FUSCC Refractory TNBC Umbrella (FUTURE) (FUTURE)

ClinicalTrials.gov Identifier: NCT03805399

Recruitment Status : Recruiting
First Posted : January 15, 2019
Last Update Posted : January 15, 2019

See **Contacts and Locations**

Sponsor:
Fudan University

Information provided by (Responsible Party):
Zhimin Shao, Fudan University

Study Description

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Brief Summary:
This is a Phase Ib/II, open-label, umbrella study evaluating the efficacy and safety of multiple targeted treatment in patients with refractory metastatic TNBC.The specific grouping of patients' depends on FUSCC 500+ gene panel testing and IHC subtype staining.

Condition or disease	Intervention/treatment	Phase
Triple-negative Breast Cancer	Drug: Pyrotinib with Capecitabine Drug: AR inhibitor with CDK4/6 inhibitor	Phase 1 Phase 2

	Drug: anti PD-1 with nab-paclitaxel Drug: PARP inhibitor Drug: BLIS with Apatinib Drug: MES with Apatinib Drug: mTOR inhibitor with nab-paclitaxel	

Detailed Description:

This is a Phase Ib/II, open-label, umbrella study evaluating the efficacy and safety of multiple targeted treatment in patients with metastatic TNBC who had disease progression during or following standard treatment with chemotherapy(anthracyclines,taxanes,platinums, vinorelbine,capecitabine,and gemcitabine included).300-400 patients will be screened and eligible participants will enter different treatment arms according to their molecular subtype (IHC staining) and FUSCC 500+ gene panel testing results. These tests would be done on their rebiopsy tumor specimen. Specifically, as to TNBC molecular subtyping,FUSCC data identified the genomic aberrations that drive each TNBC subtype by applying an integrative analysis combining somatic mutation, copy number aberrations (CNAs) and gene expression profiles, which classified TNBC patients into four subtypes, namely luminal androgen receptor (LAR), immunomodulatory (IM), basal-like immune suppressed (BLIS), and mesenchymal (MES). Then, FUSCC conducted a IHC subtyping model to replace complex genomic sequencing, which have been validated in FUSCC cohort.FUSCC 500+ gene panel was developed combining public database(TCGA, METABRIC, 560WES, MSKCC-IMPACT ect.) and FUSCC private TNBC database.New treatment arms may be added and/or existing treatment arms may be closed during the course of the study on the basis of ongoing clinical efficacy and safety as well as the current treatments available.

Study Design

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Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	140 participants
Allocation:	Non-Randomized
Intervention Model:	Parallel Assignment
Intervention Model Description:	The refractory mTNBC participants will be classified into four subtypes based on immunohistochemistry tests namely luminal androgen receptor (LAR), immunomodulatory (IM), basal-like immune suppressed (BLIS), and mesenchymal (MES).Then according to gene sequencing outcomes, different subtypes would receive different targeted therapy (combined with chemotherapy in three treatment arms).
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	Precision Treatment of Refractory Triple Negative Breast Cancer Based on Molecular Subtyping ——FUSCC-TNBC- Umbrella Trial
Actual Study Start Date :	July 17, 2018
Estimated Primary Completion Date :	January 1, 2022

Estimated Study Completion Date : June 1, 2022

Resource links provided by the National Library of Medicine

Genetics Home Reference related topics: Breast cancer

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Experimental: pyrotinib with capecitabine If patients were LAR subtype and had HER2 gene activated mutation	Drug: Pyrotinib with Capecitabine If patients were LAR subtype and had HER2 gene activated mutation, she would receive pyrotinib(EGFR-TKI) 400mg qd and capecitabine 1000mg/m2 bid(d1-d14) Other Name: SHR1258
Experimental: AR inhibitor with CDK4/6 inhibitor If patients were LAR subtype and had a wildtype RB gene,withCCDN1 amplification or CDKN2A copy number loss	Drug: AR inhibitor with CDK4/6 inhibitor If patients were LAR subtype and had a wildtype RB gene,withCCDN1 amplification or CDKN2A copy number loss, she would receive AR inhibitor SHR3680 240mg qd combined with CDK4/6 inhibitor SHR6390 150 mg qd(three week on one week off) Other Name: SHR3680 SHR6390
Experimental: anti PD-1 with nab-paclitaxel If patients were IM subtype(CD8 positive T cell more than 20%)	Drug: anti PD-1 with nab-paclitaxel If patients were IM subtype,she will receive PD-1 antibody SHR1210 200mg q2w and nab-paclitaxel 100mg qw(three week on one week off). Other Name: SHR1210
Experimental: PARP inhibitor If patients were BLIS subtype and had a BRCA gene pathogenic mutation	Drug: PARP inhibitor If patients were BLIS subtype and had a BRCA gene pathogenic mutation, she will receive PARP inhibitor SHR3162 150mg bid po. Other Name: SHR3162

Experimental: BLIS with apatinib If patients were BLIS subtype and didn't have a BRCA gene pathogenic mutation	Drug: BLIS with Apatinib If patients were BLIS subtype and didn't have a BRCA gene pathogenic mutation , she will receive VEGFR inhibitor apatinib 500mg qd. Other Name: YN968D1
Experimental: MES with apatinib If patients were MES subtype and without PI3K/AKT pathway activation	Drug: MES with Apatinib If patients were MES subtype and without PI3K/AKT pathway activation,she will receive VEGFR inhibitor apatinib 500mg qd. Other Name: YN968D1
Experimental: mTOR inhibitor with nab-paclitaxel f patients were MES subtype and had PI3K/AKT pathway activation	Drug: mTOR inhibitor with nab-paclitaxel If patients were MES subtype and had PI3K/AKT pathway activation, she will receive mTOR inhibitor 10mg qd combined with nab-paclitaxel100mg qw(three week on one week off). Other Name: everolimus

Outcome Measures

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Primary Outcome Measures :

1. Objective Response Rate (ORR) [Time Frame: Randomization until the first occurrence of disease progression or death from any cause, which ever occurs first, through the end of study (approximately 3 years)]

   The proportion of participants whose best outcome is complete remission or partial remission (according to RECIST1.1)

Secondary Outcome Measures :

1. Disease Control Rate(DOR) [Time Frame: Baseline through end of study (approximately 3 years)]

   Complete remission or partial remission or stable disease (according to RECIST1.1)

2. Progression Free Survival(PFS) [Time Frame: Randomization until the first occurrence of disease progression or death from any cause, which ever occurs first, through the end of study (approximately 3 years)]

   time to progressive disease (according to RECIST1.1)

3. Overall Survival (OS) [Time Frame: Randomization to death from any cause, through the end of study (approximately 3 years)]

   time to death due to any cause

Eligibility Criteria

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Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years to 75 Years (Adult, Older Adult)
Sexes Eligible for Study:	Female
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- ECOG Performance Status of 0, 1, or 2
- Metastatic or locally advanced, histologically documented TNBC (absence of HER2, ER, and PR expression)
- Radiologic/objective evidence of recurrence or disease progression after available standard chemotherapy regimens(anthracyclines,taxanes, platinums, vinorelbine,capacitabine, and gemcitabine included) for metastatic breast cancer(MBC)
- Availability of a representative tumor specimen that is suitable for rebiopsy, IHC staining and gene sequencing

- Adequate hematologic and end-organ function, laboratory test results, obtained within 14 days prior to initiation of study treatment.
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures as outlined for each specific treatment arm
- Measurable disease according to Response Evaluation Criteria in Solid Tumors v1.1 (RECIST v1.1)
- have the cognitive ability to understand the protocol and be willing to participate and to be followed up.

Exclusion Criteria:

- Symptomatic, untreated, or actively progressing CNS metastases
- Active or history of autoimmune disease or immune deficiency
- Significant cardiovascular disease
- History of malignancy other than breast cancer within 5 years prior to screening, with the exception of those with a negligible risk of metastasis or death
- Treatment with chemotherapy, radiotherapy,immunotherapy or surgery (outpatient clinic surgery excluded)within3 weeks prior to initiation of study treatment.
- Pregnancy or breastfeeding, or intention of becoming pregnant during the study

Contacts and Locations

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Information from the National Library of Medicine NIH NLM

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT03805399***

Contacts

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Locations

China, Shanghai

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Sponsors and Collaborators

Fudan University

Investigators

Principal Investigator: Zhimin U Shao, Professor Fudan University

More Information

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Responsible Party: Zhimin Shao, Professor, Fudan University
ClinicalTrials.gov Identifier: NCT03805399 History of Changes
Other Study ID Numbers: 1807188-16
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Studies a U.S. FDA-regulated Drug Product: No
Studies a U.S. FDA-regulated Device Product: No

Keywords provided by Zhimin Shao, Fudan University:
TNBC
Molecular Subtype
Precision Treatment
Umbrella

Additional relevant MeSH terms:

Breast Neoplasms	Antineoplastic Agents
Triple Negative Breast Neoplasms	Tubulin Modulators
Neoplasms by Site	Antimitotic Agents
Neoplasms	Mitosis Modulators
Breast Diseases	Molecular Mechanisms of Pharmacological Action
Skin Diseases	Antimetabolites, Antineoplastic
Paclitaxel	Antimetabolites
Albumin-Bound Paclitaxel	Protein Kinase Inhibitors
Capecitabine	Enzyme Inhibitors
Apatinib	Immunosuppressive Agents
Everolimus	Immunologic Factors
Sirolimus	Physiological Effects of Drugs
Poly(ADP-ribose) Polymerase Inhibitors	Anti-Bacterial Agents
Androgen Receptor Antagonists	Anti-Infective Agents
Antineoplastic Agents, Phytogenic	Antibiotics, Antineoplastic