Amended Abstract

BACKGROUND: Molecular testing of cancers is quickly becoming standard of care and is improving diagnosis and treatment. Some oncologists remain apprehensive about the clinical utility of molecular profiling, based on the degree to which information can be used in a treatment decision, and whether it leads to selection of more expensive treatments that may not be accessible.

OBJECTIVES: The aim of this study is to examine the decision impact of a multipletplatform tumor profiling service, Caris Molecular Intelligence (CMI), and evaluate CMI-guided treatment costs compared to prior and planned treatments in prospective and retrospective clinical studies.

METHODS: In 5 physician-led clinical studies, the treatment decision prior to receipt of the CMI report was captured (n=137 patients). A systematic review of treatment data from 10 clinical studies of CMI (n=385 patients) allowed a comparison of planned versus actual (n=137) and prior versus actual (n=229) treatment costs. Costing information was taken from the British National Formulary (BNF) giving a treatment cost per cycle per patient. Decision impact was changed in 88% of CMI-profiled cases compared to prior and planned treatments.

RESULTS: Decision impact was changed in 88% of CMI-profiled cases compared to 29% of NGS-only approaches. The CMI-guided treatment cost per cycle was £995 in 385 treated patients. Planned treatment costs were comparable to actual treatment costs (£979 versus £995; p=0.7123) and prior treatment costs were also not significantly different to profiling-guided treatments (£892 versus £850; p=0.6319). NGS-only guided treatments cost £2,792 per cycle per patient.

CONCLUSIONS: Treatment costs guided by a multipletplatform-profiling platform were comparable to planned and prior treatment and do not cause a cost explosion, as the majority of treatments used were conventional chemotherapies. NGS-only approaches rely on more expensive targeted therapies and higher treatment cost per cycle per patient.

Background

- Precision medicine in oncology involves the use of high throughput technologies such as immunohistochemistry (IHC) - to examine protein levels - or next-generation sequencing (NGS) - to find tumour-specific somatic mutations, including insertions/deletions (indels), single nucleotide variants, translocations, and copy number alterations to predict which treatments might be beneficial for an individual patient.
- The approaches taken by the various commercial services differ greatly in the technology components which comprise their precision medicine offerings. Predictive associations for conventional cytotoxic chemotherapies are mostly based on the alterations in protein expression, either loss or overexpression, which is found by IHC. The identification of actionable genetic alterations by NGS is typically associated with more expensive targeted therapies.
- The integration of precision medicine into routine practice is hampered by the lack of coverage and the perceived high cost of the testing.
- Various health economic models exist for the introduction of a new drug or diagnostic entity into a healthcare system.
- However, the introduction of tumor profiling is difficult as a matter of cost it is offered across all solid tumors, and the costs of drugs which are used may also vary depending on the technology platform used.
- Recent data showing the economic impact of precision medicine has focused on incremental increases in progression-free survival, total costs and cost per week of survival associated with profiling-guided therapies.

Methods

- The treatments administered following profiling were collated from 11 studies of Caris Molecular Intelligence® (CMI) 14-16 and 16 studies of FoundationOne® (F1M). 11
- In 5 studies for CMI 4 14-16 and 2 studies for F1M,27 the treatment that would have been given in the absence of profiling (i.e. the treatment of physician’s choice) was recorded. The treatment decision was considered to be changed if at least one component of a treatment regimen was different to the planned treatment.
- Treatment data was collected from 385 patients profiled with CMI. The prior line of treatment was recorded in a subgroup of 229 patients within this cohort. The planned line of treatment was collected in a subgroup of 137 patients.
- The average cost per treatment cycle was calculated from the British National Formulary BNF (version 70 dated March 2016) and based on a treatment cycle of 21 days for all oral and systemic drugs.
- List prices for CMI and F1M were used in the calculation of cost of treatment and testing per progression-free survival (PFS) gain. A list price of £5,000 was assumed for CMI and £4,650 was used for F1M.
- Cost of treatment per progression-free survival week has been described as a means of assessing cost of care in precision medicine. 28
- Prior PFS is approximately 90 days or 3 months. 29
- Unmatched PFS would be expected to be approximately one-third shorter and has been reported as 49 days in a contemporary cohort. 30
- CMI guided PFS is 120 days or 4 months. 28
- F1M guided PFS is 120 days or 4 months. 28
- All patients would receive 4 cycles of treatment.
- Statistical analysis (unpaired t-test) was performed using GraphPadPrism.

Results - Breakdown of Profiling-Guided Treatments

- The majority of CMI-guided treatments administered to a cohort of 385 patients were chemotherapy alone (70%) which is similar to those administered previously (72%) and planned to be given (66%). Patients most frequently received a combination treatment regimen.
- Sequencing guided treatment shows a shift towards targeted therapy, with 67% of treatments consisting of targeted therapy alone, which were mostly monotherapies.

Conclusions

- CMI’s multipletplatform approach results in a much higher decision impact than F1M’s NGS-only approach, based on the guidance provided towards conventional chemotherapy options rather than focusing on targeted therapies.
- The cost of treatment for CMI guided therapies is not significantly different from the treatments that had previously been given or those that would be given in the absence of profiling. This is because the majority of treatments are conventional chemotherapies. The cost of F1-directed therapies is 280% higher as the majority of sequencing-guided therapies are expensive targeted therapies.
- The incremental cost of CMI testing generates value through improved clinical outcomes.
- The improved outcomes observed with CMI mean that the cost of treatment including testing is comparable to that which could be expected with planned therapies. Although sequencing-guided treatments bring benefit, the high testing and treatment costs mean that the cost per PFS gain is greatly increased compared to the originally planned treatments.

References