Title:

Precision Oncology using a Clinician-Directed, Tailored Approach to Molecular Profiling

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Running head:

Tailoring Precision Oncology

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Abstract (248 words: max 250)

Purpose:

Precision oncology involves molecularly matching patients to targeted agents usually in early drug development (EDD) programs. Molecular profiling (MP) identifies actionable targets.

Comprehensive commercial MP platforms are costly and in resource limited environments, a more practical approach to MP is necessary to support EDD and precision oncology. We adopted a clinician-directed, tailored approach to MP to enrol patients onto molecularly targeted trials. We report the feasibility of this approach.

Methods:

All patients referred to the Royal Melbourne Hospital (RMH) EDD between Sep-2013 and Sep-2015 were identified in a prospective database. Key captured data included clinicopathological data, MP platform ordered (if any), molecular targets identified and subsequent enrolment onto clinical trials. EDD-clinician decisions to order MP and the platform utilized was guided by patient consultation, tumor type, trial availability and requirement for molecular information.

Results:

We identified 377 patients referred to RMH EDD. 216 (57%) had MP ordered. The remainder had known actionable targets (19%), or were inappropriate for clinical trials (24%). In those undergoing MP, 187 genetic aberrations were found in 113 patients with 98 considered actionable targets in 86 patients. 98 (25%) patients were enrolled onto a clinical trial, including 40 (11%) receiving molecularly matched treatments. Median progression free survival was improved in patients enrolled onto molecularly matched trials compared to those on unmatched trials (3.6 months versus 1.9 months, HR 0.58 (0.38-0.89), $p=0.013$).

Conclusion:

A clinician-directed, tailored approach to the use of MP is feasible, resulting in 11% of patients enrolled onto molecularly matched trials.

Keywords: (max 3)

Precision oncology

Molecular profiling

Matched trials

Manuscript (2,633 words: max 3,500)

Introduction

Precision medicine in oncology is a two step process which involves identifying molecular drivers in an individual's cancer and then matching therapeutics targeted towards those drivers. It is hoped that this approach improves patient outcomes while also limiting treatment toxicity. The use of anti-HER2 therapy in metastatic breast cancer was the first example of successful implementation of precision oncology^{1,2}.

In recent years, precision oncology has progressed rapidly, mainly due to next generation sequencing (NGS). NGS enables the interrogation of thousands of variants (somatic or germline) from hundreds of genes in a single test through massively parallel DNA sequencing. NGS has allowed the costs of sequencing the whole genome to fall from an estimated \$2 billion to ~\$1000³ while also reducing processing time from a decade to days⁴. Subsequent increases in accessibility to NGS in the laboratory, has led to the discovery of innumerable genetic aberrations which have provided insights into mechanisms of tumorigenesis, leading to the identification of novel therapeutic targets. As increasing numbers of targets are identified, the numbers of novel molecularly targeted agents being tested in the clinic have also increased, with many requiring a companion diagnostic for patient selection. Recent introduction of NGS into the clinic has enabled clinicians to test patients for multiple targets at the same time, shifting testing away from single or sequential individual molecular tests and allowing patients to be identified for molecularly matched treatments more efficiently.

Despite growing interest around precision medicine, the ability to personalise treatment as part of standard of care remains limited. Since 2006 the FDA has approved only 24 molecularly targeted agents that are linked to a companion diagnostic⁵, limited to only 14 unique indications involving only 11 tumour types (**Supplement A**)⁵. Subsequently, most precision oncology is currently being conducted within large early drug development (EDD) programs, where there is access to a large number of molecularly targeted agents being tested in early phase clinical trials. These programs must balance concerns regarding cost and clinical benefit^{6,7}. Commercial molecular testing using large gene panels can cost upwards of US\$5000 and current data suggests that molecular profiling results in only 4% of patients receiving a matched treatment^{8,9}.

Prior to merging with the Peter MacCallum Cancer Centre in August 2016, the Department of Medical Oncology at Royal Melbourne Hospital (RMH) ran an EDD program consisting of 15-25 open phase I clinical trials open at any one time. To support the number of trials testing molecularly targeted agents, a molecular profiling program was initiated to support the precision oncology approach. Testing utilised NGS and was tailored towards the availability and relevance to molecularly matched treatments within the EDD program. To keep costs low, custom panels only included genes of interest and cost approximately US\$300 per patient, which is an order of magnitude lower than commercial panels. Additionally, patients were only offered molecular profiling if they were deemed appropriate candidates for molecularly targeted trials.

Herein, we report the feasibility of this approach to molecular profiling. We proposed that this method would still allow a comparable number of patients to be matched to molecularly targeted agents on clinical trials. Additionally, we explore the impact of molecularly matched treatments on progression free survival (PFS) relative to unmatched trials.

Methods

Patient selection and testing

An ethics department approved prospective database recorded basic clinical, pathological and molecular information for all new cancer patients seen within the RMH EDD program. Clinical information recorded included type of cancer, treatment lines, performance status, comorbidities and eligibility/interest in early phase trials, enrolment onto early phase trials and benefit from trials,

including duration on treatment and response rates. Molecular information recorded included pre-existing known molecular aberrations (i.e. from standard-of-care companion diagnostic tests such as RAS testing for colorectal cancer), rationale for ordering (or not ordering) molecular profiling, results (if performed) and classification of results as actionable and/or druggable.

The database was interrogated in June 2016 and all new patients seen between September 2013 and September 2015 were identified.

In general, molecular testing was not offered to patients who were not candidates for early phase trials (e.g. poor performance status, deranged organ function, not willing to comply with study requirements), or who had previous molecular testing considered to be adequate (e.g. commercial platforms such as Foundation Medicine or Caris).

Mutations were deemed actionable or druggable following thorough literature review by two oncologists; literature reviews were directed at both the specific mutation identified, as well as the specific gene which held the mutation, all in the context of the patient's tumour type. Actionable mutations were deemed as either predictive or potentially druggable. A mutation was only deemed druggable if a molecularly matched treatment was easily accessible either through the EDD program or via off-label access to an approved treatment.

Patients who were enrolled onto an EDD clinical trial were classified as either receiving a molecularly matched treatment or an unmatched treatment.

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Molecular Testing

Several molecular tests were available to those who were deemed suitable. During the course of the two years, we transitioned from using the TruSeq Amplicon Cancer Panel (48 genes – **Supplement B**) to an in-house, customized somatic mutation panel (16 genes – **Supplement C**) and a specific colorectal cancer quad mutation panel (4 genes – KRAS, NRAS, BRAF, PIK3CA). Additional molecular testing offered by our program included fluorescence in-situ hybridization (FISH) used to detect amplification in ERBB-2, FGFR-1, FGFR2, FGFR-3; and immunohistochemistry (IHC) used to detect deficient mismatch repair protein (dMMR). Specimens used for molecular analysis were archival formalin fixed paraffin embedded (FFPE) specimens. If two or more specimens were available, the most recent specimen was tested. DNA was extracted as per standard protocols. If there was insufficient tissue or an unsuccessful result (e.g. DNA quality inadequate for NGS), a fresh biopsy was discussed with the patient. Results were generally received within 3 weeks of request. Patients and referring clinician were informed of the result and any potential matched treatments. Our program did not involve sequencing of germline DNA.

Patients with druggable genetic aberrations were enrolled onto trials using molecularly matched treatments where possible. When not available, patients were considered for non-matched options.

Endpoints and analysis

The primary endpoint of this study was the proportion of patients who received a molecularly matched treatment. The secondary endpoint was PFS for patients who received molecularly

matched treatment, compared to those who received non-matched treatment within our EDD list of trials. PFS was defined as the time from trial enrolment to the date of progression or the date of death from any cause. PFS was calculated using the Kaplan-Meier method and compared using the log-rank test. A univariate Cox regression analysis was performed using IBM SPSS Statistics version 21 to compare PFS for those put on matched trials versus those on unmatched trials. The difference at 4 months between the two groups was calculated by Fisher's exact test. The Kaplan-Meier estimator functions for PFS were visualized on R version 3.3.2 using the survival 2.40-1 and survminer 0.2.4 packages.

Results

We identified 377 new patients seen within our EDD program between September 2013 and September 2015. Multiple tumour sites were represented; the most common being colorectal, gynaecological, urological and upper gastrointestinal cancers (**Table 1**). Most patients (84%) were ECOG 0-1 at the time of initial consultation. The median number of prior treatments was 2. A summary of initial baseline characteristics is outlined in **Table 1**.

Following clinical review, 91 (24%) patients were deemed unsuitable for early phase trials and therefore, unlikely to benefit from MP. Of the remaining patients, 70 (19%) had a known actionable target. The remaining 216 (57%) patients had additional molecular testing ordered (**Figure 1**). 41 of the 179 (21%) NGS panels ordered were unsuccessful due to insufficient DNA (**Figure 1**).

The most common genetic aberrations identified through our molecular profiling program include TP53, KRAS, PIK3CA and BRAF (**Figure 2**). In those who underwent molecular testing through our program, we identified 187 genetic aberrations within 113 (52%) patients. Of these targets, 98 were considered actionable targets, occurring in 86 (23%) patients (**Figure 1**).

In the suitable patients who had prior molecular testing, there were 72 actionable targets in 70 patients; KRAS and BRAF mutations were most common (**Supplemental Figure D**).

Overall, of the 377 patients who were referred to our EDD program, 98 (26%) were enrolled onto an EDD clinical trial. Using our tailored approach to molecular profiling, we enrolled 40 (11% of the entire cohort) patients onto a molecularly matched treatment. **Table 2** details the types of genetic aberrations identified and the matched treatment that was received. Half of these patients (20 patients) had their actionable target identified through our clinician directed tailored molecular testing program; the remaining 20 patients had previously identified actionable targets.

We examined PFS for patients who received a matched treatment versus non-matched treatment. The median PFS in the matched group was 3.6 months versus 1.9 months in the unmatched group (Hazard ratio – HR = 0.58, 95%CI 0.38 – 0.89, p=0.013) (**Figure 3**). At four months, a significantly greater proportion of patients receiving matched treatment remained on study compared to patients receiving unmatched treatment (40% versus 21%, p=0.044).

Discussion

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This study demonstrates that a tailored, clinician directed approach to molecular testing is feasible.

The rate of patients enrolled onto matched therapies on clinical trials was 11%. When compared with more complex and costly programs, this approach did not compromise the proportion of patients receiving molecularly matched treatment through early phase clinical trials.

Other centres have reported their experience with molecular profiling and precision oncology.

Institut Gustave Roussy's MOSCATO-01 program enrolled 1110 patients and reported 19% (n=199) of patients receiving molecular matched treatment as a direct result¹⁰. MD Anderson reported 4% (n=83) in their cohort of 2000 patients⁸, while Princess Margaret Cancer Centre's IMPACT study has reported 4% (n=84) in their cohort of 1,893 patients⁹. The 11% (n=40) reported by our smaller population is within the range described. The contrast between these studies can be explained by a number of differences with respect to each institution's molecular profiling and study pipeline.

These include the types of tumours enrolled, testing platforms utilized and the accompanying range of trials available at each institution. The MOSCATO-01 program's higher rate of trial enrolment is partially explained by their procurement of fresh biopsy in most cases (948/1035) and use of array Comparative Genome Hybridisation (CGH) to detect copy number variations. Of note, they were able to action PIK3CA, EGFR, FGFR and ERBB2 amplifications whereas our testing was limited to FGFR.

Both the MD Anderson⁸ and Princess Margaret⁹ programs focused on NGS of known hotspots within key cancer genes. Despite testing a substantial proportion of patients considered to have high mutational burden (e.g. melanoma and non-small cell lung cancer), their rates of molecularly matched treatments was 4%. Our cohort had a low proportion of patients with these tumour types, reflecting a favourable comparison to these larger institutional testing strategies. Importantly, the 11% observed within our cohort is based upon all patients referred to our program, not just those deemed suitable for early phase studies and having successful molecular testing.

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The value of any precision medicine program is dependent on access to targeted agents. This was demonstrated in a pilot study conducted by the British Columbia Cancer Agency involving highly complex genomic testing, including whole genome analysis (WGA) and RNA-sequencing, to inform treatment decisions¹¹. Extensive testing of 100 patients resulted in 1 patient being enrolled onto a clinical trial. The goal of this pilot study was not to identify patients for matched treatments. However, the trial enrolment rate reported highlights that more complex molecular testing in isolation will not facilitate precision medicine. Clearly, all requisite components of a precision medicine program – molecular profiling and linked trial program – must be available to enable this to be successful, a point which the authors acknowledge. To illustrate this further, over half (n=21) of matched patients in our study were enrolled onto a pan-RAF inhibitor study (**Table 2**). If this trial had been excluded from the analysis, the proportion of patients receiving matched treatment would have been 5%, which is in agreement with other larger institutional programs^{8,9}. Molecular profiling programs must have accompanying trials to be valuable.

A major criticism of the precision oncology movement is that improvement in clinical outcomes have not been robustly demonstrated^{6,7}. The only prospective, randomized study evaluating the role of molecular profiling in informing treatment strategy did not display benefit. The SHIVA study randomized patients harbouring genetic alterations within three key pathways (hormone receptor, PI3K/AKT/mTOR, MAPK) to either a predefined molecularly matched treatment, or physicians' choice of treatment (usually chemotherapy)¹². No difference in PFS (median 2.3 versus 2.0 months, HR 0.88, p=0.41) was demonstrated. There were many criticisms of this study including the use of hormone therapy, use of only drugs licensed in France and suboptimal targeting of the

PI3K/AKT/mTOR pathway. Overall, while the SHIVA study suggests that off-label use of approved targeted agents is unlikely to provide benefit, the authors did encourage ongoing use of molecular testing to identify patients for molecularly targeted trials.

In the clinical trial setting, a number of retrospective studies have reported improved patient outcomes with molecular profiling strategies. A retrospective study from MD Anderson reported that matched treatment in the phase I setting resulted in improved median PFS (3.9 versus 2.2 months, $p=0.001$)¹³. A meta-analysis of 346 phase 1 trials also reported better outcomes in trials that used biomarkers as selection criteria for enrolment (median RR 31% vs 5% and median PFS 5.70 months vs 2.95 months)¹⁴. Our findings of improved PFS in matched versus unmatched treatments (median PFS 3.6 months vs 1.9 months, HR 0.58, $p=0.013$) adds to the literature supporting the use of molecular profiling to inform treatment decisions and improve patient outcomes.

There are a number of limitations to this study. The first is that it is a retrospective analysis of our practice patterns. Additionally, it is non-randomized and subsequently, the improved PFS observed in patients receiving matched treatments should be interpreted with caution. Like most other programs, our molecular testing was performed on archival FFPE which may have affected the number of unsuccessful tests due to poor quality specimens as formalin is known to degrade nucleic acid quality¹⁵. And like all other studies of precision medicine, poor representation of the genomic landscape as a result of tumour evolution or heterogeneity between primary and metastatic sites¹⁶,¹⁷ may influence poorer than expected response rates in the matched group. Until the development of accessible and validated non-invasive molecular profiling, we accept these as real world limitations of EDD programs at present. Finally, the application of these results in today's trial

landscape may already be outdated. The period reported (2013-2015) arguably encompassed the peak of targeted kinase inhibitor drug development, where large numbers of novel agents required companion diagnostics for selection. Most EDD programs are now increasingly focused on novel immunotherapies where the role of molecular pre-selection remains uncertain. In the absence of selective biomarkers for these agents, precision oncology and molecularly matching patients to treatments becomes more difficult. However, it is likely that our understanding of how to personalize immunotherapies will improve; the challenge for molecular profiling programs will then be to remain agile and adapt molecular testing as necessary. Importantly, this highlights the fact that molecular testing needs to be pragmatic and be tailored towards the treatments that are available to patients within individual EDD programs.

In summary, our data demonstrates that a low-cost, tailored and clinician-directed approach to molecular testing can be implemented successfully. This resulted in a comparable rate of patient enrolment onto molecularly matched trials which potentially leads to better outcomes for patients. In an era where the cost of such programs is being increasingly scrutinised, tailoring molecular testing to the available clinical trials may be a pragmatic alternative to more extensive testing.

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References

1. Slamon DJ, Leyland-Jones B, Shak S, et al: Use of Chemotherapy plus a Monoclonal Antibody against HER2 for Metastatic Breast Cancer That Overexpresses HER2 [Internet]. N Engl J Med 344:783–792, 2001 Available from: <http://www.nejm.org/doi/full/10.1056/NEJM200103153441101>
2. Mass RD, Press MF, Anderson S, et al: Evaluation of clinical outcomes according to HER2 detection by fluorescence in situ hybridization in women with metastatic breast cancer treated with trastuzumab. [Internet]. Clin Breast Cancer 6:240–246, 2005 Available from: <http://www.sciencedirect.com/science/article/pii/S1526820911707261>
3. The Cost of Sequencing a Human Genome - National Human Genome Research Institute (NHGRI) [Internet][cited 2017 Feb 23] Available from: <https://www.genome.gov/sequencingcosts/>
4. Van Dijk EL, Auger H, Jaszczyszyn Y, et al: Ten years of next-generation sequencing technology. Trends Genet 30, 2014
5. Research C for DE and: Approved Drugs - Hematology/Oncology (Cancer) Approvals & Safety Notifications [Internet][cited 2017 Feb 23] Available from: <https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm>
6. Prasad V, Fojo T, Brada M: Precision oncology: Origins, optimism, and potential [Internet]. Lancet Oncol 17:e81–e86, 2016 Available from: [http://dx.doi.org/10.1016/S1470-2045\(15\)00620-8](http://dx.doi.org/10.1016/S1470-2045(15)00620-8)
7. Tannock IF, Hickman JA: Limits to Personalized Cancer Medicine [Internet]. N Engl J Med 375:1289–1294, 2016 Available from: <http://www.nejm.org/doi/abs/10.1056/NEJMs0903885>
8. Meric-Bernstam F, Brusco L, Shaw K, et al: Feasibility of large-scale genomic testing to facilitate

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enrollment onto genomically matched clinical trials. *J Clin Oncol* 33:2753–2762, 2015

9. Bedard PL, Oza A, Clarke B, et al: Molecular profiling of advanced solid tumors at Princess Margaret Cancer Centre and patient outcomes with genotype-matched clinical trials [Internet]. *Clin Cancer Res* 22:1–12, 2016 Available from: <http://dx.doi.org/10.1186/s13073-016-0364-2>
10. Massard C, Michiels S, Ferte C, et al: High-Throughput Genomics and Clinical Outcome in Hard-to-Treat Advanced Cancers: Results of the MOSCATO 01 Trial [Internet]. *Cancer Discov* , 2017 Available from: <http://cancerdiscovery.aacrjournals.org/lookup/doi/10.1158/2159-8290.CD-16-1396>
11. Laskin J, Jones S, Aparicio S, et al: Lessons learned from the application of whole-genome analysis to the treatment of patients with advanced cancers [Internet]. *Mol Case Stud* 1:a000570, 2015 Available from: <http://molecularcasestudies.cshlp.org/lookup/doi/10.1101/mcs.a000570>
12. Le Tourneau C, Delord J-P, Gonçalves A, et al: Molecularly targeted therapy based on tumour molecular profiling versus conventional therapy for advanced cancer (SHIVA): a multicentre, open-label, proof-of-concept, randomised, controlled phase 2 trial. *Lancet Oncol* 16:1324–1334, 2015
13. Tsimberidou A-M, Wen S, Hong DS, et al: Personalized medicine for patients with advanced cancer in the phase I program at MD Anderson: validation and landmark analyses. [Internet]. *Clin Cancer Res* 20:4827–36, 2014 Available from: <http://clincancerres.aacrjournals.org/content/20/18/4827.long>
14. Schwaederle M, Zhao M, Lee JJ, et al: Association of Biomarker-Based Treatment Strategies With Response Rates and Progression-Free Survival in Refractory Malignant Neoplasms [Internet]. *JAMA Oncol* 658:1–8, 2016 Available from: <http://oncology.jamanetwork.com/article.aspx?doi=10.1001/jamaoncol.2016.2129>

- 15.** Wong SQ, Li J, Y-C Tan A, et al: Sequence artefacts in a prospective series of formalin-fixed tumours tested for mutations in hotspot regions by massively parallel sequencing [Internet]. BMC Med Genomics 7:1–10, 2014 Available from: <http://www.biomedcentral.com/1755-8794/7/23>
- 16.** Gerlinger M, Rowan AJ, Horswell S, et al: Intratumor Heterogeneity and Branched Evolution Revealed by Multiregion Sequencing [Internet]. N Engl J Med 366:883–892, 2012 Available from: <http://www.nejm.org/doi/10.1056/NEJMoa1500987>
- 17.** Tursz T, Bernards R: Hurdles on the road to personalized medicine [Internet]. Mol Oncol 9:935–939, 2015 Available from: <http://dx.doi.org/10.1016/j.molonc.2014.08.009>

Figure Legend

Table 1: Baseline characteristics of patients seen within RMH EDD Program

Total Patients in RMH EDD Clinic		377
Gender		
Male	194	51.4%
Median Age		59.9 Years
Treatment Lines		
0	23	6.1%
1	79	21.0%
2	117	31.0%
3	80	21.2%
4	34	9.0%
>4	15	4.0%
Unknown	29	7.7%
Median Treatment Lines		2
Major Tumor Types		
Colorectal	129	34.2%
Ovarian	33	8.8%
Prostate	24	6.4%
Renal	21	5.6%
Endometrial	19	5.0%

Breast	18	4.8%
Lung	18	4.8%
Pancreas	16	4.2%
ECOG at first visit		
0	117	31.0%
1	199	52.8%
2	32	8.5%
>2	9	2.4%
Unknown	20	5.3%

Table 2: Molecularly matched treatments received

Molecularly Targeted Agent(s)	Molecular Target
PI3K and FGFR inhibitors (combination)	PIK3CA mutation (3); FGFR1 amplification (1)
BRAF and EGFR inhibitors (combination)	BRAF mutation (6)
RAF-dimer Inhibitor	BRAF mutation (2); KRAS mutation (17); NRAS mutation (2)
FGFR inhibitor	FGFR1 amplification (2); FGFR3 amplification (1)
PD-1 and CTLA4 inhibitors (combination)	Deficient MMR (1)
BRAF and EGFR and PI3K inhibitors (combination)	BRAF mutation (2)
KIT targeted Antibody Drug Conjugate	KIT mutation (1)
Pan HER inhibitor	ERBB2 mutation (1)
EGFR inhibitor	EGFR mutation (1)

Figure 1: Consort diagram

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Figure 2: Genetic aberrations identified within RMH EDD program

Figure 2

Figure 3: Progression Free Survival for matched versus non-matched treatments

Supplement A: FDA approved agents approved with a molecular indication from 2006 to March

2017

Supplement B: Truseq Amplicon Cancer Panel Genes

Supplement C: Somatic Mutation Panel Genes

Supplement D: Genetic aberrations identified prior to being seen at RMH EDD Program

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