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)

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).

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.

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

Table 2: Treatment, GMI and Response

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

References

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;28(7):4877-4883.