

1162P - Analytical performance of a new liquid biopsy mutation panel for detection of clinically actionable variants

C. Svedman (Redwood City, United States of America) G. Alexander (Redwood City, United States of America) A. Bergamaschi (Redwood City, United States of America) J. Han (Redwood City, United States of America) P. B. Harrington (Redwood City, United States of America) C. Ku (Redwood City, United States of America) Y. Ma (Redwood City, United States of America) W. Gibb (Redwood City, United States of America) A. Dei Rossi (Redwood City, United States of America) L. Shen (Redwood City, United States of America) A. D. Goddard (Redwood City, United States of America) D. A. Eberhard (Redwood City, United States of America) K. M. Clark-Langone (Redwood City, United States of America)

Background Assessing genomic alterations in circulating tumor DNA (ctDNA) from liquid biopsies may better reflect tumor heterogeneity, facilitate monitoring of tumor evolution and overcome the challenges of obtaining tissue biopsies. Analytic performance of such assays should be established on a per sample basis, using clinically relevant variants at levels representative of ctDNA. Here we report the analytic performance of a 17-gene panel (Oncotype SEQ™, Liquid Select) and illustrate its ability to detect ctDNA in cancer patients.

Methods Analytical specificity and sensitivity were characterized through determination of Limit of Blank (LoB) and Limit of Detection (LoD) respectively. 73 cell-free DNA (cfDNA) samples from 60 healthy donors were used to determine the LoB and set detection thresholds. A model system using cell line DNA harboring clinically actionable variants was then used to determine the allele fraction (AF)/copy number (CN) required for a 95% rate of detection (LoD), using 30-50ng DNA input. Repeatability and reproducibility was assessed using pools of cfDNA from cancer patients. Finally, liquid biopsies from 15 stage II-IV cancer patients (on or after therapy) were assayed for genomic alterations.

Results Detection thresholds were set above the LoB corresponding to >99% per sample specificity. LoD was calculated using 105 samples for each variant tested. Mean LoDs were as follows; single nucleotide variants (SNVs), 0.56% AF; insertions/deletions (indels), 0.19% AF; fusions, 0.37% AF, and CN gain, 2.7 copies. Accuracy was verified using additional variant positive and variant negative standards. In the repeatability and reproducibility study using cfDNA pools, on average >95% of expected variants were detected in each run. 10 SNVs and 2 indels were found in the 15 patient plasma samples, ranging from <0.1-32% AF.

Conclusions The 17-gene panel (Oncotype SEQ™, Liquid Select) provides high sensitivity, detecting ctDNA at <0.1% in stage III or later disease. In addition, its high specificity and reproducibility ensures reliable patient reporting.

Legal entity responsible for the study Genomic Health

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Disclosure

C. Svedman: Employee of Genomic Health. G. Alexander, A. Bergamaschi, J. Han, P.B. Harrington, Y. Ma, A. Dei Rossi, L. Shen, A.D. Goddard, D.A. Eberhard, K.M. Clark-Langone: Stock ownership and employee of Genomic Health. C-J. Ku: Chin-Jen Ku. W. Gibb: Stock ownership and employee of Genomic Health.