Quality Assurance Audits
Preparing for Success
What is your current Position?

A. Data Management
B. Clinical Research Nurse
C. Regulatory Affairs
D. Quality Assurance
E. Administration
F. Other
What is your work setting?

A. NCORP
B. NCORP Component
C. Member Institution
D. Lead Academic Program
E. Affiliate institution
Purpose of the audit program

Verify study data that could affect the interpretation of primary study endpoints by checking compliance to protocol and regulatory requirements and accuracy of submitted data

Assessment of trial related activities and documents for adherence to Good Clinical Practice (GCP)

Provide educational support for data quality and data management practices
Scheduling of Audits

- New LAPS, Members, NCORPs – within 18 months of first patient registration
- New affiliates, components – at next parent institution audit
- Institutions audited at least once every three years but remain at risk for more frequent audits
- FDA registration studies – more frequent monitoring
FDA Registration Study Site Visits

- LungMAP – initial audit at three months after first registration to a sub-study (with registration intent), then every six months
- S1418, S1806, S1914 – initial audit at six to nine months after first registration, additional site visits dependent on accrual
- S2302 (Pragmatica) – will be audited on same schedule as treatment audits (every 3 years)
On-Site Versus Off-Site Audits

**On-site**
- LAPS / Main Member / NCORP
- Component / affiliate with large accrual
- FDA registration study site visits for sites requesting on-site audits

**Off-site**
- Most NCORP components and Main Member affiliates audited off site with parent institution
- Most FDA registration study site audits can be audited off site (remote)
Notification Process

- Scheduled three to four months prior to the audit.
- Formal notification/case list by email four to six weeks prior to the audit.
- Includes detailed instructions on how to prepare for the audit and Site Questionnaire for audit planning.
The Audit Team

QA auditor

One or more Nurse or CRA auditors

NCI-CTMB observer occasionally in attendance
Site Representatives

- CRAs
- Research Nurses
- Principal Investigator or designate
- Regulatory Representative
- Pharmacy staff
Audit Process
Audit Process

- Regulatory review (IRB, consent form content and Delegation of Task Log/Site Authority Log)
- Investigational drug accountability (drug accountability, pharmacy visit)
- Patient case review
Regulatory Review

• IRB: Regulatory documents for all protocols on the case list
• Informed consent content: minimum of four protocols’ consents reviewed
• Delegation of Task Log (DTL) and Site Authority Log
• Trial Master File (TMF): FDA registration studies
IRB Review – Local IRB

• Approvals: initial and continuing reviews, protocol updates
• **Reportable** external Safety Reports and internal SAEs
• All versions of IRB-approved consent forms or a comprehensive list
• SOPs for alternative procedures (e.g., submission of unanticipated events only)
IRB Review – CIRB

CIRB Approval of the Study-Specific Worksheet

Signatory Institution: Eastern Maine Medical Center

Re: CIRB Approval of the Annual Signatory Institution Worksheet About Local Context

Signatory Institution: Trinity Health Michigan

Documentation that CIRB is the IRB of record (Study Specific Worksheet approval)

Approved boilerplate language for ICFs

Date of local implementation of protocol updates and consent versions

Submission of unanticipated events (e.g., reportable local SAEs)

NO COPIES OF CIRB APPROVAL DOCUMENTS REQUIRED
Consent Form Content

• Compared to model consent
• Contains all elements required by federal regulations
• Updated by protocol modifications
• Specimen banking(optional) studies questions same as model
• CIRB sites: identical to approved boilerplate merged with model
Delegation of Task Log

- **Site Authority Log** (delegation of authority, signatures, handwriting samples) for key research personnel to cover all NCI sponsored studies

- Delegation of Task Log ([CTSU website](#))
  - LungMAP sub-studies
  - All registration studies (S1418, S1806, S1914)
  - All new studies that use investigational agents (since August 2020 for Ph III studies/since October 2020 for Ph I/II studies)
## Trial Master File

- Protocol
- Regulatory documents
- CLIA Certificates and list of normal lab values/range
- List of local SOPs
- Site training documents (GCP, protocol specific, etc.)
- Placeholder for centrally filed documents (e.g., CVs, 1572s)
Investigational Drug Accountability

• Review of Drug Accountability Record Forms: NCI DARF or NCI Oral DARF required for all studies using investigational agents
  • Control and satellite records
  • Complete and timely entries
  • Good documentation practices
  • Patient returns documented on Oral DARF
Investigational Drug Accountability

• Shipping receipts, transfer and return forms
  • Unused or expired drug returned or destroyed within 90 days of end of use
  • No substitution of commercial drug for investigational agent
Investigational Drug Accountability

• Cross reference DARFs against patient records to verify dose and dates of dispensing
• SOP for authorized prescriptions (ordering investigator must have active CTEP account)
• On-site audits: Tour of pharmacy
  • Assess security and storage conditions
  • Verify physical inventory
• Off-site audits: Tour of pharmacy conducted via Teams, FaceTime, WebEx, etc.
# DARF Examples – Good DARF

<table>
<thead>
<tr>
<th>Line No.</th>
<th>Date</th>
<th>Patient's Initials</th>
<th>Patient's ID No.</th>
<th>Dose</th>
<th>Quantity Dispensed or Received</th>
<th>Balance Forward</th>
<th>Manufacturer and Lot No.</th>
<th>Recorder's Initials</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7/16/93</td>
<td>RECEIVED FROM NCI</td>
<td>223344</td>
<td>170 mg</td>
<td>-30</td>
<td>30</td>
<td>ABC98765</td>
<td>EF</td>
</tr>
<tr>
<td>2</td>
<td>5/19/93</td>
<td>SENT TO XY2</td>
<td></td>
<td></td>
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<td>20</td>
<td>ABC98765</td>
<td>EF</td>
</tr>
<tr>
<td>3</td>
<td>6/19/93</td>
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<td>-2</td>
<td>18</td>
<td>ABC98765</td>
<td>EF</td>
</tr>
<tr>
<td>4</td>
<td>6/20/93</td>
<td>RG</td>
<td>223344</td>
<td>175 mg</td>
<td>-2</td>
<td>16</td>
<td>ABC98765</td>
<td>EF</td>
</tr>
<tr>
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<td>6/21/93</td>
<td>RG</td>
<td>223344</td>
<td>170 mg</td>
<td>-2</td>
<td>14</td>
<td>ABC98765</td>
<td>EF</td>
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<tr>
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<td>6/22/93</td>
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<td>12</td>
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<td>+30</td>
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<td>ABC98765</td>
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<td></td>
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<td>EF</td>
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<td>170 mg</td>
<td>-2</td>
<td>30</td>
<td>ABC98765</td>
<td>EF</td>
</tr>
</tbody>
</table>
## DARF Examples – “So-So” DARF

### Investigational Drug Accountability Record

<table>
<thead>
<tr>
<th>Line No.</th>
<th>Date</th>
<th>Patient’s Initials</th>
<th>Patient’s ID No.</th>
<th>Dose</th>
<th>Quantity (mg)</th>
<th>Manufacturer</th>
<th>Recipient’s Name</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>V/S/</td>
<td>194218</td>
<td>15mg</td>
<td>15mg</td>
<td></td>
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<td></td>
</tr>
<tr>
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<td></td>
<td>R/S/</td>
<td>194218</td>
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<td>15mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
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<td>V/S/</td>
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<td>15mg</td>
<td>15mg</td>
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<tr>
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<td>15mg</td>
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<tr>
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<td>V/S/</td>
<td>194218</td>
<td>15mg</td>
<td>15mg</td>
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<td></td>
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<tr>
<td>6</td>
<td></td>
<td>R/S/</td>
<td>194218</td>
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<td>15mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>V/S/</td>
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<td>15mg</td>
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<td>R/S/</td>
<td>194218</td>
<td>15mg</td>
<td>15mg</td>
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<td></td>
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<tr>
<td>9</td>
<td></td>
<td>V/S/</td>
<td>194218</td>
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<td>15mg</td>
<td></td>
<td></td>
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<tr>
<td>10</td>
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<td>15mg</td>
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<tr>
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<tr>
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<td>15mg</td>
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<tr>
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<td>V/S/</td>
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<td>15mg</td>
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<tr>
<td>14</td>
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<td>R/S/</td>
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<tr>
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<td>16</td>
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<td>R/S/</td>
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<td>15mg</td>
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<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Notes

- **Drug Name:** Eribulin 100 mg
- **Dose:** 2 mg/m²
- **Dispensing Area:** Phase II Selection Design Trial
- **Dispenser:** Controlled by pharmacist following DCR#123456

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*Images of other pages related to the National Cancer Institute (NCI) Clinical Trials Network are shown for context.*
# DARF Examples – Incomplete DARF

<table>
<thead>
<tr>
<th>Line</th>
<th>Date</th>
<th>Patient's Initials</th>
<th>Patient's ID No.</th>
<th>Sex</th>
<th>Dose (mg)</th>
<th>Balance Forward</th>
<th>Quantity Administered or Received</th>
<th>Balance Forward</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>J</td>
<td>123456</td>
<td>M</td>
<td>100 mg</td>
<td>1</td>
<td>100 mg</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>J</td>
<td>123456</td>
<td>M</td>
<td>100 mg</td>
<td>2</td>
<td>100 mg</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>J</td>
<td>123456</td>
<td>M</td>
<td>100 mg</td>
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<tr>
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<td>4</td>
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<td>123456</td>
<td>M</td>
<td>100 mg</td>
<td>5</td>
<td>100 mg</td>
<td>0</td>
</tr>
</tbody>
</table>

**Notes:**
- All doses are in milligrams (mg).
- Balance Forward indicates the amount of the drug to be administered.
- Quantity Administered or Received shows the actual amount administered.
- Balance Forward is updated after each administration.

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**Additional Information:**
- This record is part of the National Institutes of Health (NIH) Drug Administration Record (DARF) system.
- It is used to track the administration of drugs in clinical trials.
- The protocol number is CO8.
- The investigator is Paul Menz.
- The NCI protocol number is CO8.

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**Contact Information:**
- For questions or concerns, please contact the Clinical Trials Office.
- The protocol is under the Clinical Trials Office of the National Cancer Institute (NCI).
List of SWOG and CTSU accrual credited to SWOG over last three years

- 10% SWOG treatment and 10% SWOG non-treatment
- 10% non-SWOG treatment and 10% non-SWOG non-treatment
- Minimum of one case for each non-SWOG FDA registration study
- Minimum of three cases
- One unannounced case for on-site audits
Patient Case Review: Categories

- Informed consent
- Eligibility
- Treatment administration
- Disease / endpoint assessment
- Toxicity assessment
- General data quality – to include specimen submission and QOLs
Case Review: Categories

Chart preparation prior to audit

Shadow chart is acceptable

Recommended chart organization: Consent and screening/eligibility, then chronological by cycle / reporting period - H&P, labs, disease assessments, etc.

Color coded flagging of sections/cycles (for paper/shadow charts)

Specimen submission documents flagged (print out of specimen tracking documents)

If auditor will review records in EMR, EMR Source Documentation Locator Form must be completed prior to the audit
Informed Consent

• Most current version signed prior to registration
• Contains all required signatures
• Informed of new findings in a timely manner
• Specimen banking/optional studies offered and intent reported correctly in OPEN at time of registration
• HIPAA authorization signed
Eligibility

• Verify diagnosis by review of pathology or other diagnostic reports
• Review medical history for exclusion criteria
• Verify pre-study assessments meet protocol requirements and performed within specified time limits
• Eligibility affirmation signed prior to registration/randomization
• NO EXCEPTIONS GRANTED per Section 5.0
Treatment Administration

• BSA / dose calculations verified
• Verification of both drug orders and drug administration
• Appropriate dose modifications
• Patient diaries or other supporting documentation of compliance to oral medications
• Documentation to support delays or deviations in treatment
Endpoint Assessment

• Disease/endpoint assessments performed per protocol
• Review of radiology reports, pathology reports, lab reports, records of physical examinations, etc.
• Same method of measuring the disease at baseline and at each assessment
• Tumor measurements documented
• Off treatment follow-up conducted per protocol
Adverse Event Assessment

• Required baseline and follow-up studies performed
• Grade and attribution of AEs documented, signed off by investigator/qualified practitioner
• Documentation of immune-related status, if applicable
• Adverse events reported appropriately.
• Serious Adverse Events (SAEs) reported in a timely manner
General Data Quality

ALCOA + C to achieve data quality:
If it is not documented, it did not happen

A: Attributable

L: Legible

C: Contemporaneous

O: Original

A: Accurate

C: Complete

Adequate source documentation
Data accurately reported on the data collection forms
Timely submission of data

Specimens/images/questionnaires submitted per protocol
Good documentation practices

References:
ICH GCP E6R2 4.9.0 and ICH GCP E6R2 4.9.1
Exit Interview

- Meet with PI and staff
- Summarize findings
- Clear up any questions
- Preliminary Report indicating any major deficiencies submitted within one working day to the NCI
Audit Ratings

• Acceptable
  • See you in three years

• Acceptable, Follow-up Needed
  • A written response including a corrective and preventive action plan must be submitted.
Audit Ratings

Unacceptable

- A written response including a corrective and preventive action plan must be submitted.
- Repeat audit within 6 - 12 months.
- If repeat offender: Site Improvement Plan required / possible suspension of registration privileges.
Final Report and Follow-up Response/CAPA

Final Report sent to site and submitted to NCI within 70 days of audit

For FDA Registration Studies, Final Report must be submitted within 45 days of audit

- Site must submit Follow-up Response/CAPA for any component with Acceptable-needs follow up or Unacceptable finding
- Once Follow-up Response/CAPA reviewed and approved, site will be placed back into normal audit rotation
A Walk Through an Audit

Common things that found during the Patient Case Review
Informed Consent

Unclear specimen choice, with no documented explanation.

No initials or date next to change, no explanation.

My signature agreeing to take part in the study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the treatment study. I also agree to take part in any additional studies where I circled “yes”.

Participant’s Signature or Legally Authorized representative  
1/25/22
Date of signature

Witness’s Signature  
1/25/22
Date of signature

I conducted an informed consent discussion with the patient concerning this protocol on 1/25/22.

Physician Conducting Informed Consent Discussion  
2/1/22
Date of signature

No explanation of different dates.
Informed Consent

• The wrong version signed, when taken home to review.
• Physician or institutional HIPAA signed in place of the Research HIPAA.
• Unapproved wording in consent.
Consent Comparison

Model Consent

Site Consent
Consent Comparison

Orange highlight wording was changed.

Pink triangle means something was deleted.

Blue highlight means something was added that is not in the model consent.
Eligibility

• Performance Status (closest to registration date).

Participants’ most recent Zubrod performance status must be 0-1 (Section 10.4) and be documented within 28 days prior to sub-study randomization.

• Lack of attribution for residual adverse events.

Patients must have resolution of adverse event(s) of the most recent prior chemotherapy to Grade 1 or less, except alopecia and ≤ Grade 2 neuropathy which are allowed.

• Lack of documentation related to prior malignancy

No other prior invasive malignancy is allowed except for the following: adequately treated basal (or squamous cell) skin cancer, in situ breast or cervical cancer. Stage I or II invasive cancer treated with a curative intent without evidence of disease recurrence for at least five years.

<table>
<thead>
<tr>
<th>Medical History:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthritis</td>
</tr>
<tr>
<td>GERD</td>
</tr>
<tr>
<td>CAD</td>
</tr>
<tr>
<td>Prostate Cancer</td>
</tr>
<tr>
<td>Hip replacement</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>Grade 2</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>Grade 1</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Grade 1</td>
</tr>
<tr>
<td>HTN</td>
<td>Grade 2</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Grade 1</td>
</tr>
</tbody>
</table>
Eligibility

- Timing of tests outside the required window.

Participants must have history and physical exam must be obtained within 28 days prior to sub-study randomization.

https://www.timeanddate.com/date/duration.htm
Eligibility

• No physical or height documented in the H&P note.

Date of Service 9/1/21

Interval History
Met with patient to consider participation in S1803. We discussed the study and side effects; patient is agreeable to participation.

Subjective:
Patient complains of some fatigue. Diarrhea resolved. Denies fever, shortness of breath, nausea, vomiting or weight loss.

Objective:
B/P: 132/82, Pulse 78, Temp 97.8, Resp. 18 Weight 91.6 kg

Assessment/Plan:
Patient agreeable to participation in S1803. Required tests ordered. Plan to register next week and start treatment on 2/12/23. Return visit per research.
Eligibility

• Childbearing potential:
  • Considered to be of reproductive potential if has had menses at any time in the preceding 12 consecutive months.
  • Don’t assume a participant is post-menopausal based on age or tubal ligation.
  • Missing a negative pregnancy test.
  • Missing documentation that the patient, whether female or male, agrees to contraception use as specified in the protocol.
Eligibility

• Common missing documentation:
  • TNM staging.
  • Last date/dose of systemic treatment with corticosteroids.
  
  Participants with spinal cord compression or brain metastases must not have residual neurological dysfunction, unless no further recovery is expected, and the participant has been stable on weaning doses of corticosteroids (≤ 10 mg daily prednisone or equivalent) prior to sub-study randomization.

  • Start and stop dates of prior therapies.

<table>
<thead>
<tr>
<th>Adjuvant Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date started: 29 Mar 2019</td>
</tr>
<tr>
<td>Date completed: 12 Sep 2019</td>
</tr>
</tbody>
</table>

• Whether or not the patient had a live vaccine.
Treatment

• Patient compliance with oral medication not documented.

Date of Service 3/10/21

Interval History
Patient tolerating treatment without difficulty. No appreciable side effects, other than mild fatigue.

Assessment/Plan:
Multiple myeloma diagnosed 12/2/20, initial treatment with RVD, followed by transplant. Current treatment with Lenalidomide 10 mg/day, with Daratumumab per S1803. No concerning side effects, continue with treatment.

• When there is no diary required, there still needs to be documentation of any missed pills during the cycle.
Treatment

• Dose modification not per protocol.

Daratumumab/rHuPH20-Related Toxicity Management

If any of the following criteria are met, the daratumumab/rHuPH20 infusion must be held to allow for recovery from toxicity. The criteria for a dose delay are as follows:

• ≥ Grade 3 neutropenia and/or platelet count < 10,000/mm³

| ≥ Grade 3 neutropenia | Lenalidomide | Hold therapy (interrupt). Follow CBC on day 8, 15, 22. |

<table>
<thead>
<tr>
<th>Immune-related AEs</th>
<th>Toxicity grade or conditions (CTCAEv4.0)</th>
<th>Action taken to MK-3475 (pembrolizumab)</th>
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</thead>
<tbody>
<tr>
<td>Pneumonitis</td>
<td>Grade 2</td>
<td>Withhold</td>
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<tr>
<td></td>
<td>Grade 3 or 4, or recurrent grade 2</td>
<td>Permanently discontinue</td>
</tr>
<tr>
<td>Diarrhea / colitis</td>
<td>Grade 2 or 3</td>
<td>Withhold</td>
</tr>
<tr>
<td></td>
<td>Grade 4</td>
<td>Permanently discontinue</td>
</tr>
<tr>
<td>AST / ALT elevation or increased</td>
<td>Grade 2</td>
<td>Withhold</td>
</tr>
</tbody>
</table>
Treatment:

No documentation of required observation time.

Note that patients must remain for observation for at least 6 hours after the first dose of daratumumab (Cycle 1 Day 1).

Missing vital signs or not all vital signs documented.

Vital signs (pulse rate, respiratory rate, blood pressure & temperature) are required to be measured within 60 minutes prior to the infusion, during the infusion and within 30 minutes after the infusion.
Response Assessment

- Baseline Lesions – RECIST SECITON 10 of the protocol.
- Mis-categorizing Measurable vs Non-measurable disease.

**Measurable Disease**
- Lesions you can follow
- Baseline timepoint
- Tumor lesion measured in longest diameter
  - *EXCEPT* for lymph nodes: use short axis
- Minimum size of measurable non-nodal lesions
  - CT scan 5 mm slice: ≥10 mm
  - CT scan > 5 mm slice: 2x slice thickness
  - Calibers (clinical exam): ≥10 mm
  - Chest x-ray: ≥20 mm
  - Lymph node ≥ 15 mm

**Non-measurable Disease**
- All other lesions that do not meet the criteria to be measurable and:
  - Bone lesions
  - Leptomeningeal disease
  - Ascites
  - Pleural/pericardial effusion
  - Inflammatory breast disease
  - Cystic lesions
Response Assessment

- Not obtaining all required scans.

For studies that use disease progression as an endpoint, all potential sites of metastases should be evaluated at each time point rather than following only sites of disease identified at baseline. It is acceptable to image only the areas of the body most likely to be involved with metastatic disease for the tumor type (chest, abdomen, pelvis, and/or bone scan are typical), with the addition of any areas with suspected involvement based upon clinical symptoms. For study-specific imaging requirements, see the Study Calendar in Section 9.0.
Response Assessment

- Frequency incorrect

CT or MRI (the same method used at pre-study to meet the eligibility criteria must be repeated every 6 weeks +/- 7 days) for the first year, regardless of treatment delays, then every 12 weeks until disease progression. 6 weeks starts from sub-study registration.
Response Assessment

- Treating past progression
- PD: One or more of the following must occur:
  - 20% ↑ in the sum of appropriate diameters of target measurable lesions over smallest sum observed using the same techniques as baseline, as well as an absolute ↑ of at least 0.5 cm.
  - Unequivocal progression of non-measurable disease
  - Appearance of any new lesion.
Response Assessment

- Lymphoma & Deauville scoring

<table>
<thead>
<tr>
<th>#</th>
<th>Other Sites of Disease</th>
<th>Extent</th>
<th>Method of Assessment</th>
<th>Assessment Date</th>
<th>PET Status</th>
<th>SUV max</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Lymph Node Mediastinal &amp; Hilar</td>
<td>present</td>
<td>PET/CT</td>
<td>10 Jan 2020</td>
<td>Positive</td>
<td>(xx.xx)</td>
</tr>
<tr>
<td>2</td>
<td>Lung Single Site: LUL</td>
<td>present</td>
<td>PET/CT</td>
<td>10 Jan 2020</td>
<td>Positive</td>
<td>(xx.xx)</td>
</tr>
</tbody>
</table>

SUV max of mediastinal blood pool: (xx.xx)

SUV max of liver: (xx.xx)

Are there other FDG avid lesions that are felt to be more likely to represent something other than lymphoma? No

If yes, describe

Overall Deauville Score?:

5
Adverse Events

• Documentation of baseline events.
  • Not enough information to determine grade at BL.
  • Events occurring up to the time of the first treatment are considered baseline.

Screening Visit: (5/1/23)

<table>
<thead>
<tr>
<th>Review of Symptoms:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient considering participation in S1802. Complaints of dysuria, shortness of breath &amp; fatigue. Urinalysis shows RBCs. Denies fever, numbness, pain, nausea, vomiting, constipation, or diarrhea. Good appetite.</td>
</tr>
</tbody>
</table>

5/1/23

<table>
<thead>
<tr>
<th>WBC</th>
<th>Hgb</th>
<th>Platelets</th>
<th>ANC</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.0</td>
<td>14.0</td>
<td>213</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Creatinine 1.3
T. Bilirubin 0.9
AST 17
ALT 20
Alk Phos 81

Cycle 1 Day 1: (5/13/23)

Patient here to begin treatment on S1802. Complaints of dysuria & fatigue. No more shortness of breath, pain noticed in lower back. Denies fever, numbness, nausea, vomiting, constipation, or diarrhea. Good appetite.

5/13/23

<table>
<thead>
<tr>
<th>WBC</th>
<th>Hgb</th>
<th>Platelets</th>
<th>ANC</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.0</td>
<td>11.0</td>
<td>213</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Creatinine 1.9
T. Bilirubin 0.9
AST 17
ALT 47
Alk Phos 81
Adverse Events

Non-clinically significant laboratory are required to be reported.

- Glucose increase not reported because it was not fasting.
- Corrected calcium is within normal limits.

https://globalrph.com/medcalcs/corrected-calcium-calculator-correction-for-serum-albumin-conc/
Adverse Events

Events reported incorrectly

<table>
<thead>
<tr>
<th>Date</th>
<th>2022</th>
<th>BL</th>
<th>4/18</th>
<th>4/28</th>
<th>5/10</th>
<th>5/20</th>
<th>5/31</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tx Cycle/Day</td>
<td>4/1</td>
<td>C1/1</td>
<td>C2/1</td>
<td>C3/1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hematologic</th>
<th>EVENTS (x1000)</th>
<th>Hgb (g/dL)</th>
<th>Platelets (x1000)</th>
<th>Lymphocytes</th>
<th>ANC</th>
<th>Glucose</th>
<th>Albumin</th>
<th>Creatinine</th>
<th>T. Bilirubin</th>
<th>AST</th>
<th>ALT</th>
<th>Alt Phos</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8.8</td>
<td>14.0</td>
<td>186</td>
<td>1.0</td>
<td>4.9</td>
<td>104</td>
<td>3.6</td>
<td>0.81</td>
<td>0.3</td>
<td>10</td>
<td>12</td>
<td>69</td>
</tr>
<tr>
<td></td>
<td>8.5</td>
<td>10.0</td>
<td>166</td>
<td>1.2</td>
<td>4.0</td>
<td>112</td>
<td>3.5</td>
<td>0.75</td>
<td>0.5</td>
<td>13</td>
<td>10</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>4.0</td>
<td>9.5</td>
<td>165</td>
<td>1.1</td>
<td>3.5</td>
<td>89</td>
<td>3.4</td>
<td>0.71</td>
<td>0.5</td>
<td>30</td>
<td>28</td>
<td>74</td>
</tr>
<tr>
<td></td>
<td>1.5</td>
<td>10.1</td>
<td>151</td>
<td>0.8</td>
<td>1.4</td>
<td>90</td>
<td>3.1</td>
<td>0.8</td>
<td>0.8</td>
<td>44</td>
<td>28</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>3.0</td>
<td>11.0</td>
<td>150</td>
<td>0.8</td>
<td>1.0</td>
<td>114</td>
<td>3.5</td>
<td>0.8</td>
<td>0.6</td>
<td>45</td>
<td>35</td>
<td>74</td>
</tr>
<tr>
<td></td>
<td>2.9</td>
<td>13.0</td>
<td>120</td>
<td>1.4</td>
<td>1.0</td>
<td>89</td>
<td>3.6</td>
<td>1.4</td>
<td>1.0</td>
<td>45</td>
<td>20</td>
<td>130</td>
</tr>
</tbody>
</table>

Events occurring on Day 1 of a cycle, PRIOR to treatment being given, are recorded in the previous cycle.

When a baseline event resolves, then recurs, it then gets reported.

Report all grades if start and end dates are required.
Adverse Events

- Failure to document immune relationships or attributions.

<table>
<thead>
<tr>
<th>AE</th>
<th>Grade</th>
<th>Attribution</th>
<th>Start</th>
<th>Stop</th>
<th>Ongoing</th>
<th>Action taken</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>1</td>
<td>1</td>
<td>10/28/21</td>
<td>11/18/21</td>
<td></td>
<td>Dose not changed/no treatment for</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Verbatim term</th>
<th>CTC adverse event term</th>
<th>CTC (4.0) grade</th>
<th>CTCAE adverse event attribution code</th>
<th>Adverse event status code</th>
<th>Onset date</th>
<th>Resolution date</th>
<th>Action taken</th>
<th>Outcome of AE</th>
<th>Hospitalization (at least 24 hours)</th>
<th>Is the AE immune-related?</th>
<th>Is the AE radiation-related?</th>
<th>Treatment received for this AE?</th>
</tr>
</thead>
<tbody>
<tr>
<td>hypotension</td>
<td>Hypotension</td>
<td>1</td>
<td>Unrelated</td>
<td>New</td>
<td>No</td>
<td>28 Oct 2021</td>
<td>18 Nov 2021</td>
<td>Dose Not Changed</td>
<td>Recovered/Resolved</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
## Adverse Events

<table>
<thead>
<tr>
<th>AE</th>
<th>Grade</th>
<th>Attribution</th>
<th>Start</th>
<th>Stop</th>
<th>Ongoing</th>
<th>Immune Related</th>
<th>Is this considered a serious AE needing expedited reporting</th>
<th>Action taken</th>
</tr>
</thead>
<tbody>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Attribution: 1 definitely related; 2 unlikely related; 3 possibly related; 4 probably related; 5 unrelated

Investigators Signature: _____________________ Date: ____________________

Page: ___ of ___
Data Quality

Specimens

Questionnaires

Data entry errors

Discrepancies

Delinquent Data
Specimens & Questionnaires

Section 15 (Section 12 also for specimens).

Done at the wrong time.

Optional Specimens not drawn, when patient consented for.

Specimens drawn and submitted, when patient refused.

Specimen missed because kit not available.

EDTA and Streck cfDNA tubes: With participant's consent, collect approximately 30 mL of blood in EDTA tubes and 10 mL of blood in a Streck cfDNA tube at the following time points.

- Pre-treatment (after sub-study randomization, but prior to treatment initiation on sub-study)
- Cycles 2, 3, and 5 (at the same time as lab collection, prior to the start of cycle treatment) - Participants that go off protocol treatment are not required to continue to submit these specimens.
- First progression - First progression blood should be collected by the time of the next visit after documenting progression and prior to starting any non-protocol therapy.

If the patient consents, specimens must be submitted as follows:

Samples for unknown future studies:

I agree that my samples and related health information may be kept in a biobank for use in future health research.

- YES
- NO

Contact for Future Research

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

- YES
- NO
Data Entry Errors

Surgical Pathology Report

Requestion Physician: [redacted]  
Patient: [redacted]  
Date collected: 10/3/16  
Accession#: SS-16-02575  
Date Received: 10/3/16  
Report Date: 10/7/16

DIAGNOSIS
**CONSULTATION CASE**
Outside slides and blocks labeled S16-1681, collection date 08/19/2016.
Skin, left perianal lesion, biopsy:  
- MALIGNANT MELANOMA, MEASURING APPROXIMATELY 6.50MM IN DEPTH, ULCERATED. See Discussion and template below.

Date of initial diagnosis of NSCLC (any stage) 8/19/16
Data Entry Errors

Laboratory conversions

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free Kappa Light Chain</td>
<td>3.3 - 19.4 mg/L</td>
</tr>
<tr>
<td>Free Lambda Light Chain</td>
<td>5.7 - 26.3 mg/L</td>
</tr>
<tr>
<td>Free K/L Ratio</td>
<td>0.26 - 1.65</td>
</tr>
</tbody>
</table>

Kappa free light chain: 0.75 mg/dL
Lambda free light chain: 0.55 mg/dL
Kappa/lambda ratio (derived): 1.36
# Data Entry Errors

## Weight

<table>
<thead>
<tr>
<th></th>
<th>1/26/21</th>
<th>2/1/21</th>
<th>2/23/21</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
<td>168 cm</td>
<td>168 cm</td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>85.1</td>
<td>81.1</td>
<td>84.0</td>
</tr>
<tr>
<td>BSAM</td>
<td>1.99</td>
<td>1.95</td>
<td>1.98</td>
</tr>
</tbody>
</table>

---

Subject: E0906Z

Page: Treatment - Cycle 01

Instructions: Please complete this form after every cycle (1 cycle = 28 days). If any were not administered during this reporting period, please enter "0" for the dose value.

<table>
<thead>
<tr>
<th>Has the patient progressed or relapsed (per the definition in Section 10.0 of the protocol)?</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment for this cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reporting period start date</th>
</tr>
</thead>
<tbody>
<tr>
<td>26 Jan 2021</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reporting period end date</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 Feb 2021</td>
</tr>
</tbody>
</table>
Data Discrepancies

Adverse Events unclear

Treatment Unclear

April 6, 2023

Interval History:
Patient here for evaluation prior to Cycle 5. He has been tolerating treatment without many side effects. Continues to complain of right hip pain with some difficulty in walking, but can still play golf. Denies any nausea, vomiting, diarrhea, shortness of breath, fatigue or pain.

Pain Score: 6

<table>
<thead>
<tr>
<th>Event</th>
<th>Gr</th>
<th>ATT</th>
<th>Start</th>
<th>End</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>1</td>
<td>3</td>
<td>3/15/23</td>
<td>ongoing</td>
<td>None</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>2</td>
<td>3</td>
<td>3/15/23</td>
<td>ongoing</td>
<td>None</td>
</tr>
<tr>
<td>Pain</td>
<td>2</td>
<td>1</td>
<td>2/1/23</td>
<td>4/6/23</td>
<td>None</td>
</tr>
</tbody>
</table>

Investigator Signature: __________________ Date: 4/6/23

April 6, 2023

Medications at end of visit:
Omeprazole 20 mg
Zocor 20 mg
Immodium
Lenalidomide 15 mg.

Assessment Plan:
Myeloma, continue with treatment on S1803, Daratumumab & Lenalidomide 5 mg.
Delinquent Data

Delinquent data > than 3 months after the due date for baseline & on treatment forms & > than 6 months after the due date for follow-up data.

Section 14.4 for data

Source Doc/RAVE®

Delinquent Data

Delinquent data > than 3 months after the due date for baseline & on treatment forms & > than 6 months after the due date for follow-up data.

Section 14.4 for data

Source Doc/RAVE®
Questions?

qamail@swog.org