Targeting triple negative breast cancer metabolism with neoadjuvant chemotherapy plus fasting-mimicking diet plus/minus metformin: the BREAKFAST trial

Francesca Ligorio$^{1,2}$, Giovanni Fucà$^1$, Andrea Vingiani$^{3,4}$, Fabio Iannelli$^2$, Riccardo Lobefaro$^1$, Cristina Ferraris$^5$, Antonino Belfiore$^6$, Gianfranco Scapperotta$^8$, Catherine Depretto$^6$, Antonia Martinetti$^1$, Paola Antonia Corsetto$^7$, Giulia Valeria Bianchi$^1$, Giuseppe Capri$^1$, Secondo Folli$^5$, Saverio Minucci$^{3,8}$, Marco Foiani$^{2,3}$, Massimiliano Pagani$^{2,9}$, Giancarlo Pruneri$^{3,4}$, Filippo de Braud$^{1,3}$, Claudio Vernieri$^{1,2}$

$^1$Medical Oncology and Hematology Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Via Veneziana 1, 20133, Milan, Italy; $^2$IFOM ETS, the AIF Institute of Molecular Oncology, Via Adolfo 16, 20139, Milan, Italy; $^3$Oncology and Hemato-Oncology Department, University of Milan, Via Festa del Perdono 7, 20122 Milan, Italy; $^4$Department of Advanced Diagnostics, Fondazione IRCCS Istituto Nazionale dei Tumori, Via Veneziana 1, 20133, Milan, Italy; $^5$Breast Unit, Surgical Oncology Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Via Veneziana 1, 20133, Milan, Italy; $^6$Department of Radiology, Fondazione IRCCS Istituto Nazionale dei Tumori, Via Veneziana 1, 20133, Milan, Italy; $^7$Department of Pharmacological and Biomolecular Sciences, University of Milan, Via Festa del Perdono 7, 20122 Milan, Italy; $^8$Department of Experimental Oncology, IEO, European Institute of Oncology IRCCS, Via Adolamo 16, 20139 Milan, Italy; $^9$Department of Medical Biotechnology and Translational Medicine, University of Milan, Via Festa del Perdono 7, 20122 Milan, Italy

BACKGROUND

Cyclic fasting or fasting-mimicking diets (FMDs) enhanced the antitumor activity of chemotherapy (CT) in TNBC mouse models$^1$, while the combination of fasting and metformin resulted in impressive antitumor activity in several preclinical tumor models$^2$. The BREAKFAST study was designed to investigate if cyclic FMD, plus/minus metformin, improves the antitumor activity of neoadjuvant CT in patients (pts) with localized TNBC.

METHODS

BREAKFAST is a randomized, non-comparative, phase II trial originally designed to enrol 90 stage I-III (cT>1cm) TNBC pts candidate to receive neoadjuvant doxorubicin-cyclophosphamide q3w for 4 cycles, followed by weekly paclitaxel for 12 cycles. Pts were randomized 1:1 to receive: CT + triweekly 5-day FMD cycles (arm A), or CT + FMD + daily metformin (1700 mg) (arm B). The primary study objective was to investigate if one or both experimental treatments were able to increase pCR rates when compared to anthracycline-taxane CT alone according to historical data.

RESULTS

We enrolled 30 pts between June 2020 and February 2022, when the study was prematurely interrupted after the introduction of chemo-immunotherapy (CT-IO) as a standard neoadjuvant therapy for early stage TNBC. Of these pts, 13 were randomized to arm A and 17 to arm B. (Figure 1).

CONCLUSIONS

Preoperative CT plus cyclic FMD (plus/minus metformin) results in excellent pCR rates in early TNBC pts. Based on these findings, we recently initiated a phase II, randomized, multicentric trial, namely BREAKFAST-2, to investigate if adding cyclic FMD to neoadjuvant CT-IO increases pCR rates in stage II-III TNBC pts.

REFERENCES

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francesca.ligorio@istitutotumori.mi.it; claudio.vernieri@istitutotumori.mi.it