EDTMP and Re-186/Re-188 HEDP which are mixed gamma/beta emitters, Sn-117m DTPA which emits conversion electrons and Rd-223 which is a mixed alpha/gamma emitter.

With all these agents the primary aim has been to treat bone pain, and as part of the consent process it is important to state to the patient that these treatments are designed to treat symptoms, not the tumour.

However, the uptake of all these products depend on increased deposition in the bone matrix surrounding the tumour. It is inevitable that there will be some crossfire

ABSTRACTS

effect into the tumour and part of the tumour itself may receive a reasonable radiation dose. It had been noted by some observers that in a small group of patients treated with repeat disease of these products that the progression of bone metastases had stopped and in some cases there was evidence for disease regression.

It was also stated that treatment with these agents should be performed without any adjunctive treatment. If bisphosphonates were given this would block uptake of the agents into the bone matrix and use with chemotherapy would result in too high a toxicity to the bone marrow.

The use of high activity Sm-153 EDTMP with chemotherapy had been proposed to replace whole body irradiation in conditioning for bone marrow transplant and was found to be well tolerated (Rodriguez V et al Leuk Lymphoma 2006).

Many patients with bone metastases are treated with long term bisphosphonates and the requirement to stop these drugs before giving Sm-153 EDTMP reduced the number of patients being offered treatment. In a prospective study it was found that there was no reduced uptake of Sm-153 EDTMP when given with bisphosphonates and there was a sustained drop over over 25% in alkaline phosphatase lasting for about 8 weeks suggesting some synergy in action between the two treatment (Lam M et al EJNMMI 2008).

The next step was to look at combinations with chemotherapy agents to see if it is possible to combine chemotherapy and Sm-153 EDTMP. In a phase I study at Sloan Kettering in New York 31 patients were enrolled in a study using Sm-153 and escalating doses of paclitaxel. The toxicity was manageable and at the higher doses over 50% of patient showed disease reduction (Morris RJ et al J Clin Oncol 2009)

This has led to a series of phase II and phase III trials with a European phase II trial involving Sm-153 EDTMP and taxanes and a large world phase III trial using a combination of bisphosphonates and chemotherapy with and without Sr-89.

It looks as though radionuclides may well have a role in combination with other treatments not only in pain relief but in the treatment of bone metastatic disease

051

Results of autoradiographic uptake of Re-188-HEDP

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Abstract not available

052

Metabolic Radionuclide Therapy of Metastatic Bone Pain Using 89 SrCl (Metastron) - Review and Perspectives

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Abstract not available

053

Metabolic Radionuclide Therapy in Painful Bone Metastases with 89SrCl : Better Patients' Selection for Therapy

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The aim of this retrospective study was to evaluate the efficacy of 89-Sr in the palliation of metastatic bone pain and identification of the patients who benefit most from the radionuclide therapy. Comparing the effects of radionuclide therapy for painful bone metastases in the two main groups of patients - breast and prostate cancer patients, radionuclide therapy was not equally effective. The comparison of the effectiveness of the radionuclide metabolic therapy in early stage of metastatic disease and in later stages showed better results in early stages in all aspects of the disease, progress, pain and probably, a better life expectancy. Methods: In the period between 2001 and 2008, 89-Sr- chloride (Metastron) with 150 MBq activity was intravenously administered to 45 patients with hyperalgalic generalized bone metastases from prostate cancer (20 patients), breast cancer (20, one of them was a male patient), and other malignancies (5 patients). Pain and performance status, before and after the administration, were investigated during the follow-up. The WHO performance status (Zubrod, ECOG) scale was used to estimate the objective status of the patients, and also their subjective sensation of pain intensity was estimated by a four degree scale, showing us the analgesic effectiveness of the therapy. Results: 85 % of prostate cancer patients showed significant benefit from treatment, vs only 55% of patients with breast cancer. The percentage of patients, suffering from prostate cancer, who became free of pain was 30%, vs 20% for breast cancer patients. No effect from the radionuclide therapy was observed in two prostate cancer patients (10%) and in 9 breast cancer patients (45%). The effectiveness we observed was better in earlier stages of the malignant disease. Conclusion: Radionuclide therapy for painful bone metastases is an expensive procedure accompanied frequently with adverse reactions. Proper selection of patients, who would benefit most from that kind of therapy is essential in the therapy management.

054

Knowing People, Caring for Persons, Not Just Treating Pain: 15 years delivering radionuclides to palliate bone pain

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It is a modern topic to emphasize the importance of patient-oriented care and the human aspects of health care delivery. In these 15 years, delivering treatment to patients with bone metastases, professionals working in our Centre have learnt that looking to the person is the principal point. How many times this sentence has been said: "First patient, second patient, third patient", in order to clarify what is vital for the Centre. Since the 90's, in the Centre of Nuclear Medicine radioisotopes as P32, Sr89 and Sm 153 EDTMP were administered to patients to palliate bone pain due to metastases, mostly as ambulatory patients, with few exceptions, mainly motivated by clinical conditions, not the decision of the Nuclear Medicine Team. Each patient is a

goal, a story, a problem, a family, a solution, a friend. The main goal was to diminish pain, which was achieved in 80% of the cases, withdrawing analgesics for a long period. Pain subdued in hours, not as an effect of treatment, but mainly due to confidence, the patient was eager to receive treatment as a final point, of a long ladder of several analgesics, without effect. Magic? Medicine? Physician-patient relationship? One cannot say, but the truth is that two thirds of patients had less pain in the first 24 hours, being really due to the radiopharmaceutical in a week or two. Stories are beautiful and full of satisfactions for physicians. In many men, marriage troubles had begun, since pain derives to bad temper and so forth, making cohabitation a real stress. When pain disappeared, relationship was smooth and these patients had the fortune to be again with their family and stayed with company till the end of their lives. Problems of no availability of the radiopharmaceutical and high costs were present at the beginning. Now, Samarium is produced in Lima, and with social economical costs in mind, this is not a problem for administrating the therapy. Families are involved in the whole process. Many patients are not suitable for treatment, mostly because they have received other treatments that have made them have low platelets and white cells. Physicians and the family together as a team make nutrition a point to start and several months after, the therapy can be administered without risk. In some cases, blood transfusions are needed additionally, but food is essential in health care of these patients. Friendship has been installed with some patients and their families. After receiving treatment, some phone calls or visits are a rule, either from the physician to the patient or vice versa and many times an unexpected visit, just to say hello, has been a nice surprise in the centre. This situation is not an exception, nor a rule, but has been very frequent in these 15 years. Bone pain treatment has given not only Nuclear Medicine extra knowledge, but also a compassionate understanding of human suffering.

055

Radiosinoviolis (RSNV) con Re188-Coloide en Sinovitis Villonodular (SVN) recidivante de rodilla. Experiencia clínico terapéutica

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Introducción y concepto:La sinovitis pigmentada villonodular es un raro desorden proliferativo de la membrana sinovial, de comportamiento benigno y de etiología desconocida. Esta clase de hiperplasia sinovial permite la formación de vellosidades y nodulaciones caracterizadas por depósitos de hemosiderina intracelular. Se presenta en forma difusa y localizada (nodular).La articulación más afectada es la rodilla y la forma difusa la más común. Se presenta en personas adultas jóvenes especialmente entre la segunda y cuarta década de la vida.

El tratamiento es quirúrgico y con radioterapia externa, pero la tasa de recaída es alta (entre 8% al 46 %). Mostramos la eficacia, seguridad y respuesta en el tratamiento de SNV con Renio188-colooidal mas Metilprednisolona intraarticular valorando la respuesta clínica y cambios estructurales utilizando Resonancia magnética. **Métodos:** Presentamos una serie de casos (n=5) con diagnóstico histológico de sinovitis villonodular Difusa recurrente en rodilla izquierda, remitidos al Instituto Nacional de Cancerología, quienes recibieron tratamiento intraarticular complementario con Re188-coloide, radiomarcado en la radiofarmacia local, en el periodo de diciembre de 2007 hasta Enero de 2009. Reportamos nuestra experiencia en pacientes tratados por excisión artroscópica, sinovectomía artroscópica o abierta para sinovitis villonodular difusa seguida de tratamiento con Re188-colooidal intrarticular. Se valoró la seguridad del tratamiento así: (1) distribución del radiofármaco intraarticular por imagen gamagráfica (2) descartando la fuga del radiotrazador a ganglios linfáticos inguinales, hígado, bazo y vejiga, con gamagrafía realizada a los 30 minutos y 24 horas y (3) seguimiento de variables clínicas: fiebre, mareo, anorexia, dermatitis post radiación, en la primera semana y a los 3 y 6 meses después de la radiosinoviolisis. La eficacia clínica después del procedimiento fue valorada comparando el estado previo y a los 6 meses postratamiento. **Resultados:** Se trataron 5 pacientes con diagnóstico de sinovitis villonodular pigmentada difusa, en rodilla izquierda (4 mujeres y 1 hombre) con edad promedio al diagnóstico de 27.6 años (24 a 34 años). Número de radiosinoviolisis realizadas: 7. Dos presentaron recurrencia después de la radiosinoviolisis y se les administró segunda dosis. No hubo complicaciones tempranas o tardías regionales o sistémicas. Distribución intraarticular: difusa 7. Captación en estructuras extra articulares: 0. Dosis administrada Promedio: 22mCi (11 a 26 mCi) .La intensidad del dolor medida por Escala Analógica Visual disminuyó en 4 de 5 pacientes (80%). El rango de movilidad articular mejoró en dos pacientes (40%). El derrame articular y edema disminuyó en 4 de 5 rodillas (80%). **Conclusión:** La inyección intraarticular de Rhenio188-colooidal mostró ser una alternativa de tratamiento en recidiva de sinovitis villonodular en este grupo de pacientes, de fácil disponibilidad y marcación en la radiofarmacia del Instituto Nacional de Cancerología, cumpliendo normas de buenas prácticas y a menor costo que Ytrium-90-colooidal.

056

Estudio biocinético y dosimétrico de un kit de producción local de ¹⁷⁷Lu-EDTMP para su uso como agente paliativo del dolor.

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ABSTRACTS

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057

¹⁵³Sm-oxabiphore radionuclide therapy combined with external beam radiation therapy (8Gy) in breast cancer patients with bone metastases

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Bone metastases are the cause of excruciating pain, which increases with the development of the disease and leads to the decrease in quality of patients' life. The extent of bone affection and intensity of pain are normally uneven, in that case both local and system treatments may be required. The use of external beam radiation therapy (EBRT) combined with radionuclide therapy is assumed to be the most effective method for pain relief, though it is considered as dangerous treatment because of the possible development of myelotoxic complications. Aim: Study of effects of combined use of ¹⁵³Sm-oxabiphore and EBRT with a single dose to a target of 8Gy in treating bone metastases. Materials and methods: 20 breast cancer patients with bone metastases and pain syndrome were treated with radiation of 8Gy to a target and ¹⁵³Sm-oxabiphore (1.0mCi/kg of a body mass), which was administered on the next day after EBRT. Effectiveness and tolerance of the treatment was assessed. Dynamics of the pain syndrome was studied and the quality of life was estimated by Karnofsky scale and SF36 questionnaire. Myelotoxicity was estimated by counts of white blood cells and platelets. The estimation had been carried out for three months. The study is continued. Results: Reduction of pain during three months after the combined treatment was observed in 23 of 26 patients (88%). 20 patients (77%) reduced the use of analgesics, 6 of them (23%) could stop the use completely. Positive changes in the quality of life were found. Karnofsky score increased by more than 10% in 18 (69%) patients in three months after the treatment. In their answers to SF36 Questionnaire the patients stated positive changes in physical and emotional activities due to improvement of general and mental health, reduction of pain intensity, No confidence level for difference between scores related to general health was found. It is acceptable outcome of the palliative treatment. Reduction of anxiety measured by Spielberger's State-Trait Anxiety Inventory and Hanin's scales was found. Myelotoxicity was moderate, transient leukopenia of grades 1 or 2 was observed in 7 patients (27%). Thrombocytopenia of grades 1 or 2 was found in 6 patients (23%). Conclusions: Combination of external beam radiation (8Gy) and ¹⁵³Sm-oxabiphore (1.0mCi/kg) therapies in bone metastases patients is effective and quite safe method for pain relief, which leads to improvement of the quality of life. The project is financially supported by Russian Foundation for Humanities and the Government of Kaluga region (project № 09-06-59603 a/C)

058

Therapeutic response of radiosynovectomy with ³²P colloid in haemophilic synovitis of adolescents.

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Objective : To evaluate the efficacy of radiosynovectomy with ³²P colloid in haemophilic synovitis of adolescents. Methods: Radiosynovectomy with ³²P colloid was primarily performed on 26 haemophilic male patients (26 joints) , average age 16 years(range:11 to 21 years). The average dose of ³²P colloid was 2.1 mCi (range: 1.0 to 3.0 mCi). Results: The total efficacy of the procedure after 6-month interval was 88.5%(23/26); The median frequency of haemarthrosis was reduced from 1.9 per month of presynovectomy (range: 0.2 to 5.0) to 0.3 per month of postsynovectomy (range:0.0 to 1.0)(P < 0.05 = 61.5% of the patients(16/26) had an improvement in range of joint mobility. Conclusion Radiosynovectomy with ³²P colloid in haemophilic synovitis is a safe, brief and effective procedure, without any severe side effects. Instead of surgical synovectomy , radioisotope synovectomy (RS) is useful to treat haemophilic synovitis.

059

Development of a new ¹³¹I-labelled bisphosphonic acid for palliative therapy of metastatic bone pain

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Approximately, 80% of all patients with cancer in advance stage could develop bone metastases. Nowadays, the management of metastatic bone pain remains controversial. Analgesics are widely described according to the World Health Organization analgesic ladder supplemented by local field, external beam irradiation for persisting skeletal symptoms. In the context of advancing malignancy, however, many patients progress to multi-site, poorly localized or migratory pain, which is less amenable to local field irradiation. Wide field, hemibody radiotherapy is useful in this setting, but it is limited by significant morbidity, particularly gastrointestinal disturbance, when the abdomen and pelvis are included in the treatment field. The use of bone seeking radiopharmaceuticals represents a major advance in the management of refractory metastatic bone pain. Acting systemically, this approach allows multiple sites to be treated simultaneously with relatively sparing of healthy surrounding tissues. As a result, toxicity is low in comparison with other systemic therapies and treatment is well tolerated. Used isotopes for pain palliation by bone metastases are very expensive, with exception of ³²P, which could cause bone-marrow depression. The aim of the present work was to develop a new bisphosphonic

acid labeled with ^{131}I for metastatic bone-pain palliation. An aryl-substituted bisphosphonic acid (PICIC-1), which would easily accept the ^{131}I , was synthesized starting from DL-tyrosine. Reaction was made into three phases: 1. protection of amine group with methylchloroformiate; 2. phosphonation of carboxyl group by reaction with a mixture of phosphorous acid and phosphorous pentachloride and 3. deprotection of amine group by hydrolysis. The reaction yield was 60%. Purity of obtained compound was tested by reverse-phase HPLC using a RP18 column (4.6 mm x 100 mm) and a gradient from 0% to 100% of methanol in water as mobile phase. The chemical purity was higher than 97%. The structure of the synthesized compound was analyzed by IR and NMR spectroscopy and by electrospray mass-spectrometry. The IR spectrum showed a wide peak due to the absorbed water, because the compound was highly hygroscopic. Despite, this peak hindered the interpretation of the spectrum, there were observed characteristic peaks of phosphonic groups and aromatic ring. NMR spectrum showed characteristic peaks corresponding to main functional groups of the molecule. Mass-spectrum showed two main peaks: one at 308.9 Da related with the loss of one OH group and the other at 325.1 Da corresponding to the molecular weight of attained bisphosphonic acid. Compound was labeled with ^{131}I by using Chloramine-T method. Then, it was purified through AgCl filters. Labeling yield was higher than 95%. The stability of the label was assessed up to 72 h in PBS 0.05 M pH = 7.0-7.2 and HSA. Just after 72 h incubation, the dehalogenation was significantly higher in HSA (i.e., >15%) than, IC-1 showed satisfactory bone affinity and could be a promising new radiopharmaceutical for metastatic bone-pain palliation.

060

Radionuclide therapy in patients with painful bone metastases due to prostate carcinoma: efficacy of strontium-89 chloride

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In the past ten years, the incidence of prostate cancer raised up progressively, along with a reduction in the median age of newly diagnosed patients. It is estimated that in Romania prostate cancer represents the second major cause of mortality for cancers in men, after pulmonary cancer. From the earliest stages prostate cancer is associated with reduced quality of life, either as a result of the disease itself or from the side effects of the treatment. In advanced phases of the disease, patients may survive for years with severe pain and serious impaired mobility. There are different etiologies of pain in patients with skeletal metastases; therefore there will be different therapeutic approaches.

Vertebral body collapse, nerve root compression, pathological fractures will need different approach to pain management than skeletal pain related to osteoblastic metastasis and release of pain mediators. This paper will focus to the second situation, in which patients suffer from generalized bone pain due to multiple osteoblastic foci demonstrated on the bone scan. There is no curative treatment of bone metastases at this moment. Existing resources for bone pain palliation consists of several classes of drugs, in a 3 step approach: NSAIDs, weak opioids (e.g. codeine) and strong opioids (such morphine). All of them have significant side effects and all of them lead to significant increase of global costs of managing those patients. For this reason many efforts have been made in order to determine the reduction of analgesic needs and a better control of pain. Localized bone metastases usually can benefit from radiation therapy or surgery, while for widespread disease the preferred method is systemic therapy with bone-seeking agents: biphosphonates or systemic radiopharmaceutical therapy. Several radiopharmaceuticals are now available worldwide for the treatment of painful bone metastases: ^{32}P , ^{153}Sm , ^{89}Sr , ^{186}Re , ^{188}Re , ^{177}Lu , $^{117\text{m}}\text{Sn}$ -Pentetate. The only one available now in Romania is ^{89}Sr (Metastron, Amersham). Phosphorous-32 (^{32}P) is being used to manage bone pain for many years, the most widely used radiotracer until the 1980s. Many studies demonstrated its efficacy and cost-effectiveness, included an IAEA coordinated multinational research. Strontium-89 is a beta-emitting radionuclide that preferably localizes in areas of active bone formation (high osteoblastic activity) The local radiation results in pain relief, probably by suppressing tumor growth or by lowering the production of pain-producing mediators (the exact mechanism is still a subject of debate among researchers) Rhenium-186 HEDP and Samarium-153 EDTMP have a significantly shorter half life than Sr-89 and deliver a higher dose rate. These radiopharmaceuticals have the advantage of emitting gamma photons that allows direct measurement of biodistribution and imaging. Aim To present our experience in the field of local and biological evaluation was repeated at 3 weeks and 3-6 months after treatment. Hematological assessment was performed monthly for all patients. Results: The most important criterion of pain relief was objective pain score. Significant improvement of life quality was seen in 11 (55%) patients with major reduction of analgesic needs. In 5 patients, in addition to external beam radiotherapy we obtained a stable effect of more than 6 months. 5 patients had moderate response, one of them with an early need of a second dose after four months. No response was seen in 2 patients. Pain flare occurred in 14 cases (70%). The most serious side effect was myelosuppression, which occurred in 16 patients (80%); however this depression was mainly mild to moderate with recovery in 3-12 weeks. Discussions: Systemic radionuclide therapy of bone metastasis offers several advantages: 1. It has a proven efficacy, with a high percentage of patients with very good response. This efficacy derives from the fact that systemic therapy always allows a higher absorbed dose than any other modality of radiotherapy, because it is targeted, tumor-specific; 2. Can be administered on an out-patient basis, which may lead to

ABSTRACTS

reducing overall costs of medical care of patients; 3.It is generally well tolerated and repeatable. The major side effect of medullary suppression is temporary and mainly mild to moderate. 4.There are minimal risks to the personnel administering the agent. However, the major disadvantages of this form of therapy, at least in Romania would be: 1.It requires special license from the Nuclear Regulatory Committee; 2.It is very expensive (aprox 1300 Eu/dose); 3.There is no reimbursement. Conclusion: ^{89}Sr is effective for bone pain palliation in metastatic prostate carcinoma. It allows significant improvement of the quality of life with an easy procedure with controllable side effects and a very good compliance of patients.

061

Is radiosynoviorthesis of medium and small joints in patients with rheumatoid arthritis effective?

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Objectives: To point out a treatment asset and to describe our experience with radiosynoviorthesis (RSO) in the therapy of medium and small joints in patients with rheumatoid arthritis (RA). Methods: We included 105 patients treated for RA from 2002 to 2007. An inclusion criterion was joint destruction - Larsen stages II and III. Totally we treated 76 medium joints with 74 MBq ^{186}Re sulfide and 80 small joints with 10-40 MBq ^{169}Er citrate. A treatment effect was evaluated 6 and 12 months after RSO, comparison was done with initial state. A change of inflammation activity was assessed by means of ultrasonography, pain withdrawal, joint swelling, and motion. Statistical processing was accomplished by means of Chi-square test. Results: The best results were reached in pain reduction; the lowest success was noticed in motion modification. In treated joints the best success was observed in shoulders and elbows. The ankles had the least therapeutic answer. It was possible to observe a gradual decrease of therapeutic effect between 6 and 12 months after RSO, especially in pain ($P < 0,05$) and joint swelling ($P < 0,001$). Conclusions: RSO is a suitable treatment alternative of chronic synovitis with low potential of adverse effects, although with transient results.

062

Effect of combined Samarium-153 and adjuvant analgesic therapy for pain palliation in patients with skeletal metastases.

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Background: Systemic therapy with radionuclides is commonly used for the treatment of patients with painful skeletal metastases however complete response is rare. Typical response rate is around 75%. It has been suggested that addition of adjuvant analgesics might improve the response of samarium therapy. AIM: We undertook this study to determine the efficacy and toxicity of the combined therapy as a palliative treatment for painful skeletal metastases. Material and Methods: One hundred twenty

five patients with painful skeletal metastases from various primaries were treated with Sm-153 EDTMP at a dose of 37 MBq/kg. Along with samarium they were put on adjuvant analgesic regime containing pregabalin, mirtazapine, dexamethasone and zoledronic acid in their standard dose adjusted for body weight. The effects were evaluated according to change in eleven-point visual analogue pain score, analgesic consumption, Karnofsky performance score, ECOG score and blood count tests, conducted regularly for 16 weeks. Results: The overall response rates defined by minimum two point reduction in visual analog scale were 98.4%. Complete response was seen in 82.4%. Reduction in analgesic consumption with improvement in Karnofsky performance score was seen in all responders. One case, each of breast cancer, unknown primary did not respond to therapy. No serious side-effects were noted. Common side effects observed were drowsiness, tremor and constipation which disappeared spontaneously without needing any dose adjustment in any patient. Fall in white blood cell, platelet and haemoglobin counts, which, which are typically seen with Samarium therapy was observed in majority of patients with spontaneous recovery over six-eight weeks. Conclusion: Combination therapy of samarium and adjuvant analgesic produces grossly superior pain control with minimal toxicity. Adjuvant analgesics should be added routinely with samarium therapy in patients with skeletal metastasis.

063

The duration of pain free period after Sm-153 EDTPM palliative treatment of skeletal bone metastases in patients with moderately severe bone pain in comparison to the group of patients with severe to intolerable pain.

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Aim: To compare the duration of pain free period after Sm-153 EDTPM treatment in patients with moderately severe bone pain (1st group) and patients with severe to intolerable pain (2nd group). Material and methods: 3 patients in 1st group (all females, mean age 46,33 5.21) with multiple skeletal bone MTS with mean objective pain score according to 10 score system was 5.0 0,58 (Max-6, min-4) before treatment. 6 patients in 2nd group (5 males and 4 females, mean age 58.33 3.77) with mean objective pain score before treatment according to 10 score system was 8,50 0,22 (Max-9, min-8). All patients were examined, treated and followed up from 3 to 15 months. WB bone scan was performed from 7 to 28 days (7,0 3,18; Max - 28, min - 3) To all patients before Sm-153 EDTPM treatment and to 7 four patients 3-14 months after treatment. Sm-153 EDTPM was administered at the standard bone palliation dose of 37 MBq/kg body weight. All patients were continued to receive chemotherapy. Results: In first group of patients pain relief occurred in (4,0 0.57 days, max-5. min 3) and in a second group in (10.67 3,38 days, max-30, min-6) after Sm-153 EDTPM injection. In the first group, all patients had a complete palliative response with pain free duration more than 15 months with Sm-153 EDTPM treatment. In the

second group, patients (50%) had complete palliative response and the other three patients had partial response with mean objective pain score 1,33 0,61, max-3, min-0) and duration of pain reduction (6,33 months 1,69. min 2, max-14 months). Control WB scans in 7 patients from both groups showed decreasing quantity and intensity of bone mets. Conclusion: In patients with moderately severe bone pain, relief occurred earlier with more prolonged pain free period and complete response to Sm-153 EDTPM treatment in comparison to the group of patients with severe to intolerable pain. Although we had a small group of patients, we can expect earlier palliative treatment of bone MTS that will lead to more prolonged pain free period for those with moderately severe bone pain.

064

Possibility of using Tc99m (V) DMSA in assessment to treatment response of patients with gastro- intestinal stromal tumor.

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Introduction: Gastrointestinal stromal tumor (GIST) is the most common of the mesenchymal malignancies that may affect the gastrointestinal tract. The methods of modalities widely used for initial assessment and treatment response are CT and PET/CT. On CT images traditional anatomic tumor response criteria are based on tumor size and density, however fibrotic tissue secondary to therapy may give the same image pattern as a non- or partially responding mass, and lymph nodes which are not increased in size usually are considered as a normal, while PET/CT reflecting the metabolism of tumor cells. The role of PET/CT in assessment of treatment response is established as the most effective. In many developing countries there is a limitation or absence of PET/CT technology and using SPECT technology is one of the options. Tc99m (V) DMSA is a tumor-imaging agent, which has been used to evaluate medullary thyroid cancer and soft tissue tumors. It is a marker of phosphate metabolism and as such provides additional information on the pentose phosphate pathway and also on tumour proliferative activity, in same way fluorine-18 fluorodeoxyglucose in relation to the glycolytic pathway. Aim: To find out if Tc99m (V) DMSA could be useful tumor imaging agent for assessment and follow up of patients with GIST. Material and Methods: Patient R, male, 34 years old with GIST, liver metastases and lymphatic metastases to peritoneum, retro peritoneum complicated by ascites, Right side pleuritis and severe anemia (40gr/L). CT was done before treatment, 3 months after initial treatment (Glivec 400 mg daily) and 1,5 months after combined treatment (Glivec 400 mg daily and Avastin 500 mg every 21 days) WB scan, static images and SPECT of chest and abdomen were performed 2 hours after intravenous injection of 10 mCi Tc99m (V) DMSA, at 3 months after unsuccessful treatment by Glivec and 1,5 month after patient started to receive combined therapy Glivec and Avastin. Results: According to CT images there is significant progression of disease at 3 months after initial treatment with tumor mass in projection of stomach and

duodenum, multiple liver mets sized from 0,6 to 4,8 cm, multiple peritoneal, retroperitoneal lymph metastases, ascites and right pleuritis. CT images obtained after combined treatment show a decrease in size (0,4 to 4 cm) of liver metastases, no pleuritis, no ascites but multiple peritoneal, retroperitoneal lymph nodules and tumor mass without changes. Clinically quality of patient's life is increased, Hb rose from 40 to 110gr/L On the first WB, static and SPECT imaging with Tc99m (V)DMSA there are multiple areas of increased tracer uptake in projection of epi- and paragastrum, liver, spleen, peritoneum, retroperitoneum and mediastinum. On images after combined therapy there are multiple "cold" areas in projection of liver and spleen reflecting the presence of fibrotic tissue as a response to therapy, significant decrease of the number of "hot" areas in projection of mediastinum, peri- and retroperitoneum and decreasing tracer uptake in epi- and paragastrum. . Conclusion: Tc99m (V) DMSA demonstrated early response to treatment of a patient with GIST in comparison to CT images. Further investigations are required. This example shows that in areas where there is no or limited access to PET/CT for monitoring therapy response in GIST, conventional scintigraphy together with SPECT, using other (specific) radiopharmaceuticals, like Tc99m (V) DMSA, may be a viable option.

065

Bone pain from osteoblastic metastases

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Bone pain from osteoblastic metastases can be ameliorated 40% to 80% of the time. Although we can predict nonresponders, we cannot predict responders; however, patients with a better performance scale may have a better chance of pain relief. Radiopharmaceuticals containing phosphorus 32, strontium 89, samarium 153, rhenium 186, and tin 117m are effective, but we do not know which is the most efficacious and the safest. Toxicity includes the flare phenomenon and mild to moderate pancytopenia, but disseminated intravascular coagulation can cause severe, life-threatening thrombocytopenia. This treatment may be repeated at about 9- to 12-week intervals, perhaps earlier with 153Sm leixidronam, 186Re etidronate, and 117mSn pentetate, with a success rate approaching that of the initial injection. The duration of action of pain reduction ranges from 2 weeks to many months. Tumoural effects are probably not the only mechanism of pain relief.