sysmex | Lighting the way with diagnostics

HNSCC-SEQ

Ultra-sensitive liquid biopsy solution for the identification of gene mutations in CDKN2A, EGFR, ERBB2, FGFR3, HRAS, KRAS, NOTCH1, PIK3CA, PTEN, and TP53

HNSCC-SEQ

For emerging head and neck squamous cell cancer clinical applications

HNSCC-SEQ detects mutational drivers of head and neck squamous cell carcinoma (HNSCC). With high specificity, Plasma-Safe-SeqS technology is optimized to detect low-frequency mutant molecules, with a limit of detection of 0.04% MAF, in plasma for potential uses:

- Aid in cancer drug development
- Monitor therapeutic efficacy
- Identify treatment resistance
- Detect minimal residual disease (MRD)

Enabling discoveries in biopharma

Head and neck squamous cell carcinomas (HNSCC) develop from the mucosal epithelium in the oral cavity, pharynx, and larynx and are the most common malignancies that arise in the head and neck regions.[1]

HNSCC-SEQ has been designed for human papillomavirus (HPV)-negative patients and can be used to detect novel therapeutic targets and frequently occurring driver mutations for treatment response monitoring. HNSCC-SEQ delivers high-sensitivity mutation detection in HNSCC with a limit of detection of 0.04% MAF.

Clinical relevance

The epidermal growth factor receptor (EGFR) is an established therapeutic target in HNSCC. The first targeted therapy for HNSCC to exploit EGFR was approved in 2006,[2] and recently two immunotherapies have been incorporated into clinical practice.[3,4] However, molecular testing is not routinely performed in HNSCC evaluation, except for the presence of tumor-expressed HPV, which represents a distinct subtype with a generally favorable prognosis. Recent advances in comprehensive genomic characterization of HNSCC have revealed numerous molecular alterations that are actively being pursued as therapeutic targets.[5]

Activating mutations in HRAS and PIK3CA have been characterized for HPV-negative HNSCC and may be indications for novel personalized therapies. Analyzing circulating tumor DNA (ctDNA) is an attractive option to detect HNSCC-specific mutations via a minimally invasive blood draw. This would be a preferred method to determine the mutational profile of a patient's tumor since tissue biopsy specimens are not readily available for patients considering later line therapies.

GENE	GENE REGIONS COVERED (AMINO ACIDS)	CLINICAL RELEVANCE
CDKN2A	51–61, 80–91, 96–124, 143–152	Putative therapeutic indication Marker of poor prognosis
EGFR	283–296, 464–487, 706–725, 856–873	Therapeutic indication
ERBB2	303–315	
FGFR3	248–269, 370–392	Putative therapeutic indication
HRAS	9–27, 55–67, 105–118, 144–150	Putative therapeutic indication Marker of poor prognosis
KRAS	5–26, 141–148, 156–174	Predictive marker for anti-EGFR therapy Putative therapeutic indication
NOTCH1	184–209, 290–315, 440–468, 562–582, 1836–1862, 1979–1997	Putative therapeutic indication
PIK3CA	72–93, 108–117, 330–352, 354–371, 418–421, 440–462, 538–553, 597–614, 714–728, 970–978, 1001–1025, 1040–1056	Putative therapeutic indication
PTEN	6–26, 87–104, 117–136, 229–247, 335–342	Putative therapeutic indication
TP53	26–32, 49–77, 99–125, 126–141, 151–179, 192–219, 233–260, 262–285, 297–306, 308–331, 332–360, 368–383	Truncal mutations important for monitoring

Benefits of HNSCC-SEQ

- Quickly and accurately identify patients appropriate for treatment.
- Detect residual disease and assess response to therapy (including immunotherapy) using non-invasive, rapid, and real-time ctDNA assay.
- Avoid over-treatment in the neoadjuvant and adjuvant settings.
- Allow for individualized decisions to optimally refine treatment regimens.
- Serve as useful intermediate endpoints and improve efficiency of clinical trials.

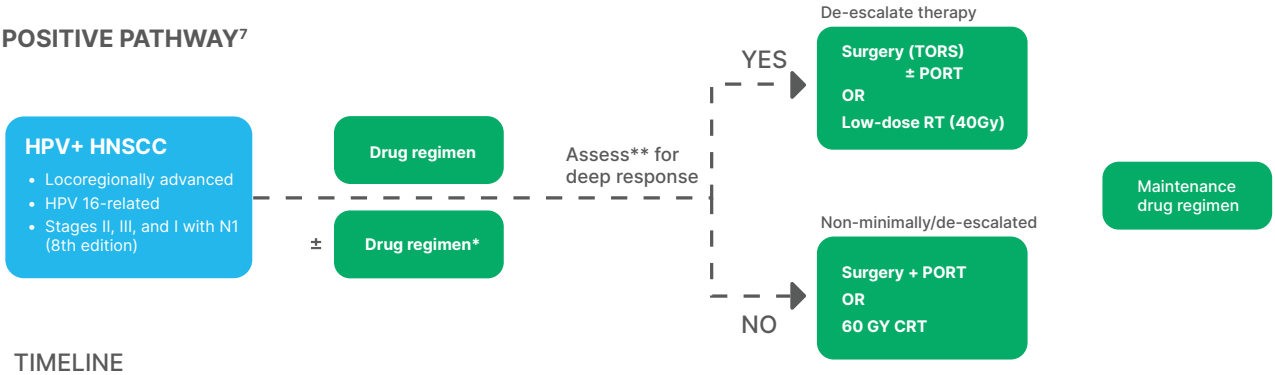
Performance data[6]

VARIANT	# OF CTDNA MOLECULES	MAF
Combined SNV Del MNV	8 or more	0.040%

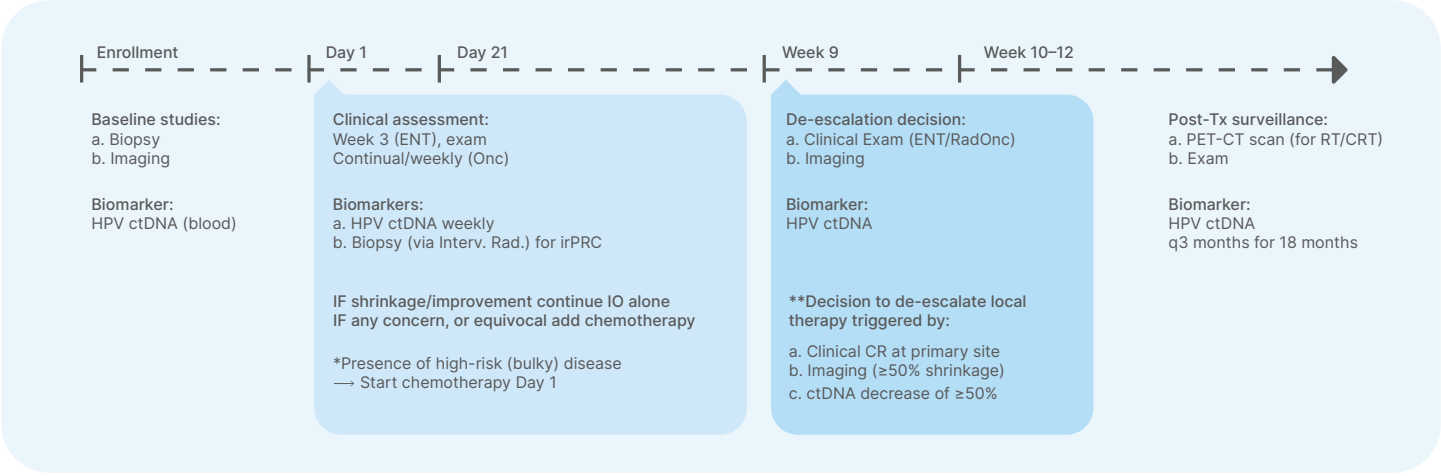
Reporting threshold is above LoD95. Corresponding MAF for 20,000 copies (~66 ng DNA).

Current ongoing clinical trial designs for HPV-positive & HPV-negative HNSCCs:

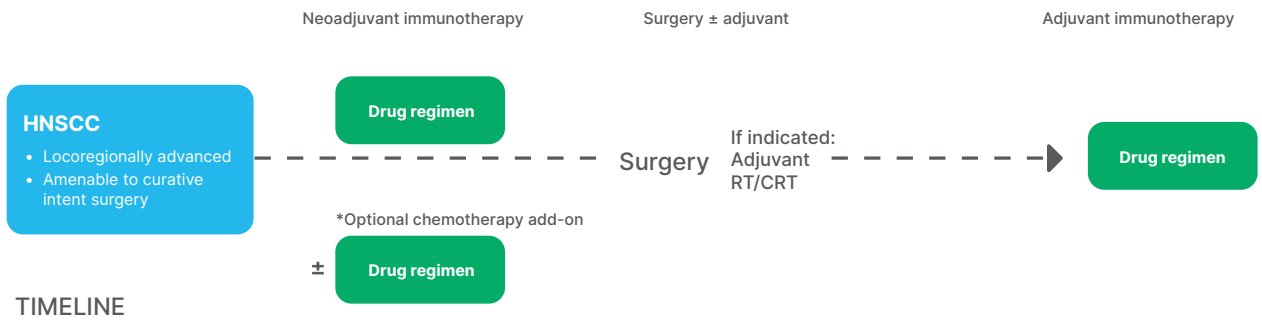
1. HPV POSITIVE PATHWAY[7]



TIMELINE



2. HPV NEGATIVE PATHWAY[8]



TIMELINE

Baseline studies:
a. Biopsy
b. Imaging

Biomarker:
Blood ctDNA

Clinical assessment:
Week 3 (ENT), exam
Continual/weekly (Onc)

Biomarkers:
a. Blood ctDNA, weekly
b. Biopsy (via interv. rad.) for irPRC

*IF shrinkage/improvement continue immunotherapy alone

IF disease worsening or equivocal add chemotherapy C2D1

(However for any clinical concern, may start earlier or later)

Surgery at week 9–12

Pre-surgery:
a. Imaging

Biomarker:
Blood ctDNA

Post-Tx surveillance for 2 years:
a. Imaging q3 months
b. Exam q3 months

Biomarker:
Blood ctDNA q3 months

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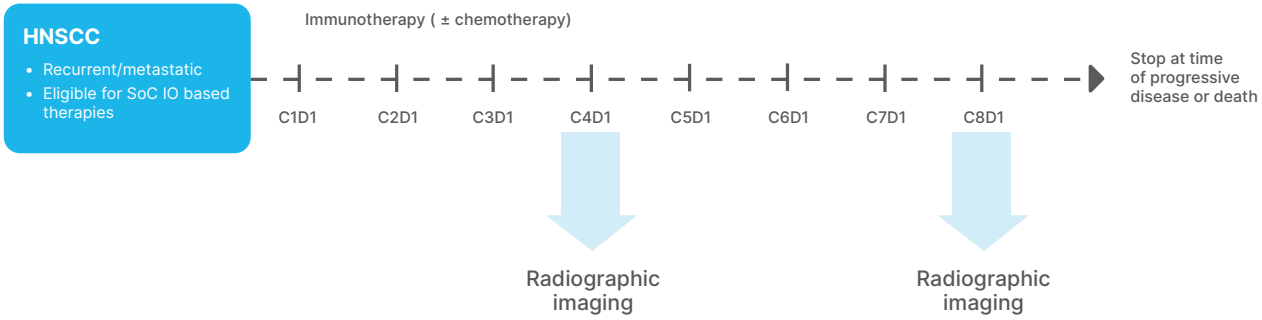
3. HPV positive and negative HNC[9]



Details:

- 2 streck tubes drawn with each cycle until time of recurrence or if stable disease, can draw every other cycle
- Total time points per patient: estimated 3 – 5
- Samples can be batched as convenient
- Both HPV positive and HPV negative disease

Sample requirements and processing time

Sample specification

2×10mL tubes of whole blood

Pre-analytical sample handling

Sysmex Inostics' validated shipping kits and temperature loggers ensure sample stability

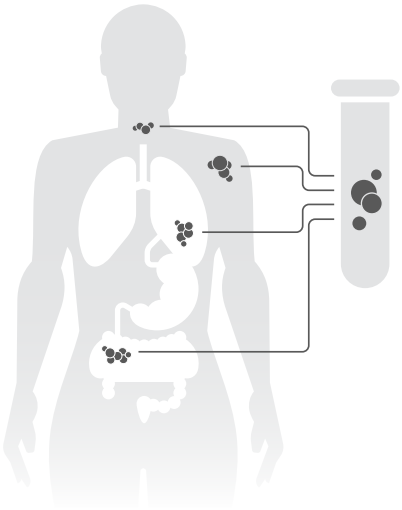
Result turnaround time

7 – 10 business days

PLASMA-SAFE-SEQS TECHNOLOGY

Ultra-sensitive across clinically relevant genomic regions

Sysmex Inostics' Plasma-Safe-SeqS technology offers highly sensitive mutation detection across the most clinically relevant gene targets. Plasma-Safe-SeqS is designed specifically for the measurement of ctDNA and panels are developed for particular clinical intended uses where highly sensitive detection may provide unique insights and improve outcomes.



Have a question about HNSCC-SEQ?
Visit: **sysmex-inostics.com/oncology/hnscc-seq#contact**

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Sysmex Inostics, Inc. 1812 Ashland Ave, Suite 500, Baltimore, MD 21205, USA
Phone Toll-Free: +1-855-232-6362 • 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

Sysmex Inostics Germany GmbH Falkenried 88, D-20251, Hamburg, Germany
info@sysmex-inostics.com

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