TREATMENT CHOICES BASED ON MULTIPLATFORM PROFILING PLATFORM, UNLIKE THOSE WITH SEQUENCING ALONE, DO NOT CAUSE A COST EXPLOSION IN REFRACTORY CANCER PATIENTS

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Amended Abstract

BACKGROUND: Molecular testing of cancers is quickly becoming standard of care using diverse approaches, either academic or commercial in origin. 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 multiplatform 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 (n=232) and treatment cost per cycle (n=292) were also compared from studies of next generation sequencing (NGS)-only approaches.

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 £945; 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 £2,795 per cycle per patient.

CONCLUSIONS: Treatment costs guided by a multiplatform-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 may 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 itself.
- 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 to model as 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.[1]

Methods

- The treatments administered following profiling were collated from 11 studies of Caris Molecular Intelligence® (CMI) [2-12] and 16 studies of FoundationOne® (FMI). [13-28]
- In 5 studies for CMI[3, 4, 8, 10, 11] and 2 studies for FMI[26, 28], 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 collated 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 FMI were used in the calculation of cost of treatment and testing per progression-free survival (PFS) gain. A list price of £5,000 was used for CMI and £4,450 was used for FMI.
- Cost of treatment per progression-free survival week has been described as a means of assessing cost of care in precision medicine.[1]
- Prior PFS is approximately 90 days or 3 months.[14, 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.[29]
- FMI-guided PFS is 120 days or 4 months.[14]
- All patients would receive 4.2 cycles of treatment.
- Statistical analysis (unpaired t-tests) was performed using GraphPad™.

Results – Decision Impact

- In 137 patients profiled using CMI, the treatment decision was changed in 120 cases (88%) and remained unchanged in 17 cases (12%).
- In 232 patients profiled using FMI, the treatment decision was changed in 67 cases (29%) and remained unchanged in 165 cases (71%).

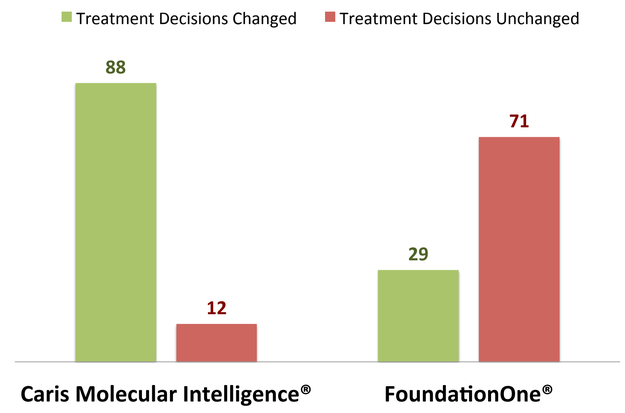

Figure 1 – Impact on Physician's Treatment Choice using Multiplatform and Next-Generation Sequencing focused Profiling Platforms

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, the majority of which were monotherapies.

	Caris Molecular Intelligence® guided treatment		Prior		Planned		FoundationOne® guided treatment	
	n	%	n	%	n	%	n	%
Total Patients	385		229		137		302	
Treatment Strategy								
Combination	238	62	142	62	60	54	76	25
Monotherapy	147	38	87	38	51	46	226	75
Treatment Types								
Chemotherapy alone	271	70	165	72	91	66	5	2
Chemotherapy plus hormone therapy	5	1	-	-	-	-	-	-
Chemotherapy plus targeted therapy	63	16	28	12	8	6	23	8
Clinical study	-	-	-	-	6	4	52	17
Hormone Therapy	12	3	8	3	2	1	2	<1
Hormone Therapy plus Targeted Therapy	3	1	-	-	-	-	-	-
Immunotherapy	1	<1	-	-	-	-	7	2
Targeted Therapy	30	8	25	11	4	3	202	67
Best Supportive Care	-	-	-	-	26	19	-	-

Table 1 – Treatment classes used in CMI-guided, Prior, Planned and FMI-guided scenarios

Results – Treatment Costs Per Patient Per Cycle

- The average treatment cost per patient per cycle of all CMI guided therapies (n=385) was £995 (range £3 - £4,446).
- The average treatment cost per patient per cycle in the prior line of treatment (n=229) was £979 (range £44 - £5,651), compared to £945 in the same patients treated according to CMI (range £3 - £4,446). This was not a significant difference (p=0.7123) but corresponds to a 3.5% reduction in average cost.
- The average treatment cost per patient per cycle in the planned line of treatment (n=137) was £892 (range £37 - £5,651), compared to an actual £850 in the same patients when treated according to CMI (range £52 - £4,446). This was not a significant difference (p=0.6319) but corresponds to a 5% reduction in average cost.
- The average treatment cost per patient per cycle of all FMI guided therapies (n=302) was £2,795 (range £3 - £8,400).

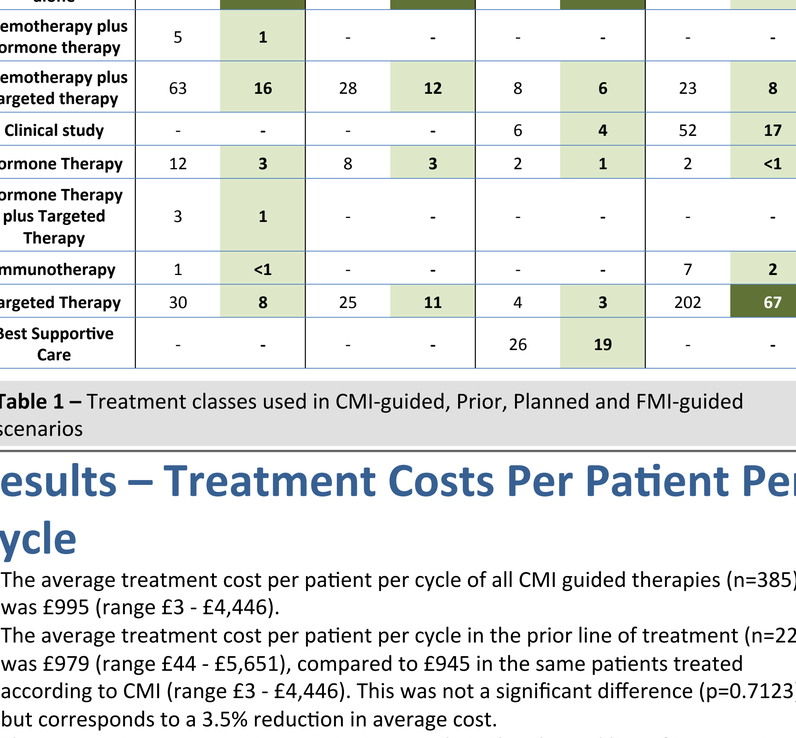

Figure 2 – Comparison of CMI-Guided Treatment Costs per Cycle Per Patient to Prior, Planned and FMI-guided treatments

Study Highlights – Testing and Treatment Cost per PFS Gain

- The planned line of treatment costs an average of £538 per week of PFS gained.
- The average cost of the prior line of treatment is £321 per week of PFS gained and is 40% lower than planned costs.
- The costs of CMI testing and CMI-guided treatment amounted to an average of £500 per week of PFS gained, 7% lower than planned treatment costs.
- The average costs of FMI testing and associated treatments was £945 per week of PFS gained, 76% higher than planned treatment costs.

	n	Average Cost of Treatment per cycle	Total Cost of Treatment	Cost of Testing	Total Cost	Median PFS	Cost per PFS month	Cost per PFS week	Cost per PFS day	% Relative costs to Planned Treatment
Prior Line	229	£979	£4,112	-	£4,112	90	£1,371	£321	£45.69	60
Planned Line	137	£897	£3,767	-	£3,767	49	£2,311	£538	£76.88	100
CMI-guided	137	£850	£3,570	£5,000	£8,570	120	£2,143	£500	£71.42	93
FMI-guided	302	£2,795	£11,739	£4,450	£16,189	120	£4,047	£945	£134.91	176

Table 2 – Cost of Testing and Associated Treatments per PFS Gained

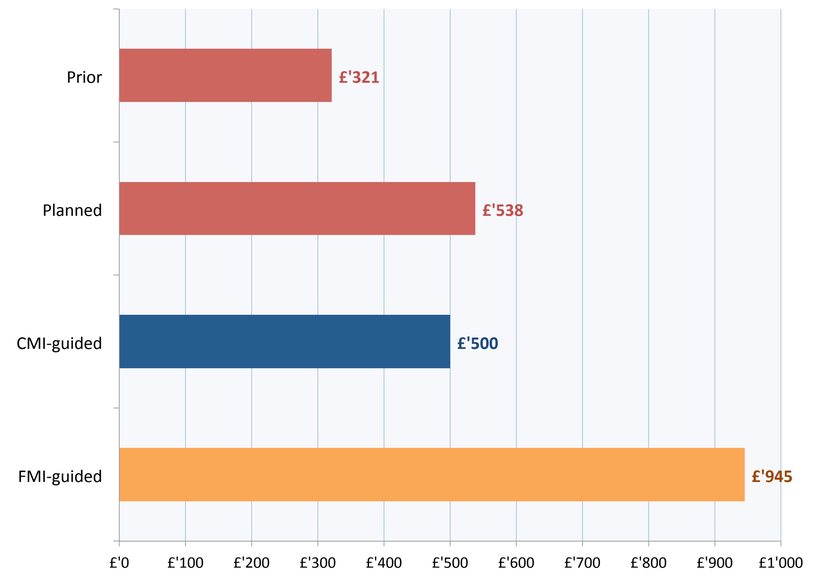

Figure 3 – Average cost of Testing and Associated Treatments per Week PFS Gained

Conclusions

- CMI's multiplatform approach results in a much higher decision impact than F1'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 treatments 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.

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