150P Association of hormone-sensitive miRNAs expression with main clinicopathologic characteristics of ER/PR-positive breast cancer

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Background: Difficulties in breast cancer (BC) treatment are associated with the occurrence of metastases at early stages of disease. It is known that ER and PR status may change during metastatic tumor progression. Recent studies have shown that changes in androgen receptor (AR) expression are associated with mammary gland carcinogenesis. Therefore a study of pathways involving these receptors might help understanding mechanisms of BC progression, as the expression of their targets, including their miRNA-targets, can also change.

Methods: The search for miRNAs whose putative promoter regions contain AR, PR or ER binding sites was performed using Biostrings (R Bioconductor package). The level of miRNAs was evaluated by RT-PCR in MCF-7 cells treated for 6, 24, 48 hours with 10 nM or 100 nM of estradiol (E2), progesterone (P4) or testosterone (T). The expression of the miRNAs most sensitive to the action of hormones was analyzed in BC samples (n=94).

Results: 15 miRNAs with high expression in the mammary gland were selected to analyze their level in the MCF-7 cells. 5 miRNAs changed 1.3-2 times under the influence of hormones: miRNA-27a (decreased after incubation with T), -190a (increased after incubation with T, decreased after incubation with P4), -190b (increased after incubation with E2), -21 (increased after incubation with T), -193b (increased after incubation with T and E2), -324 (increased after incubation with P4). MiRNA-190a, -190b (lower level in T2-T3 tumors of luminal A), -324, (lower level in T2-T3 tumors of luminal B HER2-positive subtype) were found to be associated with tumor size. The levels of miRNA-193b, -190a decreased in the tissues of patients with lymph node metastases in luminal A. In luminal B HER2-positive BC, the levels of miRNA-190a, -190b, -193b, -21 were significantly lower in the tumor tissues of patients with lymph node metastases. Association with the level of ER expression in luminal B HER2-negative BC was found for miRNA-190b (increase at a higher level of ER).

Conclusions: The study revealed an association between the expression of hormone-sensitive miRNAs (-190a, -190b, -193b, -21, -324) and T stage, N stage, the level of ER expression in some BC subtype.

Legal entity responsible for the study: The authors.

Disclosure: All authors have declared no conflicts of interest.

151P Prevalence of Anaplastic Lymphoma Kinase (ALK)+ Non-Small Cell Lung Cancer (NSCLC) in the Middle East and North Africa (MENA)

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Background: ALK gene alterations are potent oncogenic drivers in NSCLC. Tyrosine kinase inhibitors targeting the ALK pathway are effective in treating ALK+ NSCLC. Around 4—5% of Asian and Caucasian patients with NSCLC have ALK+ tumors, but ALK rearrangement prevalence data for the MENA region are lacking.

Methods: In this non-interventional epidemiology study, histologically confirmed non-squamous NSCLC samples retained for <5 years in tissue banks at 6 centers in MENA were retrospectively analyzed for ALK rearrangement using the Ventana immuno-histochemistry (IHC) method. Patient characteristics obtained from medical records were analyzed for any association with ALK rearrangement. Concordance between IHC and Vysis fluorescence in situ hybridization (FISH) ALK detection methods was assessed in a subset of samples.

Results: Overall 448 tissue samples were analyzed by IHC: 137 (30.6%) in Lebanon, 104 (23.2%) Saudi Arabia, 97 (21.7%) Egypt, 80 (17.9%) United Arab Emirates, 30 (6.7%) Morocco. Based on IHC, ALK-positivity prevalence was 8.7% (95% CI: 6.3—11.7), ALK-negativity was 91.3% (95% CI: 88.3—93.7; Table). Prevalence based on FISH (n=149) was 5.4% positivity and 81.8% negativity. Concordance between IHC and FISH (n=129) was 98.4% (95% CI: 94.2—99.8) for negative agreement and 100% (95% CI: 63.1—100) for positive agreement. Univariate analysis showed ALK rearrangement was significantly associated with epidermal growth factor (EGFR)-wild type status (p=0.03), but was not significantly associated with gender, race, smoking history, or histological subtype.

Table: 151P ALK rearrangement prevalence: ALK-IHC and ALK-FISH test				
Result	***ALK*-IHC**		***ALK*-FISH**	
	N	%	N	%
Based on all results				
Total	448	100	148	100
Positive	39	8.7	8	5.4
Negative	409	91.3	121	81.8
Non-evaluable	0	0	19	12.8
Only patients with both tests evaluable*				
Total	129	100	129	100
Positive	10	7.8	8	6.2
Negative	119	92.2	121	93.8

*Analysis of concordance in a subset of 3 centers in Saudi Arabia and Lebanon

Conclusions: Our findings suggest that ALK rearrangement prevalence is higher in MENA than elsewhere. High concordance was found between FISH and IHC methods. Except for EGFR wild-type status, no clinicopathological characteristics were associated with ALK+ NSCLC.

Legal entity responsible for the study: Pfizer Inc.

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152P Children's exposure to rare earth elements and cancer

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Background: Rare earth elements (REE) are extensively used in the renewable energy technologies such as wind turbines, batteries, catalysts and electric cars. While there are many studies about cancer epidemiology of several heavy metal, much less is known about rare earth elements despite the fact that the lanthanides included in rare-earth metals have shown interactions with cellular metabolism and physiology due particularly to their catalytic properties (impact on phosphokinase) and their radii ionic similitude with calcium (impact on Calmodulin). Our team have recently developed ICP-MS technics for hair metallic trace element screening applied to epidemiology investigation on pediatric cancer. In this abstract, we describe the first investigation on hair REE concentration in pediatric cancer among children of the Sainte-Pazanne in northern France.

Methods: Subjects. 64 children aged 5 to 15 years were included in this investigation; 20 from Sainte-Pazanne (6 500 habitants) in the Loire-Atlantique department in western France and 44 healthy children from all other part of France. Among 20 children of Sainte-Pazanne 12 suffered from cancer. Briefly, 10-50 mg of hair was washed twice and hydrolyzed in nitric acid medium during 12h. The diluted hydrolysates and External standards were tested by ICP/MS Injection Agilent 7800. Rare Earth element dosed: Lanthane (La), Cerium (Ce), Praseodyme (Pr), Neodyme (Nd), Samarium (Sm), Europium (Eu), Gadolinium (Gd), Dysprosium (Dy), Holmium (Ho), Erbium Er), Thulium (Th) and Ytterbium (Yb).

Results: 4 rare earth elements (Pr, Dy, Ho and Th) were found significatively in large proportion in Sainte-Pazanne children compared to the control population: 231% Pr, 257% Dy, 327% Ho and 400% Th respectively (n = 64, p <0.05). Within the population of the target area, the Praseodyme (Pr), and Holmium (Ho) levels were significantly high in 20% (4/20) of sick children: Pr (Patient: 0.033 ±0.01 μg/g versus healthy: 0.001 ± 0.001 μg/g) and Ho (Patient: 0.003 ±0.002 μg/g versus healthy: 0.001 ± 0.001 μg/g).

Conclusions: This result suggests that the prevalence of children cancer in lanthanide contaminated area might be much higher than elsewhere and rare earth elements could contribute to pathogenesis of pediatric cancer.

153P   The Systemic Inflammation Response Index (SIRI) is a prognostic factor that correlates with tumor burden in advanced pancreatic cancer

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Background: The SIRI, defined by neutrophil x monocyte/lymphocyte 10^9/L, has emerged as a prognostic factor for pancreatic cancer. However, the association between SIRI after chemotherapy and tumor response has not been analysed.

Methods: 161 metastatic pancreatic cancer patients were retrospectively analysed. Associations between overall survival (OS), chemotherapy, CA 199 and SIRI were evaluated. A larger number of patients with pre-treatment SIRI (pre-SIRI) were collected so, post-treatment SIRI (post-SIRI) evaluated after three cycles was adjusted for analysis.

Results: Median age 66 years. 36% received gemcitabine + nab-paclitaxel, 24% gemcitabine, 17% mFOLFIRINOX, 7% other regimens. 16% had not received treatment. Pre-SIRI$\geq 2.3 \times 10^9$/L was an independent, negative predictor of OS compared to pre-SIRI$< 2.3 \times 10^9$/L [5 versus 16 months, Hazard Ratio 2.87, Confidence Interval 95% 2.02-4.07, $P < 0.0001$]. Pre-CA199 showed no prognostic ability for OS ($P = 0.095$). SIRI values increased after treatment (median pre-SIRI: 1.6×10^9/L; post-SIRI: 2.3×10^9/L; $P = 0.007$). On the contrary, CA199 values decreased (574 versus 291 U/mL; $P = 0.008$). Thus, we analyzed the association between tumor response measured by RECIST and pre-SIRI and post- SIRI values as well as pre-CA19-9 and post CA19-9. Patients with progressive disease (PD) showed a higher pre-SIRI than those who had a response to chemotherapy (2.7×10^9/L versus 1.2×10^9/L; $P < 0.001$). Pre-CA199 was also higher in patients with PD, but not statistically significant (3089 versus 1021 U/mL; $P = 0.89$). We observed a statistically significant increase in post-SIRI values for PD compared to tumor response (3.2×10^9/L versus 1.7×10^9/L; $P = 0.012$). This was also observed for post-CA199 when PD and response values were compared (1021 versus 237; $P = 0.03$). Post-SIRI$\geq 2.3 \times 10^9$/L showed a shorter OS compared to post-SIRI$< 2.3 \times 10^9$/L (8 versus 17 months; $P = 0.016$).

Conclusions: SIRI$\geq 2.3 \times 10^9$/L was a prognostic factor for metastatic pancreatic cancer. An elevated post-SIRI associated with disease progression and had a negative impact on survival. A SIRI$\geq 2.3 \times 10^9$/L could be related to high tumor burden and be useful to select patients who would benefit of intensive first-line chemotherapy.

154P   Investigation of PD-L1 expression and tislelizumab efficacy in gastroesophageal adenocarcinoma using a novel tumor and immune cell score with VENTANA PD-L1 (SP263) assay and Combined Positive Score (CPS)

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Background: Tumor (TC) and immune cell (IC) PD-L1 expression may be associated with anti-PD-1 efficacy in gastroesophageal adenocarcinoma (GEA) and can be assessed via cell counting using the Combined Positive Score (CPS) with the Dako 22C3 assay. However, the CPS scoring method can be challenging to utilize. A novel combined algorithm, Tumor and Immune Cell (TIC) score, was developed for the Ventana SP263 assay to assess TC and IC PD-L1 expression based on tumor area. Associations between CPS and TIC scoring methods, and potential correlations with efficacy, were investigated in patients with GEA from the tislelizumab first-in-human study (NCT02407990).

Methods: PD-L1 expression was evaluated using the Ventana SP263 and Dako 22C3 assays in 74 and 49 patients, respectively. Correlation of PD-L1 TIC scores (% tumor area covered by PD-L1+ TC/IC by SP263) and CPS (by 22C3) with clinical efficacy was assessed. Cases were considered PD-L1+ at ≥ 5% for TIC or ≥ 1 for CPS. Analytical validation of TIC was further assessed by reproducibility of results.

Results: Based on statistical analysis and other considerations, TIC ≥ 5% was determined as the optimal cutoff. Response, prevalence, positive predictive value, and negative predictive value for TIC ≥ 5% and CPS ≥ 1 are shown (**Table**). At a 17.4-month median follow-up, patients with TIC ≥ 5% or CPS ≥ 1 showed survival benefit. Inter-reader and -laboratory overall agreement for TIC ≥ 5% were 99% (95% CI, 98-100) and 96% (95% CI, 94-98), respectively.

Conclusions: At evaluated cutoffs, both SP263 TIC and 22C3 CPS assays aided in the identification of patients with GEA likely to benefit from tislelizumab. TIC is a robust, reproducible scoring method. Further clinical validation is underway for TIC ≥ 5% in patients with gastric and gastroesophageal junction adenocarcinoma from a phase 3 study (NCT03777657).

Clinical trial identification: NCT02407990.

Table: 154P

Scoring Method (Cut-off)	PD-L1 Status	BEP	ORR (%)	PD-L1 Prevalence (%)	Response Odds Ratio	PPV (%)	NPV (%)	PFS HR (95% CI)	OS HR (95% CI)
TIC (SP263) ≥ 5%	+	38	18.2	51	6.67	15.8	83.3	0.497 (0.298, 0.823)	0.529 (0.295, 0.935)
	−	36	3.2						
CPS (22C3) ≥ 1	+	22	20.0	45	∞ *	18.2	88.9	0.880 (0.474, 1.606)	0.665 (0.339, 1.259)
	−	27	0						

*Odds ratio could not be estimated due to no responders in CPS <1. Abbreviations: BEP, biomarker evaluable population; CI, confidence interval; CPS, combined positive score; HR, hazard ratio; NPV, negative predictive value; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PPV, positive predictive value, TIC, tumor and immune cell.