2008P The effect of the use of complex molecular profiling in advanced solid organ tumours on clinical decision: Turkey molecular profiling in advanced cancers trial (TUMPACT)

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Background: Molecular genetic profiling (MGP) which has started to take an important part in cancer diagnosis and treatment in recent years, has entered the routine clinical practice much faster than expected. We aimed to evaluate the use of this technology in routine practice, the effect of changing the treatment decision.

Methods: Two hundred and thirty-four patients who received treatment from 21 different centers with OncoDeep MGP platform tests were included, which uses a combination of new generation sequencing (NGS), immunohistochemistry (IHC) and other specific tests (Package Plus).

Results: Summary was given in the table. Physician waited for test results in 27% (n=61) of patients for treatment decision. Prior to MGP analysis patients received median 2-lines of treatment. The median time between sending the sample abroad for testing and reaching the result by the physician was 14 days (range:5-71). With the test results, the physician changed the treatment decision in 51.8% of the patients (n=118). The most frequent way of drug supply of patients whose treatment decision were 64.4% (n = 67) from their own budget. When the treatment responses were evaluated, the disease control rate was 31.1% and the drug discontinuation was applied due to toxicity in 4 patients (3.4%). 63.6% (n = 75) of the patients were found to be alive with a median follow-up of 18.0 months. (Table).

Table: 2008P

		n:234
Gender (Male,%)		45.3
Age (Median, Min-Max)		54, 18-90
Diagnosis (%)	Breast	17.5
	Lung	16.2
	Pacreatic	14.5
	Cholangiocellular carcinoma	8.5
Comorbities (%)	Hypertension	26.5
	Diabetes Mellitus	25.5
	Benign Prostate Hyperplasia	4.1
Test Request (%)	Private Hospital	88.0
Treatment Line Before Test (%)	0	16.4
	1	22.0
	2	35.3
	3	14.7
	4	7.3
	5	4.3
Impact on Decision (Yes, %)		51.8
Decision Change Factor (%)	Package Plus	59.2
	NGS	40.8
Type of Drug Supply After Test (%)	Own Budget	64.4
	Social Security	19.2
	Private Health Insurance	4.8
	Off label	1.0
	Could Not Get	1.0

Conclusions: The first results of our study show that genetic profiling test is applicable for cancer patients in our country and when it used together with NGS and IHC, it may facilitate the clinical decision of the medical oncologist in routine clinical practice.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1314

2009P Gastric cancer in BRCA1 germ-line mutation carriers: Results of endoscopic screening and molecular analysis of tumour tissues

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Background: There are some evidences suggesting the link between BRCA1/2 germline mutations and increased risk of gastric cancer.

Methods: We performed endoscopic screening for stomach malignancies in 120 *BRCA1* mutation carriers and 110 controls.

Results: No instances of gastric cancer were detected at first visit. The analysis of atrophic changes performed by OLGA (Operative Link for Gastritis Assessment) staging revealed identical frequencies of mucosal abnormalities in carriers vs. non-carriers. *BRCA1* mutation carriers demonstrated significant association between gastric atrophy and age: OLGA stages I-IV alterations were observed in 26/41 (63%) subjects aged > 50 years old as compared to 29/79 (37%) in younger subjects ($P = 0.007$, χ^2-test). However, this age-related trend was not observed in the mutation non-carriers. One *BRCA1* mutation carrier developed gastric cancer in four years after the first visit to endoscopic examination. We performed next-generation sequencing analysis for this tumour and additional 4 archival gastric cancers obtained from *BRCA1/2* mutation carriers. Somatic loss of the remaining *BRCA1/2* allele was observed in 3 out of 5 tumours analyzed; all these carcinomas but not the malignancies with the retained *BRCA1/2* copy showed chromosomal instability.

Conclusions: Taken together, these data justify further studies on the relationships between the *BRCA1/2* and gastric cancer.

Legal entity responsible for the study: The authors.

Funding: The Russian Foundation for Basic Research [grant number 18-29-09090].

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1315

2010P Mutational profile and tumour mutational burden in Li-Fraumeni Syndrome associated cancer

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Background: Li-Fraumeni syndrome (LFS) is associated with germline mutations in the TP53 gene, which is essential in maintaining genomic integrity. Cells in patients with LFS fail to arrest secondary to DNA damage and are suggested to exhibit a 'mutator' phenotype, susceptible to multiple genomic mutations. Next generation sequencing (NGS) techniques allow us to explore the molecular landscape of cancers. The aim of our study was to delineate the mutational profile and tumour mutational burden (TMB) in LFS associated cancers with NGS.

Methods: Patients with a pathogenic germline TP53 mutation and a cancer diagnosis were identified from the Cancer Genetics Database in St. James's Hospital. Those with a TP53 mutation deemed a variant of uncertain significance were excluded. Patient demographics were collected from electronic patient records. NGS was performed on formalin fixed paraffin embedded tumour blocks with the Foundation One® CDx test. This reports on mutations in a panel of 324 genes and genomic signatures, including TMB.

Results: Nine patients have consented to participate with a total of twelve tumour specimens available for testing (3 patients with 2 separate primaries, denoted A and B where relevant below). Five patients have results to date. The remainder of the results will be included at the time of meeting presentation. Patient demographics are outlined in the table below. TMB was found to be low in all specimens (testing failed