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Future of liquid biopsies in cancer detection and therapeutics

Methylation-based multi-cancer cfDNA assay may accurately identify 50 different cancer types[1]

- Findings from ongoing **Circulating Cell-free Genome Atlas** (CCGA) study show that a cell-free DNA test has the potential to detect cancer and predict tissue of origin (TOO) early in high-risk patients.
- 15,254 participants (with/without cancer) were enrolled across 142 sites, blood and tissue samples were collected from all participants with cancer.
- **Whole-genome bisulfite sequencing was** performed better, and hence, a methylation-based assay development is being carried forward.
- The initial analysis showed that **the assay had 99% specificity and 90% accuracy in predicting TOO.**
- This assay holds great promise for early cancer detection, which could lead to a significant decrease in cancer-related mortality across many cancers.
- The test is undergoing further evaluation in the ongoing CCGA, STRIVE, and SUMMIT studies.

Imaging combined with a multi-analyte plasma test had ~50% sensitivity to detect tumors with no screening options[2]

- Per the results from the DETECT-A study, a minimally invasive multi-analyte (incorporates DNA, protein markers) blood test was found to safely detect several types of cancers in patients with previously undetectable cancers.
- Findings from this prospective, interventional study show that the addition of the plasma assay to imaging tests increased the number of cancers initially detected by current SOC tools, from 25% to a whopping 52%.
- The blood test was also able to identify 10 different tumor types, 7 of which currently have no SOC screening assays available; the assay will also be an added benefit for cancers with no established screening assays (such as ovarian, appendix, and kidney).
- Furthermore, 65% of cancers detected via this blood test were classified as a local or regional disease, opening avenues for curative treatment for such early diagnosed patients.

Feasibility of detecting MRD+ based on ctDNA in high-risk adjuvant NSCLC patients presents the opportunity for drug development[3]

- Findings from the prospective **TRACERx** study indicates that circulating tumor DNA (ctDNA) could be used as a biomarker to detect post-surgical minimum residual disease (MRD) and clonality of disease relapse in adjuvant NSCLC setting.
- Primary tumors from 78 resected Stage I-III NSCLC patients were included in this study, with post-tumor excision, multi-region sampling (involving 100 clonal SNVs, 50 sub-clonal SNVs, and 50 neo-antigens) and deep whole exome sequencing performed to develop patient-specific anchored-multiplex polymerase chain reaction (AMP) enrichment panels for further analysis.
- The AMP-MRD assay in the study was validated, and showed that sensitivity scaled in proportion with assay DNA input and number of variants tracked, with 100% specificity
- ctDNA was detected at or before clinical relapse for 38 of 42 patients (91%) who have suffered a relapse.
- This assay also allows the monitoring of clonal evolution from therapy to relapse.
- In summary, AMP personalized cfDNA enrichment can accurately detect low-frequency variant DNA and at low assay DNA inputs, consistent to an MRD setting, and opening avenues for MRD-driven adjuvant trials in NSCLC.

References:
2020 AACR Virtual Annual Meeting I; April 27-28, 2020.
1. **Thiel DD, Chen X, Kurtzman KN, et al. Abstract CT021**
2. **Papadopoulos N. Abstract CT031**
3. **Abbosh C, Frankell A, Garnett A, et al. Abstract CT023**

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