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

Title: Randomized phase IB/II study of Enzalutamide with and without Ribociclib in patients with metastatic castrate resistant, chemotherapy naïve prostate cancer that retains RB expression: Protocol CLEE011XUS12T

Sponsor: Novartis and Prostate Cancer Clinical Trial Consortium

PI: W. Kevin Kelly, DO

Rationale:
RB function is often attenuated in tumors through hyperphosphorylation - thus; RB activity can be “re-awakened” in RB+ tumors by suppressing the key kinases that phosphorylate RB (CDK4/6). Therefore, we hypothesize that the addition of ribociclib in combination with enzalutamide in patients with progressive metastatic prostate cancer despite castrate levels of testosterone that retains RB expression will significantly increase the efficacy of enzalutamide.

Study Design:
This is a Phase IB/II study of patients with mCRPC with RB positive tumors who have not received chemotherapy.

The phase IB portion will be a dose escalation study using a ‘3+3’ schema. Enzalutamide will be administered at a dose of 160 mg (40 mg X 4 pills) once daily. Ribociclib will be given orally once daily (dose levels as shown in the dose escalation schema below). Enzalutamide may be taken with or without food but should be taken at the same time every day.

<table>
<thead>
<tr>
<th>Phase IB Dose Escalation Schema</th>
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<tbody>
<tr>
<td>Dose Level</td>
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<tr>
<td>Level 1</td>
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<tr>
<td>200 mg daily</td>
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<td>Level 2</td>
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<tr>
<td>400 mg daily</td>
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<tr>
<td>Level 3</td>
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<td>600 mg daily</td>
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The phase II portion of the trial will be a randomized two arm trial utilizing the established MTD of ribociclib in combination with standard doses of enzalutamide from the phase IB component. Subjects will be randomized to either enzalutamide in combination with ribociclib or enzalutamide alone in a 1:1 ratio.
Eligibility Criteria:

1. Men with metastatic castrate resistant prostate cancer (mCRPC) who are chemotherapy naïve and retain retinoblastoma gene (RB) expression
2. Histological or cytological proof of prostate adenocarcinoma
3. Castrate serum testosterone level: ≤50 ng/dL (≤1.7 nmol/L)
4. Documented progressive mCRPC based on at least one of the following criteria:
   (a) PSA progression defined as 25% increase over baseline value with an increase in the absolute value of at least 2 ng/mL that is confirmed by another PSA level with a minimum of a 1 week interval and a minimum PSA of 2 ng/mL.
   (b) Soft-tissue progression defined as an increase ≥ 20% in the sum of the longest diameter (LD) of all target lesions based on the smallest sum LD since treatment started or the appearance of one or more new lesions.
   (c) Progression of bone disease (evaluable disease) or (new bone lesion(s)) by bone scan.
5. Willing and able to undergo a biopsy of at least one metastatic site or primary prostate. Adequate archival metastatic tissue can be used if available in lieu of a biopsy if done when patient had CRPC (within 6 months of enrollment).
6. No prior exposure to abiraterone acetate or other specific CYP-17 inhibitors.
7. No prior enzalutamide or investigational androgen receptor (AR) targeted agent
8. No prior chemotherapy
9. Patients on long term (>6 months) anti-androgen therapy (e.g., flutamide, bicalutamide, nilutamide) will need to be off anti-androgen for 4 weeks (wash out period) and show evidence of disease progression off the anti-androgen. Patients that have been on an anti-androgen 6 months or less will need to discontinue anti-androgen therapy prior to starting protocol therapy (no wash out period required).
10. ECOG PS 0-1
11. Normal organ function

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Title: Study of Gemcitabine, Abraxane® Plus Placebo Versus Gemcitabine, Abraxane® Plus 1 or 2 Truncated Courses of Demcizumab in Subjects With 1st-Line Metastatic Pancreatic Ductal Adenocarcinoma (YOSEMITE)

Sponsor: Oncomed Pharmaceuticals, Inc.

Purpose:
This is a randomized, double blind, 3 arm (1:1:1) study in subjects with 1st-line metastatic pancreatic ductal adenocarcinoma.

The purpose is to test the efficacy and safety of demcizumab, when given in combination with gemcitabine and Abraxane® compared to placebo. The administration of gemcitabine and Abraxane® is a standard treatment for patients with metastatic pancreatic ductal adenocarcinoma.
<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
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</thead>
<tbody>
<tr>
<td>Experimental: Abraxane® and gemcitabine plus placebo Abraxane® and gemcitabine plus placebo (3 cycles), Abraxane® and gemcitabine (3 cycles), Abraxane® and gemcitabine plus placebo (3 cycles) and then Abraxane® and gemcitabine until disease progression</td>
<td>Drug: Demcizumab administered intravenously Drug: Abraxane® administered intravenously Drug: gemcitabine administered intravenously Drug: Placebo</td>
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<tr>
<td>Experimental: Abraxane® and gemcitabine plus demcizumab plus placebo Abraxane® and gemcitabine plus demcizumab (3 cycles), Abraxane® and gemcitabine (3 cycles), Abraxane® and gemcitabine plus placebo (3 cycles) and then Abraxane® and gemcitabine until disease progression</td>
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<td>Drug: Demcizumab administered intravenously Drug: Abraxane® administered intravenously Drug: gemcitabine administered intravenously</td>
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**Inclusion Criteria:**
1. Subjects must have histologically confirmed metastatic pancreatic ductal adenocarcinoma. Prior chemotherapy and/or radiotherapy either in the adjuvant or neoadjuvant setting or for metastatic disease is not allowed.
2. Availability of FFPE tumor tissue (from either the primary tumor, locoregional disease or a metastatic site), either fresh core-needle-biopsied or archived (two FFPE cores preferred whenever possible). If fresh tissue is obtained, the core biopsy must be done at least 7 days prior to randomization.
3. Age ≥21 years
4. ECOG PS 0 or 1
5. Measurable disease per RECIST v1.1
6. Adequate organ and marrow function
7. For women of childbearing potential, agreement to use two effective forms of contraception

**Exclusion Criteria:**
1. Subjects with a neuroendocrine tumor of the pancreas, an acinar tumor of the pancreas or a pancreatic tumor with mixed histologies.
2. Subjects receiving heparin, warfarin, factor Xa inhibitors or other similar anticoagulants. Note: Subjects may be receiving low-dose aspirin and/or non-steroidal anti-inflammatory agents.
3. Subjects with brain metastases, leptomeningeal disease, uncontrolled seizure disorder, or active neurologic disease
4. Subjects with Grade >2 peripheral neuropathy
5. Subjects with clinically significant ascites
6. Malignancies other than pancreatic cancer successfully treated within 3 years prior to randomization, except for adequately treated carcinoma in situ of the cervix, basal or squamous cell skin cancer, treated superficial bladder cancer, localized prostate cancer treated surgically with curative intent, ductal carcinoma in situ treated surgically with curative intent
7. Significant intercurrent illness that will limit the patient's ability to participate in the study or may result in their death over the next 18 months
8. History of a significant allergic reaction attributed to humanized or human monoclonal antibody therapy
9. Subjects with known clinically significant gastrointestinal disease including, but not limited to, inflammatory bowel disease
10. Pregnant women or nursing women
11. Subjects with known HIV infection
12. Known bleeding disorder or coagulopathy

Coordinator:
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OPEN TO NETWORK PARTICIPATION:

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

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

NRG-CC001: A Randomized Phase III Trial of Memantine and Whole-Brain Radiotherapy With or Without Hippocampal Avoidance in Patients with Brain Metastases

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

N0577 (CODEL): Phase III Intergroup Study of Radiotherapy with Concomitant and Adjuvant Temozolomide Versus Radiotherapy with Adjuvant PCV Chemotherapy in Patients with 1p/19q Co-Deleted Anaplastic Glioma or Low Grade Glioma

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

EA6134: 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

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

NRG-CC003: Randomized Phase II/III Trial of Prophylactic Cranial Irradiation with or without Hippocampal Avoidance for Small Cell Lung Cancer

NRG-GY006: Randomized Phase II Trial of Radiation Therapy and Cisplatin Alone or in Combination with Intravenous Triapine in Women with Newly Diagnosed Bulky Stage II, IIIB, or IVA Cancer of the Uterine Cervix or Stage II-IVA Vaginal Cancer
Regulatory Update:
1/13/16 ECOG 2408-Amendment Ltr translated dear patient informing Chinese subjects of PI change
1/13/16 GOG 02290-Amendment Ltr 5 & 6 revisions to protocol & consent
1/19/16 RTOG 1114 Closing enrollment
1/22/16 SWOG 1318-Amendment Ltr Revision 5 revisions to protocol & consent
1/26/16 RTOG 0617-Amendment 12 revisions to protocol & consent
1/28/16 RTOG 0938-Amendment 4 revisions to protocol only
2/4/16 SWOG 1406-Amendment revision 3 revisions to protocol & consent
2/9/16 RTOG 1216-Temporary Closure Letter to accrual effective 2/22/16

Starting Wednesday evening, January 27, 2016, updates will be made to the CTSU Regulatory Support System (RSS) to automatically withdraw investigators whose CTEP investigator registration status has been suspended for greater than 1 year and associates whose CTEP associate registration status has been suspended for greater than 6 months from all rosters in RSS. The roll-out of this update will occur over three weeks on the following schedule.

<table>
<thead>
<tr>
<th>Wed., Jan 27th</th>
<th>Tues, Feb 2nd</th>
<th>Thurs, Feb 4th</th>
<th>Tues, Feb 9th</th>
<th>Thurs, Feb 11th</th>
<th>Tues, Feb 16th</th>
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<tbody>
<tr>
<td>Alliance</td>
<td>CIRB</td>
<td>SWOG</td>
<td>Other Networks</td>
<td>ECOG-ACRIN</td>
<td>COG-COGC</td>
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As appropriate, please ask associates at your organization with a suspended CTEP associate registration status to re-register at https://eapps-ctep.nci.nih.gov/iam/index.jsp. For questions, please have them contact the CTEP Associate Registration Help Desk at CTEPRegHelp@ctep.nci.nih.gov. For investigators at your organization with a suspended CTEP investigator registration status, please contact the CTEP Investigator Registration Help Desk at PMBRegPend@ctep.nci.nih.gov and provide an investigator name and a CTEP investigator ID to receive a copy of the pre-printed investigator re-registration packet by return email.

CTSU cont.
To quickly check this information for your site select the Regulatory Tab on the CTSU members website and view the browser tree on the left side of the page. Unrolling the tree under each site will provide a list of suspended investigators and associates. Click on the person’s name in the tree and details regarding the person’s CTEP registration status will display on the right side of the screen. If an associate or investigator is withdrawn as a result of the automated updates, they can request to be added back to the rosters after updating their CTEP registration status. For sites under the NCTN network, person withdrawals can be made via RUMS by your site’s lead NCTN administrator.

Oncology Patient Enrollment Network (OPEN): Regarding reimbursements associated with Biospecimen, QOL, and Imaging submissions: This is a reminder and not a notice of outstanding requirements. As of March 1, 2014 implementation of the NCTN, applicable Biospecimen, Imaging, and QOL submissions must be logged in the OPEN funding screen to be credited for reimbursement. Submissions up to February 29, 2016 must be completed in OPEN by March 1, 2016. Questions pertaining to OPEN and which submissions are required to be logged are to be directed to ctsucontact@westat.com. Sites must rely on their institutional records for submitted imaging or QOL or samples not logged in STS. Reports are not available for these submissions. Sites are strongly encouraged to enter this information into OPEN on a regular basis and into STS if applicable. For reports associated with the OPEN system, please contact the CTSU. Instructions for the OPEN system are available on the CTSU website under the OPEN tab (bottom bullet): https://www.ctsu.org/readfile.aspx?fname=OPEN/OPEN_FundingScreen_SiteUser_Guide_022614.pdf&ftype=PDF

Upcoming CTSU Webinar for the NCI “Sister” Breast Studies: Tuesday, February 23rd, 2016 at 3:00pm – 4:00pm EST. The CTSU is coordinating a webinar to discuss NCI’s “Sister” Breast Studies – five trials that are complementary to each other with respect to patient population and accrual. The following studies will be presented: A011202, NSABP B-51/RTOG-1304, A011106, EA1131, and NSABP B-55. Study Chairs will briefly discuss their trial and provide updates on protocol status, accrual, and challenges. Participants will also be able to ask questions and receive answers directly from the Study Chairs. Please monitor the CTSU website for an agenda and more details. If you would like to attend this webinar, please click on the following link, click the ‘registration’ button, and complete the required information: https://ctwestat.webex.com/ctwestat/k2/j.php?MTID=t4344fc5a89098b7162c07a6e1dde102f
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: Accrual to EA6134 is suspended effective February 2, 2016. ECOG-ACRIN has received notification from the NCI that CTEP is experiencing an acute shortage in the supply of Dabrafenib mesylate (NSC 763760) capsules and Trametinib DMSO (NSC 763093) tablets. At this time, there is only a very limited supply available for distribution for patients already enrolled to NCI trials. This shortage is NOT due to any safety issues. CTEP is working closely with the pharmaceutical collaborator to ensure that patients enrolled on study will continue to receive treatment as per protocol as well to resolve the supply/distribution issues so that study could re-open. Additional information, including information on when accrual will reopen, will be provided as soon as it is available. Patients currently on study should be treated and followed according to the protocol.

ACTIVATION OF PROTOCOL EA2133, InterAACT - An International Multicentre Open Label Randomised Phase II Advanced Anal Cancer Trial Comparing Cisplatin plus 5-fluorouracil versus Carboplatin plus Weekly Paclitaxel in Patients with Inoperable Locally Recurrent or Metastatic Disease: This study was activated on February 1, 2016 and open for registration. Please let us know if you are site is interested in participating in this trial.

PACCT-1, Program for the Assessment of Clinical Cancer Tests (PACCT-1): Trial Assigning Individualized Options for Treatment: The TAILORx Trial: and important notice on form submission was released. Effective February 10, 2016, CTSU TAILORx Data Management will NO LONGER send individual email notifications to site CRAs advising that a form could not be processed due to inappropriate form submission.

RTOG 1008, Randomized Phase II/Phase III Study of Adjuvant Concurrent Radiation and Chemotherapy Versus Radiation Alone in Resected High - Risk Malignant Salivary Gland Tumors has been amended and re-opened to accrual to further evaluate the progression-free survival (PFS) benefit in both intermediate- and high-risk patients as well as to evaluate a definitive endpoint (overall survival) in this rare disease. In order to evaluate the overall survival, the patient cohort was expanded, and the study was redesigned to add the phase III component. Please see Section 13.4 of the protocol for further details.

NRG Oncology Invoicing Guidance document: In an effort to streamline the process for distributing subject reimbursement to our NRG Oncology affiliate sites, TJU has approved the NRG Oncology Invoicing Guidance document. This document will describe the process to which affiliate sites will receive compensation for subject accrual and other study related procedures and milestones.

On Thursday, 2/11/2016, the TJU NRG Oncology affiliate sites were sent the Invoicing Guidance document via email.

Any TJU NRG Oncology affiliate site who accrued subjects from 3/1/2014 (date of NRG Oncology merger) to 12/31/2015, will follow a one-time invoice and reimbursement process for this timeframe. These sites will be contacted directly. Any subjects accrued from 1/1/2016 and moving forward will follow the NRG Oncology Invoicing Guidance document for reimbursement.

More information will be presented at the 3/15/2016 Virtual CRA Research Update Meeting.
Upcoming Events:

Jefferson Lung Cancer Symposium:  
March 11, 2016  
Philadelphia PA

- CRA Research Update: March 15, 2016 - Virtual
- SKCN Social Workers Meeting: March 18, 2016, Philadelphia, PA
- SKCN Administrators Forum: April 29, 2016, Philadelphia, PA
- 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
- CRA Research Update: June 15, 2016 - Philadelphia, PA

The Clinical Research E-News Archive is now located on the Sidney Kimmel Cancer Center webpage under the SKCN Member Area:  
http://isley.kcc.tju.edu/skcn/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.

Contact Information:

<table>
<thead>
<tr>
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NRG Update inquiries or Clinical Research E-Newsletters  
ECOG-ACRIN Update inquiries, CTSU, or CIRB  
Pending Studies or Regulatory Update inquiries

For urgent clinical trial questions or assistance please page: 877-656-9004