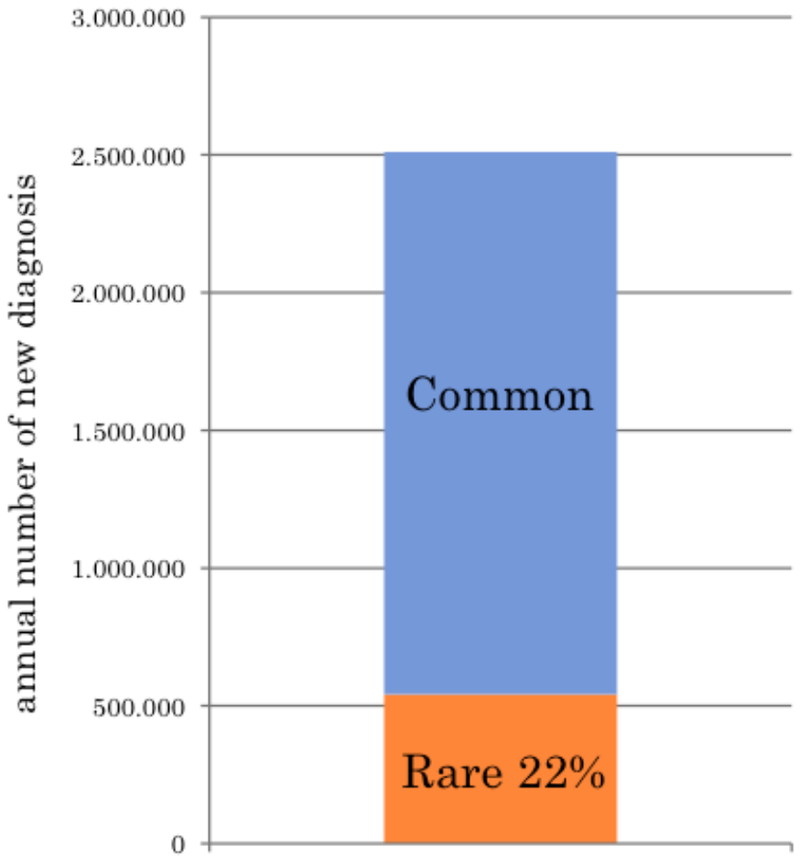
DART: *D*ual *A*nti-CTLA-4 & Anti-PD-1 blockade in *R*are *T*umors

Sandip Patel, MD
Assistant Professor
Deputy Director,
San Diego Center for Precision Immunotherapy
UCSD Moores Cancer Center

Young Chae, MD
Assistant Professor
Vice Chair, SWOG Early Therapeutics
and Rare Cancers Committee
Co-Director Developmental Therapeutics
Northwestern University

Razelle Kurzrock, MD
Professor
Chief, Division of Hematology,
Medical Oncology
Chair, SWOG Early Therapeutics
and Rare Cancers Committee
UCSD Moores Cancer Center

Rare cancers: Incidence



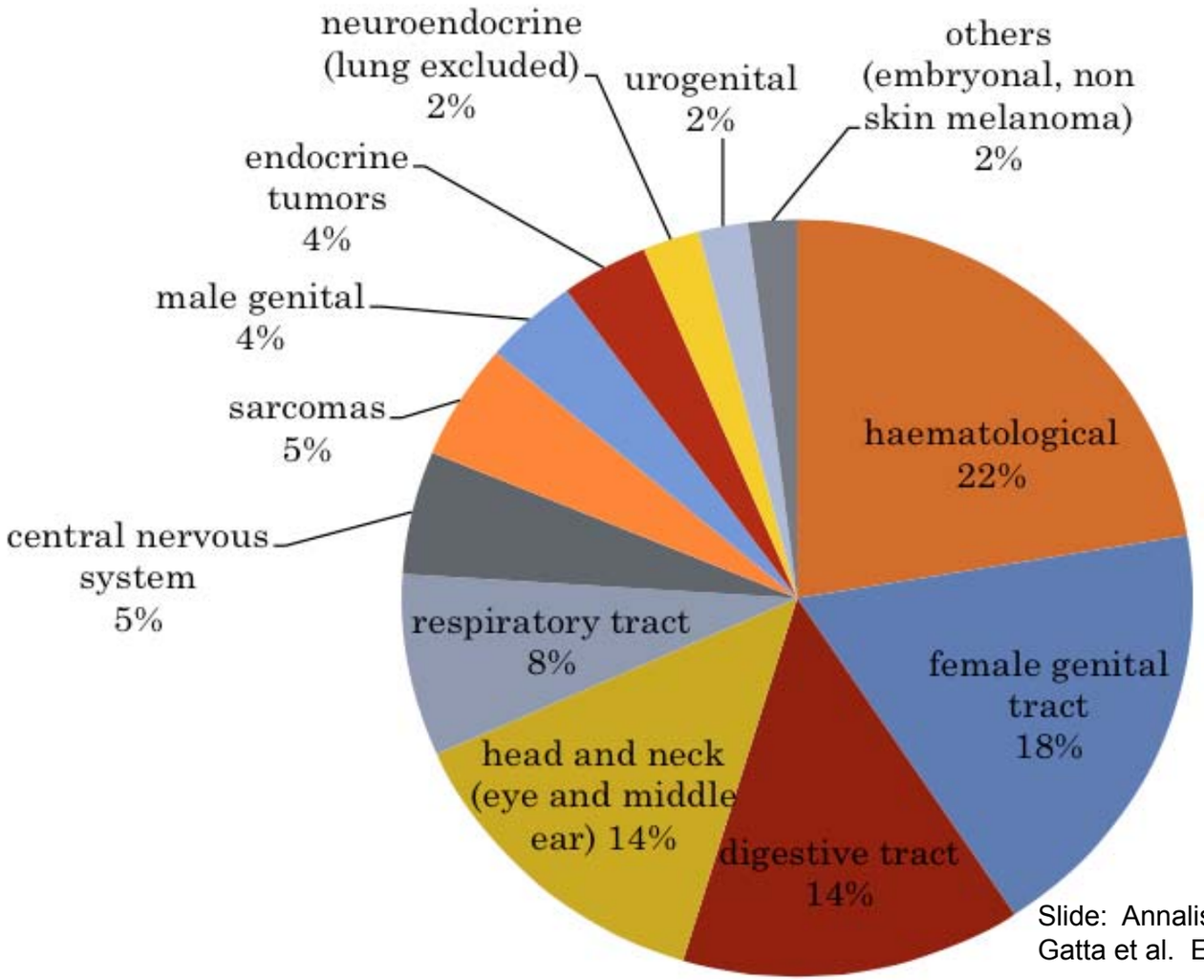
186 rare cancers

About 500,000 new cases/year in EU27

22% of all cancer diagnosed/year

Slide: Annalisa Trama, from Paper: Gemma Gatta et al. Eur J of CA 47 (2011) 2493-2511

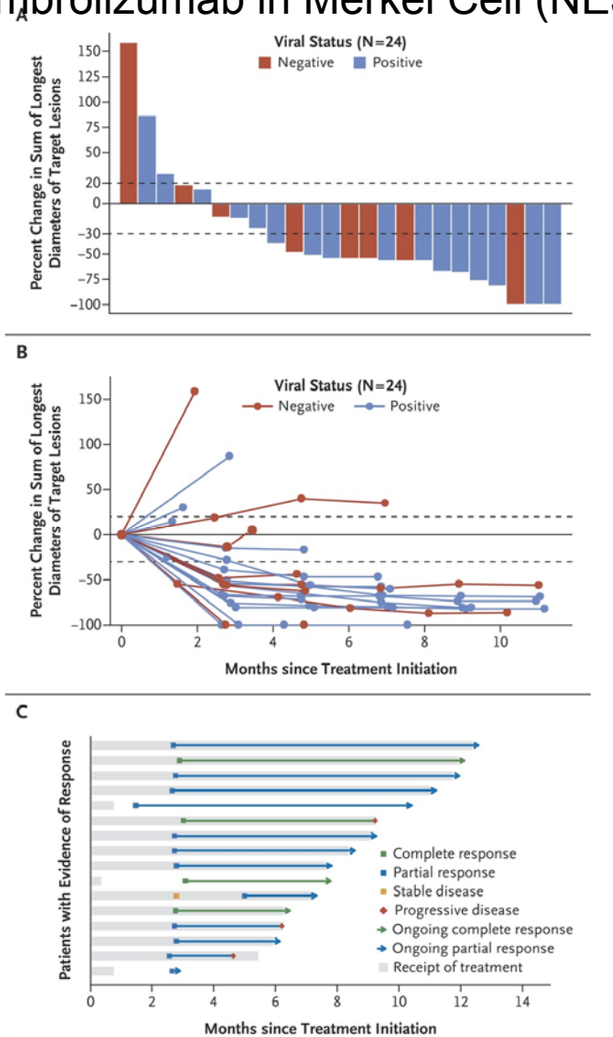
DISTRIBUTION OF MAJOR FAMILIES OF RARE TUMORS WITHIN ALL RARE CANCERS



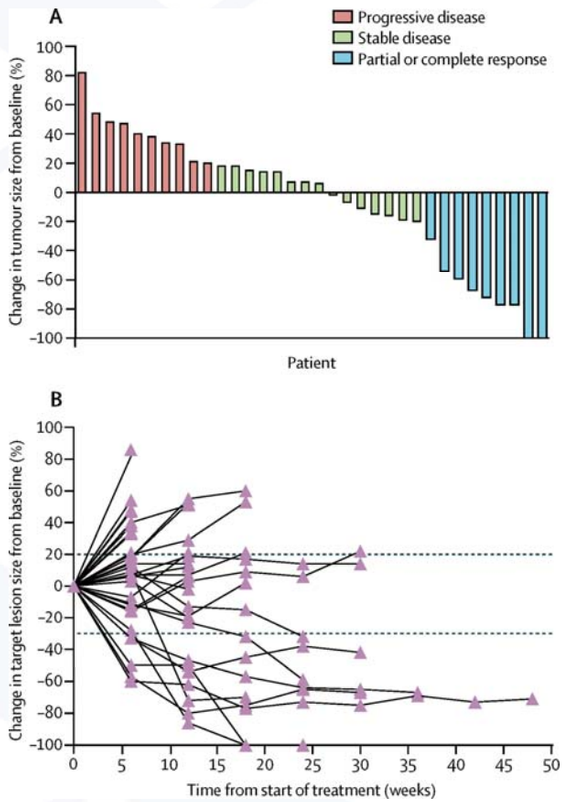
Slide: Annalisa Trama, from Paper: Gemma Gatta et al. Eur J of CA 47 (2011) 2493-2511

Responses to Immunotherapy in Rare Tumors

Pembrolizumab in Merkel Cell (NEJM 2016)

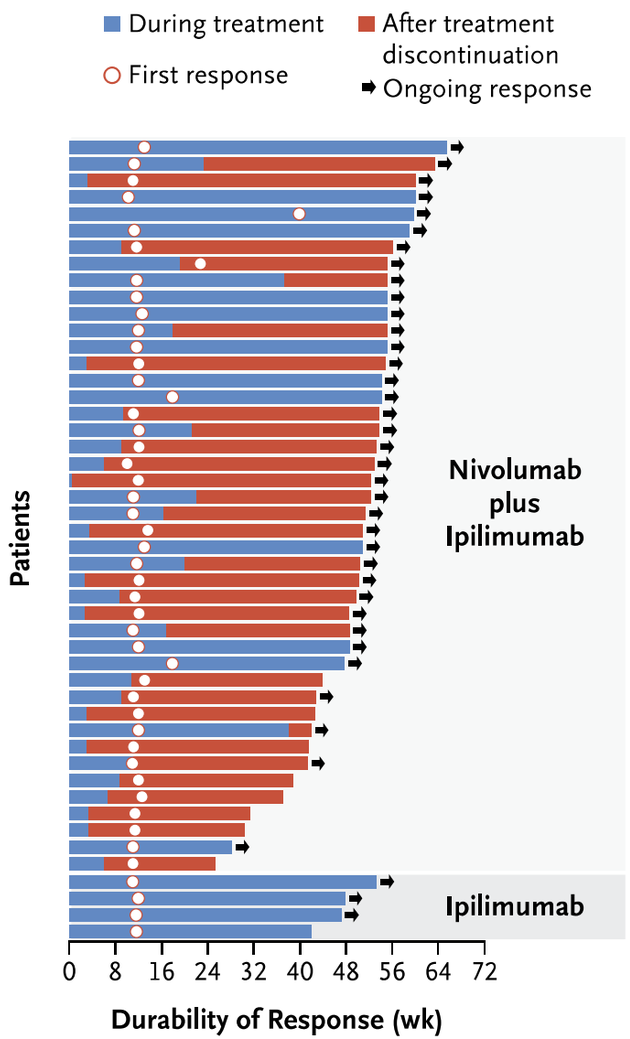


Nivolumab in Anal Cancer (Lancet Onc 2017)



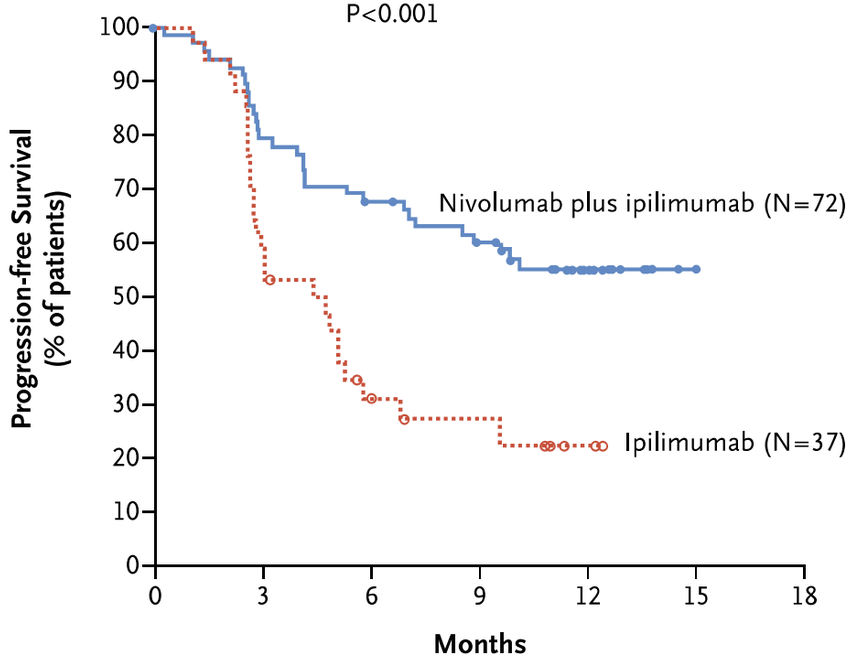
Combinatorial vs Single-Agent Immunotherapy

Postow et al. NEJM 2015



	Death or Disease Progression	Median Progression-free Survival
	no. of patients/total no.	*mo (95% CI)*
Nivolumab plus Ipilimumab	30/72	NR
Ipilimumab	25/37	4.4 (2.8–5.7)

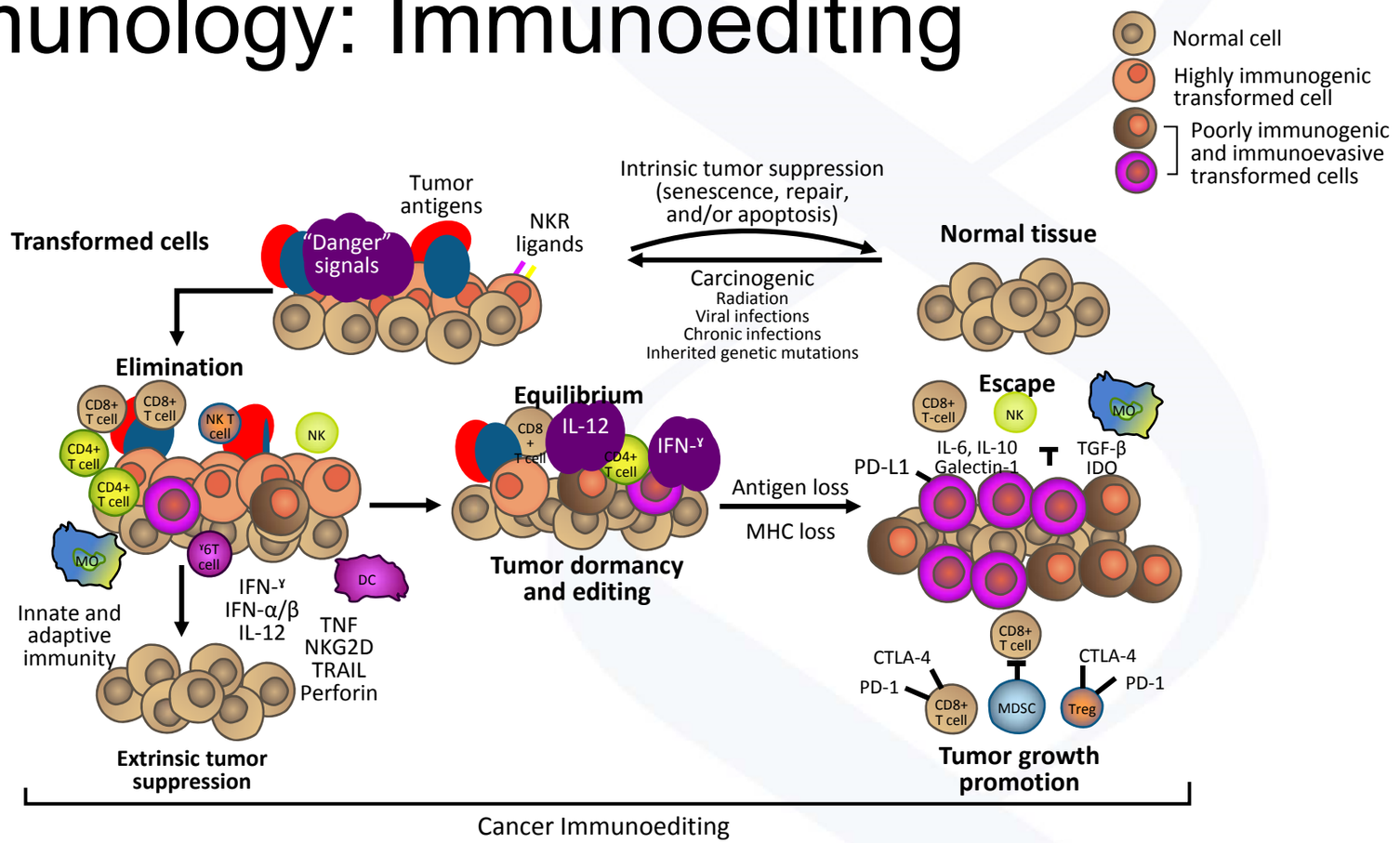
Hazard ratio, 0.40 (95% CI, 0.23–0.68)
P<0.001



No. at Risk

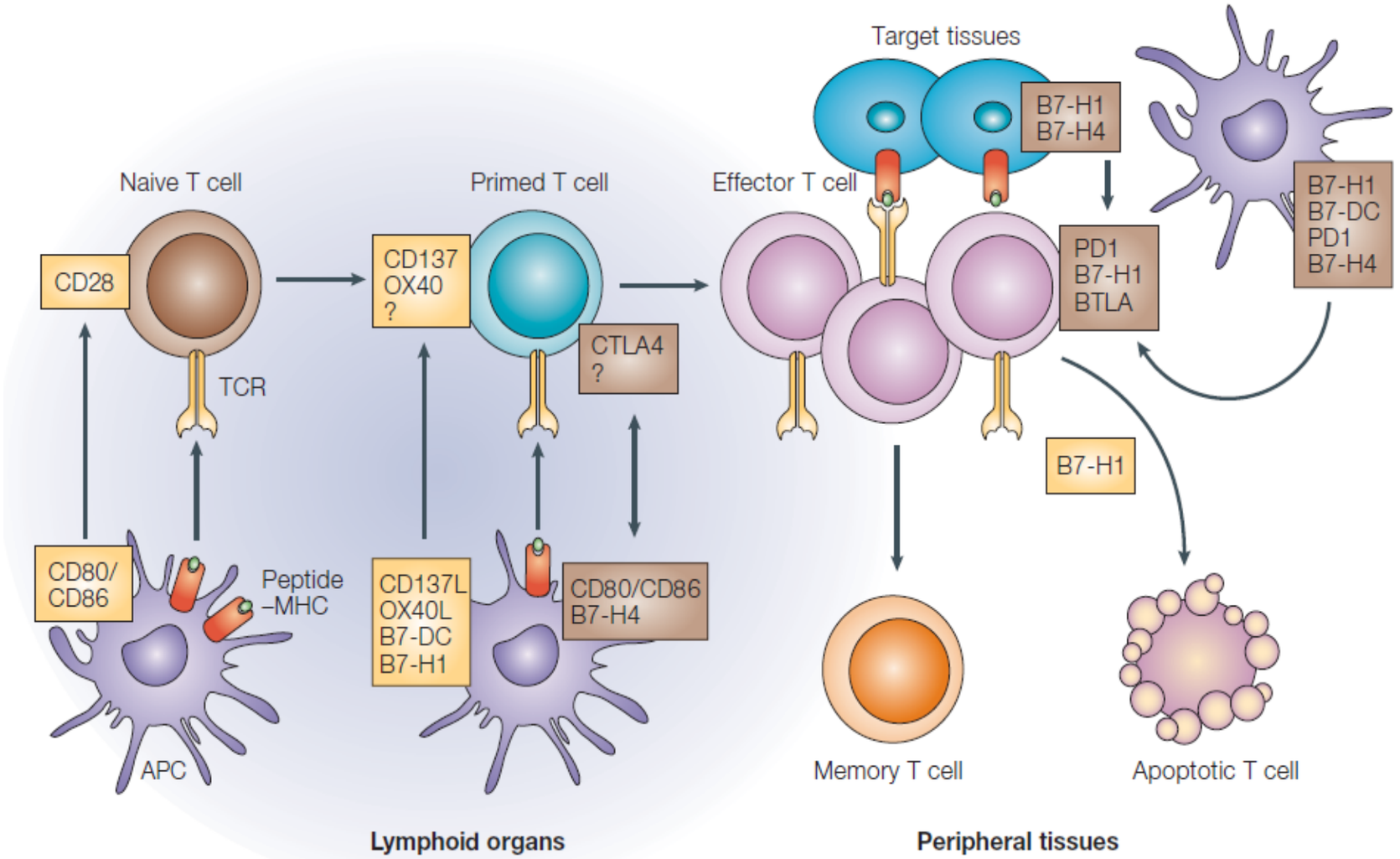
Nivolumab plus ipilimumab	72	54	45	38	20	1	0
Ipilimumab	37	20	9	6	2	0	0

Basic concepts in tumor immunology: Immunoediting



Schreiber RD, et al. Science. 2011;331:1565-1570.

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

SWOG DART
Eligibility Overview (cont'd)

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)

SWOG DART
Eligibility Overview (cont'd)

Rare Cancers Not Eligible:

- Anal cancer,
- Lymphoma,
- Merkel cell carcinoma,
- Pleural Mesothelioma,
- Sarcoma (bone & soft tissue),
- Thymic Carcinoma,
- Uterine Leiomyosarcoma.

Rare Tumors Basket Study

Rare cancers included in DART

- ✓ **Epithelial tumors of nasal cavity, sinuses, nasopharynx**
  - Squamous cell carcinoma with variants of nasal cavity, sinuses, and nasopharynx and trachea (excluding laryngeal, nasopharyngeal cancer [NPC], and squamous cell carcinoma of the head and neck [SCCHN])
  - Adenocarcinoma and variants of nasal cavity, sinuses, and nasopharynx. Some are related to dust inhalation and have p53, RAS, and p16 changes
- ✓ **Epithelial tumors of major salivary glands**
- ✓ **Salivary gland type tumors of head and neck, lip, esophagus, stomach, trachea and lung, breast and other location**
- ✓ **Undifferentiated carcinoma of gastrointestinal (GI) tract**
- ✓ **Adenocarcinoma with variants of small intestine**
- ✓ **Squamous cell carcinoma with variants of GI tract (stomach small intestine, colon, rectum, pancreas)**
- ✓ **Fibromixoma and low grade mucinous adenocarcinoma (pseudomixoma peritonei) of the appendix and ovary**
- ✓ **Pancreatic tumor including acinar cell carcinoma, mucinous or serous cystadenocarcinoma**
- ✓ **Intrahepatic Cholangiocarcinoma**
- ✓ **Cholangiocarcinoma and extrahepatic bile duct tumors**
- ✓ **Sarcomatoid carcinoma of lung)**
- ✓ **Bronchoalveolar carcinoma lung**
- ✓ **Non epithelia tumors of the ovary**
  - Germ cell tumor of ovary
  - Mullerian mixed tumor and adenosarcoma
- ✓ **Trophoblastic tumor of placenta**
  - Choriocarcinoma of placenta
- ✓ **Transitional cell carcinoma other than renal pelvis uretheral or bladder**
- ✓ **Cell tumor of the testes and extra gonadal tumors**
  - Seminoma and testicular sex cord cancer
  - Non seminomatous tumor
  - Teratoma with malignant transformation
- ✓ **Epithelial tumors of penis - squamous adenocarcinoma cell carcinoma with variants of penis**
- ✓ **Squamous cell carcinoma variants of the genitourinary (GU) system**
- ✓ **Spindle cell type of kidney, pelvis and ureter**
- ✓ **Adenocarcinoma with variants of GU system (excluding prostate cancer)**
- ✓ **Odontogenic malignant tumors**
- ✓ **Endodocrine carcinoma of pancreas and digestive tract**
- ✓ **Neuroendocrine carcinoma including carcinoid of the lung and other sides of other sites**
- ✓ **Pheochromocytoma, malignant**
- ✓ **Paraganglioma**
- ✓ **Carcinomas of pituitary gland, thyroid gland parathyroid gland adrenal cortex**
- ✓ **Dermoid tumors**
- ✓ **Peripheral nerve sheath tumors and NF1 related tumors**
- ✓ **Malignant giant cell tumors**
- ✓ **Chordoma**
- ✓ **Adrenal cortical tumors**
- ✓ **Tumor of unknown primary**
- ✓ **Other**

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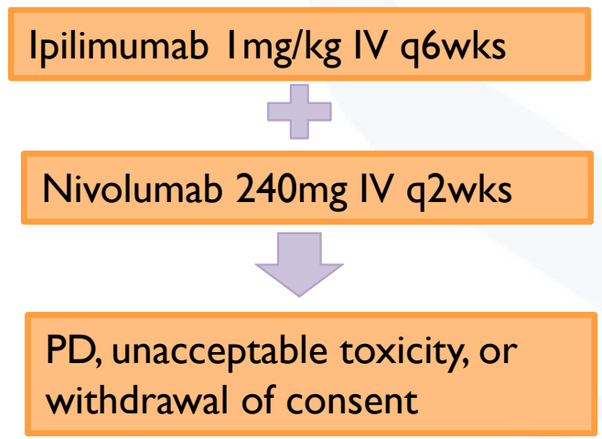
SWOG

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)

ME1

Slide 13

ME1 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

Young Kwang Chae, MD, MPH, MBA

Vice Chair, SWOG Early Therapeutics and Rare Cancer Committee

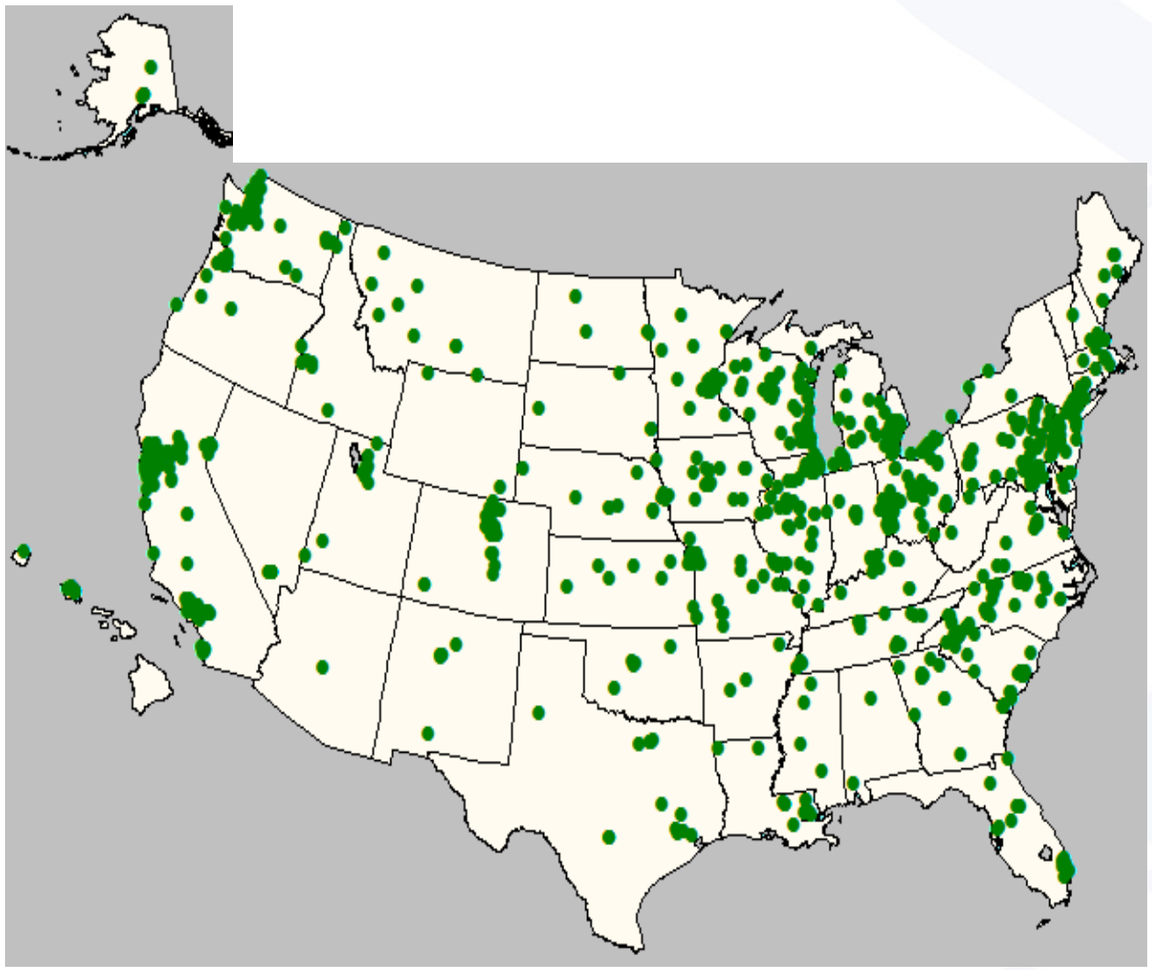
Co-Director, Early Phase Clinical Trials Unit,

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



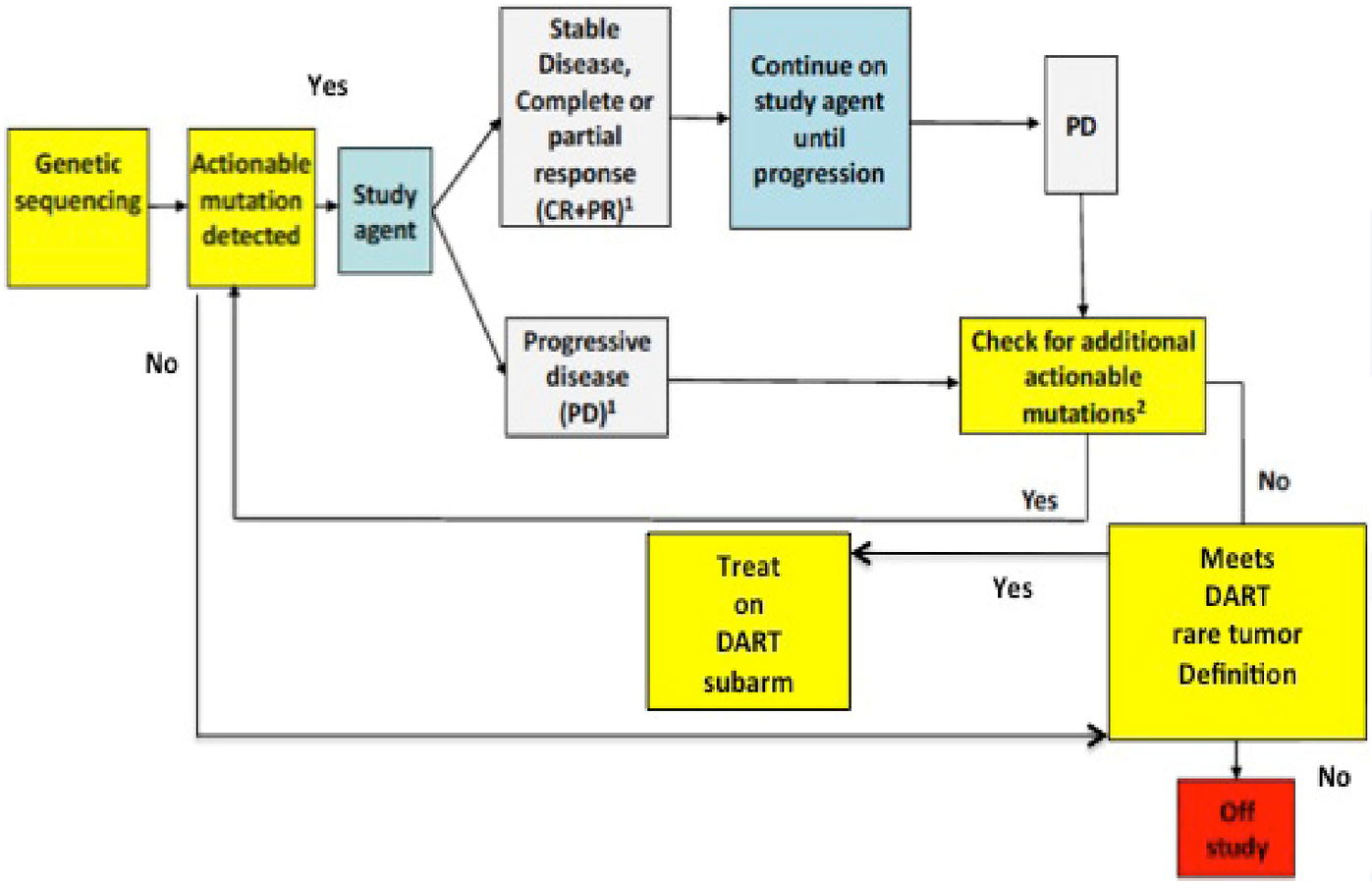
- **Trial is open and enrolling in every state, DC, and Puerto Rico**
- **50% of the 1100 sites have enrolled at least one patient for screening**

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.

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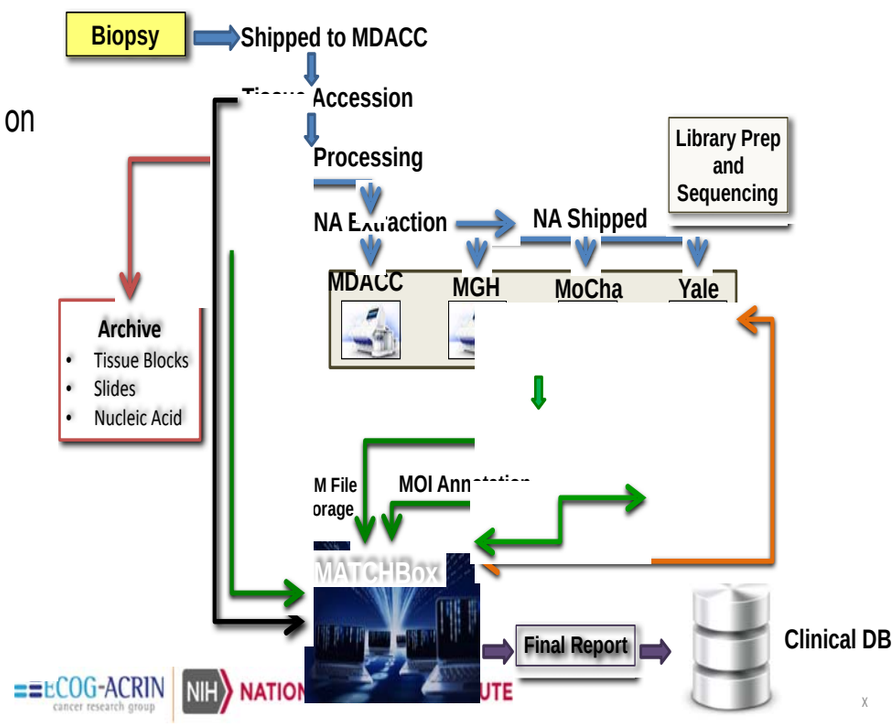
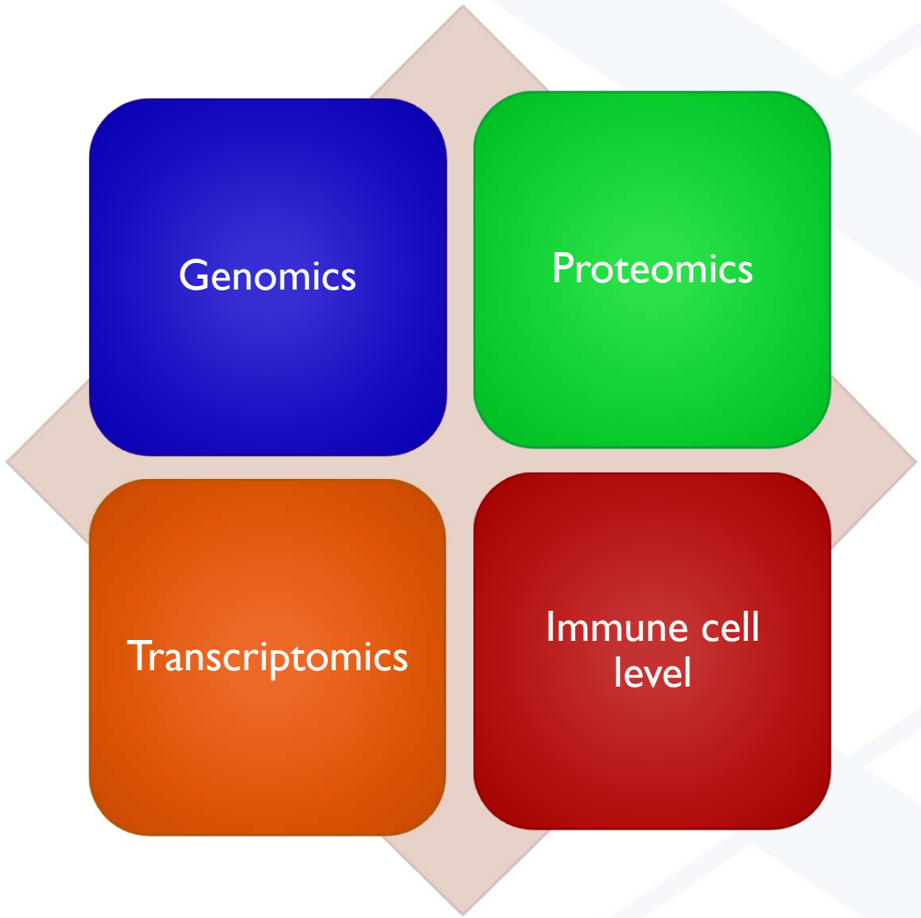
Translational Medicine in DART/MATCH

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



TM Projects



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

	PD-L1 IHC	Immune biomarkers	Germline DNA sequencing	Proteomic immune signature	cDNA sequencing	Tumor NGS
Performing Lab	**UCSD**	**Jackson Labs (JAX)**	**Counsyl**	**Biodesix**	**Circulogene**	**MatchBox**
Sample source	**Tumor tissue** (FFPE) or unstained slide	**Blood in collected in Tempus tubes** (one 2cc vial for RNA, another 2cc vial for DNA)	**Blood collected in the EDTA tube**	**Blood collected in the EDTA tube**	**Blood collected in the EDTA tube**	**Tumor tissue (FFPE) collected as part of NCI-MATCH**
Biomarker Target	PD-L1 protein expression by 28-8 IHC analysis	DNA, RNA sequencing (Nanostring) of tumor tissue and blood	Leukocyte DNA sequencing (Illumina)	Serum proteins	Cell free DNA sequencing (Illumina)	Tumor next-generation sequencing (Ion Torrent)
Specimen Estimate	150 (baseline tissue)	240 (baseline blood)	240 (baseline blood)	240 (baseline blood)	240 (baseline blood)	300 (baseline tissue)
Biomarker output	PD-L1 strata will be grouped <1%, 1-5%, 6-25%, 26-49%, >50%	Immune and Cancer pathway Nanostring (gene expression of 770 genes assaying 24 immune cell types and 500 immune response genes)	Genetic alteration	Predictive signature (good, intermediate, poor group)	Genetic alteration and mutational load	Genetic alteration and mutational load
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

Sample Type	Timepoint(s)	Sample Collection Media	Processing and Storage	Shipping
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.**	Baseline only	One 5-10 mm^3 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.	Store ambient prior to shipment. Tissue Block Size requirement: • Surface area: 25mm^2 is optimal. Minimum is 5mm^2 • Volume: 1mm^3 optimal. Minimum volume is 0.2mm^3.	Ambient, via overnight courier. Batch shipping not allowed.
8 mL blood processed to 4 mL serum	○ Baseline* ○ Cycle 2 MRI/CT* ○ Disease progression * Collection must be within 2 days prior to ipilimumab treatment.	Plastic SST If possible, Greiner Gold Top vacuette tube 4 mL, Z Serum Separator Clot Activator (SST) preferred. No glass.	Process for at least 4 mL serum by centrifugation. Transfer serum into a single plastic cryotube. Freeze upright and store in a -70 to -80°C freezer prior to shipment.	Ship (frozen) via overnight courier with dry ice (to maintain -70°C during shipment). Batch shipping not allowed.

Specimen Instructions

Sample Type	Timepoint(s)	Sample Collection Media	Processing and Storage	Shipping
4 mL whole blood	Baseline only Collection must be within 2 days prior to ipilimumab treatment.	Plastic K2EDTA or K3EDTA tube No glass.	Freeze upright in a -70 to -80°C freezer prior to shipment.	Ship (frozen) via overnight courier with dry ice (to maintain -70°C during shipment). Batch shipping not allowed.
9 mL whole blood at baseline, Cycle 2 MRI/CT and time of disease progression.	a) Baseline* b) Cycle 2 MRI/CT* c) Disease progression *Collection must be within 2 days prior to ipilimumab treatment.	Plastic K2EDTA or K3EDTA tube No glass.	After collection, invert to mix. Do not centrifuge. Refrigerate prior to shipment at 2-8°C.	Ship refrigerated with cold pack (maintain 4-10°C, during shipment). Ship overnight, same day as collected. Batch shipping not allowed.
4 mL whole blood collected in two, 2mL Tempus tubes *See below for instructions to request tempus tubes.	a) Baseline* b) Cycle 2* MRI/CT c) Disease progression *Collection must be within 2 days prior to ipilimumab treatment.	Two, 2mL tempus tubes .	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	Ship (frozen) via overnight courier with dry ice (to maintain -70°C, during shipment). Ship same day as collected. Batch shipping not allowed
5 mL whole blood at baseline **(OPTIONAL)**	Baseline only - Collection must be within 2 days prior to ipilimumab treatment.	Plastic K2EDTA or K3EDTA tube No glass.	Gently invert to mix (5 – 10 times). Do not centrifuge. Refrigerate prior to shipment at 2-8°C.	Ship refrigerated with cold pack (maintain 4 to 10°C, during shipment). Ship overnight, same day as collected. Batch shipping not allowed.

Questions

Young Chae
young.chae@northwestern.edu

Sandip Patel
sandippatel@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**

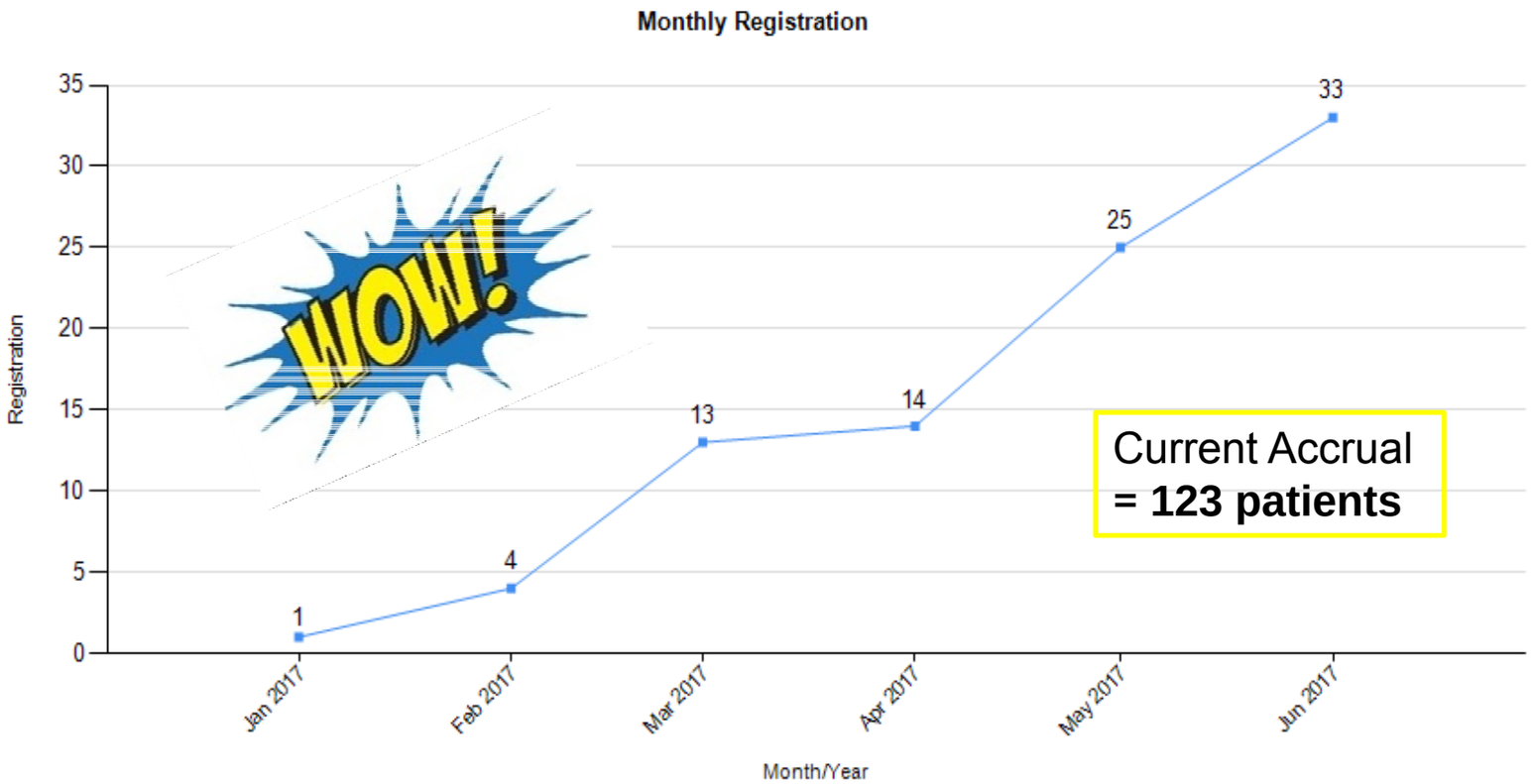
  n=16 x 36 cohorts

  + 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??



Analysis Plan

- **Primary Objective**: Overall Response (RECIST)

H_0 = 5 % H_A = 30 %

Alpha (one-sided) = 0.13

Power (1-β)= 87 %

		Truth: Positive	Truth: Negative	
Test: Positive		True Positive	False Positive Type I α	Total Testing Positive
Test: Negative		False Negative Type II β	True Negative	Total Testing Negative
		Total Truly Positive	Total Truly Negative	Total

Analysis Plan

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

Stage 1	Stage 2
• 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

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

S1609 Common Issues

Christine McLeod

Data Coordinator

SWOG Data Operations Center

S1609 Common Issues - Eligibility

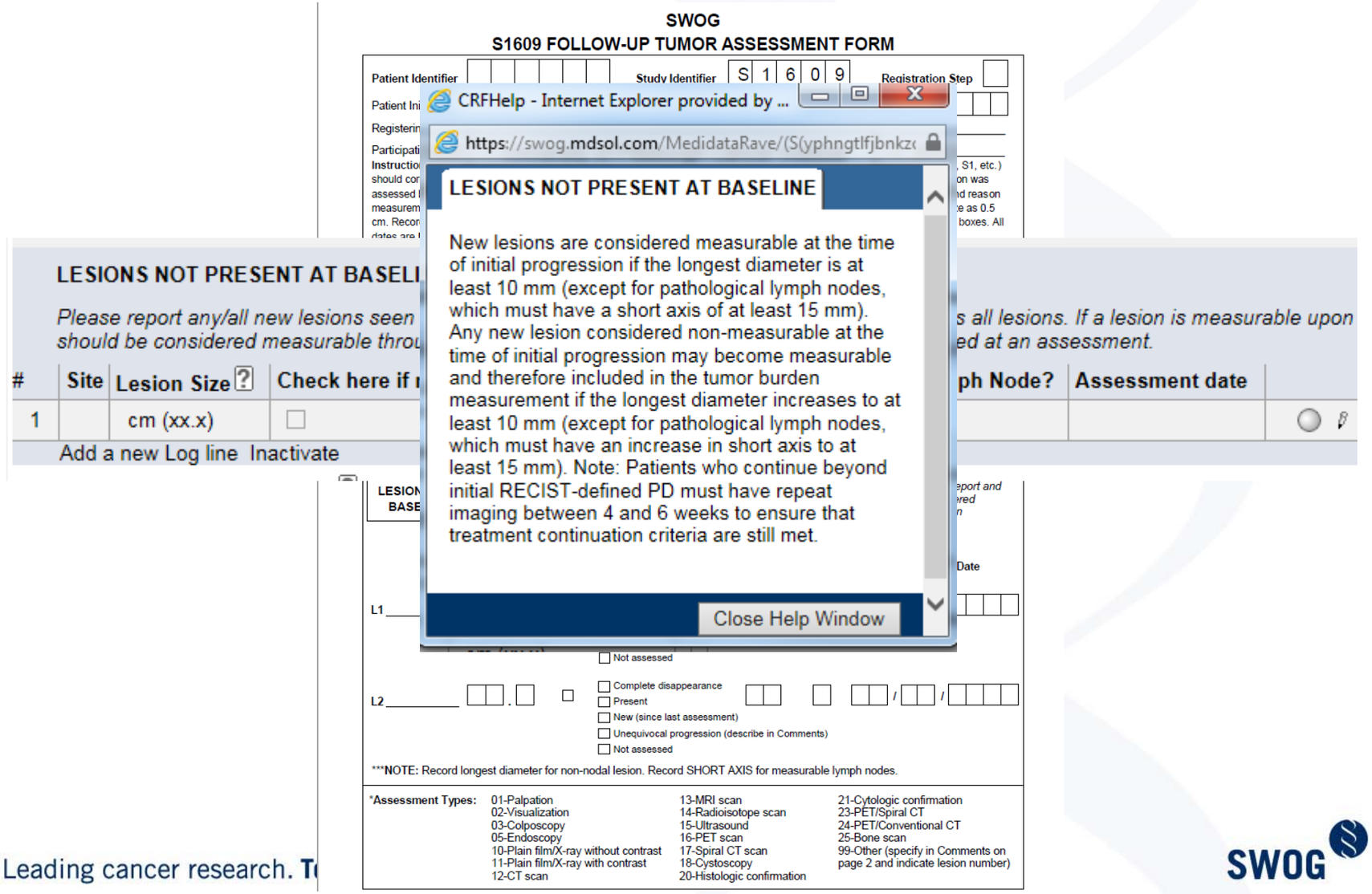
- Is my patient's tumor rare?
  - **It might be but not per protocol**
  - **Other on-going trials?**
  - When in doubt, upload redacted path report

S1609SC@swog.org

S1609 Common Issues - Data

- Disease Assessment Forms
  - **New disease since baseline**
  - **OK to remain on protocol (7.4a)**

S1609 Common Issues - FUTA



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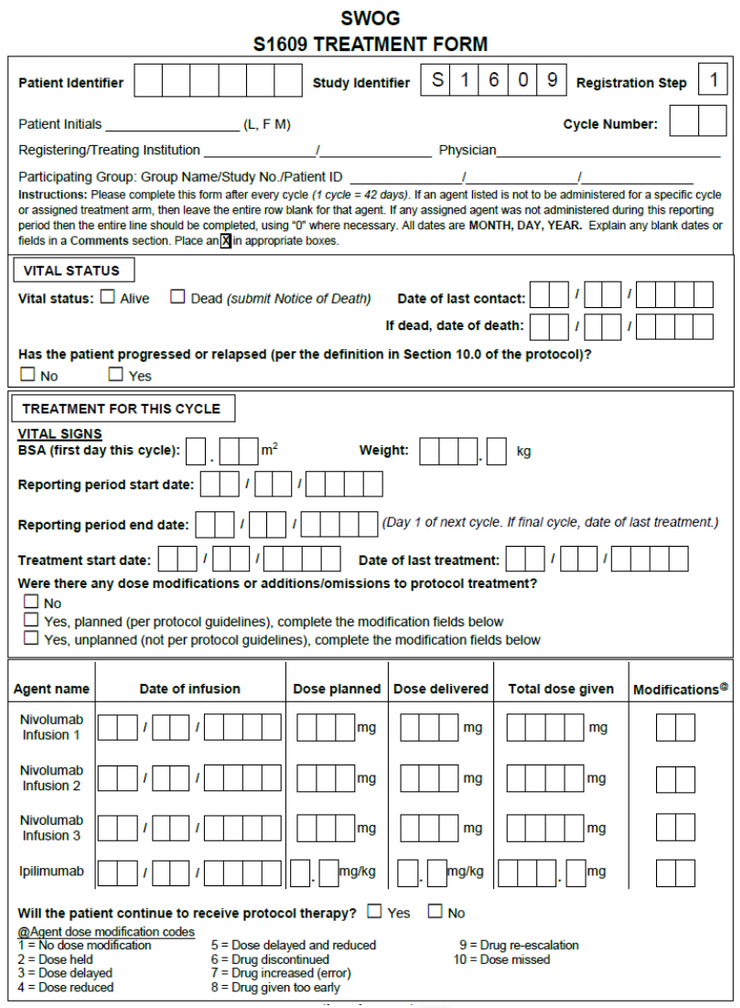
S1609 Common Issues – Tx Form



SWOG

S1609 TREATMENT FORM

Patient Identifier ☐☐☐☐☐☐ **Study Identifier** S 1 6 0 9 **Registration Step** 1

Patient Initials _____ (L, F M) **Cycle Number:** ☐☐

Registering/Treating Institution _____/_____ Physician_____

Participating Group: Group Name/Study No./Patient ID _____/_____/_____

Instructions: Please complete this form after every cycle *(1 cycle = 42 days)*. If an agent listed is not to be administered for a specific cycle or assigned treatment arm, then leave the entire row blank for that agent. If any assigned agent was not administered during this reporting period then the entire line should be completed, using "0" where necessary. All dates are **MONTH, DAY, YEAR.** Explain any blank dates or fields in a **Comments** section. Place an X in appropriate boxes.

VITAL STATUS

Vital status: ☐ Alive ☐ Dead *(submit Notice of Death)* **Date of last contact:** ☐☐/☐☐/☐☐☐☐

If dead, date of death: ☐☐/☐☐/☐☐☐☐

Has the patient progressed or relapsed (per the definition in Section 10.0 of the protocol)?

☐ No ☐ Yes

TREATMENT FOR THIS CYCLE

VITAL SIGNS

BSA (first day this cycle): ☐.☐☐ m^2 **Weight:** ☐☐☐.☐ kg

Reporting period start date: ☐☐/☐☐/☐☐☐☐

Reporting period end date: ☐☐/☐☐/☐☐☐☐ *(Day 1 of next cycle. If final cycle, date of last treatment.)*

Treatment start date: ☐☐/☐☐/☐☐☐☐ **Date of last treatment:** ☐☐/☐☐/☐☐☐☐

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

☐ No
☐ Yes, planned (per protocol guidelines), complete the modification fields below
☐ Yes, unplanned (not per protocol guidelines), complete the modification fields below

Agent name	Date of infusion	Dose planned	Dose delivered	Total dose given	Modifications@
Nivolumab Infusion 1	☐☐/☐☐/☐☐☐☐	☐☐☐ mg	☐☐☐ mg	☐☐☐☐ mg	☐☐
Nivolumab Infusion 2	☐☐/☐☐/☐☐☐☐	☐☐☐ mg	☐☐☐ mg	☐☐☐☐ mg	☐☐
Nivolumab Infusion 3	☐☐/☐☐/☐☐☐☐	☐☐☐ mg	☐☐☐ mg	☐☐☐☐ mg	☐☐
Ipilimumab	☐☐/☐☐/☐☐☐☐	☐.☐ mg/kg	☐.☐ mg/kg	☐☐☐.☐ mg	☐☐

Will the patient continue to receive protocol therapy? ☐ Yes ☐ No

@Agent dose modification codes

1 = No dose modification
2 = Dose held
3 = Dose delayed
4 = Dose reduced
5 = Dose delayed and reduced
6 = Drug discontinued
7 = Drug increased (error)
8 = Drug given too early
9 = Drug re-escalation
10 = Dose missed

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.

#	Agent name	Date of infusion	Dose planned	Dose delivered	Total dose given	Modifications	Dose modification reason	Number of days delayed (if applicable)	
1	Nivolumab Infusion 1		240	240	240				
2	Nivolumab Infusion 2								
3	Nivolumab Infusion 3								
4	Ipilimumab								

S1609 Common Issues – Tx Form

Weight 87.2 kg (xxx.x)

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.

#	Agent name	Date of infusion	Dose planned	Dose delivered	Total dose given	Modifications	Dose modification reason	Number of days delayed (if applicable)	
1	Nivolumab Infusion 1								
2	Nivolumab Infusion 2								
3	Nivolumab Infusion 3								
4	Ipilimumab		1	1	87				

S1609 Common Issues – BAB & AEs

Page: **Adverse Events: Report - Cycle 01**

Instructions: Report adverse events occurring up until the next cycle of treatment begins. Document the **worst** Grade seen during the reporting period. **Do not** code a condition existing prior to registration as an adverse event unless it worsens. Indicate if the adverse event results in inpatient hospitalization or prolongation of existing hospitalization for ≥ 24 hours. Follow instructions in Section 16.0 of the protocol for expedited reporting requirements on this study.

Do not code a condition existing prior to registration as an adverse event unless it worsens.

S1609 Common Issues – BAB & AEs

Page: **Baseline Abnormalities - Baseline**

Did the patient have any abnormalities or conditions present PRIOR to protocol treatment?

If Yes, using CTCAE 4.0 Grade definitions, please report them below

#	CTCAE(4.0) adverse event term	CTCAE(4.0) grade
1	Peripheral sensory neuropathy	1
2	Anorexia	1
3	Fatigue	2
4	Hyponatremia	1
5	Creatinine increased	1
6	Hypoalbuminemia	1

Add a new Log line Inactivate

Comments

BABs only reported on AE forms if:
Grade worsens
– or
AE completely resolves & comes back

S1609 Common Issues – BAB & AEs

#	CTC adverse event term	CTCAE (4.0) grade	CTC adverse event attribution code	CTC adverse event status code	Hospitalization *(at least 24 hours)*
1	Abdominal pain	2	Unrelated	Increased grade OR improved then worsened	☐
2	Blood bilirubin increased	2	Possible	Increased grade OR improved then worsened	☐
3	Depression	1	Unlikely	New	☐
4	Fatigue	2	Unlikely	Increased grade OR improved then worsened	☐

CTC adverse event status code

? This AE was not reported in the previous cycle. Please update Status to 1/New.

Opened To Site from DM (02 Oct 2017) ☐ Cancel

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**
  - Chris Ryan
  - Charles Blanke
  - Anne Schott
  - Michael LeBlanc
  - Nathan Eriksen
  - Casey Dawson
  - Tameka Lewis
- **SWOG Operations**
  - Cara Laubach
  - Dana Sparks
  - Gretchen Goetz
- **FHCRC**
  - Megan Othus
  - Melissa Plets
  - Eddie Mayerson
- **Data Coordinators**
  - Christine McLeod
  - Laura Kingsbury
- **SWOG Repository (Nationwide)**
  - Kae Tegtmeier
  - Matthew Dort
- **ICAN**
  - Marcia Horn
- **ITSC**
  - Edison Liu
  - David Tuveson
- **JAX**
  - Jeff Chuang
  - Karolina Palucka
- **UCSD**
  - Donna Hansel
- **CTEP**
  - Howard Streicher
  - Helen Chen
  - Elad Sharon
  - Boris Freidlin
  - Jeff Abrams
- **NCI/MATCH**
  - Alice Chen
  - Barbara Conley
- **ECOG-ACRIN/MATCH**
  - Keith Flaherty
  - Peter O'Dwyer
  - Robert Comis
- **BMS**
  - Monil Shah
  - Arvin Yang
  - Lisa Marubio