PREDICTIVE VALUE OF TOPOISOMERASE 1 BY IMMUNOHISTOCHEMISTRY (TOP1 IHC) IN PATIENTS WITH METASTATIC BREAST CANCER RECEIVING IRINOTECAN-BASED THERAPY.

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Background

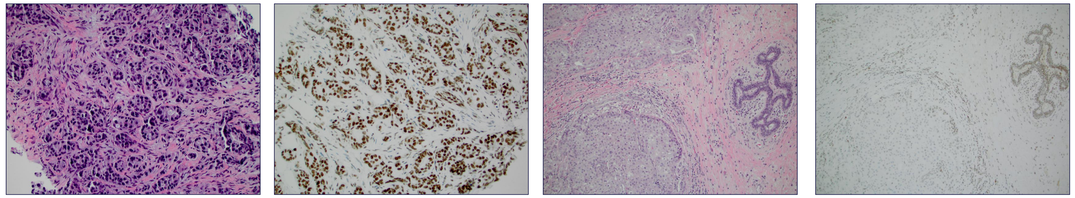
There is an unmet need for rapid assays predictive of efficacy for specific chemotherapy agents. In particular, for those patients with metastatic disease that have progressed on prior therapies. Newer multi-omic analysis can be performed on a single biopsy specimen and with rapid turn-around-time allowing greater clinical utility (1).

Methods

- ✓ 49 patients with measurable metastatic breast cancer (MBC) and with a history of prior treatments were enrolled in a prospective phase II study.
- ✓ Real-time biopsies were evaluated with a multi-omic platform which included TOP1 (1D6 antibody) measured by IHC.
- ✓ 23 of 49 tumors were TOP1 positive (positive if intensity ≥ 2+ in at least 30% tumor).

Figure 1: H&E (A) and positive staining for TOP1 (B) and H&E (C) and negative staining for TOP1 (D)

A) B) C) D)



- ✓ Each of the 23 patients received an irinotecan based regimen as follows: 11 irinotecan alone; 9 irinotecan+capecitabine or irinotecan+fluorouracil/leucovorin; 2 irinotecan+trastuzumab; 1 irinotecan+exemestane. Twenty-two patients were evaluable for analysis.
- ✓ To determine therapeutics benefit, a predetermined endpoint was used: The ratio of the progression free survival (PFS) of the new regimen divided by the PFS of the prior therapy (GMI) with a ratio of 1.3 or greater indicating improved therapeutic benefit from the new regimen (2).

Conclusions

- ✓ In this prospective phase II study in patients with advanced MBC, measurement of TOP1 predicted clinical benefit as measured by GMI, in 61% of all patients receiving irinotecan based therapy and in 6/11 (55%) patients receiving irinotecan alone.
- ✓ 73% of patients had a clinical benefit (PR and stable).
- ✓ These findings warrant further evaluation of TOP1 IHC in predicting the utility of irinotecan in the treatment of breast cancer.

Results

Table 1: Patient characteristics

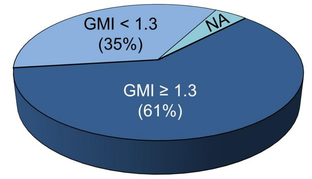
Characteristic	n	%
Gender		
Male	1	5
Female	21	95
Age, Years		
Median	66	
Range	44-74	
Ethnicity		
Not of Hispanic/Latin Origin	19	86
Hispanic/Latin Origin	3	14
Race		
White	22	100
Number of Prior Treatment Regimens		
3	3	14
4	2	9
5	3	14
6	5	23
9	4	18
10	3	14
12	2	9
Tumor Characteristics		
ER		
Positive	20	91
Negative	2	9
PR		
Positive	14	64
Negative	8	36
Her2		
Positive	2	9
Negative	19	86
Unknown	1	5

Table 2: Treatment. GMI and Response

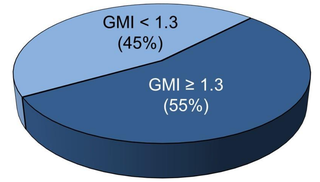
Subject ID	Treatment Received	Actual Patient GMI	Overall Best Response
01-01-101	Irinotecan	1.977	SD
01-02-105	Irinotecan	0.319	PD
01-02-107	Folfiri	1.303	SD
01-01-109	Irinotecan + Trastuzumab	7.156	SD
01-02-110	Folfiri	6.873	SD
01-02-112	Folfiri	0.046	PD
01-02-113	Irinotecan + Exemestane	2.260*	SD
01-02-115	Irinotecan + Fluorouracil	1.684	SD
01-01-117	Irinotecan	3.408	SD
01-02-118	Folfiri	2.527	PR
02-04-007	Irinotecan	0.851	PD
02-03-010	Irinotecan	3.843	SD
02-03-011	Irinotecan + Capecitabine	8.539	PR
02-03-012	Irinotecan + Capecitabine	0.366	PD
02-04-014	Irinotecan	1.373	SD
02-02-023	Irinotecan + Capecitabine	1.370	SD
02-03-027	Irinotecan	0.429	PD
02-02-029	Irinotecan	3.512	SD
02-03-037	Irinotecan	1.145	PD
02-02-036	Irinotecan	2.139	SD
02-03-039	Irinotecan + Trastuzumab	1.429	SD
02-02-041	Irinotecan	1.166	SD

GMI distribution after irinotecan-based regimen in patients with TOP1 positive staining by IHC.

All regimens (n=23)



Single agent Irinotecan (n=11)



* Patient did not have scan completed within GMI window and therefore is not considered a GMI responder.

References

1. Jameson GS et al. A pilot study utilizing multi-omic molecular profiling to find potential targets and select individualized treatments for patients with previously treated metastatic breast cancer. Breast Cancer Res Treat. 2014;147(3):579-88.
2. Von Hoff DD et al. Pilot study using molecular profiling of patients' tumors to find potential targets and select treatments for their refractory cancers. JCO 2010:4877-4883.