ONETEST™ PREMIUM: DEMONSTRATING EARLY DETECTION OF CANCER WITH PLCO SAMPLES

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ABSTRACT

20/20 BioLabs recently participated in a study under the auspices of NCI's Cancer Screening Research Network (CSRN) to investigate the performance of various multi-cancer detection (MCD) tests that are either commercially available or in development. We received a blinded set of pre-diagnostic samples that had been collected up to 6 months prior to a cancer diagnosis taken from the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Study. (It should be noted that these samples are over 30 years old.) These samples were processed using our OneTest™ Premium cancer test which utilizes a series of eight machine learning derived algorithms to interpret the results of 12 biomarker values together with age and gender to predict risk of specific cancer types including breast, colorectal, liver, lung, prostate, pancreatic, stomach and ovarian cancers. The biomarkers include AFP, CEA, CA15.3, CA125, CA19.9, CYFRA21.1, HE4, tPSA, CRP, ApoAI, Prealbimin, and β2-M. Upon unblinding of the samples, NCI indicated that of the 759 samples, 400 were controls, 91 were lung cancer, 80 prostate cancer, 76 colorectal cancer, 40 breast cancer, 21 pancreatic cancer, 17 ovarian cancer and 34 bladder cancer. Note that OTP does not include an algorithm specific to bladder cancer and as such bladder cancer was considered a "non-targeted" cancer type. Stage information was also supplied, with 53% of the cases being early stage (either stage 1 or 2). Overall sensitivities for all cancers in this pre-diagnostic cohort was 39% - 27% for early-stage cancers and 58% for later-stage. Sensitivities for early-stage pancreatic, ovarian and lung cancers were all 35% or greater. Overall specificity in the study 82%, however for any one of the cancer-type algorithms the minimum specificity was 95%.

ONETEST™ PREMIUM

OneTest™ Premium is a MCED test that predicts an individual's risk of being identified as having one or more of the eight most common cancer types, including lung, liver, colon, stomach, pancreatic, prostate (male only), breast (female only) and ovarian (female only) cancers in the coming 12 months. The test incorporates a biomarker panel consisting of 9 tumor markers and 4 inflammatory/metabolic markers. A series of cancer type specific machine-learning derived algorithms are used to analyze and interpret these marker values together with the subject's age and gender. These algorithms were derived using case-control studies including data from over 2000 individual subjects. A subsequent validation study in a cohort of >42,000 asymptomatic individuals whose cancer status was monitored for one year subsequent to testing corroborated the performance of the OneTest™ Premium algorithms. The test reports an "elevated" or "not elevated" risk and calculates risk based on the PPVs in the validation study. Because there is overlap in the markers used for each algorithm, OTP may often indicate risk for more than one type of cancer and thus risk is calculated for both the specific cancer and any cancer.

SAMPLES

A set of pre-diagnostic samples that had been collected up to 6 months prior to a cancer diagnosis were taken from the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Study. Samples had not been subjected to more than one prior freeze-thaw cycle. Samples were blinded with 20/20 BioLabs only knowing that roughly half the samples were cases and half controls. Upon unblinding the nature of the samples was revealed as indicated in the table below:

Sample Type	Control	Lung Cancer	Prostate Cancer	Colo-rectal Cancer	Breast Cancer	Pancreatic Cancer	Ovarian Cancer	Bladder Cancer
Number	400	91	80	76	40	21	17	34

METHODS

These samples were tested for 12 biomarkers, including AFP, CEA, CA15.3, CA125, CA19.9, CYFRA21.1, HE4, tPSA, CRP, ApoAI, Prealbimin, and β2-M. All of the protein tumor markers were tested on a Roche Cobas e411 using manufacturer supplied test kits. The four inflammatory/metabolic markers were tested on an Abbott Alinity c again using manufacturer supplied test kits. The IFUs for each test were followed as per protocol in our CAP/CLIA laboratory. Results were processed using our OneTest™ Premium cancer test which utilizes a series of eight machine learning derived algorithms to interpret the results of 12 biomarker values together with age and gender to predict risk of specific cancer types including breast, colorectal, liver, lung, prostate, pancreatic, stomach and ovarian cancers.

RESULTS

Sensitivities and specificities for the overall test, combining all algorithms, and for each individual algorithm are tabulated below:

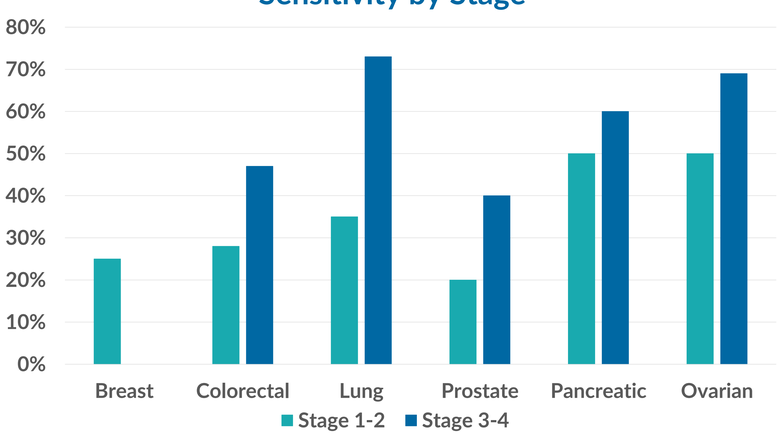
Cancer Type (all stages)	Number	Specificity (out of 400 Controls)	Sensitivity by Specific Algorithm	Sensitivity by Any Algorithm
ALL	359	82%	-	39%
Bladder	34	-	-	15%
Breast	40	100%	0%	25%
Colorectal	76	96%	14%	37%
Liver	0	95%	-	
Lung	91	95%	36%	52%
Prostate	80	98%	31%	34%
Stomach	0	97%	-	
Pancreatic	21	95%	19%	57%
Ovarian	17	96%	65%	65%

RESULTS (Cont.)

- Overall specificity in the study 82%, however for any one of the cancer-type algorithms the minimum specificity was 95%.
- Overall sensitivities for all cancers in this pre-diagnostic cohort was 39%.
- Sensitivities ranged from a low of 15% for bladder cancer – note that OTP does not include a specific algorithm for bladder cancer and was not trained using bladder cancer – to as high as 65% for ovarian cancer.
- Sensitivities for Lung, Pancreatic and Ovarian cancers were all above 50%.
- Sensitivities for Prostate and Colorectal cancers were 34 and 37% respectively.

Stage information was also supplied, with 53% of the cases being early stage (either stage 1 or 2). Sensitivities by stage for each cancer type is presented in the chart below (Note that all breast cancer cases were early stage):

Sensitivity by Stage



- Sensitivities for early-stage cancers ranged from 20% for prostate cancer to 50% for Pancreatic and Ovarian cancers.

CONCLUSIONS

OneTest™ Premium was challenged using samples obtained from the PLCO cohort. The test demonstrated significantly high sensitivities among early-stage pre-diagnostic samples with an overall sensitivity amongst early-stage cancers of 27%. In general, the response to an elevated OneTest™ Premium result should be determined by a health care professional who is familiar with the individual patient's health history. Follow-up will include further screening or diagnostic testing which may include repeat testing with OneTest™ Premium at a greater frequency, the use of another MCED, or cancer-type specific diagnostic tests.