POSTER #235

Lessons from the routine tumor molecular profiling in Russia

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BACKGROUND

- Cost-effectiveness is one of the major limitations for tumor molecular profiling.
- Small fraction of patients can benefit from precision oncology approach.
- We describe our experience of providing affordable molecular profiling (AMP) in routine settings
- We provide the data of the first 79 patients tested within the 1st half of 2018

OBJECTIVES

This study was aimed to evaluate the pipeline of an affordable tumor profiling based on focused biomarker panels and thorough selection of patients for testing:

- Define clinical characteristics of patients eligible for testing
- Estimate the probability of actionable biomarkers to be found
- Follow-up of the patients received molecular targeted therapy

METHODS

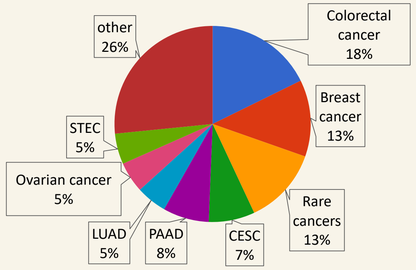
- NGS assays were performed with AmpliSeq-based targeted NGS panels
- Data were analyzed with the proprietary bioinformatic pipeline
- We analyzed using NGS: SNVs (including splice-affecting variants), CNVs, TMB (tumor mutational burden)
- Additional biomarkers comprised: MSI-assay, FISH (gene fusions), PD-L1, IHC

Patients should met the following criteria:

- Exhausted therapy options OR Molecular profiling is considered in Guidelines
- ECOG<3
- Expected probability of detecting actionable biomarkers to be over 2%

RESULTS

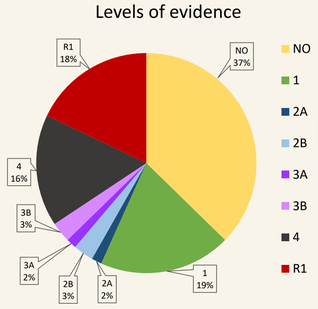
Cancer types



- Totally 16 cancer types were presented in the tested cohort
- The most common cancer types in the tested cohort were Colorectal and Breast cancer as the most prevalent in general population.
- Rare cancers, Pancreatic and Stomach carcinomas were overrepresented because of lack of conventional therapy options.
- The most prevalent stage was the 4

- We used MSK-IMPACT levels of evidence
- In 47% of cases we found at least 1 actionable biomarker
- The 1 level was predominantly represented by MSI-H or PD-L1 and BRCA mutations.
- R1 level referring to biomarkers of resistance was observed in 18% of cases. The most common R1 was KRAS
- Few cases of matched therapy including uncommon findings were the patients were thoroughly evaluated (table below)

Levels of evidence



CANCER TYPE	BIOMARKER	MATCHED DRUG	Response
Cervical carcinoma	EGFR amplification	Afatinib	CR
Colorectal cancer	FLT3 amplification	Sorafenib	PR
Pancreatic adenocarcinoma	PALB2 slpicing-site mutation	Olaparib	PR
Lung adenocarcinoma	MET exon skipping	Crizotinib/cabozantinib	*ND*
Head and neck cancer (salivary)	HRAS	Tipifarnib	*ND*

RESULTS

	Cancer	LoE	Findings
MSI-H	BRCA	1, 3B	MSI-H, BRCA1
	CESC	1	MSI-H
	CRC	1	MSI-H
	CRC	1, R1	MSI-H, KRAS
	CRC	1, 3B, R1	MSI-H, PTCH1, KRAS
	LUAD	1	MSI-H
	OV	1, 1, 2B	MSI-H, BRCA1, TCS2
	RARE	1	MSI-H
	UCS	1, 4	MSI-H, NF1

- MSI-H status was observed in 11% of cases that makes most of them eligible candidates for immunotherapy
- MSI-H often co-occurred with other biomarkers (left table)
- Other Immunotherapy biomarkers also have been found: PD-L1, High TMB and PBRM1mut.

- The most common reason why patients didn`t get molecular matched therapy was the absence of the related clinical trial or regulatory issues with off-label treatment.
- Immunotherapy is the most prospective molecular-matched therapy for the selected cohort of patients giving the prevalence of biomarkers.
- Unexpected actionable findings substantiate to expand the criteria of patient selection. For example revealed co-occurrence of MSI-H and KRASmut or FLT3 amplification in colorectal cancer.

CONCLUSION

Both, prevalence of identified actionable biomarkers and success cases of molecular-matched treatment proves the reasonability of further development of affordable molecular treatment. From the other hand it should be considered wether it si possible to provide appropriate treatment based on molecular profile. So the healthcare management issues tend to be a stumbling block of widespread use of routine molecular profiling.

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