Genomic Characterization of a PDX Model of T-DM1-resistant HER2+ Invasive Ductal Carcinoma Using Augmented Exome Sequencing

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Materials and Methods

Tumor Samples and PDX Model

The fibroblast sample (PM) from a metastatic lung lesion was used to establish a human PDX model from a patient with HER2+ invasive ductal carcinoma. This model was found resistant to T-DM1 within 10 days of initiating therapy. We performed whole-genome sequencing and copy-number analysis to identify the somatic and tumor genome composition and overall survival compared to standard therapy and thus considered as standard of care. Despite these favorable evolution traits, most patients eventually progressed. The prevalence of resistance to the conventional therapy was not outstripped. Acquisition resistance to T-DM1 has been shown, but has not been shown to occur in an invasive system.

As PDX tumor model was used to establish a human PDX model from a patient with HER2+ invasive ductal carcinoma. This model was found resistant to T-DM1 within 10 days of initiating therapy. We performed whole-genome sequencing and copy-number analysis to identify the somatic and tumor genome composition and overall survival compared to standard therapy and considered as standard of care. Despite these favorable evolution traits, most patients eventually progressed. The prevalence of resistance to the conventional therapy was not outstripped. Acquisition resistance to T-DM1 has been shown, but has not been shown to occur in an invasive system.

In the same patient, we used immune to establish a human PDX model from a patient with HER2+ invasive ductal carcinoma. This model was found resistant to T-DM1 within 10 days of initiating therapy. We performed whole-genome sequencing and copy-number analysis to identify the somatic and tumor genome composition and overall survival compared to standard therapy and thus considered as standard of care. Despite these favorable evolution traits, most patients eventually progressed. The prevalence of resistance to the conventional therapy was not outstripped. Acquisition resistance to T-DM1 has been shown, but has not been shown to occur in an invasive system.

Results

PDX Model Concordance

We measured concordance of T-DM1 treatment in vivo for our PDX model as well as other HER2+ PDX models derived from HER2+ metastatic breast cancer patients, who were treated with standard therapies. We also measured concordance of T-DM1 treatment in vivo for our PDX model as well as other HER2+ PDX models derived from HER2+ metastatic breast cancer patients, who were treated with standard therapies.

To determine the accuracy of the T-DM1 treatment in vivo for our PDX model as well as other HER2+ PDX models derived from HER2+ metastatic breast cancer patients, who were treated with standard therapies.

Conclusions

T-DM1 is effective in treating advanced HER2+ breast cancer patients who have progressed on standard therapies, but the efficacy is short-lived. Here we used whole-genome and transcriptome analysis to identify the somatic and tumor genome composition and overall survival compared to standard therapy and thus considered as standard of care. Despite these favorable evolution traits, most patients eventually progressed. The prevalence of resistance to the conventional therapy was not outstripped. Acquisition resistance to T-DM1 has been shown, but has not been shown to occur in an invasive system.

1. Personalized Cancer Therapy - Knowledge based on Personal Medicine. MB: Johnson Cancer Center; Midwest Hospital.
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References

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