detection of the high relevance of IDH1 mutation, it remains to be determined which phenotypic alterations are driving its prognostic value.

OC-0323 Serum microRNAs as xerostomia biomarkers in oropharyngeal cancer patients undergoing radiotherapy

B. Tomasik[1,2,3], A. Papis-Ubych[4], J. Fijuth[3], P. Kędzierawski[5], J. Sadowski[5], R. Stando[5], R. Bibik[6], Ł. Graczyk[6], T. Latusek[7], T. Rutkowski[8], P. Widłak[9], W. Fendler[1,10]

[1]Medical University of Lodz, Department of Biostatistics and Translational Medicine, Lodz, Poland ; [2]Medical University of Warsaw, Postgraduate School of Molecular Medicine, Warsaw, Poland ; [3]Medical University of Lodz, Department of Radiotherapy, Lodz, Poland ; [4]N. Copernicus Memorial Regional Specialist Hospital, Department of Radiotherapy, Lodz, Poland ; [5]Holycross Cancer Centre, Radiotherapy Department, Kielce, Poland ; [6]Oncology Center of Radom, Department of Radiation Oncology, Radom, Poland ; [7]Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology - branch in Gliwice, Radiotherapy Department, Gliwice, Poland ; [8]Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology - branch in Gliwice, I Radiotherapy and Chemotherapy Clinic, Gliwice, Poland ; [9]Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology - branch in Gliwice, Center for Translational Research and Molecular Biology of Cancer, Gliwice, Poland ; [10]Dana-Farber Cancer Institute, Department of Radiation Oncology, Boston, USA

Purpose or Objective

Severe xerostomia is noted in up to 75% of patients irradiated for oropharyngeal cancer (OPC). Currently, we do not possess effective tools for measuring radiation sensitivity that would allow tailored therapy. Preliminary literature reports indicate that extracellular microRNAs (miRNAs) may be a new class of biomarkers that will pave the way for further personalization of radiotherapy (RT). Hence, the aim of this study was to analyze temporal changes in expression levels of miRNAs circulating in the serum and to create an efficient test for patient-rated xerostomia 3 months after primary treatment with IMRT with or without chemotherapy for OPC.

Material and Methods

The study was designed as a prospective cohort study that enrolled OPC patients treated with IMRT (total dose of 70 Gy or equivalent) from June 2016 to December 2018 in four oncological centers in Poland. One hundred fifty-two patients with OPC diagnosis were assessed for eligibility and 111 patients were finally qualified for the study. Side effects were prospectively assessed using EORTC QLQ-C30 and EORTC H&N-35 questionnaires. We randomly selected a group of 10 patients with severe (grade ≥3) xerostomia and matched a comparative group of 10 patients without severe xerostomia. We collected serum samples before RT, after receiving 20 Gy and within 24 hours after the end of the treatment. qPCR arrays (miRCURY LNA, Human panels I II, Exiqon, Copenhagen, Denmark) were used to quantify miRNA expression levels. Data were normalized toward the average expression of miRNAs detectable in all samples. MiRNAs were shortlisted on the basis of univariate, Benjamini-Hochberg adjusted, p values. The classifier for xerostomia was created using a stepwise, 5-fold cross-validated, logistic regression model. The results were validated in a group of 60 patients (30 patients with grade ≥3 xerostomia and 30 patients without severe xerostomia).

Results

Severe xerostomia 3 months after the end of RT was reported by 63 patients (56.8%). The model based on miR-185-5p and miR-425-5p expression levels measured before the start of RT had a very good discriminatory ability - AUC 0.96 (95% CI: 0.88-1.00). The model based on the expression of the same miRNAs maintained a very high discriminatory power when parameters were measured after 20 Gy (AUC 0.90 (95% CI: 0.75-1.00)). Changes in the expression levels of miR-185-5p and miR-425-5p in the samples from the validation group were also confirmed to be significant. The model based on the expression levels of these two miRNAs measured before radiotherapy was characterized by an AUC 0.80 (95% CI: 0.70 -0.91). In samples taken after 20 Gy, the use of expression levels of these two miRNAs resulted in AUC 0.83 (95% CI: 0.73-0.94).

Conclusion

The expression levels of miR-425-5p and miR-185-5p measured in the serum of patients with OPC before the start of RT and during therapy (after 20 Gy) have a significant prognostic value for the occurrence of severe xerostomia 90 days after the end of RT.

OC-0324 Prefoldin overexpression associates with the risk of mortality and metastasis in lung cancer

P. Romero Pareja[1], S. Chávez de Diego[2], X. Peñate[2], J. Reyes[3], B. Vieites[4], M. Borrego[1], S. Perez[1], J. Jaen Olasolo[5], B.D. Delgado[1], J.M. Praena Fernández[6], J.L. Lopez Guerra[1]

[1]Virgen del Rocio University Hospital, Radiation Oncology, Sevilla, Spain ; [2]Universidad de Sevilla-CSIC-Hospital Universitario V. del Rocio, Instituto de Biomedicina de Sevilla, Sevilla, Spain ; [3]Junta de Andalucia-University of Pablo de Olavide-University of Seville-C, Andalusian Center of Molecular Biology and Regenerative Medicine-CABIMER, Sevilla, Spain ; [4]Virgen del Rocio University Hospital, Pathology, Sevilla, Spain ; [5]University Hospital Puerta del Mar, Radiation Oncology, Cadiz, Spain ; [6]Universidad de Sevilla, Nursing, Sevilla, Spain

Purpose or Objective

Prefoldin (*PFDN*) is a co-chaperone that contributes to both cytoplasmic and nuclear biological processes. Canonical *PFDN* has a heterohexameric jellyfish-like structure. Four ß-type subunits (*PFDN1, 2, 4* and *6*) form two dimers onto two subunits of the α type (*PFDN3* and *5*). *PFDN2* and *6* are also components of the URI-prefoldin-like complex, which has been described to promote cancer. It has been shown that *PFDN1* overexpresion promotes epithelial-mesenchymal transition (EMT) and lung cancer (LC) progression in different LC cell lines and murine models whereas cyclin A knockdown alone induces EMT and increases cell migration and invasion ability. We investigated whether this putative involvement of canonical *PFDN* in LC translates into the clinic.

Material and Methods

58 non-small cell LC patients with available tumor tissue samples (59% squamous and 41% adenocarcinoma) were assessed. The stages were as follows: 24% I, 7% II, 61% III, and 8% IV. 90% of patients were primarily treated with surgery and 69% received chemotherapy. 86% underwent thoracic radiotherapy either primarily (41%) or after locorregional recurrence (45%). The levels of *PFDN1, 3, 5* were examined by immunoblotting. Additionally, the mRNA expression of 518 LC cases from The Cancer Genome Atlas (TCGA) database was evaluated. To assess the risk of mortality and recurrences we used Kaplan-Meier and Cox proportional hazards analyses.

Results

PFDN1, 3, 5 and cyclin A overexpression (+++) were found in 22 (38%), 31 (53%), 24 (41%), and 14 (24%) tumor samples. After a follow up of 40 months, 39 (67%) patients were alive and 34 (58%) had experienced a recurrence (24 were distant metastasis). Body surface area and stage associated with overall survival (OS; p=0.01 and p=0.036, respectively), disease-free survival (DFS; p=0.033 and p=0.038, respectively), and distant metastasis-free survival (DMFS; p=0.002 and p=0.025, respectively) in the univariate analysis. In addition, the use of radiotherapy and chemotherapy also associated with DMFS (p=0.005 and p=0.015, respectively). *PFDN1, 3* and *5* overexpression were associated with lower OS (p=0.002, p=0.015, and p=0.002, respectively), lower DFS (p=0.01, p=0.042, and p=0.055, respectively), and lower DMFS (p=0.011, p=0.036, and p=0.11, respectively). There was not any association with local recurrence. In the multivariate analysis, the *PFDN5* retained significance for OS (HR 5.09; p=0.007) and the *PFDN1* for DFS (HR 5.15; p=0.01) and DMFS (HR 5.45; p=0.05). In the TCGA adenocarcinoma cohort, there was a high correlation between *PFDN1* and *5* (Pearson coefficient: 0.53; p <0.0001), a high mRNA expression of *PFDN3* in the tumor compare with the normal tissue (p <0.0001), and *PFDN1* overexpression showed lower OS (p=0.034).

Conclusion

Overexpression of canonical PFDN associates with the risk of mortality and metastasis in non-small cell LC. These response markers may be usefull biomarkers for guiding therapy intensity in an individualized therapy.

Proffered Papers: Proffered papers 16: Breast

OC-0325 Postmastectomy RT in high-risk breast cancer. A 30-year update of the DBCG 82bc randomized trial.

M. Overgaard[1], H. Melgaard Nielsen[2], T. Tramm[3], I. Højris[2], T. Grantzau[4], J. Alsner[1], B.V. Offersen[1], J. Overgaard[1]

[1]Aarhus University Hospital, Department of Experimental Clinical Oncology, Aarhus N, Denmark ; [2]Aarhus University Hospital, Department of Oncology, Aarhus N, Denmark ; [3]Aarhus University Hospital, Department of Pathology, Aarhus N, Denmark ; [4]Rigshospitalet, Department of Pathology, Copenhagen, Denmark

Purpose or Objective

Almost at the same time as the first ordinary ESTRO meeting in London 1982, did the Danish Breast Cancer Group (DBCG) include the first patient in what became the World largest randomized trial to evaluate the role of postmastectomy irradiation to high-risk pre- and postmenopausal (<70 years) breast cancer patients who also received adjuvant systemic therapy alone. The initial results were published in NEJM (1997) and Lancet (1999). We hereby present 30-year long-term follow-up of the cancer therapeutic effect as well as a focus on the potential late cardiac and secondary cancer risk.

Material and Methods

Between 1982 and 1990, a total of 3,083 patients with pathological stage II and stage III breast cancer were after mastectomy randomly assigned to receive adjuvant systemic therapy and postoperative irradiation to the chestwall and regional lymph nodes (1,538 pts), or adjuvant systemic therapy alone (1,545 pts). Pre- and menopausal patients received 8-9 cycles of CMF with an interval of 4 weeks, whereas postmenopausal patients received tamoxifen 30 mg daily for one year. The median potential follow-up time was 33 (range 29-37) years. The endpoints were loco-regional control, freedom for distant metastases, overall survival and irradiation related late morbidity.

Results

Overall the 30-year cumulative incidence of loco-regional recurrence was 10% in irradiated patients vs 38% in patients who received adjuvant systemic therapy alone (HR: 0.22 [95% cfl 0.19-0.27]). Distant metastasis probability at 30 years was 49% in irradiated patients compared to 59% in non-irradiated (HR: 0.78 [0.70-0.85]). These figures were also reflected in a superior breast survival HR: 0.75 [0.68-0.83], and overall of the irradiated patients (19% versus 14% at 30 years (p<0.0001), HR: 0.84 [0.78-0.91]. Radiotherapy did not result in any significant excess death of other courses, such as ischemic heart disease, HR: 0.90 [0.69-1.16]; or secondary lung cancer HR: 1.41 [0.91-2.16]. (see figure)

Conclusion

The study definitely demonstrate that optimal long-term treatment benefit of high-risk breast cancer can only be achieved if both loco-regional and systemic tumor control are aimed for. Therefore, radiotherapy has an important role in the multidisciplinary treatment of breast cancer. The RT treatment did not result in excess ischemic heart damage, nor in other non-cancer related death.

OC-0326 DBCG-IMN: Long-term survival gain with internal mammary node irradiation to breast cancer patients

L.B.J. Thorsen[1], J. Overgaard[1], S.V. Holm-Hansen[2], M. Berg[3], I. Jensen[4], C. Kamby[5], M.H. Nielsen[6], M. Overgaard[1], B.V. Offersen[7]

[1]Aarhus University Hospital, Department of Experimental Clinical Oncology, Aarhus, Denmark ; [2]Herlev University Hospital, Department of Oncology, Herlev, Denmark ; [3]Vejle Hospital, Department of Oncology, Vejle, Denmark ; [4]Aalborg University Hospital, Department of Oncology, Aalborg, Denmark ; [5]Rigshospitalet, Department of Oncology, Copenhagen, Denmark ; [6]Odense University Hospital, Department of Oncology, Odense, Denmark ; [7]Aarhus University Hospital, Department of Oncology, Aarhus, Denmark

Purpose or Objective

The DBCG-IMN study demonstrated improved 8-year overall survival (OS) with internal mammary node irradiation (IMNI) in patients with early node-positive breast cancer (BC). Here, we report updated results on long-term OS in the DBCG-IMN cohort.

Material and Methods

During 2003-2007, the DBCG-IMN study, a nationwide, prospective cohort study, allocated 3,089 patients with early, unilateral, node-positive BC, age<70 years and no prior malignancies to adjuvant radiotherapy (RT) +/- IMNI based on laterality of disease. This method was chosen to avoid cardiac irradiation in patients with left-sided BC: Patients with right-sided BC received IMNI (n=1,492), whereas patients with left-sided BC did not (n=1,597). All other treatments were provided independently of BC laterality. Median patient age was 56 years and 41% were premenopausal. Surgery was mastectomy (65%) or breast conserving surgery (BCS, 35%), all with axillary clearance. Tumors were pT2 or larger in 58%, with medial/central location in 40%. Nodal stage was pN2 or worse in 41% of patients. IMNI targeted the first four intercostal spaces. All patients received adjuvant RT 48 Gy/24 fractions to chest wall/residual breast and the periclavicular area. In 18% of patients, the axillary level I was treated, and 32% of