Supplementary Information File

Article: Comparing survival outcomes for advanced cancer patients who received complex genomic profiling using a synthetic control arm

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Supplementary Information

Supplementary Table S1. CGP Informed Treatment Detail (N=25)			
Therapeutic	**Access**	**Variant**	**Frequency**
MEK & CDK4/6 inhibitor	Trial	SDHB m (g)	1
MEK & CDK4/6 inhibitor	Trial	KRASm	1
MEK & CDK4/6 inhibitor	Trial	CDKN2A focal deletion	1
PARP Inhibitor	Trial	BRCA1 m (1s, 1g)	2
RET inhibitor	Trial	RET m	4
TRK inhibitor	Trial	ETV6-NTRK3 fusion	1
KIT Tyrosine Kinase Inhibitor	Off Label	KIT m	2
Anti PD1 & MEK Inhibitor	Off Label	NRAS m	1
BRAF & MEK inhibitor	Off Label	BRAFm	1
Parp Inhibitor	Off Label	BRCA2 m (g)	1
SMO Inhibitor	1 SOC, 1 Off Label	PTCH1 m	2
Anti HER2	Trial	ERBB2 m	1
Anti HER2	Trial	ERBB2 m	1
Cisplatin as opposed to BSC	SOC	BRCA2 m	1
Anti PD-L1	Trial	Focal CD274 amp	1
Addition of anti CTLA-4 to anti PD1	Off Label	JAK1m	1
MEK & RAF Dimer inhibitor	Trial	NF1 m	1
FGFR inhibitor	Trial	FGFR2-BICC1 fusion	1
FGFR inhibitor	Trial	FGFR2 m	1

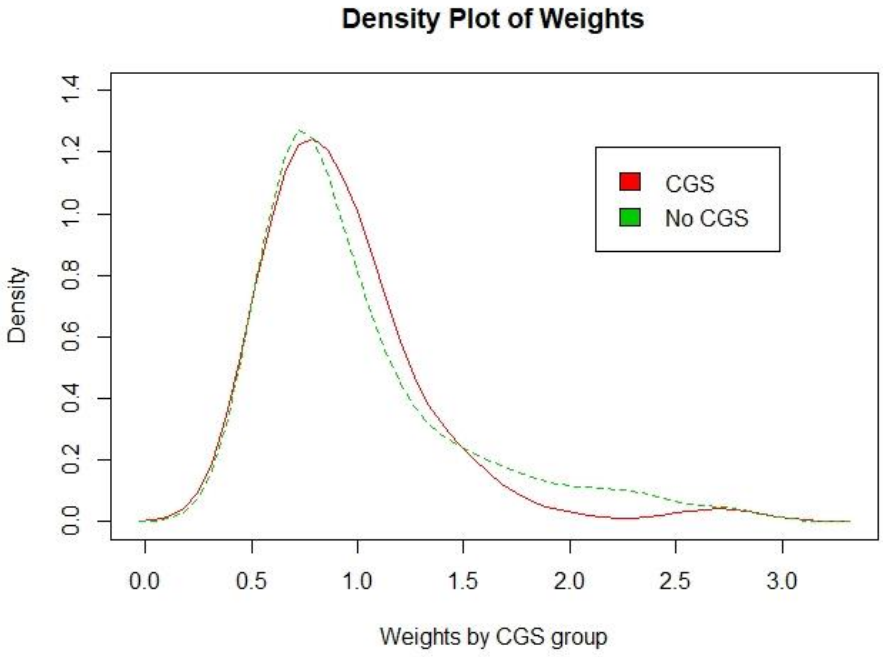
m; mutation (SNV), s; somatic, g; germline, amp; amplification, SOC; standard of care

Supplementary Table S2. Propensity Score Model (π=probability of receiving CGP)			
	Coefficient	Standard Error	*p* value
Age	-0.018	0.011	*0.106*
Sex			
M	-0.252	0.293	*0.389*
ECOG			
0	Ref		
1	-0.322	0.301	*0.284*
2	-0.243	0.574	*0.672*
Failed Lines of Systemic Treatment	-0.524	0.147	*<0.000***
Therapeutic Options Remaining*			
0	Ref		
1	-0.026	0.331	*0.938*
2 or more	0.583	0.646	*0.367*
Primary			
CUP	-1.600	0.754	*0.034**
GU	-1.255	0.774	*0.105*
Gynae	0.433	0.635	*0.495*
H&N/NM Skin	-1.329	0.642	*0.038**
Lung	Ref		
Melanoma	0.814	0.837	*0.331*
Other Rare	-0.459	0.703	*0.514*
Sarcoma	-0.691	0.688	*0.316*
UGI	-1.112	0.561	*0.047**
Rare Cancer			
Yes	0.761		*0.086*
AIC	358.28		
Hosmer-Lemeshow Goodness of Fit (g=10)	*p*=0.1772		

AIC, Akaike Information Criterion. *p<0.05, **p<0.01

Supplementary Figure S1

Kernel density plot of inverse probability of treatment weights by CGP group



Supplementary Notes

NGS Assay Description - Targeted gene sequencing of coding regions and splice sites was performed on DNA extracted from tissue and matched blood. Libraries were prepared and enriched using SureSelect XT target enrichment (Agilent Design ID 3016871). Indexed libraries were pooled and sequenced to a targeted coverage of 500/100 reads/base (tumour/blood) on Illumina NextSeq500 using 2x75bp reads. Seqliner v0.7 was used to generate aligned reads and call variants against the hg19 human reference genome. PathOS v1.3 was used to annotate and transform variants to standard nomenclature and filter for rare, non-synonymous variants within 20bp of coding exons. Germline (blood) analysis was limited to 76 genes with evidence for cancer predisposition (modified from Rahman, Nature 2014;16;505(7483):302-328). Copy number loss was detected using GAFFA2. Structural variants were detected using GRIDSS (https://github.com/PapenfussLab/gridss). Variants are described according to HGVS nomenclature version 15.11 (http://varnomen.hgvs.org/) with minor differences in accordance with Molecular Pathology policy. The policy as it pertains to this report is available by contacting the laboratory on the number below. Therapeutic implications are adapted from AMP/ASCO/CAP guidelines for the interpretation of somatic variants.