复旦团队新方案为“最毒乳腺癌”患者带来更大生机

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复旦团队新方案为“最毒乳腺癌”患者带来更大生机。中新网上海10月24日电(陈静 王广兆)三阴性乳腺癌患者数约占所有乳腺癌患者数的15%-20%，因其恶性程度高、容易复发转移，相较于其他类型乳腺癌治疗手段单一、缺乏有效治疗靶点，素有“最毒乳腺癌”之称。

中国专家团队基于自主研发的“多基因模型(三阴性乳腺癌预后预测模型)”，针对有“最毒乳腺癌”之称的三阴性乳腺癌，采用精准治疗方案(“蒽环紫杉”序贯“吉西他滨”联合“卡铂”)，让高危患者生存率提升超过10%。这改变了传统三阴性乳腺癌辅助化疗“千人一方”的局面。



RESEARCH

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Intensive chemotherapy versus standard chemotherapy among patients with high risk, operable, triple negative breast cancer based on integrated mRNA-lncRNA signature (BCTOP-T-A01): randomised, multicentre, phase 3 trial

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ABSTRACT

OBJECTIVE
To evaluate the feasibility of using a multigene signature to tailor individualised adjuvant therapy for patients with operable triple negative breast cancer.

DESIGN
Randomised, multicentre, open label, phase 3 trial.

SETTING
7 cancer centres in China between 3 January 2016 and 17 July 2023.

PARTICIPANTS
Female patients aged 18-70 years with early triple negative breast cancer after definitive surgery.

INTERVENTIONS
After risk stratification using the integrated signature, patients at high risk were randomised (1:1) to receive an intensive adjuvant treatment comprising four cycles of docetaxel, epirubicin, and cyclophosphamide followed by four cycles of gemcitabine and cisplatin (arm A; n=166) or a standard treatment of four cycles of epirubicin and cyclophosphamide followed by four cycles of docetaxel (arm B; n=170). Patients at low risk received the same adjuvant chemotherapy as arm B (arm C; n=168).

MAIN OUTCOME MEASURES
The primary endpoint was disease-free survival in the intention-to-treat analysis for arm A versus arm B. Secondary endpoints included disease-free survival for arm C versus arm B, recurrence-free survival, overall survival, and safety.

RESULTS
Among the 504 enrolled patients, 498 received study treatment. At a median follow-up of 45.1 months, the three year disease-free survival rate was 90.9% for patients in arm A and 80.6% for patients in arm B (hazard ratio 0.51, 95% confidence interval (CI) 0.28 to 0.95; P=0.03). The three year recurrence-free survival rate was 92.6% in arm A and 83.2% in arm B (hazard ratio 0.50, 95% CI 0.25 to 0.98; P=0.04). The three year overall survival rate was 98.2% in arm A and 91.3% in arm B (hazard ratio 0.58, 95% CI 0.22 to 1.56; P=0.27). The rates of disease-free survival (three year disease-free survival 90.1% v80.6%; hazard ratio 0.57, 95% CI 0.33 to 0.98; P=0.04), recurrence-free survival (three year recurrence-free survival 94.5% v83.2%; 0.42, 0.22 to 0.81; P=0.007), and overall survival (three year overall survival 100% v91.3%; 0.14, 0.03 to 0.61; P=0.002) were significantly higher in patients in arm C than in those in arm B with the same chemotherapy regimen. The incidence of grade 3-4 treatment related adverse events were 64% (105/163), 51% (86/169), and 54% (90/166) for arms A, B, and C, respectively. No treatment related deaths occurred.

CONCLUSIONS
The multigene signature showed potential for tailoring adjuvant chemotherapy for patients with operable triple negative breast cancer. Intensive regimens incorporating gemcitabine and cisplatin into anthracycline/taxane based therapy significantly improved disease-free survival with manageable toxicity.

TRIAL REGISTRATION
ClinicalTrials.gov NCT02641847.

WHAT IS ALREADY KNOWN ON THIS TOPIC

The prognosis of early stage triple negative breast cancer is unsatisfactory, and a need for optimisation of adjuvant therapy remains

A prospectively validated signature for triple negative breast cancer that can predict prognosis and guide adjuvant treatments is lacking

An integrated mRNA-lncRNA signature has been previously developed to provide prognostic information in triple negative breast cancer

WHAT THIS STUDY ADDS

This study is the first to use a multigene signature to tailor individualised adjuvant therapy for patients with operable triple negative breast cancer

The intensive chemotherapy regimen significantly improved disease-free survival compared with standard chemotherapy in patients identified as being at high risk

The prognostic value of the multigene signature was prospectively validated, with better survival outcomes in patients at low risk than in those at high risk receiving the same standard therapy

Introduction

Triple negative breast cancer, characterised by the absence of expression of oestrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 (HER2), accounts for 15-20% of all invasive breast cancers and is associated with a high risk of early recurrence and mortality.[1 2] Adjuvant anthracycline/taxane based chemotherapy is a standard treatment for early stage triple negative

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国际知名医学期刊之一的《英国医学杂志》(TheBMJ)24日刊登了中国专家团队的相关研究成果。(复旦大学附属肿瘤医院供图)

国际知名医学期刊之一的《英国医学杂志》(The BMJ)24日刊登了复旦大学附属肿瘤医院乳腺外科邵志敏教授、王中华教授、江一舟教授团队领衔相关研究的成果。

近年来，越来越多的研究认为，三阴性乳腺癌具有极高的异质性，可进一步被细分。在临床上，医生也发现，虽然三阴性乳腺癌患者整体预后欠佳，但并非所有患者都会出现复发转移，更精准的治疗策略亟待探索。

但是，目前三阴性乳腺癌的辅助化疗只能沿用传统的“千人一方”的治疗方案。因为当前乳腺癌研究领域缺乏经过临床队列验证的针对三阴性乳腺癌特异的工具或模型，无法精确地预测患者的复发转移风险，进而实现对患者风险分层进而开展个性化精准治疗。

2015年，邵志敏教授、江一舟教授团队自主研发构建了由5个RNA组成的三阴性乳腺癌预后预测模型(简称“多基因模型”)，为三阴性乳腺癌的精准化疗提供了理论依据。

复旦大学附属肿瘤医院乳腺外科副主任王中华教授介绍，此次研究中，其所在科室领衔中国(大陆)其他6家中心开展协作临床研究。他们将入组患者依据多基因模型检测结果，分为高危组和低危组。其中，高危组患者按照1:1比例，随机接受强化或标准方案辅助化疗。经过中位45个月的随访，接受强化治疗的高危患者3年无病生存率为90.9%，明显优于标准治疗组患者80.6%，疾病风险降低49%；强化治疗组患者的3年无复发生存率为92.6%，也高于标准治疗组的83.2%，可以降低高危患者50%的复发风险。

邵志敏教授指出，多基因模型指导下的精准化疗方案让低危患者的生存率提升也接近10%。王中华教授表示，这项研究成果在国际上前瞻性验证了三阴性乳腺癌多基因模型指导精准化疗和预测患者预后的价值。

复旦大学附属肿瘤医院副院长、临床研究中心主任江一舟教授透露，基于已获得的研究结果，医院正在准备开展针对多基因模型预测的低危三阴性乳腺癌患者的降阶梯治疗。(完)

（原标题：中国专家“预测预后+精准化疗方案”为“最毒乳腺癌”患者带来更大生机）

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