Breast Cancer RESEARCH

LETTER

Individual xenograft as a personalized therapeutic resort for women with metastatic triple-negative breast carcinoma

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Findings

A localized left breast ductal invasive triple-negative breast carcinoma (TNBC) was diagnosed in a 44-year-old woman. After surgery, she was treated with chemotherapy and radiation therapy in accordance with national guidelines. At the end of treatment, she had local and metastatic relapse with multiple sub-diaphragmatic lymph nodes.

With her written consent, imagery-guided biopsies of a metastatic lymph node were performed, one sample being used for genomic analyses and another for immediate xenograft (Additional file 1: Supplementary methods). Because of the early metastases after docetaxel and epirubicin-cyclophosphamide, she received cisplatin but the disease progressed after 3 months.

Meanwhile, the transcriptomic analysis of the metastatic sample enabled a molecular subclassification as Basal-Like 2 with *EGFR* mRNA overexpression [1,2]. We did not find any *EGFR* or *K-RAS* mutation. After successful engraftment of the metastastic samples, we tested eight different chemotherapies over 1 month on the xenograft model. The combination of paclitaxel and cetuximab was the most efficient (Figure 1A), so it was offered to the patient. After 3 months of this second-line treatment, the metabolic response was almost complete (Figure 1B, C).

In compliance with French bioethics law (#2004-800, 06/08/2004), the patient had been informed of the research use of the part of her biopsy samples remaining after diagnosis had been established and did not oppose it. The treatment combining paclitaxel and cetuximab was discussed and approved in a multidisciplinary meeting and then offered to the patient. Informed written consent was obtained from the patient. The Clinical Research Board Ethics Committee (in French, 'Comité de Protection des Personnes') approved this study (CPP Ile-de-France #13218). The University Institute Board Ethics Committee for experimental animal studies approved this study (#2012-15/728-0115).

The occurrence of metastases heavily affects prognosis for women with TNBC, with a median survival of under 15 months [3]. In addition, when progression occurs after first-line chemotherapy, there is no standard care.

Primary tumors are heterogeneous at the cellular and molecular level [4], and metastases derive from aggressive clones that have usually acquired resistance to first-line treatments. These tumor cells, which may be a minority in the primary tumor, are precisely those on which drug efficiency needs to be tested for individualized treatments for patients with metastases.

Recently, a molecular subclassification of TNBC was established, a new step toward innovative personalized treatments for patients with TNBC [1,2]. However, molecular analyses still have limitations, since molecular biomarkers are integrated into complex pathways and can rarely be directly used in daily oncologic practice. These limitations make it necessary to implement a different, complementary method. Individual xenografts from metastatic samples of TNBC are an additional, innovative tool and are more physiological than genomic analysis, as the tumor is in a mammalian environment and can be followed up over time. In pancreatic cancer, which shares poor prognosis and high metastatic potential with TNBC, individual xenografts have been proposed in a pilot study for personalized treatments [5]. Individual xenografts could also be proposed as a personalized therapeutic resort for women with metastatic TNBC.

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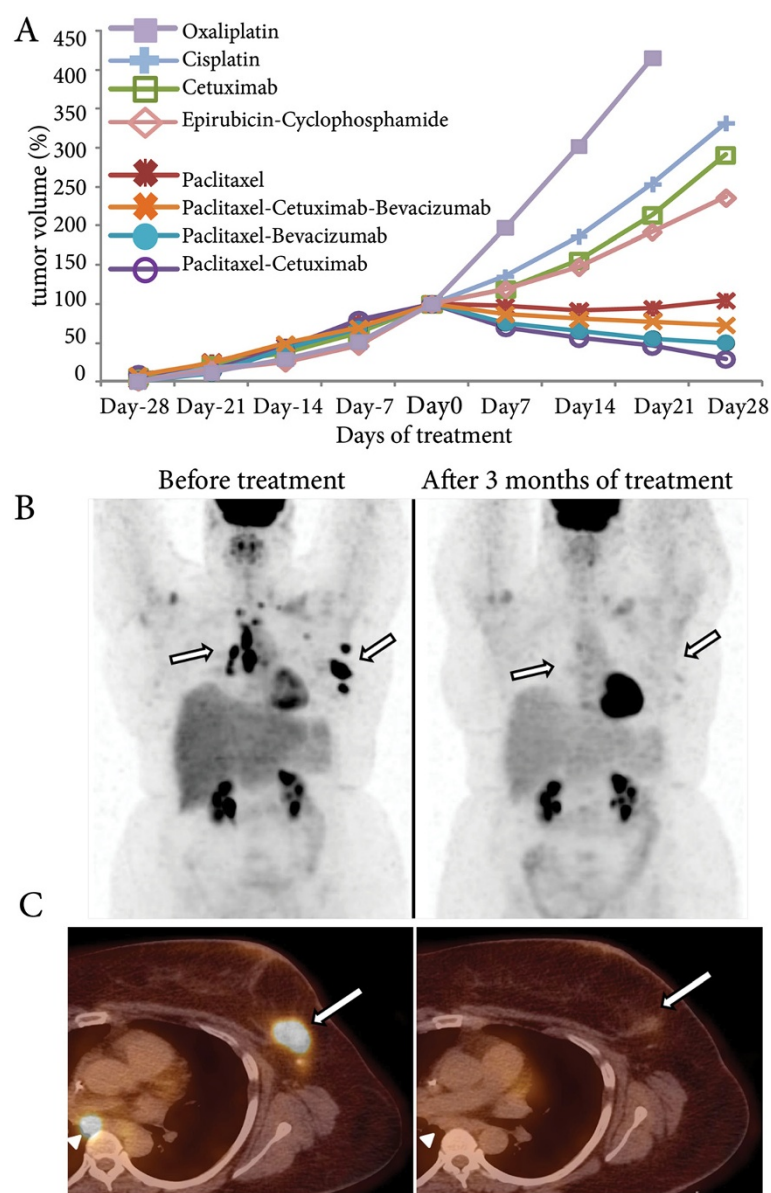Full list of author information is available at the end of the article

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Figure 1 Individual xenograft efficiently guided treatment of a patient with metastatic triple-negative breast carcinoma. (A) *In vivo* effects of drugs or combination of drugs in the xenograft model obtained from metastatic triple-negative breast carcinoma. Mice (n = 5 per group of treatment) were treated with drugs or combinations of drugs. Tumors were measured every week, from 4 weeks before the treatment started to 4 weeks after treatment. Tumor volumes were calculated at each time-point. The greatest tumor growth inhibition is observed with the combination of paclitaxel and cetuximab (purple circle). **(B)** Positron emission tomography (PET), maximum intensity projection. The left panel shows baseline PET with intense fluoro-deoxyglucose (FDG) uptake in sub-diaphragmatic breast and lymph node lesions (white arrows); the right panel shows PET after two cycles of combined paclitaxel and cetuximab. There is a marked decrease (88%) of SUV_{max} (maximum standardized uptake value within the region of interest) in target lesions (white arrows) and thus a partial metabolic response according to PERCIST (PET Response Criteria in Solid Tumors) criteria. **(C)** Fused PET/computed tomography. The left panel shows an image at baseline with intense FDG uptake in a left breast lesion (SUV_{max} = 17.2, white arrow) and in a subcarinar lymph node (SUV_{max} = 14.3, white arrowhead); after two treatment cycles (right panel), SUV_{max} of both target lesions (white arrow, white arrowhead) is below background level.

Additional file

Additional file 1: Supplementary methods.

Abbreviation
TNBC: Triple-negative breast carcinoma.

Competing interests
The authors declare that they have no competing interests.

Authors' contributions
GB conceived and designed the study, provided the study material or patient, collected and assembled the data, provided data analysis and interpretation, and drafted the manuscript. J-PF provided data analysis and interpretation, and performed the statistical analyses. IF collected and assembled data and performed the xenografts. LV collected and assembled data, provided data analysis and interpretation, and performed the positron emission tomography/computed tomography. NJ provided data analysis and interpretation. PB provided the study material. CdB provided the study material or patient and performed tumor biopsies. EB provided the study material or patient. AJ conceived and designed the study, located financial support, provided administrative support, provided the study material or patient, collected and assembled data, provided data analysis and interpretation, and drafted the manuscript. All authors read and approved the final manuscript.

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