JOURNAL WATCH

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Our panel of experts highlight the most important research articles across the spectrum of topics relevant to the field of lung cancer management.

Expert panel: Antonio Rossi, Division of Medical Oncology, SG Moscati Hospital, Avellino, Italy; Sarah Beth Harrington, University of Arkansas, Little Rock, AR, USA; Matthew Steliga, University of Arkansas, Little Rock, AR, USA

Yamashita F, Azuma K, Yoshida T *et al.* Prognostic value of *EGFR* mutation and ERCC1 in patients with non-small cell lung cancer undergoing platinum-based chemotherapy. *PLoS ONE* 8(8), e71356 (2013).

This retrospective study analyzed the relationships between *EGFR* mutations or excision repair cross-complementing 1 (ERCC1) expression and progression-free survival (PFS) in patients with non-small-cell lung cancer (NSCLC) treated with platinum-based chemotherapy. The peptide nucleic acid-locked nucleic acid PCR clamp method was used to determine *EGFR* mutation status, and immunohistochemistry was used to examine the expression of ERCC1 in tumor samples obtained from the patients.

EGFR mutations were identified in 46 out of 103 patients, while ERCC1 expression was only detected in 51 patients for whom adequate tumor specimens were available. ERCC1 expression resulted positive in 28 patients. Among the NSCLC patients who received platinum-based chemotherapy, the median PFS was significantly better in those who had never smoked and those with exon 19 deletion, and the median overall survival (OS) was significantly better in those who had never smoked, those with exon 19 deletion and women. Cox regression analysis revealed that exon 19 deletion and having never smoked were significantly associated with both PFS and

OS. Subset analysis revealed a significant correlation between ERCC1 expression and *EGFR* mutation, and ERCC1-negative patients with exon 19 deletion had a longer PFS than the other patients; ERCC1-positive patients without exon 19 deletion had a shorter PFS than the other patients.

These results indicate that NSCLC patients with exon 19 deletion have a longer PFS and OS, and that platinum-based chemotherapy is more effective against ERCC1-negative and exon 19-positive NSCLC patients. However, these are further retrospective findings from a small sample of NSCLC patients receiving platinum-based chemotherapy. A large amount of data evaluating the predictive role of activating *EGFR* mutations, including exon 19 deletion, in patients receiving platinum-based chemotherapy is already available in literature both retrospectively, from larger samples of patients, and prospectively, from Phase III randomized trials. All of these results, including all outcomes, are contrasting and only an improbable large prospective randomized Phase III trial addressing this issue might reach firm conclusions. Recently, Phase III randomized trials investigating customized chemotherapy failed to demonstrate prospectively the prognostic value of ERCC1, also underlining the need to optimize the methods to determine its expression.

– Written by Antonio Rossi

News & Views

News

Journal Watch

Interview

Planck M, Isaksson S, Veerla S, Staaf J. Identification of transcriptional subgroups in *EGFR*-mutated and *EGFR/KRAS*-wild type lung adenocarcinoma reveals gene signatures associated with patient outcome. *Clin. Cancer Res.* 19(18), 5116–5126 (2013).

The aim of this study was to determine whether transcriptional subgroups of clinical relevance exist within *EGFR*-mutated, *KRAS*-mutated or *EGFR* and *KRAS* wild-type (*EGFR*wt/*KRAS*wt) lung adenocarcinomas.

A total of 1186 lung adenocarcinomas, including 215 *EGFR*-mutated, 84 *KRAS*-mutated and 219 *EGFR*wt/*KRAS*wt tumors were studied for gene-expression profiles. They were assembled and divided into four discovery ($n = 522$) and four validation cohorts ($n = 664$). Subgroups within the mutation groups were identified by unsupervised consensus clustering, significance analysis of microarrays (SAM analysis) and centroid classification across discovery cohorts. Genomic alterations in identified mutation subgroups were assessed by integration of genomic profiles for 158 cases with concurrent data. Multicohort expression subgroup predictors were built for each mutation group using the discovery cohorts, and validated in the four validation cohorts. Consensus clustering within the mutation groups identified reproducible transcriptional subgroups in *EGFR*-mutated and *EGFR*wt/*KRAS*wt tumors, but not in *KRAS*-mutated tumors. The failure to identify reproducible subgroups within *KRAS*-mutated tumors could be due to the lower number of available tumors and/or a potential biological or etiological heterogeneity among these tumors. Subgroups displayed differences in genomic alterations, clinicopathological characteristics and overall survival. Multicohort gene signatures derived from the mutation subgroups added independent prognostic information in their respective mutation group, for adenocarcinoma in general and stage I tumors specifically, irrespective of mutation status, when applied to the validation cohorts. High-risk subgroups showed higher expression

of proliferation-related genes, higher frequency of copy number alterations/amplifications and association with a poorly differentiated tumor phenotype. All these characteristics were consistent with their worse clinical outcome.

This study identified transcriptional subgroups in *EGFR*-mutated and *EGFR*wt/*KRAS*wt adenocarcinomas with significant differences in clinicopathological characteristics and patient outcome, not limited to a mutation-specific setting. These results extend and reinforce other recent findings on this topic. Further analyses in larger well-characterized cohorts are required to determine the predictive values of the identified gene signatures in a mutation-specific and general context.

– Written by Antonio Rossi

Freeman RK, Ascioti AJ, Mahidhara RS. A propensity-matched comparison of pleurodesis or tunneled pleural catheter in patients undergoing diagnostic thoracoscopy for malignancy. *Ann. Thorac. Surg.* 96, 259–264 (2013).

Malignant pleural effusion can lead to significant dyspnea and need for repeat thoracenteses. Both tunneled pleural catheter (TPC) and talc pleurodesis (TP) can be used after thoracoscopy and provide relief from dyspnea with decreased need for subsequent intervention. The authors performed a retrospective propensity-matched analysis to compare outcomes in 30 patients who received TPC and 30 matched controls receiving TP at a single center.

The mean length of stay (LOS) was 6 days (range: 4–13 days) for TP and 3 days (range: 1–6 days) for TPC. In addition to LOS, successful palliation was defined as: improvement in Zubrod performance status and lack of reintervention. Neither criteria differed between the groups. Interval between TP or TPC and initiation of systemic treatment was longer in the TP group (17 vs 9 days). The TP group had six reported morbidities (respiratory insufficiency, atrial fibrillation and

pulmonary embolus) and one death. The TPC group had no perioperative morbidity or mortality.

Perioperative pain was not reported, but in general, placement of a TPC is associated with the same size incision, but often less pain, than a chemical pleurodesis. Cost analysis was not reported, but the shorter LOS probably more than compensated for the cost of the TPC and necessary drain bottles.

This retrospective single-center report illustrates that for patients with malignant pleural effusion, a TPC may be associated with a shorter LOS, less morbidity and sooner initiation of systemic therapy compared with TP, while providing similar improvement in performance status without need for reintervention.

– Written by Sarah Beth Harrington and Matthew Steliga

Koczywas M, Cristea M, Thomas J et al. Interdisciplinary palliative care intervention in metastatic non-small-cell lung cancer. *Clin. Lung Cancer* doi:10.1016/j.clcc.2013.06.008 (2013) (Epub ahead of print).

It is well established in current literature that patients with metastatic non-small-cell lung cancer (NSCLC) have significant physical, psychological, social and spiritual needs. Despite growing evidence that early palliative care can improve patient-reported symptoms and quality of life, challenges remain in practical palliative care integration into routine oncology care in the outpatient setting. This article presents quality of life data from the 'usual oncology care' arm of the study in order to tailor an outpatient interdisciplinary palliative care intervention.

A total of 130 patients with stage IV NSCLC were recruited into this prospective longitudinal study over a 1-year period. Of those, 114 patients had evaluable data, which included quality of life surveys at baseline, 6, 12 and 24 weeks. Physical function, cognitive status, nutritional status, social activity and support were all assessed. An extensive symptom

assessment was documented over time, which included physical, psychological and spiritual symptoms.

Findings demonstrated significant declines in physical and cognitive function over time, coupled with worsening symptom distress in this cohort of patients with metastatic NSCLC. This study is one of the more comprehensive ones in the current literature and describes the decline in quality of life over several domains. It also

points to the need for improved models of palliative care that focus on minimizing expected symptom burden and improving overall quality of life for patients with advanced lung cancer. The results informed the development of an interdisciplinary palliative care intervention, which will be tested over the next 2 years.

– Written by Sarah Beth Harrington and Matthew Steliga

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Journal Watch highlights some of the most important papers recently published in the field of lung cancer management and research. The editorial team welcomes recommendations for relevant papers for inclusion in future issues.

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