recommendations, yet tuned to the national context and the economic specificities of the country.
The first work-packages of the HERO project have objectivized a large variation within European countries in resource availability and in actual needs for radiotherapy provision, related to the national cancer incidence. It also showed a remarkable lack of guidance for radiotherapy planning, with national recommendations mostly duplicating the available recommendations from international organizations or projects, without any attempt to streamline them to the needs of the individual country.
Due to the growing awareness of resource limitations and tightening budgets, the weighing of costs and outcomes as performed in economic evaluations have become an integral part of the health resource allocation processes in many countries. Whereas cost-effectiveness data are typically required prior to the introduction of new drugs, they gradually also become more frequently requested to support radiotherapy financing. In order to make valid recommendations, the economic evaluations should however mimic the actual clinical and economic situation of the specific country. Yet, cost-effectiveness data from one country are not necessarily representative for another.
The next step within the HERO-project is to develop a costing model that provides accurate radiotherapy resource cost data, based on the available resources, the cancer epidemiology and the radiotherapy practice of individual European countries. Time-driven activity-based costing, a cost-accounting method specifically developed to capture product complexity and variability, is highly suitable for that purpose. A final step will be to evaluate how these cost data can be combined with effectiveness data – derived from international studies but applicable to a country-specific environment – in an adaptable economic evaluation model, relevant for individual countries in the heterogeneous European context.

SP-0395

The equity gap in access to radiotherapy in the world. How do we close the divide?

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Abstract not received.

Proffered Papers: Radiobiology 3: Genetic predictors of tumour response

OC-0396

Identification of a microRNA signature associated with risk of distant metastasis in nasopharyngeal carcinoma

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Purpose/Objective: Despite significant improvement in locoregional control in the contemporary era of nasopharyngeal carcinoma (NPC) management, patients still suffer from a significant risk of distant metastasis (DM). Identifying those patients at risk of DM would aid in personalized treatment in the future. MicroRNAs (miRNAs) play many important roles in human cancers; hence, we proceeded to address the primary hypothesis that there is a miRNA expression signature capable of predicting DM for NPC patients.
Materials and Methods: The expression of 734 miRNAs was measured in 125 (Training Set) and 121 (Validation Set) clinically annotated NPC diagnostic biopsy samples.
Results: A 4-miRNA expression signature associated with risk of DM was generated by fitting a penalized Cox Proportion Hazard regression model to the Training data set (HR 8.25; $p<0.001$). This signature was subsequently tested in the Validation set, and maintained a significant relationship with DM (HR 3.2; $p=0.01$). In addition, multivariate analysis determined that this 4-miRNA signature was the strongest independent predictor when clinical factors were included. Finally, pathway enrichment analysis indicated that targets of the miRNAs comprising the final signature appear to be converging on cell cycle regulation.
Conclusions: This 4-miRNA signature adds to the prognostic value of the current 'gold standard' of TNM staging. In-depth interrogation of these 4-miRNAs will provide important biological insights that could facilitate the discovery and development of novel molecularly targeted therapies to improve outcome for future NPC patients.

OC-0397

A LAMP3 single nucleotide polymorphism associated with poor prognosis in breast cancer

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Purpose/Objective: Lysosome-associated membrane protein (LAMP)-3 is regulated by the unfolded protein response pathway. Our preclinical data suggest that LAMP3 plays an important role in autophagy induction during the response of breast cancer cells to various treatments and stress factors. We have shown that radiation therapy (RT), tamoxifen and hypoxia can induce *LAMP3* and that high expression of *LAMP3* is associated with resistance to RT and tamoxifen in breast cancer cells. Moreover, patients with high levels of *LAMP3* mRNA had more locoregional recurrences. Here, we investigate the occurrence and clinical associations of a frequent non-synonymous single nucleotide polymorphism (SNP) in the *LAMP3* gene (rs482912, Ile318Val) in 626 breast cancer patients.
Materials and Methods: A custom TaqManÒ SNP Genotyping Assay targeted to our SNP of interest (rs482912) was used to assess its occurrence in breast cancer patients. We analysed the SNP's association with several clinical factors by Pearson Chi-square tests, and performed Kaplan-Meier survival and Cox regression analyses to investigate a relation with locoregional control.
Results: In our cohort, the minor allele frequency for the *LAMP3* rs482912SNP was 0.718, which is similar to the frequency in the European population. The SNP was not associated with menopausal status, type of operation, use of

RT, histological grade, tumour size or nodal stage. However, patients carrying the LAMP3 rs482912 SNP either homozygously (n=323) or heterozygously (n=253) had fewer locoregional recurrences than those carrying the reference allele (n=50, Hazard Ratio (HR) = 0.389, 95% Confidence Interval (CI) = 0.196-0.771, *P* = .007) (figure). This prognostic value was limited to patients treated with breast-conserving therapy including RT (HR = 0.265, CI = 0.104-0.674, *P* = .005), which is in line with a role for LAMP3 in radiosensitivity. Furthermore, the LAMP3 SNP was only prognostic in grade III tumours (HR = 0.270, *P* = .005), tumours larger than 2 cm (HR = 0.357, *P* = .011), and in patients with involved lymph nodes (HR = 0.154, *P* < .001).

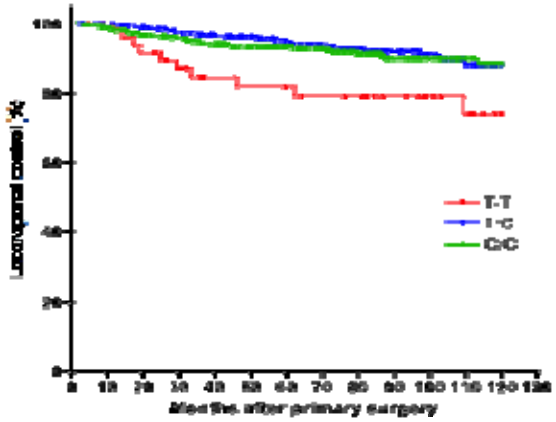

Figure: Breast cancer patients that carry the LAMP3 rs482912 SNP allele (C) either homozygously or heterozygously have better locoregional control (P = .007).

Conclusions: The *LAMP3* rs482912 SNP is associated with locoregional control in a cohort of 626 breast cancer patients. This is specifically the case after RT as part of breast conserving treatment and for patients with more advanced or aggressive tumours.

OC-0398

HSPB1 rs2868370 predicts risk of relapse in patients with lung cancer treated with radio(chemo)therapy

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Purpose/Objective: The incidence of relapse of locally advanced lung cancer after treatment with radio(chemo) therapy is still high. The significance of biologic markers such as heat shock protein (HSPB1) for predicting recurrence has been increasingly emphasized by recent investigations. We investigated prospectively the association between single nucleotide polymorphisms (SNPs) in the HSPB1 gene and the risk of relapse in patients with lung cancer.
Materials and Methods: The data set consist of 156 lung cancer patients with available genomic DNA samples and treated with radio(chemo)therapy from January 2013 to September 2014. Median age was 63 years-old (range, 37-89) and the Karnofsky performance status was ≥70 except for 6 cases. The most common histology for non-small cell lung cancer patients (79%) was squamous cell carcinoma (65%). Seventythree percent of patients had Stage III disease, 92.3% received platinum-based chemotherapy, and received doses between 39 Gy and 70 Gy (median, 63 Gy). We genotyped three SNPs of the HSPB1 gene (rs2868370, rs2868371, and rs7459185) by the TaqMan assays. Cox proportional hazards analysis was performed to calculate the hazard ratio (HR) and confidence interval (CI) of each genotype on relapse risk. Multivariate analyses were performed using a logistic regression model, with a stepwise backward elimination procedure. A P value of 0.05 or less was considered statistically significant.
Results: The distribution of the HSPB1 genotype was: rs2868370, 65% GG, 32% AG, 3% AA; rs2868371, 77% CC, 18% CG, 5% GG; rs7459185, 51% GG, 39% CG, 10% GG).The incidence of relapse was 31% (24% locoregional and distant, 18% only locoregional, and 58% only distant). In univariate analysis, CG/GG genotypes of HSPB1 rs2868371 were associated with a statistically significantly lower risk of any relapse (HR = 0.47; 95% CI, 0.23 to 0.97; p = 0.042) and distant recurrence (HR = 0.40; 95% CI, 0.17-0.93; p = 0.033) compared with the CC genotype. In addition, AG/AA genotypes of HSPB1 rs2868370 were associated with a statistically significantly higher risk of distant relapse (HR = 2.19; 95% CI, 1.11 to 4.35; p = 0.024) compared with the GG genotype. In multivariate analysis, only the rs2868370 SNP retained significance (HR = 2.47; p = 0.010).
Conclusions: Our results showed that the AG/GG genotypes of HSPB1 rs2868370 gene were associated with a higher risk of distant relapse in patients with lung cancer treated with radio(chemo)therapy and thus may serve as a reliable predictor of recurrence. This response marker may be used for guiding therapy intensity or as a selection criteria for a clinical trial in an individual patient, which would further the goal of individualized therapy.

OC-0399

The clinical impact of hypoxia-regulated gene expression in loco-regional gastroesophageal cancer

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Purpose/Objective: In a former study (1), the hypoxia gene expression classifier, developed in head and neck squamous cell carcinomas, was applied in 89 patients with loco-regional gastroesophageal cancer (GC). Analysis of the 15 genes was indicative of hypoxia being more profound in esophagus squamous cell carcinomas (ESCC) compared with adenocarcinomas of the esophago-gastric junction and the stomach (AC), and was a potential prognostic marker in patients with ESCC. The purpose of the present study was to confirm these results.
Materials and Methods: The study population consisted of 152 patients with GC treated with neoadjuvant or definitive chemoradiotherapy or perioperative chemotherapy. Based on formalin-fixed, paraffin-embedded, diagnostic biopsies, gene expression of the 15 hypoxia-induced and pH-independent genes was obtained with qPCR. Sufficient amounts of RNA for gene analyses were available in 135 patients; ESCC: 89