INTRODUCTION

The ability of a multi-cancer test to detect UCT and uncommon cancers may indicate MCED.

When transitioning from such a case-control study to application in the clinic, a classifier performance on the TO type-specific detection of cases with UCT, MP, and UP.

METHODS

CCGA (plasma) samples from a prespecified subset (Figure 1) were subjected to targeted methylation (Illumina) assay.

Median values per DNA fragment across 1,000,000 targeted genomic regions were input to a classifier that detects cancer site and provides TOO: TDO (class definitions in training dataset), ovary, uterus, cervix, rectum, bladder, bladders, female, female genital, female genitalia, and as well as plasma, male genital, and prostate.

A noninvasive cell-free DNA (cfDNA) blood test with the ability to detect multiple cancer types at the preclinical stage (eg, in stages II/III) could improve cancer mortality.

To be effective at population scale, such a multi-cancer test should:

- Detect as many cancer types as possible, to maximize the total number of cancer cases detected and intercept as many cancers as possible before they reach metastatic stages.
- Have several false positive results (FPRs) per high specificity to minimize potential harms, with compelling sensitivity, and a low number of false negative results (FNRs) per high signal.
- Be acceptable to patients and healthcare providers.

The previously reported multi-cancer detection test in plasma cfDNA (AstraZeneca (MSK) ClinicalTrial.gov #NCT02076137) was a case-control study with 1,646 cancer and 1,375 non-cancer cases in the training set and 740 cancer and 614 non-cancer cases in the validation set.

The classifier performance of a cfDNA-based multi-cancer detection test on uncommon cancer types showed the classifier detection and TOO results for UP.

Conversely, TOO classification may provide clinical and research implications for the clinic as the TOO test can direct the clinical workflow.

- Given that further classification development is ongoing (see poster #21149), it is possible that the classifier performances of the prespecified TooD class and the TOO accuracy, may improve over time.
- Detection and TOO predictions for MP further suggest that the test handles expression of signals from existing TOO categories, and could lead to awareness of one of the prespecified TooD classes.
- In general, TOO predictions for detected UCTs were consistent with biologic features of reported cases.

Overall, these data suggest that the MCED test classifier exploits general features associated with malignancy, and supports its population-scale multi-cancer early detection.

CONCLUSIONS

1. The TOO classifier results for UCT-confirmed cases of cancers and for cases with a TOO assigned in the prespecified TOO classes and/or the TOO accuracy, may increase over time.

2. The classifier classification may provide clinical and research implications for the clinic as the TOO test can direct the clinical workflow.

3. Given that further development is ongoing (see poster #21149), it is possible that the classifier performances of the prespecified TooD class and the TOO accuracy, may improve over time.

4. Detection and TOO predictions for MP further suggest that the test handles expression of signals from existing TOO categories, and could lead to awareness of one of the prespecified TooD classes.

5. In general, TOO predictions for detected UCTs were consistent with biologic features of reported cases.

Overall, these data suggest that the TOO classifier exploits general features associated with malignancy, and supports its population-scale multi-cancer early detection.