Multi-Cancer Detection Test to Aid Clinically Presenting Head and Neck Cancer Diagnosis

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INTRODUCTION

- Delayed diagnostic resolution in individuals seeking care for signs and symptoms suspicious for cancer can affect outcome, patient experience, and the efficiency of care delivery.[1-6]
- The Circulating Cell-free Genome Atlas (CCGA; NCT02889978) study was designed to develop and validate a multi-cancer detection test.
- This blood-based multi-cancer detection test uses a cell-free DNA (cfDNA)-based targeted methylation assay to detect cancer signals across multiple cancers, including head and neck cancer, and predict cancer signal origin (ie, the tissue where the primary tumor arose).[7]

OBJECTIVE

- To evaluate performance of the multi-cancer detection test in a subgroup of clinically presenting cancer participants, including a smaller subgroup of head and neck cancer, and non-cancer participants.

RESULTS

Study Population

- A total of 518 clinically presenting cancer participants, 25 of which had head and neck cancer were included in the analysis. A subgroup of 327 clinically presenting cancer participants with single known primaries and a trained, predicted CSO (not including a CSO prediction of "other") were included in the accuracy of CSO prediction analysis.
- In addition, 398 non-cancer participants with confirmed non-cancer status at Year 1 follow-up were analyzed. Also, 16 participants who had significant non-malignant medical conditions at enrollment were analyzed.

Specificity

- The multi-cancer detection test correctly identified 396 of 398 non-cancer participants (non-cancer status confirmed at Year 1 follow-up) as not having cancer (**Table 1**), corresponding to a false positive rate of <1%.
- High specificity was also observed in non-cancer participants with non-malignant confounding conditions.

Sensitivity

- Sensitivity of the multi-cancer detection test in participants with clinically presenting cancers and the subgroup of participants with head and neck cancers was comparable (**Table 2**).
- Sensitivity was generally higher for head and neck cancers at later clinical cancer stages, as expected.
  - It should be noted that the wide confidence intervals may be attributed to small sample size.

Cancer Signal Origin Prediction

- Accuracy of CSO prediction for participants with head and neck cancers was high, and similar to that of all clinically presenting cancer participants (**Table 3**).

Table 1. Specificity

Group	Cancer Signal Not Detected/ Total	% (95% CI)
Non-cancers with non-cancer status confirmed at Year 1 follow-up	396/398	99.5% (98.2-99.9%)
Non-cancers with non-malignant confounding conditions at enrollment	15/16	93.8% (71.7-99.7%)

CI, confidence interval.

Table 2. Sensitivity

Group	Cancer Signal Detected/Total	% (95% CI)
All Clinically Presenting Cancer	344/518	66.4% (62.2-70.3%)
Clinically Presenting Head and Neck Cancer	18/25	72.0% (52.4-85.7%)
Stage I	2/3	66.7% (20.8-98.3%)
Stage II	1/4	25.0% (1.3-69.9%)
Stage III	5/6	83.3% (43.6-99.1%)
Stage IV	10/12	83.3% (55.2-95.3%)

CI, confidence interval.

Table 3. Cancer Signal Origin Prediction Accuracy

Group	Correct Signal Origin Detected/Total	% (95% CI)
All Clinically Presenting Cancer[a]	300/327	91.7% (88.3-94.3%)
Clinically Presenting Head and Neck Cancer	16/18	88.9% (67.2-96.9%)

[a]Excludes participants with multiple or unknown primaries or other cancers.
CI, confidence interval.

CONCLUSIONS

- The multi-cancer detection test performed with high specificity while detecting cancer signals and predicting cancer signal origin in individuals with symptomatic cancer, including in those with head and neck cancer.
- These findings support the potential use of this multi-cancer detection test for diagnostic resolution of symptomatic cancers.

References

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METHODS

Multi-Cancer Detection Test

- This test detects cancer signal and predicts cancer signal origin through machine-learning analysis of methylation patterns in cfDNA circulating in the blood.[7]
  - Targeted methylation sequencing of 10^6 CpG sites in cfDNA isolated from a blood draw is performed.
  - A machine-learning algorithm differentiates abnormal tumor cfDNA methylation patterns from normal cfDNA methylation patterns.
  - When a cancer signal is detected, the machine-learning algorithm discerns cancer type-specific differences in methylation to predict cancer signal origin.

Study Design and Participants

- The CCGA study is a prospective, longitudinal, multicenter, case-control study with the objective to develop and validate a multi-cancer detection test.
  - In the second CCGA substudy, the multi-cancer detection test performance was assessed in a training set and an independent validation set.[7]
  - Test performance is reported from the validation set from the second CCGA substudy of participants.
- Specificity was assessed in non-cancer participants who had confirmed non-cancer status at Year 1 follow-up and in a subgroup of non-cancer participants with significant non-malignant medical conditions at enrollment (eg, oral/pharyngeal/nasal lesion).
- Sensitivity and cancer signal origin prediction accuracy were assessed in a subgroup of participants with clinically presenting cancers and a smaller subgroup of participants with head and neck cancer from the second CCGA substudy.

Measures

- **Specificity**: Estimated as the proportion of non-cancer participants with a "cancer signal not-detected" result.
- **Sensitivity**: Estimated as the proportion of cancer participants with a "cancer signal detected" result.
- **Sensitivity by clinical stage**: Estimated as the proportion of participants with a "cancer signal detected" result among cancer participants with a clinical stage.
- **Accuracy of cancer signal origin (CSO) prediction**: Estimated as the proportion of participants with a true positive cancer signal detected result and with a correctly predicted trained cancer signal origin.