Cost-Consequence Model of Whole-Exome, Whole-Transcriptome Sequencing Versus 50-Gene Panels for Genomic Profiling in Advanced Solid Tumors

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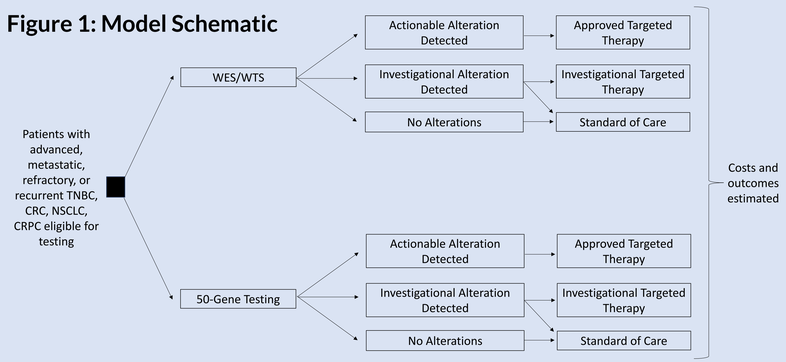
BACKGROUND

- In oncology practice, predictive biomarkers are increasingly being used in guiding treatment decision making.[1]
- Next-generation sequencing (NGS) allows for detection of multiple genomic alterations which can be used to determine treatment eligibility, especially within advanced cancers.[2]
- NGS panels vary significantly in the number and type of genomic alterations assessed, and can roughly be divided into small panels assessing 50 genes or less, and large panels, assessing greater than 50 genes.
- Given cost and test performance tradeoffs, the clinical and economic consequences of using different genomic profiling panels is not fully understood.

METHODS

- A previously published model [3,4] (Figure 1) was used to assess whole-exome, whole-transcriptome (WES/WTS) testing in advanced triple negative breast cancer (TNBC), non-small cell lung cancer (NSCLC), colorectal cancer (CRC), and castrate-resistant prostate cancer (CRPC).
- WES/WTS testing was compared with four 50-gene panels that differed in assessed genes, three commercially-available and one custom panel designed to maximize identification of alterations across all solid tumors.
- Alteration prevalence (Figure 2) was based on an analysis of tissue samples obtained from testing patients in real-world practice, with minor assumptions informed by published literature incorporated in cases of missing data (e.g., PD-L1 measures).[5]
- Test results were grouped as:
  - Actionable Alterations- Alteration with an approved therapy indicated for that cancer type.
  - Investigational Alterations- Alteration with potential treatment being studied in clinical trials or an associated therapy approved in a different tumor type.
  - No Alterations- No actionable or investigational alteration included in this analysis identified.
- Treatments were assigned based on test result, which was informed by the prevalence of included alterations and the set of genes assessed in each test panel.
- Other model inputs, including testing and treatment costs and the proportion of patients enrolling in clinical trials, were estimated from published literature.[3,6]
- Model outcomes were calculated when increasing use of WES/WTS testing in place of 50-gene panels within a hypothetical one-million-member plan and included number of patients changing treatment and per-member per-month (PMPM) costs over one-year.
- Parameter uncertainty was explored in one-way sensitivity analyses.

Figure 1: Model Schematic



Patients enter the model with diagnosed cancer. Two scenarios are compared, differing by testing approach used. Based on test result, patients are directed to treatments options that impact costs.
Abbreviations: CRC: colorectal cancer; CRPC: castrate resistant prostate cancer; NSCLC: non-small cell lung cancer; TNBC: triple-negative breast cancer; WES: whole-exome sequencing; WTS: whole-transcriptome sequencing

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Based on real-world evidence, use of whole-exome, whole-transcriptome sequencing in four common cancers increases treatment options for patients with a negligible impact on costs.

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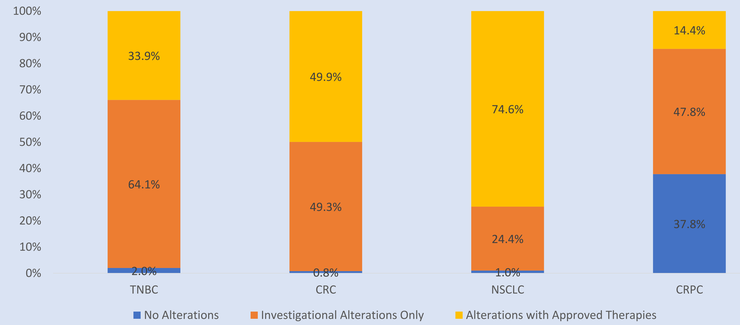
RESULTS

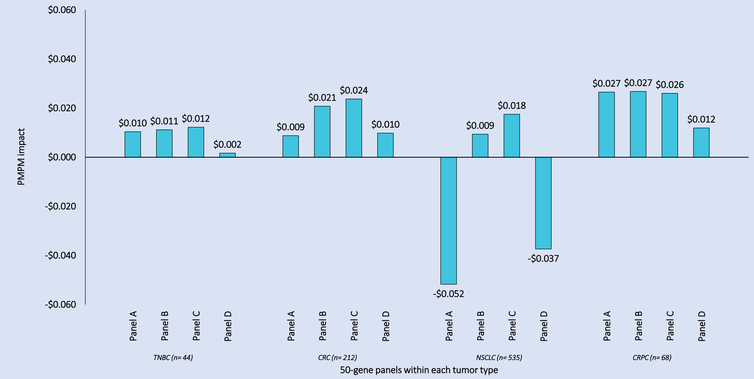
- Within a one-million-member plan, 858 patients with TNBC, NSCLC, CRC, and CRPC were eligible for testing and included in the analysis.
- When compared to use of each of the four 50-gene panels, the number of patients changing treatments when using WES/WTS testing was 1-2 (TNBC), 1-6 (NSCLC), 4-6 (CRC), and 3-5 (CRPC), with the range reflecting differences between each 50-gene panel.
- An increase in utilization of WES/WTS testing had a negligible impact on PMPM costs, with slight increases in TNBC, CRC, and CRPC, and cost savings within NSCLC depending on the specific 50-gene panel (Figure 3), with testing costs only accounting for 1-2% of total costs in all cancers.
- In sensitivity analyses, results were most sensitive to varying assumptions around treatment costs. Other inputs, including the proportion of patients enrolling in clinical trials and testing costs, were less influential.

Figure 2: Alteration Prevalence by Tumor Type



Alteration status by cancer type, based on real-world evidence, is shown. No Alterations indicates that no alteration included in this analysis was identified.
Abbreviations: CRC: colorectal cancer; CRPC: castrate resistant prostate cancer; NSCLC: non-small cell lung cancer; TNBC: triple-negative breast cancer.

Figure 3: PMPM Impact of Increasing Use of WES/WTS Testing



Results show the incremental PMPM impact when using WES/WTS testing instead of each of four 50-gene panel tests within a population. Positive numbers indicate an increased cost with WES/WTS testing.
Abbreviations: CRC: colorectal cancer; CRPC: castrate resistant prostate cancer; NSCLC: non-small cell lung cancer; PMPM per-member per-month cost; TNBC: triple-negative breast cancer.

DISCUSSION

- Strengths include consideration of four distinct panels within four common cancers, and exploration of uncertainty in sensitivity analyses. Limitations include simplifying assumptions around treatment pathways as necessary in modeling and a focus on short-term outcomes.
- Model results may underestimate the benefits of WES/WTS testing by only considering a subset of known alterations but are consistent with real-world analyses that found use of larger panels increased detection of biomarkers.[7-10]
- Findings indicate that use of WES/WTS testing instead of 50-gene panel testing supports precision oncology by expanding available treatment alternatives to patients with a minimal budget impact.

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