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Molecular screening and early phase trial inclusion for head and neck squamous cell carcinoma's patients

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BACKGROUND

Head and neck squamous cell carcinoma (HNSCC) is the seventh most common cancer in the world.
Despite important drug development for HNSCC prognostic is still pejorative.
HNSCC's patients cannot easily benefit of molecular screening (MS) and molecular characteristics are not used to decide treatment in standard of care

OBJECTIVE

The aim of the study was to evaluate the impact of MS on patient's treatment and outcome in HNSCC.

PATIENTS AND METHODS

We retrospectively collected data from patients with recurrent or metastatic HNSCC included in MS studies (MATCH R, STING, STARTRK, RAGNAR, MOSCATO) in Gustave Roussy Cancer Campus between June 2012 and April 2021.
Molecular screening was different between studies (Table 1). Patients could be included in multiple studies and have iterative MS.
We then analyzed molecular results and access of targeted therapies related to molecular alterations.
236 patients were discussed in a molecular tumor board and analysed in this study. 135 patients had metastatic disease and 101 loco regional relapse only, 40% were oral cavity SCC. Only 7% had MS before the first line.
We focus on 78 patients eligible for a targeted early phase trial. Most of them (75.6%) could not access to targeted therapy in an early phase trial for many causes (Fig 1).

RESULTS

Fig. 1: Flow chart

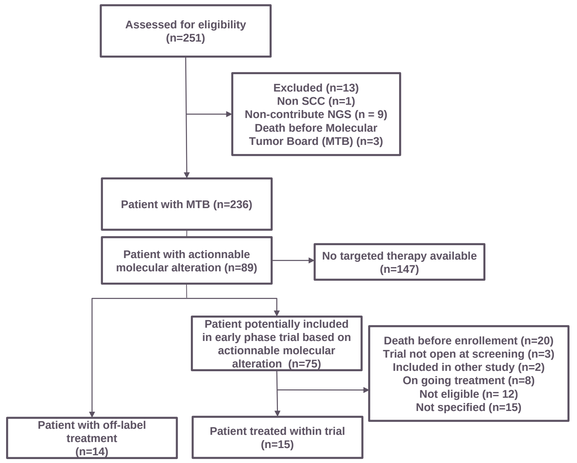

Table. 1: Molecular panel

	STING	STARTRK/RAGNAR	MOSCATO	MATCH R
Number of genes studied	321	324	30 to 74	161
Number of patients	63	63 + 50	95	4

***Fig. 2: 90 molecular alterations in 75* Patients potentially included in early phase trial based on actionnable molecular alteration**

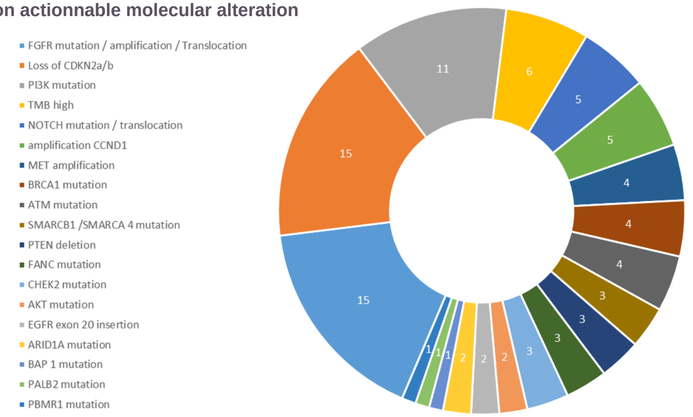

Table 2. Characteristics of patients with actionable molecular alterations And potentially included in early phase trial

	n =15	n = 60
Sex - no (%)		
Male	15 (100)	57 (95)
Female		3 (5)
Median age at MTB - years (range)	64 (32 – 70)	59,6 (25-81)
Primary tumor site – no (%)		
Oral cavity	5 (33)	28 (47)
Oropharynx	4 (22)	14 (23)
Hypopharynx	1 (6)	8 (13)
Larynx	5 (28)	6 (10)
Sinus	2 (11)	4 (7)
Extent of disease – no (%)		
Only locoregional	4 (27)	25 (42)
Metastatic	11 (73)	35 (58)
Number of lines of chemotherapy at MTB – no (%)		
0		
1	1 (7)	22 (37)
2	5 (33)	21 (35)
>2	0 (0)	12 (20)
	9 (60)	5 (8)

Table 3. Outcomes for 15 patients treated based on molecular alterations in early phase trial

Molecular anomalies	FGFR mutation / amplification / translocation	PI3K mutation / amplification	Loss of CDKN2a/b	BAP1 mutation	PBMR1 mutation	PTEN deletion	MET amplification	NOTCH2 translocation
Number of patients	5	3	2	1	1	1	1	1
Type of treatment	FGFR inhibitor	PI3K inhibitor AKT inhibitor	MTAP ihibitor Cell cycle inhibitor	ATR + PARP inihibitor	Niraparib	AKT inhibitor	MET inhibitor	NOTCH inhibitor
ORR	SD : 3 PD : 2	PR : 1 PD : 2	PD : 2	PR	SD	SD	PD	PD
Mediane PFS (month) [95% CI]	1.9 [1.3; 3.3]							
Mediane OS (month) [95% CI]	11.6 [3.1; 16.5]							

CONCLUSION

In this retrospective cohort, 35% of patients had actionable molecular alterations and only 16% of them could be treated in an early phase trial based on their actionable molecular alteration.

For this patients, outcomes in early phase trial are interesting, even if bias of hyper selection. Molecular alterations can lead to targeted therapies strategy and are an entry point to early phase trial. These results highlight the importance of early and iterative molecular screening for patients with recurrent or metastatic HNSCC.

We need to simplify molecular screening access for HNSCC's patients and understand molecular alterations evolution after chemotherapy and/or immunotherapy.

MOLECULAR ANALYSIS FOR PRECISION ONCOLOGY CONGRESS MAP
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