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Mutational landscape and therapeutic implications in squamous cell carcinomas

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BACKGROUND

Disseminated squamous cell carcinomas (SCCs) are traditionally considered void of actionable molecular targets, in contrast to adenocarcinomas, where an increasing number of targets are identified. SCC rarely undergo routine molecular testing and approved targeted therapies are rare in this population.

Access to extensive molecular profiling and subsequent matching with experimental therapies may improve the outlook for patients (pts) with SCC. We report the mutational landscape in SCC using comprehensive molecular and subsequent therapeutic implications.

METHODS

Pts with late stage SCCs (head and neck cancer, non-small-cell lung cancer, cervical cancer, thymic carcinoma or unknown primary tumor) referred to a Phase I facility were included in a prospective, single-center, single-arm open-label genomic profiling study (NCT02290522). Fresh tumor tissue was obtained for whole exome sequencing or whole genome sequencing, RNA sequencing and chromosomal aberrations. Circulating tumor DNA was obtained when fresh tumor biopsy was not feasible. Each individual genomic report was reviewed and discussed by a multidisciplinary tumor board dedicated to precision medicine. When possible, pts were treated with regimen matched to the genomic profile.

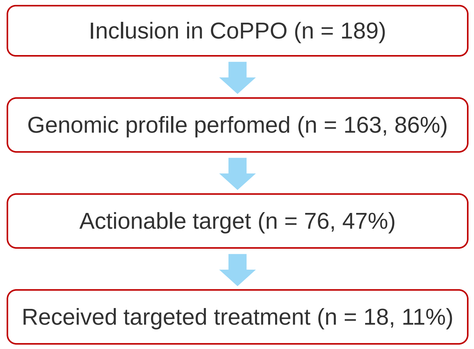


Figure 1: CoPPO study

METHODS

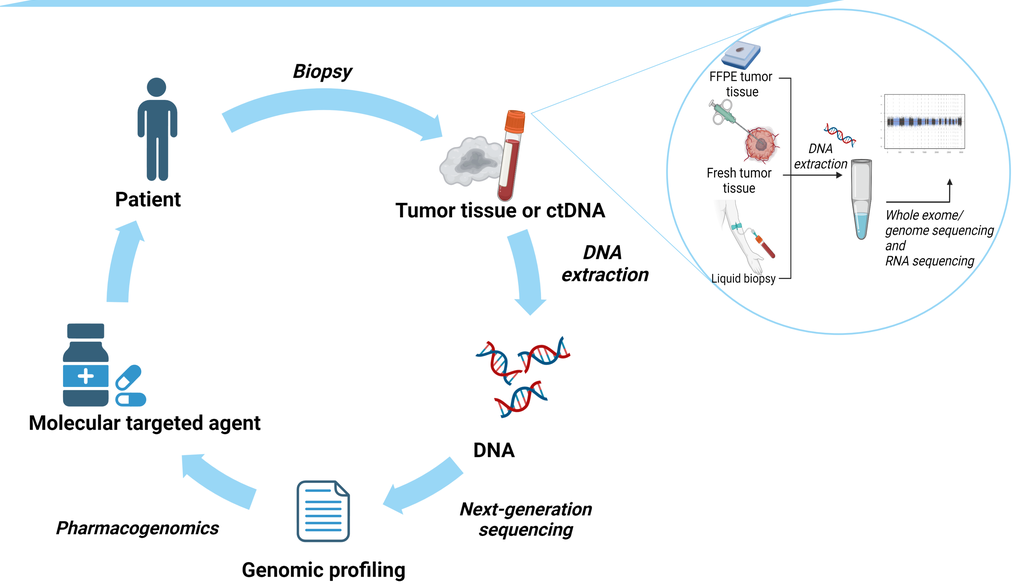


Figure 2 : Principles of genomic profiling

RESULTS

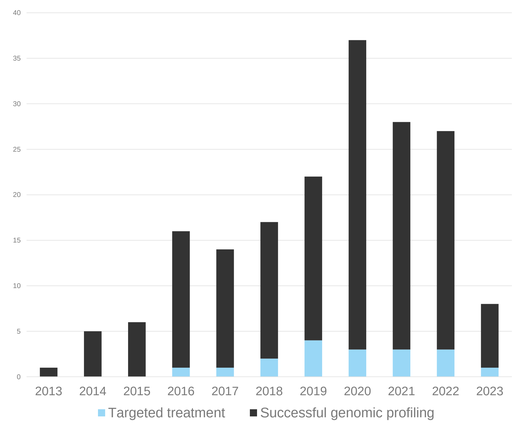


Figure 3a : Successful genomic profiles for pts with SCC throughout the years compared to pts receiving targeted therapy

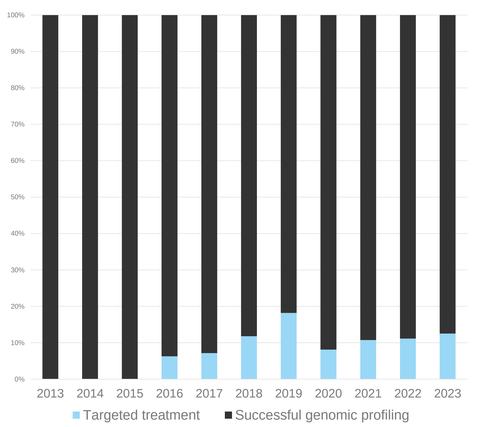
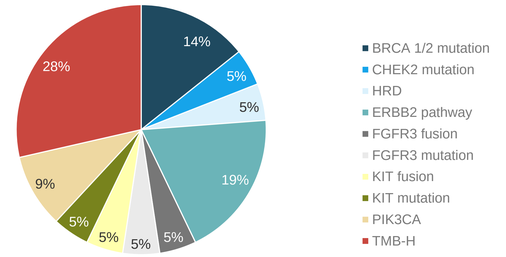


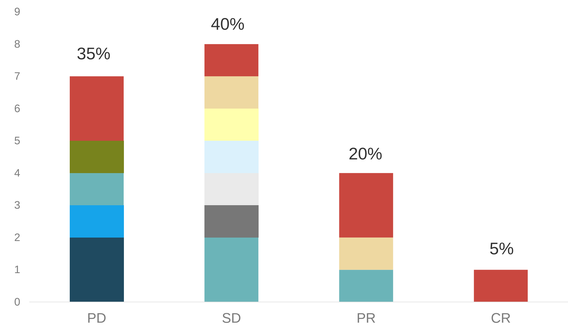
Figure 3b : The relative relation between successful genomic profiles compared to pts receiving targeted therapy. Notably >70% of the pts receiving targeted therapy were from 2019.

RESULTS



TMB-H = High tumor mutational burden > 10mut/Mb

Figure 4 : Targets for the patients treated with tailored therapy
18 patients were treated with targeted therapy. Three patients were treated twice with tailored therapy



PD = progressive disease, SD = stable disease, PR = partial response, CR = complete response

Figure 5: Outcome for the patients treated with targeted therapy
(N = 18, three patients were treated twice). In total 21 treatment regimens were initiated and 20 pts were evaluable by RECIST. Overall response rate (ORR) in the treated population 25% (95% CI:6% - 44%).

CONCLUSIONS

- Druggable targets were identified in 47% of pts (95% CI: 39% - 54%)
- Targeted treatment were initiated in 11% of pts (95% CI: 6% - 16%)
- ORR in the treated group was 25% (95% CI:6% - 44%)

This study illustrates increasing targeted treatment options for SCCs and high ORR, thereby emphasizing the importance of genomic profiling.

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