

# A Case of Stage IIA Anal Squamous Cell Carcinoma Detected Using a Multi-Cancer Early Detection Test

AACR 2023  
April 14–19, 2023  
Orlando, Florida

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## INTRODUCTION

- Anal cancer is a less common cancer that represents 0.5% of all new cancer cases in the US<sup>1</sup>
  - Most anal cancers are linked to human papillomavirus (HPV) infection<sup>2</sup>
- The 5-year relative survival for localized, regional, and distant stage anal cancer is 83.3%, 67.3%, and 35.9% respectively,<sup>1</sup> underscoring the need for early detection to maximize chances for long-term survival
- Although some anal cancers can be detected early via screening (anal Pap test), the anal Pap test is not routinely recommended for the general population due to the low prevalence of anal cancer<sup>3,4</sup>
- A multi-cancer early detection (MCED) test (Galleri<sup>®</sup>,\* GRAIL, LLC, Menlo Park, CA) is available as a complement to existing single cancer screening tests and as a screening option for cancers that do not have USPSTF-recommended or other screening<sup>5-7</sup>
  - This MCED test detects a shared cancer signal from abnormal methylation patterns of tumor cell-free DNA in blood using a targeted methylation assay and machine learning algorithm
  - When a cancer signal is detected, a 'cancer signal detected' result (positive result) is reported with 1 or 2 predicted cancer signal origin(s) (CSO)
  - Importantly, this test may detect cancers at a late stage or not detect a cancer at all as sensitivity of cancer signal detection for this MCED test was 51.5% in the Circulating Cell-free Genome Atlas (CCGA) study (NCT02889978)<sup>7</sup>
  - In the CCGA study, the overall CSO prediction accuracy of the top-predicted CSO was 89%<sup>7</sup>
  - Despite high average CSO prediction accuracy, the biological similarity among HPV-related cancers of the anogenital tract and head and neck (H&N),<sup>8</sup> may lead to CSO misclassification<sup>9</sup>

## OBJECTIVE

- Here, an HPV-driven anal squamous cell carcinoma (SCC) case is reported to review the diagnostic journey following a 'cancer signal detected' test result and misclassified CSO prediction

## SUPPORTING INFORMATION

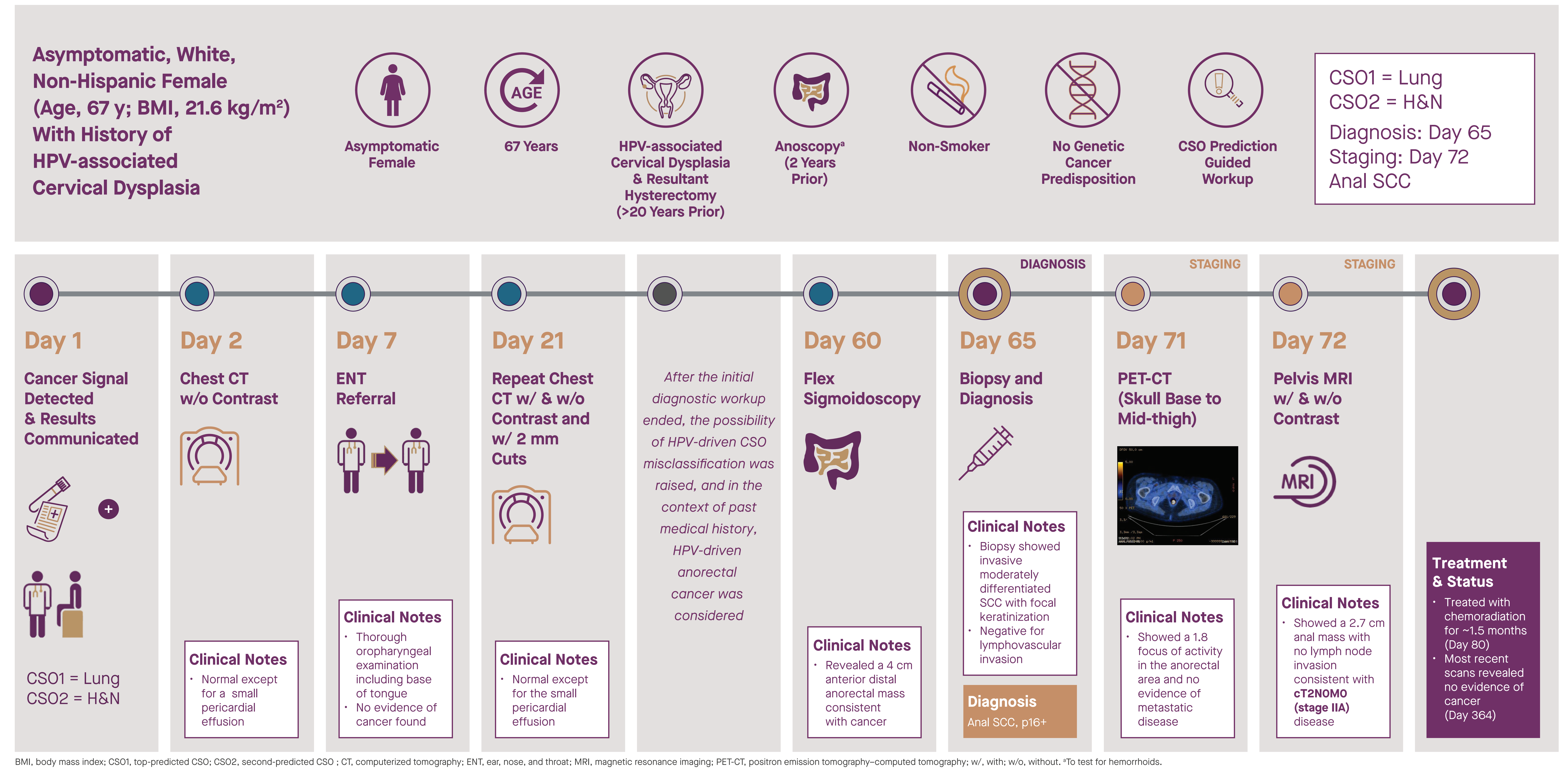
### Supporting Data

- In the CCGA study, an observational, multicenter, case-control study, sensitivity of cancer signal detection was 75.0% in stage II anal cancer<sup>7</sup> (Table S1)

Table S1. Sensitivity of Cancer Signal Detection in Anal Cancer by Stage

| Clinical stage | Total | Test positive | Sensitivity (95% CI)  |
|----------------|-------|---------------|-----------------------|
| All            | 22    | 18            | 81.8% (61.5%–92.7%)   |
| I              | 4     | 1             | 25.0% (1.3%–69.9%)    |
| II             | 4     | 3             | 75.0% (30.1%–98.7%)   |
| III            | 13    | 13            | 100.0% (77.2%–100.0%) |
| IV             | 1     | 1             | 100.0% (5.1%–100.0%)  |

## KEY RESULTS: THE MCED TEST DETECTED A CANCER SIGNAL FOR A STAGE IIA ANAL SCC. BIOLOGICAL SIMILARITIES ACROSS TISSUES CAUSED CSO MISCLASSIFICATION; HOWEVER, PHYSICIAN EDUCATION AROUND TEST PERFORMANCE HELPED DIRECT DIAGNOSTIC EVALUATION



## CONCLUSIONS

- The MCED test detected a cancer signal for an asymptomatic individual with stage IIA anal SCC
  - Anal cancer does not have USPSTF-recommended or other routine screening;<sup>3</sup> without the MCED test, this cancer may not have been detected until clinical presentation
- HPV infection can induce similar epigenetic changes across multiple

tissues (anogenital tract, lung, H&N), which likely explains the CSO misclassification in this case;<sup>9</sup> despite this phenomenon, the detection of a cancer signal by the MCED test prompted aggressive cancer workup and led to early detection and treatment with curative intent

- Based on this case, CSO misclassification may be considered in patients with an HPV medical history

- Future versions of the MCED test may take HPV status into account when predicting CSO
- The use of this MCED test led to early detection of cancer and treatment (chemoradiation) with curative intent
- Detection of a less common cancer in the real world by the MCED test is notable

### References

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### Disclosures

DAM serves on a speaker's bureau for GRAIL, LLC, with equity in Illumina, Inc. BW is an employee of GRAIL, LLC, with equity in Illumina, Inc.

### Acknowledgements

Funders: GRAIL, LLC. Writing provided by Grace Wang (GRAIL, LLC, Menlo Park, CA). Editorial and graphic assistance provided by Kristi Whitfield from PosterDocs (Oakland, CA).

\*The Galleri<sup>®</sup> test was developed and its performance characteristics were determined by GRAIL, LLC. The Galleri<sup>®</sup> test has not been cleared or approved by the Food and Drug Administration. GRAIL's clinical laboratory is regulated under Clinical Laboratory Improvement Amendments to perform high-complexity testing. The Galleri<sup>®</sup> test is intended for clinical purposes.

