DART: *Dual Anti-CTLA-4 & Anti-PD-1 blockade in Rare Tumors*

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UCSD Moores Cancer Center

Leading cancer research. *Together.*
RARE CANCERS: INCIDENCE

186 rare cancers

About 500,000 new cases/year in EU27

22% of all cancer diagnosed/year

DISTRIBUTION OF MAJOR FAMILIES OF RARE TUMORS WITHIN ALL RARE CANCERS

- Central nervous system: 5%
- Respiratory tract: 8%
- Head and neck (eye and middle ear): 14%
- Digestive tract: 14%
- Female genital tract: 18%
- Haematological: 22%
- Others (embryonal, non-skin melanoma): 2%
- Urogenital: 2%
- Endocrine tumors (lung excluded): 2%
- Male genital: 4%
- Sarcomas: 5%

Responses to Immunotherapy in Rare Tumors

Pembrolizumab in Merkel Cell (NEJM 2016)

Nivolumab in Anal Cancer (Lancet Onc 2017)
Combinatorial vs Single-Agent Immunotherapy

Postow et al. NEJM 2015

**Death or Disease Progression**
- Nivolumab plus Ipilimumab: 30/72
- Ipilimumab: 25/37
  - Median Progression-free Survival
    - Nivolumab plus Ipilimumab: 4.4 (2.8–5.7) mo (95% CI)
    - Ipilimumab: NR
  - Hazard ratio, 0.40 (95% CI, 0.23–0.68)
    - P < 0.001

**Progression-free Survival**
- Nivolumab plus ipilimumab (N=72)
- Ipilimumab (N=37)

**No. at Risk**
- Nivolumab plus ipilimumab: 72 54 45 38 20 1 0
- Ipilimumab: 37 20 9 6 2 0 0

**Durability of Response (wk)**
- Patients
- Nivolumab plus Ipilimumab
- Ipilimumab
**Basic concepts in tumor immunology: Immunoediting**

Transformed cells

Elimination

Transformed cells

"Danger" signals

Tumor antigens

NKR ligands

Intrinsic tumor suppression (senescence, repair, and/or apoptosis)

Carcinogenic
Radiation
Viral infections
Chronic infections
Inherited genetic mutations

Innate and adaptive immunity

Extrinsic tumor suppression

Trm

CD8+ T cell

CD4+ T cell

NK cell

Transformed

Highly immunogenic transformed cell

Poorly immunogenic and immunoevasive transformed cells

Normal tissue

Normal cell

Cancer Immunoediting

Immune checkpoint inhibition by location and type of immune cells: CTLA-4 and PD-1

Chen L. Nature Reviews Immunology vol 4 May 2004 p336
DART: Dual Anti-CTLA-4 & Anti-PD-1 blockade in Rare Tumors

Primary study objective:

• To evaluate the overall response rate (ORR) in patients with advanced rare cancers treated with ipilimumab plus nivolumab combination therapy
  • Primary Endpoint: Overall response rate (ORR) as assessed by traditional RECIST v1.1 measurement criteria will be used.

Secondary objectives:

• To evaluate toxicities in each cohort
• To estimate overall survival, progression-free survival, and immune-related ORR, PFS in each cohort
1. Rare Cancer histologic subtypes
   (incidence of < 6/100,000 persons/year).
   a. NCI-MATCH screen or treatment failures, w/o further MATCH options (Amendment 1, 2)
      • Amendment 3: Direct Enrollment Onto DART
   b. Histologic subtypes (n=33 cohorts: added adenoid cystic carcinoma, vulvar cancer, metaplastic breast carcinoma)
Rare Cancers Not Eligible:

• Anal cancer,
• Lymphoma,
• Merkel cell carcinoma,
• Pleural Mesothelioma,
• Sarcoma (bone & soft tissue),
• Thymic Carcinoma,
• Uterine Leiomyosarcoma.
### Rare cancers included in DART

<table>
<thead>
<tr>
<th>Category</th>
<th>Cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transitional cell carcinoma other than renal pelvis, ureteral or bladder</td>
<td></td>
</tr>
<tr>
<td>Cell tumor of testes and extra gonadal tumors</td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma of the head and neck (SCCHN)</td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma and variants of nasal cavity, sinuses, and nasopharynx</td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma with variants of nasal cavity, sinuses, and nasopharynx and trachea (excluding larynx), nasopharyngeal cancer (NPC), and squamous cell carcinoma of the head and neck (SCCHN)</td>
<td></td>
</tr>
<tr>
<td>Epithelial tumors of major salivary glands</td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma with variants of small intestine</td>
<td></td>
</tr>
<tr>
<td>Undifferentiated carcinoma of gastrointestinal (GI) tract</td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma with variants of small intestine</td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma with variants of GI tract (stomach, small intestine, colon, rectum, pancreas)</td>
<td></td>
</tr>
<tr>
<td>Fibromyxoma and low grade mucinous adenocarcinoma (pseudomyxoma peritonei) of the appendix and ovary</td>
<td></td>
</tr>
<tr>
<td>Pancreatic tumor including adrenal cell carcinoma, mucinous or serous cystadenocarcinoma</td>
<td></td>
</tr>
<tr>
<td>Intrahepatic Cholangiocarcinoma</td>
<td></td>
</tr>
<tr>
<td>Cholangiocarcinoma and extrahepatic bile duct tumors</td>
<td></td>
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<tr>
<td>Sarcomatoid carcinoma of lung</td>
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<tr>
<td>Bronchoalveolar carcinoma lung</td>
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<tr>
<td>Non epithelia tumors of the ovary</td>
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<tr>
<td>Germ cell tumor of ovary</td>
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<tr>
<td>Mullerian mixed tumor and adenosarcoma</td>
<td></td>
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<tr>
<td>Trophoblastic tumor of placenta</td>
<td></td>
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<tr>
<td>Choriocarcinoma of placenta</td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma variants of the genitourinary (GU) system</td>
<td></td>
</tr>
<tr>
<td>Spindle cell type of kidney, pelvis and ureter</td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma with variants of GU system (excluding prostate cancer)</td>
<td></td>
</tr>
<tr>
<td>Odontogenic malignant tumors</td>
<td></td>
</tr>
<tr>
<td>Endodocrine carcinoma of pancreas and digestive tract</td>
<td></td>
</tr>
<tr>
<td>Neuroendocrine carcinoma including carcinoid of the lung and other sites of other sites</td>
<td></td>
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<tr>
<td>Pheochromocytoma, malignant</td>
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<tr>
<td>Paraganglioma</td>
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<tr>
<td>Carcinomas of pituitary gland, thyroid gland, parathyroid gland, adrenal cortex</td>
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<tr>
<td>Dermoid tumors</td>
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<tr>
<td>Peripheral nerve sheath tumors and NPY related tumors</td>
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<tr>
<td>Malignant giant cell tumors</td>
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<tr>
<td>Chondroma</td>
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<tr>
<td>Adrenal cortical tumors</td>
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<tr>
<td>Tumor of unknown primary</td>
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<tr>
<td>Other</td>
<td></td>
</tr>
</tbody>
</table>
SWOG DART Treatment/ Schema

- Basket study in rare tumors
- Concurrent Combination Immunotherapy:
  Ipilimumab 1 mg/kg IV every 6 weeks and nivolumab 240mg IV (fixed dose) every 2 weeks
  - Nivolumab monotherapy permitted for patients who experience severe immune-related toxicity on combination ipilimumab/nivolumab
- Treatment cycle length: 6 weeks
- Imaging assessments: every 12 weeks
DART To Date

DART Activated: 1/13/17; First Patient Treated: 1/30/17

As of **9/27/17**:

- 709 sites approved to enroll through CTSU
- Total enrollment: 123 patients
- Six Cohorts Completed 1st Stage Accrual
  - Salivary gland type tumors of head and neck, lip, esophagus, stomach, trachea and lung, breast and other location
  - Fibromixoma and low grade mucinous adenocarcinoma (pseudomixoma peritonei) of the appendix and ovary
  - Intrahepatic cholangiocarcinoma
  - Cholangiocarcinoma and extrahepatic bile duct tumors
  - Neuroendocrine carcinoma including carcinoid of the lung
  - Cancer of Unknown Primary (CuP)
Is this true? Not sure how we verified this...

Mayerson, Eddie, 9/8/2017
NOC cohort inquiries

- Translocation RCC
- Esthesioneuroblastoma
- Metastatic adamantinoma
- Pilomatricoma
More Common Tumor Types that are Not Eligible FAQs

- Pancreatic Adenocarcinoma
- Primary peritoneal/ epithelial ovarian/ high-grade serous ovarian/ ovarian serous cystadenocarcinoma cancers
- Endometrial adenocarcinomas
- Squamous cell carcinoma or adenocarcinoma of the uterine cervix
- Squamous cell carcinoma of the skin
- Common cancers with rare metastases
Amendment 3 Revisions

- Direct enrollment onto DART (independent of MATCH)
- Added arms for adenoid cystic carcinoma, vulvar cancer, metaplastic breast carcinoma, GIST
- Direct specimen submission to DART, FFPE tissue block or 25-30 unstained slides
- ACTH or cortisol in range
- Imaging/Treatment Calendar Resync
- Other Minor Changes to irAE Tables
The DART Story Part II

Collaboration with NCI MATCH & Translational Medicine

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Vice Chair, SWOG Early Therapeutics and Rare Cancer Committee
Co-Director, Early Phase Clinical Trials Unit,
Robert H. Lurie Comprehensive Cancer Center of Northwestern University
NCI MATCH

- First federally funded pathway-based histology-agnostic targeted therapy basket trial initiated by NCI and ECOG-ACRIN.
- 30 subarms
- SWOG PI, Dr. Villalobos from ETRC committee
- A quarter of patients enrolled have rare cancers.
- In June, 2017, the trial successfully reached its goal to sequence the tumors of 6K patients, nearly two years early.
- Its availability through more than 1100 participating sites reflects the broad interest in the promise of genomics, and the ability of such a study to deliver that promise to the community.
MATCH Distribution of ~1100 Participating Sites

- Trial is open and enrolling in every state, DC, and Puerto Rico
- 50% of the 1100 sites have enrolled at least one patient for screening
MATCH – DART Collaboration

- Match maker: NCI CTEP
- Common goal: help patients with rare cancers
- Leverage: (1) utilization of NCI MATCH sites (>700 sites) (2) use of NCI MATCH molecular biomarker screening test results for translational medicine

- Current DART patients should be have been enrolled to the NCI MATCH trial. (1) screen-failed (2) progressed on the matched therapy on trial
- Treatment is allowed between the two trials.
NCI MATCH DART
DART to become a Stand-Alone Trial

• No more fresh biopsy requirement for the DART
• No need for MATCH enrollment to enroll into the DART
• Protocol amendment no. 3 to be approved and activated very soon.
• Many more sites will join with the activation of the new amended protocol.
Translational Medicine in DART/MATCH

**CLIA LAB NETWORK**

- Genetic platform: Thermo Fisher Ampliseq custom panel running on S5 sequencer ONCOMINE Cancer Research Panel
  - 20 ng DNA/RNA
  - 143 genes
  - SNV, indel, CNV, targeted translocations
- Validation within and across sites: same SOP
- Selected IHC, FISH
- MoCHA plus Competitively chosen lab sites:
  - MD Anderson (Hamilton)
  - MGH (Iafrate)
  - Yale (Sklar)
  - New site to be chosen

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**NCI-MATCH Assay System & Work Flow**

- ~ 14 Day Turnaround Time
- Biopsy
  - Review and Sign off
  - Ion Reporter
- Shipped to MDACC
- Tissue Processing
  - Archive
    - Tissue Blocks
    - Slides
    - Nucleic Acid
- PTEN IHC NA Extraction
- Tissue Accession
- NA Shipped
- MATCHBox
  - BAM File Storage
  - MDACC
  - MGH
  - MoCHA
  - Yale
- Library Prep and Sequencing
- Final Report
- Clinical DB
TM Projects

Genomics  
Proteomics  
Transcriptomics  
Immune cell level
TM samples

1. **Tissue**: pretreatment fresh biopsy or **archived tissue** (<6 months) – Coordination with NCI MATCH team and individual sites participating required

2. **Blood**: three time points (at baseline, at the first imaging, and at PD):
   - **Current**: only at baseline
   - **Next amendment**: two more blood samples.
## Precision Immuno-oncology

<table>
<thead>
<tr>
<th>Performing Lab</th>
<th>PD-L1 IHC</th>
<th>Immune biomarkers</th>
<th>Germline DNA sequencing</th>
<th>Proteomic immune signature</th>
<th>cDNA sequencing</th>
<th>Tumor NGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>UCSD</td>
<td>Jackson Labs (JAX)</td>
<td>Counsyl</td>
<td>Biodesix</td>
<td>Circulogene</td>
<td>MatchBox</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sample source</th>
<th>Biomarker Target</th>
<th>Specimen Estimate</th>
<th>Biomarker output</th>
<th>Statistical Considerations</th>
<th>Sample time points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor tissue (FFPE) or unstained slide</td>
<td>PD-L1 protein expression by 28-8 IHC analysis</td>
<td>150 (baseline tissue)</td>
<td>PD-L1 strata will be grouped: &lt;1%, 1-5%, 6-25%, 26-49%, &gt;50%</td>
<td>Binary endpoint by strata</td>
<td>Tissue: Baseline</td>
</tr>
<tr>
<td>Blood in collected in Tempus tubes (one 2cc vial for RNA, another 2cc vial for DNA)</td>
<td>DNA, RNA sequencing (Nanostring) of tumor tissue and blood</td>
<td>240 (baseline blood)</td>
<td>Immune and Cancer pathway Nanostring (gene expression of 770 genes assaying 24 immune cell types and 500 immune response genes)</td>
<td>Log-expression</td>
<td>Tissue: baseline Blood: DNA and RNA at three time points</td>
</tr>
<tr>
<td>Blood collected in the EDTA tube</td>
<td>Leukocyte DNA sequencing (Illumina)</td>
<td>240 (baseline blood)</td>
<td>Genetic alteration</td>
<td>Categorical variable</td>
<td>Blood at baseline</td>
</tr>
<tr>
<td>Blood collected in the EDTA tube</td>
<td>Serum proteins</td>
<td>240 (baseline blood)</td>
<td>Predictive signature (good, intermediate, poor group)</td>
<td>Categorical variable</td>
<td>Blood: at three time points</td>
</tr>
<tr>
<td>Blood collected in the EDTA tube</td>
<td>Cell free DNA sequencing (Illumina)</td>
<td>240 (baseline blood)</td>
<td>Genetic alteration and mutational load</td>
<td>Percentile rank of mutational load</td>
<td>Blood: at three time points</td>
</tr>
<tr>
<td>Tumor tissue (FFPE) collected as part of NCI-MATCH</td>
<td>Tumor next-generation sequencing (Ion Torrent)</td>
<td>300 (baseline tissue)</td>
<td>Genetic alteration and mutational load</td>
<td>Percentile rank of mutational load</td>
<td></td>
</tr>
</tbody>
</table>

**Statistical Considerations**
- Binary endpoint by strata
- Log-expression
- Categorical variable
- Categorical variable
- Percentile rank of mutational load
- Percentile rank of mutational load

**Sample time points**
- Tissue: Baseline
- Tissue: baseline Blood: DNA and RNA at three time points
- Blood at baseline
- Blood: at three time points
- Blood: at three time points
- Tissue: baseline
### Specimen Instructions

<table>
<thead>
<tr>
<th>Sample Type</th>
<th>Timepoint(s)</th>
<th>Sample Collection Media</th>
<th>Processing and Storage</th>
<th>Shipping</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFPE tissue block or 25 to 30 unstained slides for QC Pathology Review and translational medicine as indicated in Sections 12.0 and 15.1a. Tissue block strongly preferred.</td>
<td>Baseline only</td>
<td>One 5-10 mm³ paraffin embedded tissue block (FFPE) OR If site is unable to release tissue block, 25 to 30 recently cut, 4-5 micron, unstained sections, on positively charged slides preferred. If sufficient tissue is not available, a minimum 10 freshly cut, serially sectioned and numbered 4-5 micron, unstained sections on positively charged slides must be submitted.</td>
<td>Store ambient prior to shipment. Tissue Block Size requirement: Surface area: 25mm² is optimal. Minimum is 5mm². Volume: 1mm³ optimal. Minimum volume is 0.2mm³.</td>
<td>Ambient, via overnight courier. Batch shipping not allowed.</td>
</tr>
<tr>
<td>8 mL blood processed to 4 mL serum</td>
<td>* Baseline* * Cycle 2 MRI/CT* * Disease progression * Collection must be within 2 days prior to ipilimumab treatment.</td>
<td>Plastic SST If possible, Greiner Gold Top vacutette tube 4 mL Z Serum Separator Clot Activator (SST) preferred. No glass.</td>
<td>Process for at least 4 mL serum by centrifugation. Transfer serum into a single plastic cryotube. Freeze upright and store in -70°C to -80°C freezer prior to shipment.</td>
<td>Ship (frozen) via overnight courier with dry ice (to maintain -70°C during shipment). Batch shipping not allowed.</td>
</tr>
<tr>
<td>Sample Type</td>
<td>Timepoint(s)</td>
<td>Sample Collection Media</td>
<td>Processing and Storage</td>
<td>Shipping</td>
</tr>
<tr>
<td>---------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>--------------------------------</td>
<td>---------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>4 mL whole blood</td>
<td>Baseline only. Collection must be within 2 days prior to ipilimumab treatment.</td>
<td>Plastic K2EDTA or K3EDTA tube</td>
<td>Freeze upright in a -70 to -80°C freezer prior to shipment.</td>
<td>Ship (frozen) via overnight courier with dry ice (to maintain -70°C during shipment). Batch shipping not allowed.</td>
</tr>
<tr>
<td>9 mL whole blood</td>
<td>a) Baseline*&lt;br&gt;b) Cycle 2*&lt;br&gt;c) Disease progression&lt;br&gt;&quot;Collection must be within 2 days prior to ipilimumab treatment.&quot;</td>
<td>Plastic K2EDTA or K3EDTA tube</td>
<td>After collection, invert to mix. Do not centrifuge. Refrigerate prior to shipment at 2-8°C.</td>
<td>Ship refrigerated with cold pack (maintain 4-10°C, during shipment). Ship overnight, same day as collected. Batch shipping not allowed.</td>
</tr>
<tr>
<td>4 mL whole blood</td>
<td>a) Baseline*&lt;br&gt;b) Cycle 2*&lt;br&gt;c) Disease progression&lt;br&gt;&quot;Collection must be within 2 days prior to ipilimumab treatment.&quot;</td>
<td>Two, 2mL tempus tubes</td>
<td>After collection, tempus tubes must be shaken immediately and vigorously for at least 20 seconds, or vortexed for at least 10 seconds. This is critical to planned future research. Do not centrifuge. Freeze upright in a -70 to -80°C freezer</td>
<td>Ship (frozen) via overnight courier with dry ice (to maintain -70°C during shipment). Ship same day as collected. Batch shipping not allowed.</td>
</tr>
<tr>
<td>5 mL whole blood</td>
<td>Baseline only. Collection must be within 2 days prior to ipilimumab treatment.</td>
<td>Plastic K2EDTA or K3EDTA tube</td>
<td>Gently invert to mix (5 – 10 times). Do not centrifuge. Refrigerate prior to shipment at 2-8°C.</td>
<td>Ship refrigerated with cold pack (maintain 4 to 10°C, during shipment). Ship overnight, same day as collected. Batch shipping not allowed.</td>
</tr>
</tbody>
</table>

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**Specimen Instructions**

Leading cancer research. Together.
Questions

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Sandip Patel
sandippatelpatel@ucsd.edu
Statistics Behind S1609

Melissa Plets, M.S.
Secondary Statistician

Megan Othus, PhD
Primary Statistician

Eddie Mayerson, M.S.
Secondary Statistician
Accrual goals

- Maximum = 707 total patients
  - n=16 x 36 cohorts
  - + n=60 in NOC cohort
  - + 10% not eligible / not evaluable
Accrual goals

- Hoping for at least **9 patients/month**
- <100 patients in first 2 years = feasible study??

Current Accrual = **123 patients**
Analysis Plan

- **Primary Objective**: Overall Response (RECIST)
  \[ H_0 = 5\% \quad H_A = 30\% \]

  Alpha (one-sided) = 0.13
  Power \((1-\beta)\) = 87\%
## Analysis Plan

### Two-stage design - For each cohort (except CuP & NOC)

<table>
<thead>
<tr>
<th>Stage 1</th>
<th>Stage 2</th>
</tr>
</thead>
</table>
| • Accrue **6 eligible patients**  
• Temporarily close cohort  
• If ≥ 1 response, reopen  
• If 0 responses, permanently close cohort | • Accrue **10 additional** eligible patients  
(total n=16 /cohort)  
• Permanently close cohort  
• ≥ 2 responses, further study in this subtype |

**CuP cohort:** accrue 16 eligible patients; no formal first stage response assessment

**NOC cohort:** accrue 60 eligible patients; ongoing monitoring; used to potentially open additional cohorts
Analysis Plan

Two-stage design

Pros

- Minimize number of patients treated with ineffective drug
- “Screening” for drugs worthy of further development (resources)

Challenges

- Lose accrual momentum
- Difficult to close at n=6 in cooperative group setting
- Evaluating eligibility in “real time”
- Ongoing monitoring of response data
## Current Open/Close Status of Cohorts

Registrations ending August 4, 2017; Data as of August 4, 2017

<table>
<thead>
<tr>
<th>Cohort Number</th>
<th>Histology</th>
<th>Patients Enrolled</th>
<th>Percent of Total N</th>
<th>Open Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Salivary gland type tumors of head and neck, lip, esophagus, stomach, trachea and lung, breast and other location</td>
<td>11</td>
<td>10.5</td>
<td>Temp Closed</td>
</tr>
<tr>
<td>7</td>
<td>Fibromixoma and low grade mucinous adenocarcinoma (pseudomixoma peritonei) of the appendix and ovary</td>
<td>10</td>
<td>8.4</td>
<td>Temp Closed</td>
</tr>
<tr>
<td>9</td>
<td>Intrahepatic cholangiocarcinoma</td>
<td>9</td>
<td>8.4</td>
<td>Temp Closed</td>
</tr>
<tr>
<td>10</td>
<td>Cholangiocarcinoma and extrahepatic bile duct tumors</td>
<td>9</td>
<td>8.4</td>
<td>Temp Closed</td>
</tr>
<tr>
<td>23</td>
<td>Neuroendocrine carcinoma including carcinoid of the lung</td>
<td>13</td>
<td>10.5</td>
<td>RE-OPENED</td>
</tr>
<tr>
<td>32</td>
<td>Tumor of unknown primary (Cancer of Unknown Primary; CuP)</td>
<td>9</td>
<td>8.4</td>
<td>RE-OPENED</td>
</tr>
<tr>
<td>33</td>
<td>Not Otherwise Categorized (NOC) Rare Tumors</td>
<td>14</td>
<td>12.6</td>
<td>Open</td>
</tr>
</tbody>
</table>
S1609 Common Issues

Christine McLeod
Data Coordinator
SWOG Data Operations Center
S1609 Common Issues - Eligibility

- Is my patient’s tumor rare?
  - It might be but not per protocol
  - Other on-going trials?
  - When in doubt, upload redacted path report

S1609SC@swog.org
• Disease Assessment Forms
  ◦ New disease since baseline
  ◦ OK to remain on protocol (7.4a)
S1609 Common Issues - FUTA
S1609 Common Issues – Tx Form

<table>
<thead>
<tr>
<th>Field</th>
<th>Details</th>
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<tbody>
<tr>
<td>Patient Identifier</td>
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<tr>
<td>Study Identifier</td>
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<td>Patient Initials</td>
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<td>Treatment Information</td>
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<td>Vital Status</td>
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<td>Date of last contact</td>
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<td>Date of death</td>
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<tr>
<td>Has patient progressed or relapsed</td>
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<tr>
<td>Treatment for this cycle</td>
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<tr>
<td>Tumor type</td>
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<tr>
<td>Reporting period start date</td>
<td></td>
</tr>
<tr>
<td>Reporting period end date</td>
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<tr>
<td>Treatment start date</td>
<td></td>
</tr>
<tr>
<td>Date of last treatment</td>
<td></td>
</tr>
<tr>
<td>Modifications/restored modifications</td>
<td></td>
</tr>
<tr>
<td>Agent Name</td>
<td></td>
</tr>
<tr>
<td>Date of infusion</td>
<td></td>
</tr>
<tr>
<td>Dose planned</td>
<td></td>
</tr>
<tr>
<td>Dose delivered</td>
<td></td>
</tr>
<tr>
<td>Total dose given</td>
<td></td>
</tr>
<tr>
<td>Modifications</td>
<td></td>
</tr>
<tr>
<td>Will continue to receive protocol therapy?</td>
<td></td>
</tr>
</tbody>
</table>
S1609 Common Issues - Data

**Treatment Forms**
- Nivolumab to be reported in mg for planned, delivered & total doses
- Ipilimumab to be reported in mg/kg for planned and delivered doses, mg for total dose
### S1609 Common Issues – Tx Form

Were there any dose modifications or additions/omissions to protocol treatment?

*For Nivolumab, report planned and delivered doses in mg. Report total dose in mg.*

*For Ipilimumab, report planned and delivered doses in mg/kg. Report total dose in mg.*

<table>
<thead>
<tr>
<th>#</th>
<th>Agent name</th>
<th>Date of infusion</th>
<th>Dose planned</th>
<th>Dose delivered</th>
<th>Total dose given</th>
<th>Modifications</th>
<th>Dose modification reason</th>
<th>Number of days delayed (if applicable)</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Nivolumab Infusion 1</td>
<td>240</td>
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<tr>
<td>3</td>
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<tr>
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<td>Ipilimumab</td>
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<td>240</td>
<td>240</td>
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<td></td>
<td></td>
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</tbody>
</table>
## S1609 Common Issues – Tx Form

<table>
<thead>
<tr>
<th>#</th>
<th>Agent name</th>
<th>Date of infusion</th>
<th>Dose planned</th>
<th>Dose delivered</th>
<th>Total dose given</th>
<th>Modifications</th>
<th>Dose modification reason</th>
<th>Number of days delayed (if applicable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nivolumab</td>
<td>Infusion 1</td>
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<td>1</td>
<td>1</td>
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<tr>
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<td>Nivolumab</td>
<td>Infusion 2</td>
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<td>1</td>
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<tr>
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<td>Nivolumab</td>
<td>Infusion 3</td>
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<td></td>
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<td></td>
</tr>
<tr>
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<td>Iplilumab</td>
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<td>1</td>
<td>87</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

 Were there any dose modifications or additions/omissions to protocol treatment?

For Nivolumab, report planned and delivered doses in mg. Report total dose in mg.

For Iplilumab, report planned and delivered doses in mg/kg. Report total dose in mg.
Do not code a condition existing prior to registration as an adverse event unless it worsens.
S1609 Common Issues – BAB & AEs

BABs only reported on AE forms if:
Grade worsens
– or
AE completely resolves & comes back
**Status Codes on AE forms:**
If not reported in previous cycle = 1/ New
S1609 Common Issues

- **S1609SC@swog.org**
  - SCs, PC, Data Coordinators
    - Histologic Eligibility, Treatment

- **RareTumors@crab.org**
  - Statisticians, Data Coordinators
    - General eligibility, statistical considerations, data

- **SWOG Statistics and Data Management Center at Cancer Research And Biostatistics**
  - (206) 652 -2267
Thank You

- **Mentors/Co-Chairs**
  - Razelle Kurzrock
  - Francis Giles

- **SWOG**
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  - Charles Blanke
  - Anne Schott
  - Michael LeBlanc
  - Nathan Eriksen
  - Casey Dawson
  - Tameka Lewis

- **SWOG Operations**
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  - Dana Sparks
  - Gretchen Goetz

- **FHCRC**
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  - Melissa Plets
  - Eddie Mayerson

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  - Laura Kingsbury

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  - Matthew Dort

- **ICAN**
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- **ITSC**
  - Edison Liu
  - David Tuveson

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  - Jeff Chuang
  - Karolina Palucka

- **UCSD**
  - Donna Hansel

- **CTEP**
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  - Helen Chen
  - Elad Sharon
  - Boris Freidlin
  - Jeff Abrams

- **NCI/MATCH**
  - Alice Chen
  - Barbara Conley

- **ECOG-ACRIN/MATCH**
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  - Peter O'Dwyer
  - Robert Comis

- **BMS**
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  - Arvin Yang
  - Lisa Marubio