NEW FEATURED TRIAL AT THE SIDNEY KIMMEL CANCER CENTER AT JEFFERSON UNIVERSITY:

Title: A Randomized, Double-Blind, Placebo-Controlled Phase 2 Study of Paclitaxel in Combination with Reparixin Compared to Paclitaxel Alone as Front-Line Therapy for Metastatic Triple-Negative Breast Cancer

PI: Laura Austin, MD

Sponsor: Dompé

Purpose: The current phase 2 study thus aims to evaluate the Progression Free Survival of patients with metastatic TNBC [relapsed following neoadjuvant chemotherapy] receiving reparixin in combination with paclitaxel versus paclitaxel alone.

Treatment:
Arm 1: Experimental: paclitaxel 80 mg/m² i.v. (Days 1, 8, and 15) + reparixin oral tablets 1200 mg t.i.d. continuing from D 1 to Day 21 of 28-day cycle
Arm 2: Active Comparator: paclitaxel 80 mg/m² i.v. (Days 1, 8, and 15) + placebo oral tablets 1200 mg t.i.d. continuing from D 1 to Day 21 of 28-day cycle

Inclusion Criteria:
1. Female aged > 18 years.
2. Patients with pathologically documented metastatic triple negative breast cancer (TNBC), eligible for treatment with paclitaxel. Paraffin-embedded tissue must be available from metastatic sites, if reasonably accessible, or from the primary tumor, to confirm the diagnosis of TNBC and for correlative studies (only on metastatic tissue). Fifteen slides can be obtained if the full block is not available to be sent or released.
   A. TNBC will be defined as breast cancer with <1% ER+ and <1% PgR+ cells, and HER2 immunohistochemistry score of 0 or 1+ and/or in situ hybridization (ISH) with HER2 gene copy number <4 or a ratio of less than 2 between HER2 gene copy number and centromere of chromosome 17. Patients whose metastatic disease is TNBC are eligible even when their primary tumor expressed hormone receptors and/or HER2.
3. Patients must have relapsed following a prior neoadjuvant chemotherapy regimen. If a taxane (i.e., paclitaxel or docetaxel) was administered as part of the neoadjuvant regimen, PD must have occurred > 12 months from the end of previous neoadjuvant treatment. For non-taxane (neo)adjuvant regimen, PD must have occurred > 6 months from the end of previous (neo)adjuvant treatment
4. Patients with at least one baseline measurable lesion according to RECIST criteria version 1.1.
5. No history or evidence by CT scan or MRI, of brain metastases or leptomeningeal disease.

Exclusion Criteria:
1. Newly diagnosed metastatic TNBC and TNBC not previously treated with neoadjuvant chemotherapy
2. Prior therapy for metastatic TNBC (chemotherapy, hormone therapy or biological therapy). Patients may receive bisphosphonates and other therapies to treat bone metastases, however if used, bone lesions will not be considered as measurable disease.
3. Less than four weeks since last radiotherapy (excluding palliative radiotherapy).
Title: Phase Ib/II Study of Neoadjuvant Pembrolizumab (MK-3475) with Gemcitabine-Cisplatin (cisplatin eligible) or Gemcitabine (cisplatin-ineligible) in Subjects with T2-4aN0M0 Urothelial Cancer: HCRN GU14-188

PI: Jean Hoffman- Censits, MD

Sponsor: Hoosier Cancer Research Network

Purpose: This study is to determine the safety and efficacy of neoadjuvant pembrolizumab (MK-3475) in combination with gemcitabine-cisplatin or gemcitabine in subjects with cT2-T4a N0 M0 urothelial cancer (UC).

Treatment:

Phase Ib:
- Cohort 1 (Cisplatin Eligible)
  - Pembrolizumab every 3 weeks times 5 doses + Gemcitabine-Cisplatin every 21 days times 4 cycles

Phase II:
- Cohort 1 (Cisplatin Eligible)
  - Arm A - Pembrolizumab every 3 weeks times 5 doses + Gemcitabine-Cisplatin every 21 days times 4 cycles
- Cohort 2 (Cisplatin Ineligible)
  - Arm B - Pembrolizumab every 3 weeks times 5 doses + Gemcitabine every 28 days times 3 cycles

Inclusion Criteria:
1. Have histologically confirmed muscle invasive disease of the urinary bladder, renal pelvis, or ureters with surgical intent for radical cystectomy (RC) or nephroureterectomy (NU).
2. Histology must be urothelial carcinoma or urothelial carcinoma with mixed histology.
3. Clinical stage cT2-T4a N0 M0.
4. Have archived tissue available to submit for PD-L1 expression or able to undergo biopsy procedure
5. Have ECOG performance status of 0, 1, 2

Cohort I – Cisplatin eligible
In addition to the inclusion criteria listed above, Cohort I subjects must satisfy all of the following criteria:
- Glomerular filtration rate (GFR) or creatinine clearance (Ccr) ≥ 50 mL/min. (24 hour urine preferred). The cisplatin dose will be split over two days for values between 50-59 mL/min
- ECOG PS 0, 1 (and not 2)
- Hearing impaired ≤ grade 1 (may or may not be enrolled in a monitoring program)
- Peripheral neuropathy ≤ grade 1

Cohort II – Cisplatin Ineligible
In addition to the inclusion criteria listed above, Cohort II subjects must also meet any one of the following criteria:
- GFR or Ccr: 30-49 (24 hour urine preferred). OR
• ECOG PS 2 OR
• Hearing impaired ≥ grade 2 as assessed by treating physician (may or may not be enrolled in a monitoring program). OR
• Peripheral neuropathy of Grade 2-4

Exclusion Criteria:
1. Is not a surgical candidate.
2. Has abdomino-pelvic short axis lymph node of ≥ 15mm without biopsy.
3. Has a diagnosis of immunodeficiency or is receiving systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to study registration.
4. Has had a prior monoclonal antibody within 28 days prior to study registration or who has not recovered from adverse events due to agents administered more than 28 days earlier.
5. Has a known additional malignancy that is progressing or requires active treatment. Exceptions include basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or in situ cervical cancer that has undergone potentially curative therapy.
6. Has active New York Heart Association (NYHA) Stage III/IV heart failure.
7. Has known active central nervous system (CNS) metastases and/or carcinomatous meningitis.
8. Has an active autoimmune disease requiring systemic treatment within the past 3 months or a documented history of clinically severe autoimmune disease, or a syndrome that requires systemic steroids or immunosuppressive agents.
9. Has evidence of interstitial lung disease or active, noninfectious pneumonitis.
10. Has an active infection requiring systemic therapy.
11. Has received prior therapy with an anti-PD-1, anti-PD-L1,anti-PD-L2, anti-CD137, or anti-Cytotoxic T-lymphocyte associated antigen-4 (CTLA-4) antibody (including ipilimumab or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways).
12. Has a known history of HIV, a known active Hepatitis B, or Hepatitis C
13. Has received a live vaccine within 30 days prior to study registration.

Coordinator:
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Title: A Phase 3 Placebo-Controlled Study of Carboplatin/Paclitaxel With or Without Concurrent and Continuation Maintenance Veliparib (PARP inhibitor) in Subjects with Previously Untreated Stages III or IV High-Grade Serous Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer

PI: Russell Schilder, MD

Sponsor: AbbVie, Inc.

Purpose: The primary objective of the study is to evaluate whether progression-free survival (PFS) is prolonged when veliparib is added to standard platinum-based chemotherapy and then continued as maintenance (Arm 3 versus Arm 1). Progression-free survival as the primary study endpoint will be evaluated in both the whole subject population, as well as a more selective cohort of subjects with BRCA-deficient tumors (gBRCA and/or sBRCA).
Treatment:
Once pre-therapy procedures are complete and eligibility is confirmed, subjects will be randomized 1:1:1 to one of the following three arms:
Arm 1: Carboplatin/paclitaxel plus placebo for six 21-day cycles followed by placebo maintenance therapy for 30 additional 21-day cycles;
Arm 2: Carboplatin/paclitaxel plus veliparib for six 21-day cycles followed by placebo maintenance therapy for 30 additional 21-day cycles;
Arm 3: Carboplatin/paclitaxel plus veliparib for six 21-day cycles followed by veliparib maintenance therapy for 30 additional 21-day cycles

During the Combination Therapy Phase, subjects will receive veliparib/placebo orally (PO) twice daily (BID) in combination with intravenous (IV) carboplatin/paclitaxel for six cycles (Cycle 1 through Cycle 6). Subjects who complete the Combination Therapy Phase and who have not progressed will receive veliparib 400 mg/placebo orally twice daily maintenance therapy for an additional 30 cycles (Cycles 7 – 36) during the Maintenance Therapy Phase.

Inclusion Criteria:
1. Subjects with a histologic diagnosis of epithelial ovarian, fallopian tube, or primary peritoneal carcinoma, FIGO Stage III or IV with appropriate tissue available for histologic evaluation.
2. Subjects will be required to have high-grade serous adenocarcinoma to be eligible.
3. Subject is willing to undergo testing for gBRCA.
4. Subject must have adequate hematologic, renal, and hepatic function as follows:
   a. Hemoglobin ≥ 9.5 g/dL (5.89 mmol/L);
   b. Absolute neutrophil count greater than or equal to 1,500/μL;
   c. Platelet count greater than or equal to 100,000/μL;
   d. Serum creatinine ≤ 1.0 × ULN range; subjects with a serum creatinine >1.0 × ULN range must have a creatinine clearance ≥ 60 mL/min (according to the Cockcroft-Gault equation);
   e. Total bilirubin ≤ 1.5× ULN. Subjects with Gilbert's Syndrome may have a bilirubin ≥ 1.5 × the ULN range if no evidence of biliary obstruction exists;
   f. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase must be less than or equal to 2.5 × ULN;
   g. Albumin ≥ 3.0 g/dL.
5. Subjects with neuropathy (sensory and motor) less than or equal to Grade 1.
6. Subjects must have an ECOG performance status of 0, 1, or 2.
7. Subject is able to swallow and retain oral medication and does not have uncontrolled emesis.
8. Subjects who undergo primary cytoreductive surgery must be entered between 1 and 12 weeks after surgery. Subjects undergoing interval surgery must have a needle core biopsy confirming the histological diagnosis prior to enrollment.
9. Subjects with measurable disease and non-measurable disease are eligible. Subjects may or may not have cancer-related symptoms.
10. Subject has one of the following available for PD analyses including somatic BRCA testing:
    a. Archived diagnostic formalin-fixed paraffin embedded (FFPE) tumor tissue; or tumor tissue biopsy collected prior to Cycle 1 Day 1.
Exclusion Criteria:
1. Subjects with the following histologic cell types are ineligible: endometrioid adenocarcinoma, carcinosarcoma, undifferentiated carcinoma, mixed epithelial adenocarcinoma, adenocarcinoma not otherwise specified, mucinous adenocarcinoma, clear cell adenocarcinoma, low-grade serous adenocarcinoma, or malignant Brenner's tumor.
2. Subjects with synchronous primary endometrial cancer, or a past history of endometrial cancer unless all of the following conditions are met: endometrial cancer stage not greater than IA, no vascular or lymphatic invasion, no poorly differentiated subtypes including serous, clear cell, or other FIGO grade 3 lesions.
3. Subjects with a history of other invasive malignancies, with the exception of non-melanoma skin cancer, are excluded if there is any evidence of other malignancy being present within the last 3 years.
4. Subjects are also excluded if their previous cancer treatment contraindicates this protocol's therapy. Subjects who have received prior radiotherapy to any portion of the abdominal cavity or pelvis are excluded.
5. Subjects who have received prior chemotherapy for any abdominal or pelvic tumor are excluded.
6. Subject has a clinically significant uncontrolled condition(s), including but not limited to:
   A. Uncontrolled seizure disorder, or focal or generalized seizure within the last 12 months;
   B. Active infection that requires parenteral antibiotics;
   C. Known active hepatitis B or hepatitis C with abnormal liver function test or organ dysfunction;
   D. Symptomatic congestive heart failure; unstable angina pectoris; serious ventricular cardiac arrhythmia (i.e., ventricular tachycardia or ventricular fibrillation) or serious cardiac arrhythmia requiring medication (this does not include asymptomatic atrial fibrillation with controlled ventricular rate); or myocardial infarction within the last 6 months;
   E. Uncontrolled hypertension (sustained systolic blood pressure > 150 mmHg or diastolic pressure > 100 mmHg despite optimal medical management);
   F. Bowel obstruction or gastric outlet obstruction. Note: Subjects requiring drainage gastrostomy tube and/or parental hydration and/or nutrition are not eligible;
   G. Psychiatric illness/social situations that would limit compliance with study requirements;
   H. Any medical condition which in the opinion of the Investigator places the subject at an unacceptably high risk for toxicities.
7. Known history of allergic reaction to Cremophor-paclitaxel, carboplatin, Azo-Colourant Tartrazine (also known as FD&C Yellow 5 or E102), Azo-Colourant Orange Yellow-S (also known as FD&C Yellow 6 or E110) or known contraindications to any study supplied drug.
8. Subjects with history or evidence upon physical examination of central nervous system (CNS) disease, including primary brain tumor, any brain metastases, or history of cerebrovascular accident (CVA, stroke), transient ischemic attack (TIA) within 6 months of Cycle 1 Day 1.
9. Subjects under the age of 18.

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NRG BR003: A Randomized Phase III Trial of Adjuvant Therapy Comparing Doxorubicin Plus Cyclophosphamide Followed by Weekly Paclitaxel with or Without Carboplatin for Node-Positive or High-Risk Node-Negative Triple-Negative Invasive Breast Cancer

SWOG 1318: A Phase II Study of Blinatumomab (NSC-765986) and POMP (Prednisone, Vincristine, Methotrexate, 6-Mercaptopurine) for Patients >/= 65 Years of Age with Newly Diagnosed Philadelphia-Chromosome Negative (Ph-) Acute Lymphoblastic Leukemia (ALL) and of Dasatinib (NSC-732517), Prednisone and Blinatumomab for Patients >/= 65 Years of Age with Newly Diagnosed Philadelphia-Chromosome Positive (Ph+) ALL

A091401: Randomized Phase II Study of Nivolumab with or Without Ipilimumab in Patients with Metastatic or Unresectable Sarcoma

EA6134: A Randomized Phase III Trial of Dabrafenib + Trametinib Followed by Ipilimumab + Nivolumab at Progression vs. Ipilimumab + Nivolumab Followed by Dabrafenib + Trametinib at Progression in Patients with Advanced BRAFV600 Mutant Melanoma

NSABP B-52: A Randomized Phase III Trial Evaluating Pathologic Complete Response Rates in Patients with Hormone Receptor-Positive, HER2-Positive, Large Operable and Locally Advanced Breast Cancer Treated with Neoadjuvant Therapy of Docetaxel, Carboplatin, Trastuzumab, and Pertuzumab (TCHP) With or Without Estrogen Deprivation

RTOG 1201: A Phase II Randomized Trial for Locally Advanced Unresectable Pancreatic Cancer

CTSU Update:
NCTN and NCORP graphic identity badges now appear on protocol-specific-webpages. NCI created these for the NCTN and NCORP programs for NCI grantees to identify being part of these programs and to also highlight trials led by each network. These badges have been added to the protocol-specific pages on the CTSU website and appear at the top of each page next to the protocol number. The NCTN badge is displayed when NCTN is sponsoring a trial and identifies the study as a cancer treatment trial. The NCORP badge appears when NCORP is sponsoring a trial and identifies the study as a cancer control or prevention trial. Clinical trials sites funded by either NCI program are encouraged to participate in both NCTN and NCORP studies that best meet the needs of their site’s expertise and patient population.

The CTSU released its Fall 2015 Edition Newsletter on Thursday December 17th. This Newsletter can be found on the CTSU site. I would like to highlight some key topics:
CTSU cont.

CTSU Support for National Coverage Analysis: the CTSU is working with NCI, the NCTN Network Groups, and NCORP Research Bases to provide National Coverage Analysis (NCA) support for NCI-sponsored trials. To address this new effort, the CTSU has created and is leading a Coverage Analysis Working Group that will establish standard processes and procedures for the development and ongoing maintenance of coverage analysis documents that will be posted on the CTSU website for select NCI trials. CTSU support for NCA development will begin sometime in early 2016. In addition to this new effort, the CTSU is working with an experienced billing compliance consultant to provide NCA documents for select trials which will be posted on the CTSU website and announced in the CTSU Bi-Monthly Broadcast as they become available in early 2016.

CTSU Report and Information Subscription Portal (CRISP): CRISP allows CTSU website users to subscribe to and manage e-mail notifications. The CRISP button is accessible from any page on the CTSU website and is located in the banner, next to “My Account.” A pop-up will appear so make sure any pop-up blockers are turned off. Currently one can subscribe to the following weekly alerts: summary of multi-step enrollments, summary of changes to person roster, new protocols in my area of interest, expiring IRB approvals and changes to Site Registration statuses. Additional options will be available in the Spring of 2016.

Roster Update Management System (RUMS): RUMS was developed to streamline and standardize the rostering process. RUMS is an application hosted on the CTSU website that allows the management of institution and person roster data through a direct link with the Regulatory Support System (RSS). Training materials are available in the RUMS tab, including a video and User Guide.

Google Search Feature: The CTSU website is an enormous repository of documents and information. To help better navigate the wealth of available information, we have brought Google Search, a trusted search engine, to the CTSU website. The search feature is located in the upper-right hand corner of the public and members’ websites. Simply enter a keyword to search and click GO. A listing of all documents and CTSU website locations that contain the keyword will appear on the screen with a URL location for each entry. Once you have found what you are searching for, simply click on the link to go directly to that document or section of the website. We encourage you to take advantage of this feature and hope it improves your ability to find information quickly and easily.

A041202, A Randomized Phase III Study of Bendamustine Plus Rituximab Versus Ibrutinib Plus Rituximab Versus Ibrutinib Alone in Untreated Older Patients (>= 65 Years of Age) with Chronic Lymphocytic Leukemia (CLL), is approaching its accrual goal and permanently closed to new patient pre-registration (Step 0) on December 28, 2015. Patients pre-registered (Step 0) to this study on or before December 28 will be able to be registered/randomized (Step 1) to the study provided they meet all registration eligibility criteria. Notice of closure of registration/randomization (Step 1) will be announced at a later date. Patients on treatment should continue to be treated and followed as required per protocol.

EAY131 - Molecular Analysis for Therapy Choice (MATCH): A pause to all new accrual to the Screening (Step 0) portion of EAY131 started as of November 4, 2015. Screening (Step 0) accrual and related biospecimen processing have reached the accrual goals necessary to conduct a study-specified planned analysis. EAY131’s protocol design has a built-in review after 500 patients are enrolled for mutation screening. The trial’s enrollment has now reached 500 patients. To perform the review required by the protocol, new enrollments must pause until the analysis can be conducted. During this pause, the study team will use the time to thoroughly review data from the first 500 patients, and also examine all of the processes that support the study. The study team will continue to add new treatment arms to the trial as planned, to improve the frequency of matching mutations to drugs. This trial is expected to reopen in early 2016 with additional treatment trials available. Additional information will be provided as soon as it is available.

The Thomas Jefferson University application to the NCI Central Institutional Review board for the EAY131 protocol was approved on October 22, 2015. If your site is interested in participating please contact Joshua Schoppe at your earliest convenience.

ECOG-ACRIN Laboratories December Holiday Schedule: The ECOG-ACRIN Biorepository and Pathology Facility (CBPF) will be closed on December 24 through December 26, 2015. The ECOG-ACRIN Biorepository and Pathology Facility (CBPF) will also be closed on January 1 and January 2, 2016. Do not
ECOG cont.
collect specimens for EAY131 (NCI MATCH) on December 23 through December 25, 2015 or on December 31 through January 1, 2016. Do not ship frozen specimens on December 23, 2015. Hold and ship on December 28, 2015. Do not ship frozen specimens on December 31, 2015. Hold and ship on January 4, 2016. ECOG-ACRIN Central Biorepository can be reached at 1-(844) 744-2420 or eacbpf@mdanderson.org

ECOG-ACRIN Upcoming Performance Monitoring:
The next Performance Monitoring data cut-off date of December 31, 2015 is approaching. Any data received on or before December 31, 2015 will be included in the upcoming Performance Monitoring. Data received after December 31, 2015 will be considered late. It is important to remember that data timeliness will be evaluated by assessing two components: The rate of CRF submitted and the rate of survival follow-up. To avoid penalties, each evaluable ECOG institution must have a score of 90% or better on each component. ECOG-ACRIN has designed an application where sites can look-up information about specific affiliate sites, protocols and patients. The Performance Monitoring link is only available to ECOG-ACRIN sites. The link for this website here: http://webapps.ecog.org/Performance. You will need to use your CTEP user name and password to access this site.

NSABP B-43, B-47, B-52, The Pittsburgh Center has reviewed the updated trastuzumab IB, Version 15, dated October 2015 (with a safety data cut-off dated September 24, 2015) and has determined that no changes are needed in the protocols and consent forms at this time. A Summary of Significant Changes begins on page 2 of the IB.

Please submit the information to your IRB according to your local policy and procedures. It is not necessary to submit documentation regarding IRB review of the updated IB to NRG Oncology or CTSU; this documentation should be maintained in your local study records.

Affiliate Invoicing for NRG Oncology Trials: As an effort to streamline the process for reimbursement, we are in the process of finalizing a guidance document that describes the process by which affiliate sites will submit invoices for compensation for participant accrual and other study related procedures and milestones. This process will involve the TJU NRG Oncology affiliate sites, the Sidney Kimmel Cancer Network (SKCN), and the Office of Research Administration. More information to follow.

Upcoming Events:

- **Jefferson Lung Cancer Symposium:** March 11, 2016 - Philadelphia, PA
- **CRA Research Update:** March 18, 2016 - Virtual
- **SKCN Social Workers Meeting:** TBA
- **SKCN Navigators Meeting:** May 13, 2016 - Philadelphia, PA
- **ECOG-ACRIN Spring 2016 Meeting:** May 12-14, 2016 - Boston, MA
- **Palliative Care Symposium:** June 3, 2016 - Philadelphia, PA

NRG Semi-Annual Meeting:
January 21-24, 2016
Atlanta, GA
The Clinical Research E-News Archive is now located on the Sidney Kimmel Cancer Center webpage under the JKCCN Member Area: http://www.kimmelcancercenter.org/jkccn/e-newsletters.html

Sidney Kimmel Cancer Network Homepage: http://isley.kcc.tju.edu/skcn/ -This page contains links to the Remote Access Portal as well as the clinical trial document repository.

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