SafeSEQ Head and Neck Cancer Panel

Lighting the way with diagnostics

Ultra-high sensitivity NGS-based circulating tumor DNA detection for emerging clinical applications

Background

Head and neck squamous cell carcinoma (HNSCC) affects approximately 600,000 globally[1], where about half will ultimately succumb to this disease.

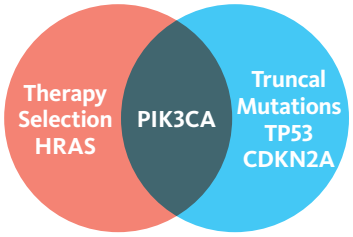
The first targeted therapy for HNSCC to exploit the epidermal growth factor receptor (EGFR) was approved in 2006[2] and recently two immunotherapies have been adopted into clinical practice[3,4]. However, molecular testing is not routinely performed in HNSCC except for the presence of tumor expressed human papillomavirus (HPV), which represents a distinct subtype with generally favorable prognosis. Recent advances in comprehensive genomic characterization of HNSCC have revealed numerous molecular alterations that are actively being pursued as therapeutic targets.[1]

Activating mutations in HRAS and PIK3CA have been characterized for HPV-negative HNSCC, and may be indications for novel precision therapies. Circulating tumor DNA (ctDNA) is an attractive option for mutation detection in HNSCC via a minimally-invasive blood draw to capture the mutational profile across a patient's tumor burden since tissue biopsy specimens are not readily available for patients considering later line therapies.

Sysmex Inostics' SafeSEQ Head and Neck Cancer Panel has been designed for HPV- patients (~75% of HNSCC patients) and can be used to detect novel therapeutic targets and frequently occurring driver mutations for treatment response monitoring.

Gene List for the SafeSEQ HNSCC Panel
HRAS
PIK3CA
TP53
CDKN2A

Rationale for genes in the SafeSEQ HNSCC Panel



Sensitivity matters

Mutations in HRAS occur infrequently in HNSCC but have been recently shown to impart unique sensitivity to a novel therapeutic class known as farnesyltransferase inhibitors.[5]

In newly diagnosed patients, HRAS mutations are only detected in about 1 in 20 cases and may be acquired in a much larger proportion of patients that have undergone treatment with anti-EGFR therapy.[6]

Blood-based testing can enable access to a greater number of patients and can deliver clinically important results, however, a primary challenge in blood-based mutation testing is the limited quantity of ctDNA that has been observed in HNSCC patients with advanced and metastatic disease. For example, a recent study comparing four different

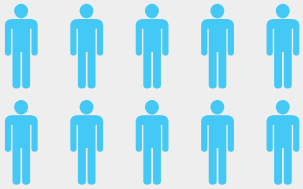
Sensitivity matters for detection of rare, low-frequency therapeutic indications for HNSCC

Only 1 in 20 HNSCC patients is HRAS+ at first diagnosis

12% of ctDNA plasma mutations observed >1% MAF

88% of ctDNA plasma mutations observed <1% MAF

For enrollment of 50 patients based on HRAS mutation status

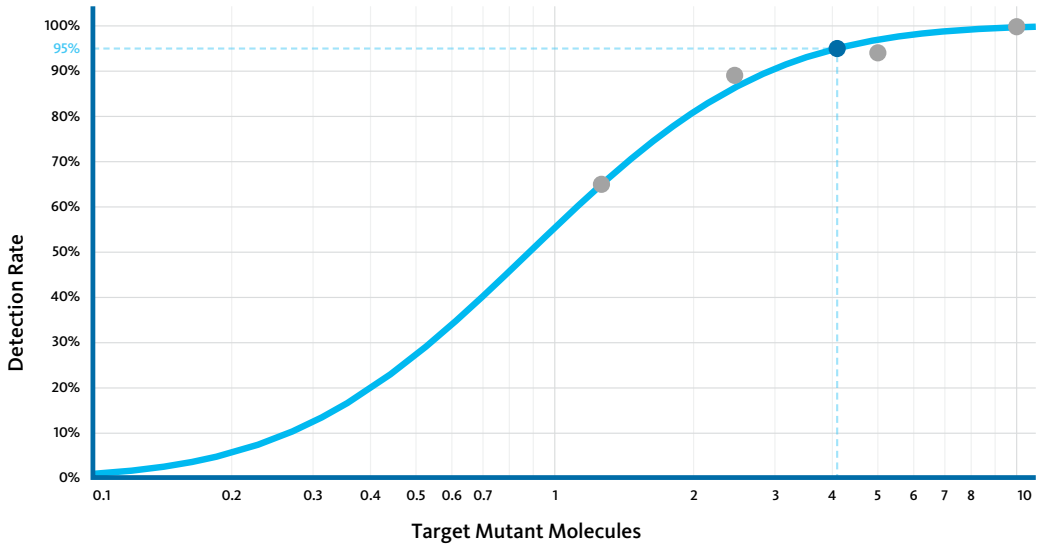


Screen 1,000 patients using SafeSEQ to identify 50 HRAS+

$1x total screening cost

Screen over 9,000 patients using an assay that is unreliable below 1% MAF to identify 50 HRAS+

>$9x total screening cost



Reliable high-sensitivity detection of low-frequency mutations

Figure 1: Sensitivity (LoD95) is established using the SeraCare Seraseq ctDNA Mutation Mix v2 (6 mutations) with a background of 10K wildtype GE and the indicated number of target mutant molecules.

commercial broad coverage ctDNA tests has revealed poor agreement below 1% mutant allele fraction (MAF), with a greater proportion of false positive and negative calls at low frequencies. This makes such tests unsuitable for HNSCC[7] as the vast majority (88%) of HNSCC patients have been shown to have detectable ctDNA at levels well below 1% MAF[8].

SafeSEQ delivers high sensitivity mutation detection in HNSCC with a limit of detection of 0.05% MAF, which is orders of magnitude more sensitive than broad based plasma NGS panels and can greatly improve the rapid identification of patients eligible for novel targeted therapies (figure 1). Importantly, reliable detection of low-frequency mutations directly impacts the cost of clinical development. For example, to enroll 50 patients into a clinical study based on HRAS mutation status, many more patients must be tested if the assay cannot reliably detect mutations below 1% MAF, which increases both time and cost.

Sysmex Inostics SafeSEQ HNSCC Panel is a focused, ultrahigh sensitivity solution which prioritizes depth and quality of information over breadth of genomic coverage, making it ideal for cost-effective clinical development for targeted therapies. This purpose-designed panel can also be used for high sensitivity molecular monitoring to help gauge patients' response to different therapeutic modalities, with the potential to exceed the resolution offered by current imaging techniques.

Challenge of HNSCC in clinical practice

- 5% of HNSCC patients are HRAS mutation-positive
- No routine molecular testing
- Undue biopsy risk and long turnaround times for FFPE testing
- Mutations occur at low MAF for ctDNA testing

A choice:

- an invasive tissue biopsy or
- screen patients for HNSCC specific mutations with a minimally invasive, highly sensitive, blood-based approach

To learn more about **SafeSEQ Head and Neck Cancer Panel** or other highly sensitive ctDNA tests from Sysmex Inostics, please contact us today at info@sysmex-Inostics.com or visit our website at **www.sysmex-inostics.com**

References

1. Ferlay, J. et al. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int. J. Cancer 127, 2893–2917 (2010
2. U.S. Food and Drug Administration, Center for Drug Evaluation and Research. Erbitux BLA 125084/SUPPL-46 supplement, 1 Mar 2006. Accessed 9 Oct 2018, from https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2006/125084s046LTR.pdf
3. FDA Approves Pembrolizumab for Head and Neck Cancer. 24 Aug 2016. Retrieved 9 Oct 2018 from, https://www.cancer.gov/news-events/cancer-currents-blog/2016/fda-pembrolizumab-hnscc.
4. FDA Approved Nivolumab for Head and Neck Cancer. 1 Dec 2016. Retrieved 9 Oct 2018 from, https://www.cancer.gov/news-events/cancer-currents-blog/2016/fda-nivolumab-scchn.
5. Ho AL, Chau N, Bauman J, and Gualberto A et al. 1046O Preliminary results from a phase II trial of tipifarnib in squamous cell carcinomas (SCCs) with HRAS mutations, Annals of Oncology, Volume 29, Issue suppl_8, October 2018. https://academic.oup.com/annonc/article/29/suppl_8/mdy287.002/5140721
6. Braig F, Voigtlaender M, and Binder M et al. Liquid biopsy monitoring uncovers acquired RAS-mediated resistance to cetuximab in a substantial proportion of patients with head and neck squamous cell carcinoma. Oncotarget. 2016 7(28):42988-42995. doi: 10.18632/oncotarget.8943
7. Stetson D. and Dougherty B.A. JCO Precision Oncol (2019). Orthogonal Comparison of Four Plasma NGS Tests With Tumor Suggests Technical Factors are a Major Source of Assay Discordance. https://ascopubs.org/doi/10.1200/PO.18.00191
8. Wang Y. and Agrawal N. et al. Sci Transl Med. 7(293):293ra104 (2016). Detection of somatic mutations and HPV in the saliva and plasma of patients with head and neck squamous cell carcinomas. doi: 10.1126/scitranslmed.aaa8507

For research use only. Not for use in diagnostic procedures.

Sysmex Inostics GmbH Falkenried 88, 20251 Hamburg, Germany • Phone +49 40 325907-0 • Fax +49 40 325907-6699 • info@sysmex-inostics.com • **www.sysmex-inostics.com**

Sysmex Inostics, Inc. 1812 Ashland Ave, Suite 500, Baltimore, MD 21205, USA • Phone Toll-Free: +1-855-BEAM-DNA (232-6362) • info@sysmex-inostics.com • **www.sysmex-inostics.com**

Sysmex Corporation 1-5-1 Wakinohama-Kaigandori, Chuo-ku, Kobe 651-0073, Japan • Phone +81 78 265 0500 • Fax +81 78 265-0524 • **www.sysmex.co.jp**

SAFESEQHNSCC.EN.N.09/2019