**CONTENTS**

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Patient Registrations to Studies
by 12 Month Intervals
SYMPTOM CONTROL AND QOL COMMITTEE
As Primary Committee

Screening registrations and registrations to Biologic only studies are excluded.
**Patient Registrations to Studies**

by 12 Month Intervals

SYMPTOM CONTROL AND QOL COMMITTEE
As Secondary Committee

Screening registrations and registrations to Biologic only studies are excluded.
### Patient Registrations by Study and Arm

**SYMPTOM CONTROL AND QOL COMMITTEE**

As Primary or Secondary Committee

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*Studies with Symptom Control and QOL as a secondary committee*
### Non-SWOG Studies with SWOG-Credited Registrations

**SYMPTOM CONTROL AND QOL COMMITTEE**

**As Primary Committee**

Studies with Accrual from July 2017 - December 2018

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### Non-SWOG Studies with SWOG-Credited Registrations

**SYMPTOM CONTROL AND QOL COMMITTEE**

**As Secondary Committee**

Studies with Accrual from July 2017 - December 2018

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Non-SWOG Studies with SWOG-Credited Registrations (cont.)

SYMPTOM CONTROL AND QOL COMMITTEE
As Secondary Committee
Studies with Accrual from July 2017 - December 2018

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APRIL 24 - 27, 2019
### Non-SWOG Studies with SWOG-Credited Registrations (cont.)

**SYMPTOM CONTROL AND QOL COMMITTEE**  
As Secondary Committee  
Studies with Accrual from July 2017 - December 2018

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<td>Nasopharyngeal , Individual Tx EBV</td>
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**Date Activated:**
- 05/17/18
- 04/12/10
- 01/13/12
- 12/07/15
- 11/07/17
- 02/04/16
- 05/12/17
- 04/21/14
- 12/24/13
- 07/07/11
S1207 Phase III

Coordinating Group: SWOG

Phase III Randomized, Placebo-Controlled Clinical Trial Evaluating the Use of Adjuvant Endocrine Therapy +/- One Year of Everolimus in Patients with High-Risk, Hormone Receptor-Positive and Her2/neu Negative Breast Cancer.

**E3 Breast Cancer Study - Evaluating Everolimus with Endocrine therapy**

**Participants:**
SWOG, CTSU (Supported by Alliance, NRG)

**Date Activated:**
09/03/2013

**Study Chairs:**
M Chavez MacGregor, L Pusztai, P Ganz (NRG), P Rastogi (CTSU), M Goetz (Alliance)

**Statisticians:**
W Barlow, J Miao, D Lew

**Data Coordinator:**
I Syquia

**SCHEMA**

To compare whether the addition of one year of everolimus to standard adjuvant endocrine therapy improves overall survival (OS) and distant recurrence-free survival (DRFS) in this patient population.

To evaluate the safety, toxicities, and tolerability of one year of everolimus in combination with standard

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**Objectives**

To compare whether the addition of one year of everolimus (10 mg daily) to standard adjuvant endocrine therapy improves invasive disease-free survival (IDFS) in patients with high-risk, hormone-receptor (HR) positive and HER2-negative breast cancer.
adjuvant endocrine therapy and compare it with standard adjuvant endocrine therapy plus placebo in this patient population.

To determine whether the benefit of one year of everolimus use in addition to standard adjuvant endocrine therapy varies by recurrence score (RS), nodal status, or other commonly used prognostic factors.

**Patient Population**
Patients must have histologically confirmed invasive breast carcinoma with positive ER and/or PgR status and negative HER-2, for whom standard adjuvant endocrine therapy is planned. Patients must not have metastatic breast cancer. Patients with multifocal, multicentric, synchronous bilateral, and primary inflammatory breast cancers are allowed. Patients must be high risk as defined in the protocol, based on Recurrence Score or MammaPrint and grade, number of positive nodes, and prior therapy. Patients with micrometastases as the only nodal involvement (pN1mi) will be categorized as node negative.

Patients must have completed either breast-conserving surgery or total mastectomy with negative margins and appropriate axillary staging. Patients must have completed appropriate radiation therapy as described in the protocol. Patients must have completed standard neoadjuvant or adjuvant taxane and/or anthracycline based chemotherapy prior to randomization. Patients may have started endocrine therapy at any time after the diagnosis of the current breast cancer. Patients must not be receiving or planning to receive trastuzumab. Concurrent bisphosphonate therapy is allowed. Patients must not have prior exposure to mTOR inhibitors.

Patients must be at least 18 years of age, have a Zubrod performance status of 0-2, and have adequate hematologic, hepatic, renal, and cardiac function. Patients must not have received immunization with an attenuated live vaccine within seven days prior to registration. Patients must be able to take oral medications. Patients at NCORP institutions must be offered the opportunity to participate in the Behavioral and Health Outcomes (BAHO) substudy.

**Stratification/Descriptive Factors**
Patient randomization will be stratified by risk level as described in the protocol based on Recurrence Score or MammaPrint and grade, number of positive nodes, and prior therapy.

**Accrual Goals**
The accrual goal is 1,900 patients. Interim analyses are planned for after approximately 40%, 60%, and 80% of the events in the control arm have been observed.

**Summary Statement**
For the current status of this study, please refer to the Breast chapter.
S1418 Phase III

Coordinating Group: SWOG

A Randomized, Phase III Trial to Evaluate the Efficacy and Safety of MK-3475 (Pembrolizumab) as Adjuvant Therapy for Triple Receptor-Negative Breast Cancer with ≥ 1 cm Residual Invasive Cancer or Positive Lymph Nodes (ypN1mi, ypN1-3) after Neoadjuvant Chemotherapy

Participants: SWOG, CTSU (Supported by NRG)

Date Activated: 11/15/2016

Study Chairs: L Pusztai, J Mammen, P Ganz (NRG)

Statisticians: W Barlow, J Miao, D Lew

Data Coordinators: I Syquia, J Scurlock

SCHEMA

![SCHEMA Diagram]

*PD-L1 status determined by central laboratory

Objectives
To compare invasive disease-free survival (IDFS) of patients with triple-negative breast cancer (TNBC) who have either >1 cm residual invasive breast cancer and/or positive lymph nodes (>ypN+) after neoadjuvant chemotherapy randomized to 1 year of MK-3475 (pembrolizumab) adjuvant therapy compared to no MK-3475 (pembrolizumab), in both the entire study population and also in the PD-L1 positive subset.

To compare the effects of MK-3475 (pembrolizumab) on overall survival (OS) and distant recurrence-free survival (DRFS) between the two
randomized arms for the PD-L1 positive patients and then all patients.

To assess the toxicity and tolerability of MK-3475 (pembrolizumab) in this patient population with or without radiation therapy.

To examine the association between biomarkers of inflammation and quality of life and patient-reported outcomes between the two groups during and shortly after the end of therapy.

To examine the long-term and late effects of treatment on patient-reported outcomes.

**Patient Population**

Patients must have histologically confirmed ER-, PR- and HER2-negative breast cancer (triple-negative, TNBC) with residual invasive disease after completion of neoadjuvant chemotherapy. Patients with HER2 equivocal that do not receive HER2-targeted therapy are eligible. Patients with weakly ER or PR positive disease are eligible if patients are not eligible for adjuvant endocrine therapy. Residual disease must be $\geq 1$ cm in greatest dimension, and/or have positive lymph nodes (ypN1mi, ypN1, ypN2, ypN3) determined as described in the protocol. Patients must not have metastatic disease. Patients must have adequate tumor tissue for PD-L1 testing.

Patients must have received neoadjuvant chemotherapy as recommended by NCCN guidelines for TNBC. Patients may receive post-operative (adjuvant) chemotherapy at the discretion of the treating physician. Patients who receive adjuvant chemotherapy with capecitabine as standard of care must be registered no later than 35 days after final dose of treatment, and may be registered either before or after initiation of adjuvant chemotherapy, to be given concurrently with protocol treatment. Any other adjuvant chemotherapy must be completed or discontinued prior to step1 registration, with registration to step1 within 35 days after the final dose of adjuvant chemotherapy. Patients must have completed their final breast surgery with clear resection margins for invasive cancer and DCIS within 270 days prior to registration. Patients may receive concomitant radiation therapy (XRT) or XRT prior to registration; the intention to use XRT and the extent of intended XRT must be specified at registration if it has not been initiated. Patients must not have had prior immunotherapy with anti PD-L1 or anti-CTLA4 or similar drugs.

Patients must be at least 18 years of age, have a Zubrod performance status of 0-2, and must not have received live vaccines within 30 days prior to registration. Patients must not be known HIV positive or have known active hepatitis B or C. Patients must not have active autoimmune disease that has required systemic treatment in the past two years, non-infectious pneumonitis, or an active infection requiring systemic therapy. Patients who speak/read English must agree to participate in the Behavioral and Health Outcomes (BAHO) substudy.

Patients must be registered to Step 2 for randomization within 14 calendar days of receiving e-mail notification that the patient's tissue specimen was adequate for PD-L1 testing. Patients must have adequate hematologic, hepatic, renal and thyroid function prior to randomization.

**Stratification/Descriptive Factors**

Randomization will be stratified by the following factors: (1) nodal stage: ypN0 vs ypN+; (2) residual tumor size: $\leq 2$ cm vs $> 2$ cm; (3) PD-L1 status: positive vs negative; and (4) Post-operative (adjuvant) chemotherapy (either received, receiving, or planned): yes vs. no

**Accrual Goals**

The accrual goal is 1,000 patients to achieve 910 eligible patients. Two interim analyses will be performed when approximately 50% and 75% of the IDFS events in the PD-L1 positive population have been observed.

**Summary Statement**

For the current status of this study, please refer to the Breast chapter.
S1600 Phase III

Coordinating Group: SWOG

A Randomized Phase III Double-Blind Clinical Trial Evaluating the Effect of Immune-Enhancing Nutrition on Radical Cystectomy Outcomes

Participants: SWOG, CTSU

Study Chairs: J Hamilton-Reeves, J Holzbeierlein

Statisticians: J Unger, D Lew

Data Coordinators: S Dzingle, R Topacio

SCHEMA

Objectives
To compare the impact of consuming perioperative specialized immune-modulating drinks (SIM, Impact Advanced Recovery, Nestle) to oral nutrition supplement control drinks (ONS, Oral Nutrition Control, Nestle) on post-operative complications (any vs. none) within 30 days after scheduled radical cystectomy (RC).

To assess whether SIM use compared to ONS reduces skeletal muscle wasting.

To assess whether SIM use compared to ONS reduces high grade post-operative complications.

To assess whether SIM use compared to ONS reduces readmission rates.

To assess whether SIM use compared to ONS improves quality of life.

To assess whether SIM use compared to ONS improves disease-free survival and overall survival.

To assess whether SIM use compared to ONS reduces infections.

DATE ACTIVATED: 02/21/2019

R A N D O M I Z E

SIM nutrition drink

C Y S T E T C T O M Y

ONS control drink

SIM nutrition drink

ONS control drink
**Patient Population**

Patients must have a tissue diagnosis of primary cell carcinoma of the bladder by TURBT or partial cystectomy. Patients may not have any evidence of unresectable disease or metastatic disease as assessed by exam under anesthesia or imaging (CT, MRI, PET). Patients must be planning to undergo radical cystectomy within 28 days after registration, and the surgery must be planned to be performed under pre-approved, study-specific surgical guidelines.

Patients must have completed any neoadjuvant chemotherapy or immunotherapy (intravesical or systemic) at least 14 days prior to registration and any toxicities resolved to ≤ Grade 2. Patients must not be planning to receive adjuvant chemotherapy within 90 days after radical cystectomy. Patients may have received prior partial cystectomy and/or prior radiation therapy; these must have been completed at least 180 days prior to registration.

Patients must be at least 18 years old, be able to understand and speak English, and not have known galactosemia or active viral infections such as HIV or hepatitis. Patients must have their baseline nutrition status assessed using the Patient-Generated Subjective Global Assessment (PG-SGA) within 14 days prior to registration and must not have a global category rating of Stage C (severely malnourished). Patients must be able to swallow liquid and have no refractory nausea, vomiting, malabsorption, or significant small bowel resection that would preclude adequate absorption. Patients on tube feeding are not eligible.

Patients must consent and be willing to have specimens collected and submitted as described in the protocol.

**Stratification/Descriptive Factors**

Patient randomization will be stratified by the following factors: (1) planned diversion type: neobladder vs other; (2) prior neoadjuvant therapy: any vs none; and (3) baseline nutrition status as assessed by the PG-SGA: well nourished (Stage A) vs moderate malnutrition (Stage B).

**Accrual Goals**

The accrual goal is 200 patients to achieve 190 eligible patients.

**Summary Statement**

This study was activated on February 21, 2019.
S1602 Phase III

Coordinating Group: SWOG

A Phase III Randomized Trial to Evaluate the Influence of BCG Strain Differences and T Cell Priming with Intradermal BCG before Intravesical Therapy for BCG-Naïve High-Grade Non-Muscle Invasive Bladder Cancer

Participants: SWOG, CTSU (Supported by Alliance, ECOG-ACRIN, NRG)

Study Chairs: R Svatek, A Alva, M Woods (Alliance), V Master (NRG), J Mark (ECOG-ACRIN)

Statisticians: C Tangen, M Plets, E Mayerson

Data Coordinator: J Sanchez

Date Activated: 02/07/2017

SCHEMA

R A N D O M I Z A T I O N

High-grade BCG-naïve non-muscle invasive bladder cancer

Arm 1: BCG LIVE (TICE®)

Arm 2: Tokyo-172 BCG

Arm 3: Intradermal Priming + Tokyo-172 BCG

Objectives

To compare whether time to high-grade recurrence (TTHGR) for patients with BCG-naïve, non-muscle invasive bladder cancer (NMIBC) receiving Tokyo-172 BCG (Arm 2) is non-inferior to patients receiving BCG LIVE (TICE® BCG) (Arm 1).

To test whether TTHGR for patients with BCG-naïve, NMIBC receiving intradermal Tokyo-172 BCG vaccination followed by intravesical Tokyo-172 BCG instillation (Arm 3) is superior to patients receiving intravesical Tokyo-172 BCG instillation without prior intradermal BCG vaccination (Arm 2).

To compare time to recurrence (TTR) with any-grade (AG) bladder cancer between: (1) patients receiving Tokyo-172 versus BCG LIVE (TICE® BCG) strain; and (2) patients receiving intradermal + intravesical versus intravesical only Tokyo-172 BCG.
To compare progression-free survival (PFS) between:
(1) patients receiving Tokyo-172 versus BCG LIVE (TICE® BCG) strain; and (2) patients receiving intradermal + intravesical versus intravesical only Tokyo-172 BCG.

To estimate the complete response (CR) rate for CIS patients at 6 months in patients receiving intravesical Tokyo-172 BCG (Arms 2 & 3 will be evaluated separately).

To evaluate the duration of CR by treatment arm for patients with CIS who have a CR at 6 months.

To test whether TTHGR for patients with BCG-naïve NMIBC receiving intradermal Tokyo-172 BCG vaccination followed by intravesical Tokyo-172 BCG instillation is superior to patients receiving intravesical TICE® BCG strain.

To compare the change (baseline to 6 month) in patient-reported bladder cancer-specific quality of life between TICE® and Tokyo BCG strains.

To compare the change (baseline to 6 month) in patient-reported quality of life between priming and no priming.

To test the hypothesis that changes in urinary symptoms during BCG treatment predict time to high-grade recurrence (TTHGR).

**Patient Population**
Patients must have high-grade, histologically proven Ta, carcinoma in situ (CIS) or T1 stage urothelial cell carcinoma of the bladder and must have had all visible papillary tumors removed. Patients with pure adenocarcinoma, pure squamous cell carcinoma, micropapillary components, nodal involvement or metastatic disease are excluded.

Patients must not have received prior intravesical or intradermal BCG. Patients must not be taking oral glucocorticoids and must not be planning to receive concomitant biologic therapy, hormonal therapy, chemotherapy, surgery, or other cancer therapy while on study.

Patients must not have a known history of tuberculosis and must have a negative PPD test within 90 days prior to registration. Patients must complete Patient Reported Outcomes (PRO) forms in English or Spanish must complete the baseline Bladder Cancer Index (BCI), EORTC QLQ-C30 and AUASS forms.

Treating physician must confirm availability and access to BCG LIVE (TICE® BCG).

**Stratification/Descriptive Factors**
Patient randomization will be stratified according to the following factors: (1) age: ≤ 75 vs > 75; and (2) clinical stage: Ta vs T1 vs CIS only vs CIS with either Ta or T1.

**Accrual Goals**
The accrual goal for this study is 969 patients to achieve 924 eligible patients. Interim analyses will be conducted when 22%, 45%, and 70% of the expected number of pooled TTHGR events have occurred.

**Summary Statement**
For the current status of this study, please refer to the Genitourinary chapter.
S1614 Phase III

Coordinating Group: SWOG

A Phase III Randomized Trial of Prophylactic Antiviral Therapy in Patients with Current or Past Hepatitis B Virus (HBV) Infection Receiving Anti-Cancer Therapy for Solid Tumors

Participants: SWOG, CTSU (Supported by ECOG-ACRIN)

Study Chairs: J Hwang, A Lok, E Mitchell (ECOG-ACRIN)

Statisticians: J Unger, E Mayerson

Data Coordinators: K Carvalho, S Dzingle

Date Activated: 02/21/2019

SCHEMA

Cohort 1:
Chronic HBV

Prophylactic Antiviral Therapy

Upon Indication Antiviral Therapy

Cohort 2:
Past HBV

Upon Indication Antiviral Therapy

Usual Care Antiviral Therapy
Objectives

Co-primary objectives:

To compare the effect of prophylactic tenofovir alafenamide (TAF) therapy versus upon indication TAF therapy on time-to-adverse liver outcomes of liver failure or liver-related death in patients with chronic HBV infection (HBsAg+ and anti-HBc+) receiving anti-cancer therapy for solid tumors.

To compare the effect of upon indication TAF therapy versus usual care on time-to-adverse liver outcomes of liver failure or liver-related death in patients with past HBV infection (HBsAg- and anti-HBc+) receiving anti-cancer therapy for solid tumors.

Secondary objectives:

Using time-to-event analysis, to compare the effect of TAF therapy versus upon indication TAF therapy on HBV reactivation, on the combined endpoint of adverse liver outcomes (liver failure or liver-related death) and HBV reactivation, and on HBV flare by arm in patients with chronic HBV infection receiving anti-cancer therapy for solid tumors.

Using time-to-event analysis, to compare the effect of upon indication TAF therapy versus usual care on HBV reactivation, on the combined endpoint of adverse liver outcomes (liver failure or liver-related death) and HBV reactivation, and on HBV flare by arm in patients with past HBV infection receiving anti-cancer therapy for solid tumors.

Patient Population

Patients must be diagnosed with Stage I-III solid tumor malignancy not involving the liver. Patients must have HBV infection as indicated through positive HBsAg or anti-HBc tests. Patients must not have lymphoma, leukemia, or myeloma. Patients must not have primary liver cancer or evidence of any malignancy that involves the liver.

Patients must be planning to receive a new regimen of systemic anti-cancer therapy for their solid tumor malignancy and must have discontinued all previous therapies. Patients must not have received anti-CD20 cancer therapy regimens nor had a hematopoietic stem cell transplant. Patients must have discontinued any antiviral medications active against HBV at least 90 days prior to registration, and discontinue any contraindicated medications as identified in the protocol at time of registration.

Patients must have a Zubrod performance status of 0-2, and have adequate liver, renal, and coagulation function. Patients must not have known cirrhosis, known hepatitis-C infection, or history of human immunodeficiency infection proven by an HIV test within the past 365 days. Patients must have complete results for HBsAg, anti-HBc, anti-HBs, and HBV DNA lab tests as specified in the protocol. Patients must be able to take oral medications.

Patients must be willing to submit specimens for ongoing testing of HBV reactivation. Patients must be offered the opportunity to participate in the translational medicine studies.

Stratification/Descriptive Factors

Patients with chronic HBV infection will be randomized within Cohort 1, with randomization balanced by planned cancer therapy type: any cytotoxic therapy vs immunotherapy alone vs targeted therapy alone vs immunotherapy and targeted therapy.

Patients with past HBV infection will be randomized within Cohort 2 with randomization balanced by the following factors: (1) planned cancer therapy type: any cytotoxic therapy vs immunotherapy alone vs targeted therapy alone vs immunotherapy and targeted therapy; and (2) anti-HBs status: positive vs negative.

Accrual Goals

The accrual goal for this study is 444 patients, 222 patients per cohort to achieve 200 eligible patients per cohort. A single formal interim analysis for efficacy for each cohort will be conducted when one half of patients have reached one year of follow-up.

Summary Statement

This study was activated on February 21, 2019.
S1714 Observational Cohort

Coordinating Group: SWOG

A Prospective Observational Cohort Study to Develop a Predictive Model of Taxane-Induced Peripheral Neuropathy in Cancer Patients

Participants:
SWOG, CTSU

Date Activated:
03/01/2019

Study Chairs:
M Trivedi, D Hershman

Statisticians:
J Unger, A Darke

Data Coordinators:
K Carvalho, M Yee

Objectives
To develop and validate a clinical risk prediction model using clinical factors for the development of peripheral neuropathy in patients receiving taxane-based chemotherapy regimens.

To examine patient-reported outcomes (PROs) and objective measures of chemotherapy induced peripheral neuropathy (CIPN) to better define the phenotype of peripheral neuropathy in this patient population.

To assess the incidence of CIPN within one year in this patient population.

To identify predictors of treatment dose reductions, delays, and discontinuations associated with CIPN symptoms in this patient population.

Patient Population
Patients must have Stage I, II, or III primary nonsmall cell lung, primary breast, or primary ovarian cancer.

Patients must plan to start treatment with one of the study-approved taxane-based chemotherapy regimens within 14 days after registration, and must not have received a taxane, platinum, vinca alkaloid, or bortezomib-based chemotherapy regimen prior to registration.

Patients may have pre-existing neuropathy.

Patients must be able and willing to complete questionnaires in English or Spanish, agree to submit all required specimens for translational research, and be offered the opportunity to submit additional optional specimens for banking.

Stratification/Descriptive Factors
Patients will be classified by the following factors: (1) primary cancer: lung vs breast vs ovarian, and (2) planned taxane regimen: paclitaxel vs docetaxel.

Accrual Goals
A total of 1050 patients will be accrued to achieve 1000 eligible patients. When 525 patients have been accrued to the paclitaxel or docetaxel group, that group will be closed to further accrual. When 250 lung cancer patients have been accrued, the lung cancer category will be closed to further accrual.

Summary Statement
This study was activated March 1, 2019.
S1802 Phase III

Coordinating Group: SWOG

Phase III Randomized Trial of Standard Systemic Therapy (SST) versus Standard Systemic Therapy Plus Definitive Treatment (Surgery or Radiation) of the Primary Tumor in Metastatic Prostate Cancer

Participants: SWOG, CTSU (Supported by Alliance, CCTG, ECOG-ACRIN)

Date Activated: 09/17/2018

Study Chairs: B Chapin, A Aparicio, R Valicenti, M Alemozaffarr (ECOG-ACRIN), D Scherr (Alliance), M Gleave (CCTG)

Statisticians: C Tangen, E Mayerson

Data Coordinator: S O'Bryan

SCHEMA

*Step 1 registration can occur prior to start of SST or up to 28 weeks after SST start
Objectives
To compare overall survival in metastatic prostate cancer patients who are randomized to standard systemic therapy (SST) plus definitive treatment of the primary tumor versus SST alone.

To compare overall survival in metastatic prostate cancer patients who received SST plus surgical excision of the primary tumor versus SST alone in the subset who specify the surgical intent stratification factor.

To compare the rate of symptomatic local progression between the treatment arms.

To compare progression-free survival between the two treatment arms.

To compare rates of progression-free survival between arms for the subsets of patients with and without metastasis directed therapy to oligometastatic sites.

To compare between arms patient-reported urinary function and urinary bother over time (after initiation of SST at 6 months, 1, 2, and 3 years) using the Expanded Prostate Cancer Index Composite (EPIC) and patient-reported pain and physical functioning using the EORTC QLQ-C30 between patients receiving standard systemic therapy and those receiving systemic therapy and definitive management of the primary prostate cancer.

Patient Population
Patients must have a histologically or cytologically proven diagnosis of adenocarcinoma of the prostate. Patients must not have pure small cell carcinoma, pure sarcomatoid or pure squamous cell carcinoma of the prostate. Patients must have an intact prostate, and evidence of metastatic disease. Patients must not have known brain metastases. To be randomized, patients must have no evidence of disease progression during induction SST, must have a consultation with a urologist, and must have surgically resectable disease, regardless of definitive treatment intent.

Patients must have received no more than 28 weeks of SST for metastatic disease prior to registration. Patients must not have received any prior local therapy for prostate adenocarcinoma. Prior local therapy for benign conditions is allowed. Metastases-directed radiotherapy is allowed for up to four sites during the first 28 weeks of SST. To be randomized, patients must have received between 22 and 28 weeks of SST, must not have progressed, and any toxicities from SST must resolve to Grade 1 or better. Patients must not be planning to receive docetaxel after randomization.

Patients must have a CT/MRI and bone scan obtained within 42 days prior to registration. Patients must have a documented PSA and testosterone measurement prior to initiation of SST. To be randomized, patients must have a testosterone measurement below 50 ng/dL, a PSA measurement and Zubrod performance status of 0-1 within 28 days prior to randomization.

Patients who can complete patient-reported outcome instruments in English, Spanish or French must participate in the quality of life studies. All patients must be offered the opportunity to participate in specimen banking for future use.

Stratification/Descriptive Factors
Patient registration to induction therapy will be described by time between initiation of standard systemic therapy and study registration: no SST at registration or < 8 weeks vs ≥ 8 weeks.

Patient randomization will be stratified according to the following factors: (1) intended treatment of the primary tumor: radical prostatectomy vs radiation therapy; (2) receipt of docetaxel during induction SST: yes vs no; (3) PSA level at randomization timepoint: ≤ 4 ng/mL vs > 4 ng/mL; and (4) disease volume by conventional imaging: polymetastatic vs oligometastatic and no prior treatment vs oligometastatic and prior treatment.

Accrual Goals
The accrual goal for this study is 1,273 patients to achieve 1,066 eligible, randomized patients. Three interim analyses are planned for when 39%, 60%, and 79% of the expected deaths have occurred.

Summary Statement
For the current status of this study, please refer to the Genitourinary chapter.
S1806 Phase III

Coordinating Group: SWOG

Phase III Randomized Trial of Concurrent Chemoradiotherapy With or Without Atezolizumab in Localized Muscle Invasive Bladder Cancer (SWOG/NRG 1806)

**Participants:**
SWOG, CTSU (Supported by Alliance, CCTG, ECOG-ACRIN, NRG)

**Study Chairs:**
P Singh, S Lerner, J Efstathiou (NRG), B Costello (Alliance), S Sridhar (CCTG), N Hahn (ECOG-ACRIN)

**Statisticians:**
C Tangen, M Plets

**Data Coordinator:**
J Sanchez

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**SCHEMA**

*Chemotherapy choices: gemcitabine, cisplatin, 5-FU+mitomycin-C

**Objectives**

To compare bladder intact event-free survival (BI-EFS) for concurrent chemoradiation therapy with and without atezolizumab in localized muscle invasive bladder cancer.

To compare overall survival between the two arms.

To compare modified bladder intact event-free survival (mBI-EFS) including cancer related death between arms.

To compare complete and partial pathologic response between arms at 3 months after completing chemoradiation therapy.
To estimate metastases-free survival by arm.

To compare the qualitative and quantitative adverse events from each arm.

To estimate the rate of non-muscle invasive bladder cancer recurrence by arm.

To estimate the rate of salvage cystectomy and reasons for cystectomy by arm.

**Patient Population**

Patients must have histologically proven T2-T4a N0 M0 muscle invasive urothelial carcinoma of the bladder. Patients must not have small cell carcinoma or diffuse CIS of the bladder. Patients must have undergone a TURBT within 70 days prior to randomization. The treating urologist must have attempted maximal resection of all visible tumor. Patients must not have had urothelial carcinoma or histological variant at any site outside of the urinary bladder within the previous 24 months, with exception of Ta/T1/CIS of the upper urinary tract. Patients must have undergone radiological staging using CT or MRI within 70 days prior to randomization.

Patients must be planning to receive one of the protocol-specified chemotherapy regimens. Patients must not have had prior treatment for muscle invasive bladder cancer or prior pelvic radiation for any reason. Patients must not have received any prior systemic therapy for non-muscle invasive bladder cancer, but prior intravesical therapies are allowed. Patients must not have received any of the prohibited therapies listed in the protocol, or had a major surgical procedure within 28 days prior to randomization. Patients must not have received treatment with systemic immunosuppressive medications within 14 days prior to randomization. Patients must not have received a live attenuated vaccine within 28 days prior to randomization or anticipate that such a vaccine will be required while on protocol treatment and up to five months after the last dose of protocol treatment. Patients must not ever have undergone prior allogeneic bone marrow transplantation or prior solid organ transplantation.

Patients must have a Zubrod performance status of 0-2 and have adequate hematologic, hepatic, and renal function. Patients must not have clinically significant liver disease that precludes them from treatment regimens prescribed in the protocol. Patients must have an ECG performed within 28 days prior to randomization. Patients must not have an active infection requiring oral or IV antibiotics within 14 days prior to randomization. Patients must not have a history of active tuberculosis or an active autoimmune disease that required systemic treatment within two years prior to randomization. Patients must not have history of idiopathic pulmonary fibrosis, pneumonitis, organizing pneumonia, or evidence of active pneumonitis. Patients positive for HIV or with a known history of HBV or HCV must meet criteria specified in the protocol. Female patients of childbearing potential must have a serum pregnancy test prior to randomization. Patients must not have a known allergy to Chinese hamster egg.

Patients who can complete patient-reported outcome instruments in English or Spanish must agree to complete the baseline quality of life questionnaires.

Patients must be offered the opportunity to participate in specimen banking for future studies.

**Stratification/Descriptive Factors**

Patients registered to step 1 will be described by the following factors: (1) planned RT modality: 3DCRT vs IMRT; and (2) first patient treated with RT modality at this site: yes vs no.

Patient randomization will be stratified according to the following factors: (1) clinical stage: T2 vs T3/T4a; (2) intended chemotherapy regimen: cisplatin vs 5-FU + mitomycin-C vs gemcitabine; (3) radiation field: small pelvis vs bladder only; and (4) performance status: 0-1 vs 2.

**Accrual Goals**

The accrual goal for this study is 475 patients to achieve 432 eligible patients. Interim analyses will be conducted when 30%, 48%, 68%, and 85% of the expected B1-EFS events have occurred.

**Summary Statement**

For the current status of this study, please refer to the Genitourinary chapter.
S1826 Phase III

Coordinating Group: SWOG

A Phase III, Randomized Study of Nivolumab (Opdivo) or Brentuximab Vedotin (Adcetris) Plus AVD in Patients (Age ≥ 12 Years) with Newly Diagnosed Advanced Stage Classical Hodgkin Lymphoma

Participants:
SWOG, CTSU (Supported by Alliance, COG, ECOG-ACRIN)

Study Chairs:
A Herrera, J Friedberg, S Castellino (COG), S Rutherford (Alliance), N Khan (ECOG-ACRIN)

Statisticians:
M LeBlanc, H Li

Data Coordinator:
I Syquia

SCHEMA

Objectives
To compare the progression-free survival in patients with newly diagnosed advanced stage classical Hodgkin lymphoma randomized to N-AVD (nivolumab, doxorubicin, vinblastine, dacarbazine) versus that obtained with BV-AVD (brentuximab vedotin, doxorubicin, vinblastine, dacarbazine).

To compare overall survival in patients randomized to N-AVD versus BV-AVD.

To compare event-free survival in patients randomized to N-AVD versus BV-AVD.

To compare the metabolic complete response (CR) rate at the end of treatment in patients randomized to N-AVD versus BV-AVD.

To compare the physician-reported treatment-related adverse event rates between arms stratified by age groups.
To compare patient-reported symptoms using selected PRO-CTCAE items between arms stratified by age groups.

To compare the safety and tolerability of N-AVD versus that of BV-AVD.

To compare between arms patient-reported fatigue, neuropathy and health-related quality of life over time (baseline, beginning of Cycle 3, 4-8 weeks after completion of treatment, and 1 and 3 years after randomization) using the PROMIS-Fatigue, the FACT/GOG-Ntx, and the PROMIS Global, respectively.

**Patient Population**
Patients must have histologically confirmed newly diagnosed, previously untreated Stage III or IV classical Hodgkin lymphoma (nodular sclerosing, mixed cellularity, lymphocyte-rich, or lymphocyte-depleted, or not otherwise specified). Patients must have bidimensionally measurable disease and a whole body or limited whole body PET-CT scan performed within 42 days prior to registration. Patients who have nodular lymphocyte predominant Hodgkin lymphoma or known central nervous system disease are not eligible.

Patients must not have received any prior chemotherapy, radiation, or antibody-based treatment for classical Hodgkin lymphoma. Pre-treatment steroid use is permitted with restrictions as outlined in the protocol and must be discontinued prior to initiation of protocol treatment. Patients must not have had prior solid organ transplant, or prior allogeneic stem cell transplantation. Patients must not have received a live vaccine within 30 days prior to planned protocol therapy.

Patients must be at least 12 years of age and have a performance status corresponding to Zubrod score of 0, 1, or 2. Patients 17 years of age or less will be graded according to the Lansky play-performance scale. Patients must have adequate renal, hepatic, and cardiac function. HIV infected patients on effective anti-retroviral therapy with undetectable or unquantifiable viral load within six months prior to registration are eligible. Patients must not have known active Hepatitis B (HBV) or Hepatitis C (HVC) virus at time of registration. Patients must not have a history of active interstitial pneumonitis or interstitial lung disease, had a diagnosis of inherited or acquired immunodeficiency with exceptions, any known uncontrolled intercurrent illness. Patients must not have a condition requiring systemic treatment with either corticosteroids or other immunosuppressive medication within 14 days prior to registration or must not have active autoimmune disease that has required systemic treatment in past two years. Patients must not have Grade 2 or higher peripheral neuropathy. Patients must not have second prior malignancy except for adequately treated basal (or squamous cell) skin cancer, any in situ cancer or other cancer for which the patient have been disease free for two years. Women of childbearing potential must have a negative pregnancy test within 28 days prior to registration.

Patients who can complete Patient-Reported Outcome instruments in English, Spanish, or French must complete the required instruments prior to registration. Patients must have sufficient diagnostic tissue specimen collected prior to registration. Patients must be offered the opportunity to participate in specimen banking for future studies.

**Stratification/Descriptive Factors**
Randomization will be stratified by the following factors: (1) age (years): 12-17 vs 18-60 vs > 60; and (2) international prognostic score: 0-3 vs 4-7; and (3) pre-specified plan to use Residual PET Radiation Therapy (Residual PET RT): yes vs no. All pediatric patients enrolled by COG will be stratified to Residual PET RT.

**Accrual Goals**
The accrual goal of this study is 987 patients to achieve 940 eligible patients. Three interim analyses will be performed when approximately 25%, 50%, and 75% of anticipated progressions or deaths in the pooled arms have been observed.

**Summary Statement**
For the current status of this study, please refer to the Lymphoma chapter.