## 10P Clinical and morphological pattern of malignant tumors with microsatellite instability (MSI)

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**Background:** Solid tumors with microsatellite instability (MSI), regardless of location, are highly susceptible to immune checkpoint inhibitors. The aim of the study was to investigate clinical and morphological features of tumors with MSI.

**Methods:** The study included 787 tumor samples of the following localizations: 530- colorectal cancer (CRC), 95- endometrial carcinoma (EC), 87- gastric cancer (GC), 20- ovarian cancer, 18- pancreatic cancer, 15- cervical cancer, 15- esophageal cancer, 7- cancers of unknown primary site. The study of MSI was carried out using fragment analysis by determining mononucleotide markers: BAT-25, BAT-26, NR-21, NR-24, NR-27. Data of preoperative level of CEA and CA19-9 were obtained in 185 patients with CRC.

**Results:** The prevalence of MSI in CRC was 6.8%, in EC- 27.4%, in GC - 6.9%, in ovarian cancer - 5%. MSI was not found in other localizations. The characteristic clinical and morphological features of MSI-positive CRC were younger age ($p=0.032$), right-sided localization ($p<0.0001$), presence of multiple primary tumors ($p=0.041$), absence of distant metastases ($p=0.013$), presence of carcinoma G3 ($p=0.0008$), mucinous component ($p<0.0001$), Crohn-like reaction ($p=0.0063$) and tumor-infiltrating lymphocytes ($p<0.0001$). Also, in patients with CRC with MSI, the preoperative level of CEA was lower than in patients with MSS tumors: the median was 2.0 ngml (interquartile range (IQR): 0.7-3.4; $n=20$) and 3.9 ng/ml (IQR: 1.1-13.1; $n=165$), respectively ($p=0.0061$). No differences in smoking status, tumor size and the presence of diseases associated with an increase of CEA were shown between the MSI and MSS CRC. For EC with MSI, there were the following features: endometrioid adenocarcinoma ($p=0.017$), high grade tumors ($p=0.0054$), presence of cribriform growth pattern ($p=0.0084$) and tumor-infiltrating lymphocytes ($p=0.0019$), as well as a higher level of mitotic activity ($p=0.002$). MSI-positive GC was more often found in women ($p=0.033$), was characterized by older age ($p=0.001$), distal tumor localization ($p=0.022$), presence of high-grade tumors ($p=0.012$) and tumor-infiltrating lymphocytes ($p=0.009$).

**Conclusions:** Common features for CRC, EC and GC with MSI are the presence of a high-grade tumors and tumor-infiltrating lymphocytes.

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## 11P ROS1-gene rearranged lung adenocarcinomas: Demographic, clinicopathologic and treatment profile in a cohort of Indian patients

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**Background:** ROS1 translocations are seen in 1%-2% of non-small cell lung cancer (NSCLC) patients. There is limited data on the clinicopathologic profile of ROS1 translocated NSCLC.

**Methods:** The study included 409 patients with NSCLC who were referred for molecular testing. Fluorescent in situ hybridisation (FISH) assays were performed to detect ROS1 gene rearrangements on 3-5µm tissue section from formalin-fixed-paraffin embedded (FFPE) tumor tissue. ZytoLight SPEC ROS1 Dual Color Break Apart FISH Probe (ZytoVision, Germany) was used. Clinicopathologic profiles of the FISH-positive patients were documented.

**Results:** Out of 409 cases of stage IV NSCLC, 18 (4.4%) cases were positive for a ROS1 gene rearrangement. Of the positive cases 11 were females and 7 were males. Smoking history was known for 11 patients of which 2 were smokers (all males) and 9 were non-smokers (7 females and 2 males). The median age was 49 years (range 28 - 65 years). The histopathology was adenocarcinoma in all cases with the solid subtype of adenocarcinoma being the most common histologic subtype (6 cases) followed by solid type with macronuclei (5 cases). Fifteen patients were treated with crizotinib of whom 4 received the drug in the first-line and 11 in the second-line. The overall response rate for crizotinib was 10/15 (66.6%) all of which were partial responses (PR). The disease control rate (PR + stable disease) was 14/15 (93.3%). One patient had disease progression on first-line crizotinib. The median duration of response was 9 months (range 1 to 19 months). After progression on crizotinib; immunotherapy with pembrolizumab was given in 3 patients with PD-L1 IHC of 13%, 65% and 5%. Peripheral edema was the most common toxicity with crizotinib and was reported in 6 (40%) of the patients.

**Conclusions:** ROS-1 rearranged NSCLC represents 4% of all advanced stage NSCLC patients. Most patients were females, non-smokers and are diagnosed at a younger age (median 49years) compared to NSCLC with other driver mutations. Most patients present in an advanced stage. The response rates to crizotinib (most commonly used drug) is 66.6% with all of them being partial responses. Crizotinib is well tolerated in our cohort of patients.

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## 12P Molecular features of KRAS mutant NSCLC: Weaving a future score for immune-checkpoint inhibitors (ICI)

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**Background:** KRAS mutation is present in almost 33% of NSCLC patients. Retrospective trials have shown a tendency of higher efficacy of ICI in this subgroup, and prospective trials with KRAS inhibitors are emerging. If KRAS could take part as a biomarker score for ICI or KRAS inhibitors efficacy is still unknown.

**Methods:** A retrospective analysis was done in our center, from all NSCLC patients with either tissue DNA and/or ctDNA NGS analyses, treated with schemes including ICI. NGS methods included: Oncomine V3.0, Guardant 360, and Foundation liquid.

**Results:** Two hundred one patients had NGS done with 51(25.4%) with KRAS mutation detected. Median age was 62 years old, and 53% had PDL1 >1%, within 21% with >=50%. High CD8 T Cell infiltration was detected in 18% but was unknown in 51%. KRAS most frequent mutations detected were G12C (43,9%) and G12D (17,1%). TP53 co-mutation was present in 29% (KP group), NF1 in 11.3% and STK11 in 9,7% (KL group). Most KRAS G12C, had PDL1 positive (69%) and 25% had PDL1 >=50%. TILs infiltration in 25% with high infiltration KL group had PDL1 positive in 20% (anyone with PDL1 50%) and without CD8 T-cell infiltration. A combination of chemo-immunotherapy (anti-PDL1) was administered in 26% of all, and chemotherapy monotherapy in 53%. Patients KRASmut and PDL1 positive, showed better median OS than PDL1 negative (28 vs 21,9 months, p=0,25), and those with PDL1 >=50% expression reached median survival of 39 months. Patients KRASmut and PDL1 negative, obtained similar low survival rates regardless of treatment (OS 15%). In KP group, PDL1 negative showed mOS of 12 months compared to 21 months if PDL1 positive. Survival was lower in STK11mut respect to STK11wt (17 vs 24,8 months). In KL group, treatment did not affect survival (mOS 10 months). Globally, more than one co-mutation tended to worse survival (14 months).

**Conclusions:** Our sample represents general NSCLC patients. KP group shows an immune phenotype (high PDL1, CD8 Tcells infiltration) and better survival rates for ICI included therapy. KL group is a challenging group without real ICI efficacy and results from KRAS inhibitors early trials have shown major benefit in this group. Our study shows a potential molecular score to select treatment. A wider sample is expected to support this observation.

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## 13P Incidental germline findings from tumor molecular profiling for precision oncology: Is it common and how to manage?

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**Background:** A fraction of patients referred for tumor-only complex molecular profiling may harbor germline variants in genes associated with the development of hereditary cancer syndromes (HCS). Bioinformatic management and reporting of such incidental germline findings are not standardized.

**Methods:** Data from NGS sequencing of tumor-only samples from patients referred for complex molecular profiling were analyzed in order to identify germline variants in HCS-associated genes. Analysis of variant origin was performed employing bioinformatic algorithms followed by manual curation. If possible, variant origin was