intermediate doses of radioactivity are suitable for these relatively slow-growing tumors ("long-term low dose, not short term high dose concept"). After each 2 treatment cycles, restaging is performed by morphologic (CT/MRI) and molecular imaging (Ga-68 SSTR PET/CT), blood chemistry and tumor markers. All data are entered in a prospective structured database (over 250 items per patient).

**NET Center Bad Berka - Results**

Retrospective analysis was performed in 1000 patients (age 4 - 85 years) with metastatic and / or progressive NETs, undergoing 1 - 9 cycles of PRRT at our center using Lu-177 (n=331), Y-90 (n=170) or both (n=499). Median total administered activity was 17.5 GBq. Patients were followed up for up to the first 1 cycle of PRRT. Well-differentiated NETs (G1-2) accounted for 54 %. Most patients (95.6 %) had undergone at least 1 previous therapy (surgery 86.8 %, medical therapy 55 %, ablative therapy 14.2 % and radiotherapy 3.4 %). The median overall survival (OS) of all patients from the start of PRRT was 52 months (mo). Median OS according to radionuclide used: Y-90 24 mo, Lu-177 55 mo, both (TANDEM or DUO PRRT) 64 mo; according to the grade of tumor: G1 87 mo, G2 55 mo, G3 28 mo, unknown 50 mo; and according to origin of primary tumors: pancreas 45 mo, small intestine 77 mo, unknown primary 55 mo, lung 36 mo. Median OS of progression-free survival of smaller metastases in the last therapy cycle was 22 mo, comparable for pancreatic (23 mo) and small intestinal (25 mo) NETs. The use of a combination of Lu-177 and Y-90 takes this heterogeneity into account. Sequential administration of Y-90 and Lu-177 labeled analogues is useful for the treatment of larger tumors and allows the treatment of smaller metastases respectively in further treatment cycles. Conclusions PRRT lends a significant benefit in progression free survival as well as in overall survival in metastasized and / or progressive G1-2 NETs as compared to other treatment modalities and regardless of previous therapies. Combination of Lu-177 and Y-90 (DUO) based PRRT may be more effective than either radionuclide alone. Up to 10 cycles of PRRT, given over several years were tolerated very well by most patients. Severe renal toxicity can be completely avoided or reduced by nephroprotection applying aminocids; haematological toxicity is usually mild to moderate (except for MDS which occurs in approx. 3-5% of all patients treated). Quality of life can be significantly improved. PRRT should only be performed at specialized centers as NET patients need highly individualized interdisciplinary treatment and long term care.

**NETTER-1 is the first Phase III multicentric, randomized, controlled trial evaluating Lu-177 (Lutathera®) in patients with inoperable, progressive, somatostatin receptor positive midgut NETs.** 230 patients with Grade 1-2 metastatic midgut NETs were randomized to receive Lutathera 7.4 GBq every 8 weeks (x4 administrations) versus Octreotide LAR 60 mg every 4-weeks. The primary endpoint was PFS per RECIST 1.1 criteria, with objective tumor assessment performed by an independent reading center every 12 weeks. Secondary objectives included objective response rate, overall survival, toxicity, and health-related quality of life. Enrollment was completed in February 2015, with a target of 230 patients randomized (1:1) in 35 European and 15 sites in the United States. At the time of statistical analysis, the number of centrally confirmed disease progressions or deaths was 23 in the Lutathera group and 67 in the Octreotide LAR 60 mg group. The median PFS was not reached for Lutathera and was 8.4 months with 60 mg Octreotide LAR [95% CI: 5.8-11.0 months], p<0.0001, with a hazard ratio of 0.21 [95% CI: 0.13-0.34].

Within the current evaluable patient dataset for tumor responses (n=201), the number of CR/PR was 18 (18%) in the Lutathera group and 3 (3.0%) in the Octreotide LAR 60 mg group (p=0.0008). Although the OS data are not mature enough for a definitive analysis, the number of deaths was 13 in the Lutathera group and 22 in the Octreotide LAR 60 mg group (p=0.019 at interim analysis) which suggests an improvement in overall survival. The Phase III NETTER-1 trial provides evidence for a clinically meaningful and statistically significant increase in PFS and ORR, and also suggests a survival benefit in patients with advanced midgut NETs treated with Lutathera.

---

**Teaching Lecture: Radiotherapy for paediatric brain tumours**

**SP-0571 Radiotherapy for paediatric brain tumours**

R.D. Kortmann
1University of Leipzig, Radiation Therapy, Leipzig, Germany

**Introduction**

Radiation therapy is an integral component in the management of childhood CNS malignancies. Although high cure rates can be achieved, detrimental long term side effects often hamper the functional outcome.

**Technologies**

Stereotactic conformal radiation therapy, IMRT, tomodotherapy, image-guided radiation therapy and proton therapy are increasingly used to provide an excellent coverage of the target. Modimodality imaging such as MRI, PET and spectroscopy are implemented in treatment planning and allow for an exact definition and delineation of the target and organs at risk. Novel fractionation schedules exploit the radiobiological measured and excellent dose homogeneity throughout the target volume. Especially proton therapy has the ability to decrease the dose exposure to whole body and surrounding normal tissue thereby reducing the risk of acute and late effects. The major developments in radiation therapy of pediatric tumours are aimed to individually tailor radiation therapy to the target especially in irradiation of the tumours site such as ependymoma, low grade glioma. With the increasing complexity of radiation techniques in the treatment of CNS malignancies formalised systems and comprehensive quality assurance programmes were introduced to provide an optimal and reproducible treatment on a high quality level. To reduce late effects RT parameters can be modified by the investigation of novel radiotherapy dose prescriptions and reducing dose exposure to neighbouring normal tissue with a maximal sparing of normal brain. The introduction of models to predict the impact of radiotherapy dose volume parameters on long-term neuropsychological function will help to further reduce the risk for late effects.

**Conclusion**

The rapid developments and small patient numbers as well as the lack of appropriate measurement instruments and difficult endpoints like quality of survival preclude the necessity to investigate the role of these new technologies within prospective randomised trials. Paediatric oncologists should therefore not refrain from including new technologies in their prospective trials as part of treatment standards. A detailed assessment of the long-term benefits and side effects is however necessary to define their precise role in the management of childhood CNS malignancies.

**Teaching Lecture: Role and validation of deformable image registration in clinical practice**

**SP-0572 Role and validation of deformable image registration in clinical practice**

M. van Herk1,2
1University of Manchester, Manchester Academic Health Science Centre, Manchester, United Kingdom
2The Christie NHS Foundation Trust, Medical Physics, Manchester, United Kingdom

Image registration is the process of finding the transformation between two image sets. It is used widely in...