Abstract # 165624

Value of Sequencing-Guided Treatment for Patients with Advanced Malignancies

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BACKGROUND

- Current approaches in the treatment of advanced cancer are based predominantly upon lessons learned from the cytotoxic era. Our current approaches have yielded incremental steps forward, but most patients who develop metastatic disease still die and the costs of care are soaring
- Rational combination approaches that are selected based upon computational analysis of multi-platform molecular data, tailored for each patient based upon their past medical history, performance status and unique molecular profile, and curated to prevent the development of resistance represent a possible solution that warrants further exploration
- The optimal treatment strategy for patients with advanced breast or ovarian cancer is currently unknown. Resistance to standard therapies like anthracyclines and taxanes limit the number of treatment options in many patients to a small number of non-cross-resistant regimens
- We hypothesized that genomic and proteomic profiling of samples from advanced patients would identify genomic alterations that are linked to targeted therapies, and that this could facilitate a personalized approach to therapy for our patients

METHODS

- Single center analysis of 150 advanced breast or ovarian cancer patients seen over a 24 month period (May 2014 through April 2016)
- Most patients were re-biopsied after consultation with the genomic oncology service
- Most tissue samples were sent for FoundationOne© and/or TheraLink© (proteomics) and blood samples were sent for Guardant360© starting in the summer of 2015
- All metastatic biopsies were obtained at same center (Avera Cancer Institute) and same protocol was used for all samples
- Routine pathology was completed predominantly at Avera, including IHC and FISH for HER2 if applicable
- All FFPE samples sent to Foundation Medicine and Theranostics were obtained and processed based upon instructions from both companies
- All patients were enrolled in a sequencing protocol (NCT02470715) with no standardized treatment provided
- All treatment suggestions were made by a formal sequencing review team
- Response rates were based upon RECIST 1.1 measurements whenever possible

RESULTS

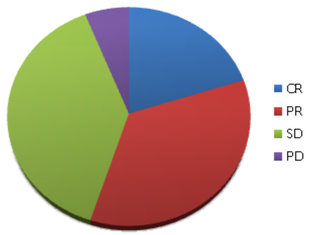
- 100 Evaluable patients
- Over 60% of patients were able to receive full recommended therapy
- Average lines of previous therapy was over 3

Table 1. Best Response Rate for Fully Evaluable Patients

	Full (n =61)	Partial (n =12)	None (n = 27)
CR	20%	8%	8%
PR	35%	42%	-
SD	39%	25%	24%
PD	6%	25%	68%
CBR	**94%**	**75%**	**32%**

Full - patient received all of recommended therapy
CR – no detectable disease
PD - progressive disease
Partial - patient received at least 1 of the recommended therapies,
PR – greater than 30% disease reduction
Clinical Benefit Rate (CBR) = CR + PR + SD
SD – overall no or minimal change

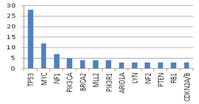
Best Outcome

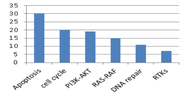


- Over 55% of advanced patients on MEM therapy have responded positively (Complete response or partial response)
- More than 90% of the patients got their disease under control
- The treatment was ineffective in only 6% of patients

RESULTS

Most Frequently Seen Gene Alterations in Metastatic Ovarian Cancer



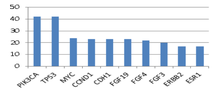


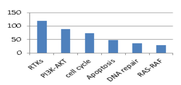
pathway	Frequency
Apoptosis	30
cell cycle	20
PI3K-AKT	19
RAS-RAF	15
DNA repair	11
RTKs	7

Rank	Gene	Frequency
1	*TP53*	28
2	*MYC*	12
3	*NF1*	7
4	*PIK3CA*	5
5	*BRCA2*	4
5	*MLL2*	4
5	*PIK3R1*	4
8	*ARID1A*	3
8	*LYN*	3
8	*NF2*	3
8	*PTEN*	3
8	*RB1*	3
8	*CDKN2A/B*	3

Among the 33 metastatic ovarian cancer patients, 58 different gene mutations has been detected by FoundationOne test. Genes that alters the apoptosis pathway *(TP53, BCL2L1, BCOR, PUMA, MCL1* and *BCL6)* appeared to be the most seen alterations.

Most Frequently Seen Gene Alterations in Metastatic Breast Cancer



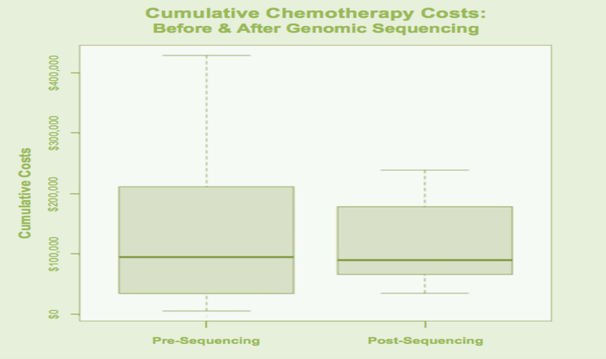


Pathway	Frequency
RTKs	121
PI3K-AKT	89
cell cycle	74
Apoptosis	48
DNA repair	36
RAS-RAF	29

Rank	Gene	Frequency
1	*PIK3CA*	42
1	*TP53*	42
3	*MYC*	24
4	*CCND1*	23
4	*CDH1*	23
4	*FGF19*	23
7	*FGF4*	22
8	*FGF3*	20
9	*ERBB2*	17
9	*ESR1*	17

Among the 116 metastatic breast cancer patients, 147 different gene mutations has been detected by FoundationOne test. The RTKs *(FGFs, ERBBs and IGF1R)* appeared to be the most seen alterations.

RESULTS



DISCUSSION

- Molecular profiling patients with advanced breast or ovarian cancer has yielded actionable targets in a majority of cases
- Presently, we are predominantly using FDA approved drugs in combinations based upon the molecular and proteomic information and seeking insurance approval for the treatment
- Biggest challenge has been working with insurance companies to grant approval for off-label treatments/combinations
- Our remarkable initial data provides very strong evidence that it is critical to incorporate multi-platform profiling as early as possible (preferably at diagnosis) in the disease course to allow for the best chance of benefit
- Off-label drug use in a variety of combinations can be utilized safely and effectively in a community cancer center and make a significant impact in patient outcomes

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