52 ORAL

D-lysine for reduction of renal [In-111-DTPA,D-Phe-1]-octreotide and [Y-90-DOTA,D-Phe-1,Tyr-3]octreotide uptake

Marion de Jong[1], Bert Bernard[1], Wout Breeman[1], Willem Bakker[1], Theo Visser[1], Helmut Mäcke[2], Eric Krenning[1]. [1]*Dept of Nuclear Medicine, University Hospital Dijkzigt, Rotterdam, The Netherlands;* [2]*Dept of Nuclear Medicine, Kantonspital Basel, Basel, Switzerland*

In-111-DTPA-octreotide (In-111-DTPAOC), successfully used to image somatostatin receptor-positive lesions, is now applied for peptide-receptor-radionuclide therapy (PRRT). For the latter purpose [DOTA,D-Phe-1,Tyr-3]octreotide (DOTATOC), suitable for stable radiolabelling with Y-90, is even more promising. However, significant renal (re-)uptake and retention of these analogues exists, reducing the detection sensitivity of perirenal tumours and increasing radiotoxicity in the kidney during PRRT. We studied the inhibitory effects of D- and L-lysine on kidney uptake of In-111-DTPAOC and Y-90-DOTATOC.

Methods: Wistar rats were given In-111-DTPAOC (0.2 MBq, 0.5 μg–0.5 mg; iv, ip or orally) or Y-90-DOTATOC (1 MBq, 0.5 μg; iv), with or without D- or L-lysine. At several time points, organs were isolated and counted.

Results: D- or L-lysine, iv, 400 mg/kg, resulted in >50% inhibition of kidney In-111-DTPAOC uptake. Higher or repeated doses of lysine did not increase inhibition. Oral and ip administration of lysine was less effective. However, after L-lysine also uptake of In-111-DTPAOC in target organs was decreased. D-lysine did not have this negative effect. Renal uptake of Y-90-DOTATOC was reduced by 65% by D-lysine iv; uptake in target organs was unaffected.

Conclusion: D- and L-lysine are promising for reduction of nephroradiotoxic effects during PRRT by preventing tubular re-uptake of the radiolabel. This method may be useful in other nephrotoxic modalities as well. D-lysine is preferred to obtain maximal radioactivity in the tumour.

53 ORAL

Randomised controlled trial of supportive care in radical pelvic radiotherapy: Does it influence radiation morbidity?

S. Faithfull[1], D.P. Dearnaley[2], R.A. Huddart[2]. [1]*Centre for Cancer and palliative Care Studies, Institute of Cancer Research;* [2]*Academic radiotherapy, Royal Marsden NHS Trust, UK*

Purpose: This study evaluates the effect of a patient focused approach led by a nurse specialist vs. conventional management. The hypothesis is that supportive care could prevent and minimise the impact of radiation induced side-effects.

Methods: This study is designed as a randomised controlled clinical trial with a sample of 115 men who have undergone radical pelvic radiotherapy (64Gy) for prostate (n = 95) or bladder cancer (n = 20). Data for each patient was collected during radiotherapy and in a 5 month follow up period from entering the study; patients completed EORTC QL30 and self report visual analogue scale of symptoms, satisfaction with care and economic costs.

Results: Initial analysis suggests a reduction in bladder ($p = 0.04$) and bowel morbidity ($p = 0.01$) in the early part of radiotherapy treatment and better emotional functioning at 6 weeks ($p = 0.04$) in the intervention group. This resulted in improvement of global quality of life scores ($p = 0.02$), although some of these advantages are lost by 12 weeks.

Conclusion: These results suggest that that non pharmacological management of symptoms was effective in reducing symptoms and in improving quality of life of patients during radiotherapy. This study identifies the value of nurse specialist care, within a multidisciplinary team, not only economically but also for patients quality of life.

54 ORAL

Post radiation severe xerostomia relieved by pilocarpine: A prospective French cooperative study

J.C. Horiot, F. Lipinski, S. Schraub, C. Maylin, R.J. Bensadoun, J.M. Ardiet, M. Bolla, Y. Coscas, F. Baillet, B. Coche-Dequéant, M. Urbajtel, X. Montbarbon, S. Bourdin, P. Wibault, F. Pene, M. Alfonsi, G. Calais, P. Desprez, M. Lapeyre, J. Vinke, M. Labart, J. Savary. *Centre G.F. Leclerc, Radiotherapy, B.P. 1544, 21034 Dijon, France*

From June 1995 to February 1996, 156 patients (pts) with severe radiation induced xerostomia received Pilocarpine hydrochloride orally, 15 mg per day with a 5 mg optional increase at 5 weeks up to a daily dose of 25 mg beyond 9 weeks. The aim of the study was 1) to confirm the action of the drug against xerostomia, 2) to correlate the response to dose/volume radiotherapy parameters. 145 patients are fully evaluable. Treatment compliance was 75%. 38 pts (26%) stopped treatment before week 12 for acute intolerance (sweating, nausea, vomiting) or no response. No severe complication occurred. 97 pts (67%) reported a significant relief of symptoms of xerostomia at 12 weeks. Within 12 weeks, the size of the subgroup with normal food intake almost doubled (13 to 24 pts) while the size of the subgroup with (nearly) impossible solid food ingestion decreased by 38% (47 vs 29 pts). The impact on quality of life was considered important or very important by 77% of the responders. No difference was found according to dose/volume radiotherapy parameters suggesting that oral Pilocarpine hydrochloride 1) acts primarily by stimulating ectopic salivary glands, 2) can be of benefit to pts suffering of severe xerostomia regardless of radiotherapy dose/volume parameters. 3) All responders are identified at 12 weeks.

55 ORAL

A phase III randomised study of carboplatin and amifostine (A) vs carboplatin and G-CSF in patients with inoperable non small cell lung cancer (NSCLC)

H. Anderson[1], V. Mercer[1], L. Russell[2], N. Habboubi[2], N. Thatcher[1]. [1]*Christie and Wythenshawe Hospitals, Manchester;* [2]*US Bioscience, Croxley Green, UK*

Purpose: Amifostine is an organic thiophosphate which protects normal tissues from the effects of chemotherapy. This study is designed to compare the haematological toxicity seen when either A or G-CSF is given to patients with advanced NSCLC treated with carboplatin at a dose of AUC 9.

Methods: Patients are randomised to receive carboplatin AUC 9 with either A 740 mg/m^2 pre and 2 hours post carboplatin or G-CSF (263 μg/day) from days 2–15. Treatment is repeated every 28 days. 20 patients are currently evaluable for haematological toxicity, 9 with G-CSF and 11 with A.

Results: Of those patients treated with G-CSF, 4 have developed Grade 3 and 5 have developed Grade 4 thrombocytopenia. The dose of carboplatin has been reduced in 5 patients and 3 patients have required platelet transfusions. In contrast, only 2 patients receiving A have developed grade 3 and no patients have developed grade 4 thrombocytopenia. There has been 1 dose reduction and no platelet transfusions administered. No patients have developed grade 4 neutropenia. The response rate and survival are preliminary at this stage but there is no evidence of reduced antitumour activity with A.

Conclusion: The data suggest that amifostine protects against both neutropenia and thrombocytopenia whereas G-CSF protects against neutropenia alone.

56 ORAL

Amifostine protects against acute cisplatin/ifosfamide-induced kidney damage assessed by measurement of glomerular and tubular enzymes

C. Bokemeyer[1], J.T. Hartmann[1], L. Fels[2], S. Knop[1], H. Stolte[2], L. Kanz[1]. [1]*Dep Hematology/Oncology, Eberhard-Karls-University Medical Center II, 72076 Tübingen,* [2]*Dep of Experimental Nephrology, Hannover University Medical School, Hannover, Germany*

Purpose: This study evaluates the degree of kidney damage during cisplatin (P)/ifosfamide (IFO)-combination chemotherapy (CTX) and its possible prevention by amifostine (AMI) using an established model for the quantification of urinary markers.

Patients and Methods: 26 pts with solid tumours stratified according to pretreatment who received VIP- or TIP-regimen containing P (50 mg/m^2, d1 over 1 h) and IFO (4 g/m, d1 over 16 h) were randomized to VIP/TIP+G-CSF alone or with AMI 910 mg/m^2 given as a short infusion prior to CTX. For all pts creatinine-clearance (Cc), serum creatinine and electrolytes including magnesium (Mg) were determined prior to and after each cycle. Differential urinary protein and enzyme excretion was measured at days 0, 3 and 5 after CTX. High molecular weight proteins (HMW) were used to target the glomerular, low molecular weight proteins (LMW) and N-acetyl-D-glucosaminidase (NAG) excretion to detect proximal tubular damage.

Results: 26 pts were evaluable (14 with AMI and 11 controls) for urinary markers and 30 pts for Cc and Mg values. AMI prevented a significant reduction in Cc after application of 2 cycles of P/IFO-based CTX and reduced the excretion of tubular markers (LMW, NAG) by appr. 50% (day 5) as compared to controls ($p < 0.05$). The degree of prevention was more pronounced with every cycle of CTX. Cc was 121 ml/min (65–159) prior to and 126 ml/min (80–162) after CTX in the AMI-group, whereas in the