

# Innovation in SWOG Clinical Trials

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Early Therapeutics/Rare Cancers Committee

Melanoma Committee

Gastrointestinal Committee

Genitourinary Committee

# in·no·va·tion

/ˌɪnəˈvāSH(ə)n/

*noun*

noun: innovation

the action or process of innovating.

*synonyms:* change, alteration, revolution, upheaval, transformation, metamorphosis,  
breakthrough, new measures, new methods, modernization, novelty, newness;  
creativity, originality, ingenuity, inspiration, inventiveness

a new method, idea, product, etc.

Origin

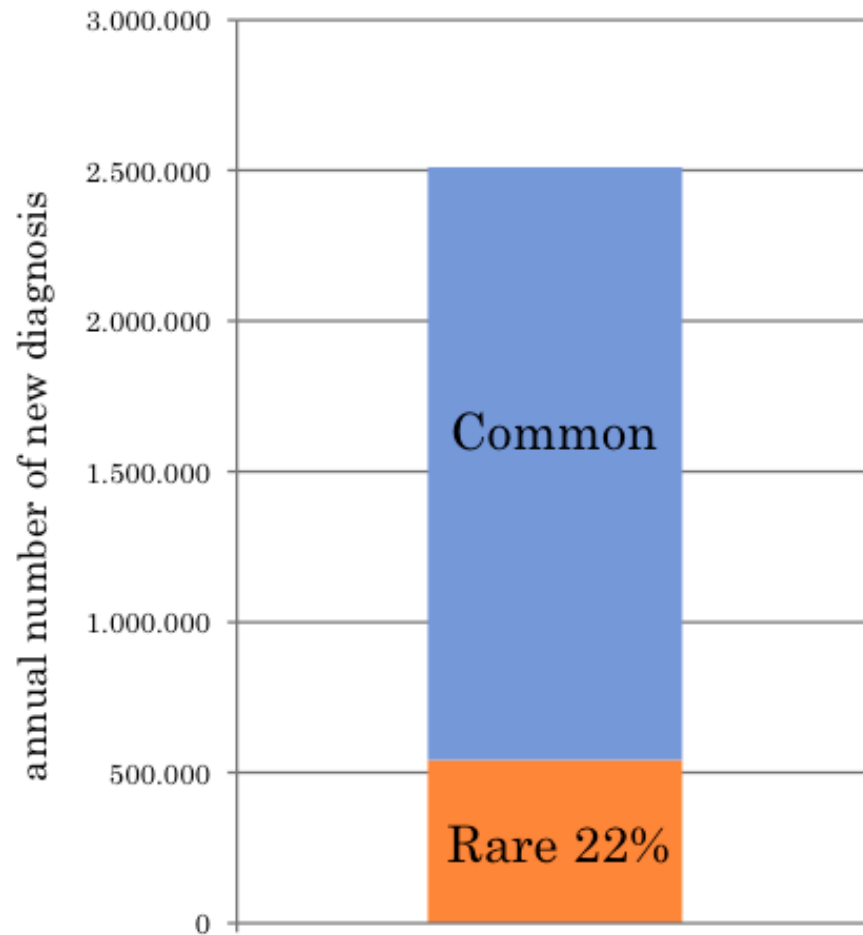


# Innovation:

## Early Therapeutics<sup>✓</sup> Committee *and Rare Cancers*

- Historically, classic phase I trials, limited institutions
- Evolution to molecularly-defined trials
- 2013 - SWOG Rare Cancers Task Force
  - Reduce barriers to participation in rare cancers trials

# 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



# Innovation: *Metamorphosis*

## Early Therapeutics<sup>✓</sup> Committee

### *and Rare Cancers*

- Engagement across specialities
  - JAK1 inhibitor in sarcoma – Dr. Villalobos
  - Anti-mesothelin ADC in peritoneal mesothelioma – Dr. Raghav
  - Tissue of origin testing in CUP – Dr. Yentz
  - Bretuximab in systemic mastocytosis – Dr. Borate

# Innovation:

## S1609: DART

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

*Sandip Patel, MD*

University of California, San Diego  
Moore's Cancer Center

*Francis Giles, MD*

Comprehensive Cancer Center of  
Northwestern University

*Young Chae, MD*

Assistant Professor  
Northwestern University

*Razelle Kurzrock, MD*

University of California, San Diego  
Moore's Cancer Center

# S1609: DART

## Primary study objective:

- To evaluate the overall response rate in patients with advanced rare cancers treated with ipilimumab plus nivolumab combination therapy
- 6-16 patients per stratum

### 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)
- ✓ Fibromyxoma 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 urethral 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
- ✓ Endocrine 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
- ✓ Adenocarcinoma of unknown primary
- ✓ Tumor of unknown primary
- ✓ Other

# Innovation: Integrating with EAY131: NCI-MATCH

THIS PRECISION MEDICINE TRIAL  
EXPLORES TREATING PATIENTS  
BASED ON THE MOLECULAR  
PROFILES OF THEIR TUMORS

NCI-MATCH\* IS FOR ADULTS WITH:

- solid tumors (including rare tumors) and lymphomas
- tumors that no longer respond to standard treatment



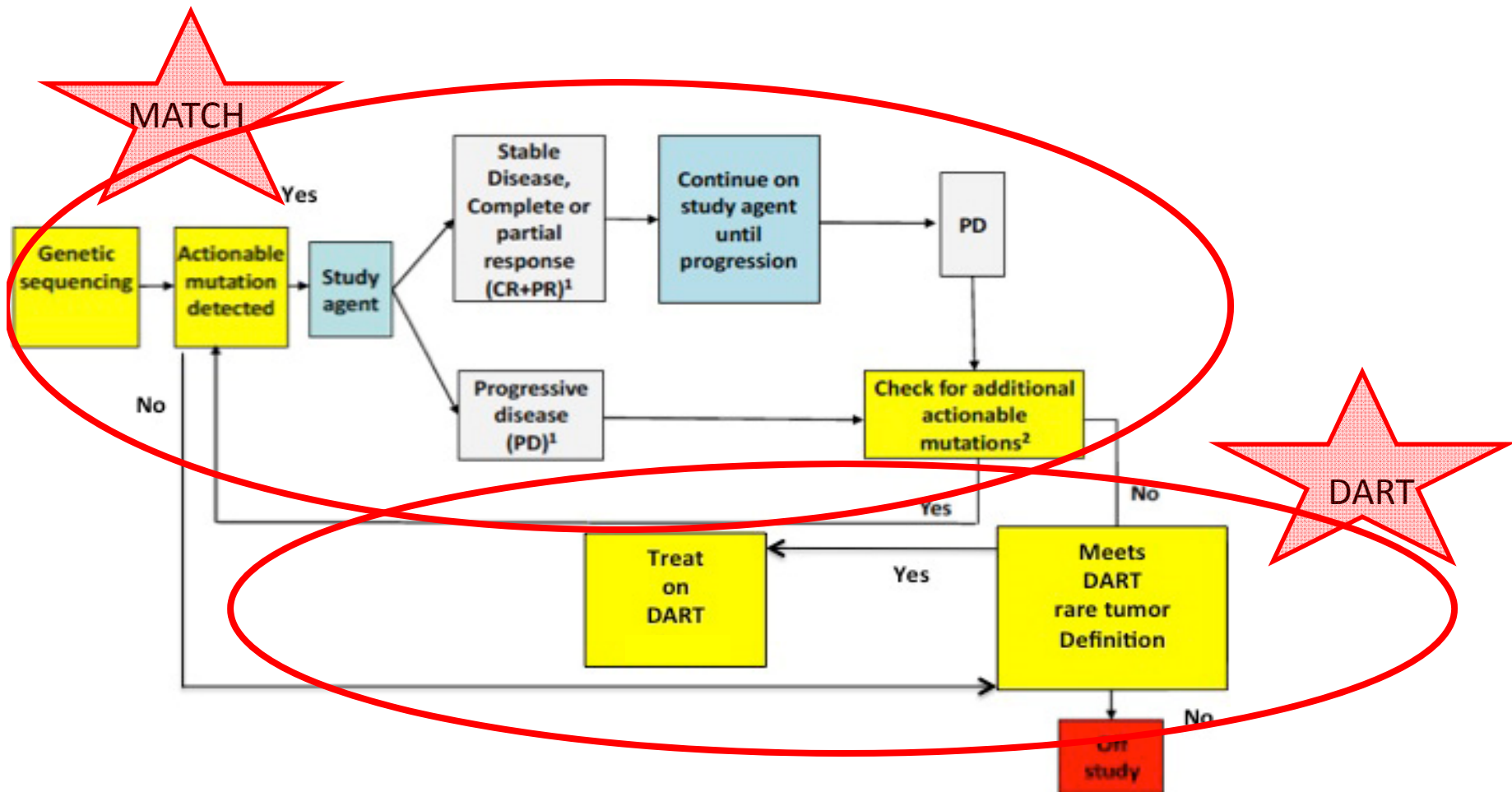
ABOUT 6,000  
CANCER PATIENTS  
WILL BE  
SCREENED WITH A  
TUMOR BIOPSY

- “a goal for NCI-MATCH is for about 25% of total patients enrolled in the trial to have rare cancers”

From [www.cancer.gov](http://www.cancer.gov)



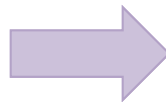
# S1609 DART Treatment/ Schema



Ipilimumab 1mg/kg IV q 6wks



Nivolumab 240mg IV q2wks

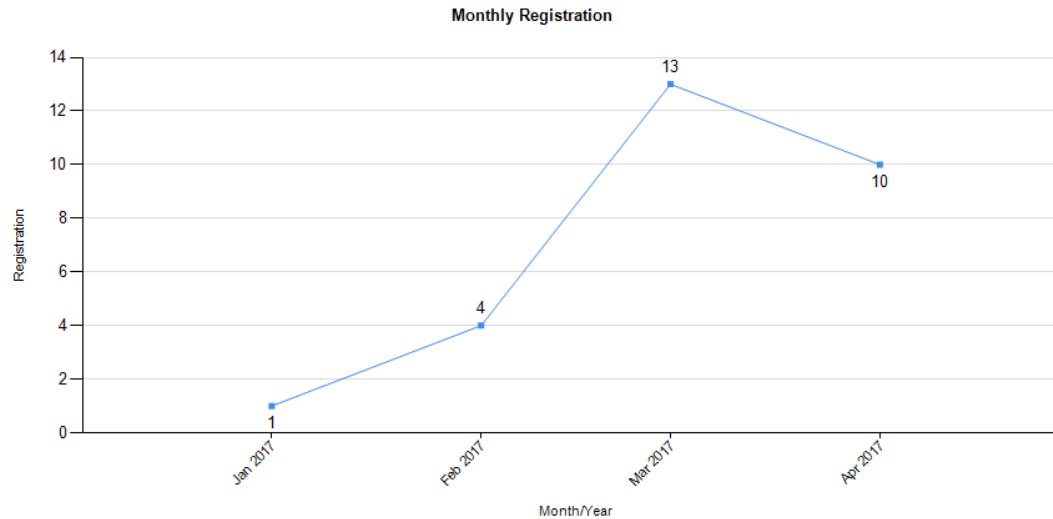


PD, unacceptable toxicity, or withdrawal of consent

Innovation: *Ingenuity*  
DART + MATCH = Symbiosis



# S1609 DART Accrual



Histologic Cohort	TOTAL REGS
Salivary gland type tumors	7
Adenocarcinoma with variants of small intestine	4
Squamous cell carcinoma with variants of GI tract	2
Pancreatic tumor including acinar cell carcinoma, mucinous or serous cystadenocarcinoma	1
Intrahepatic Cholangiocarcinoma	3
Cholangiocarcinoma and extrahepatic bile duct tumors	2
Germ cell tumor of the testes and extragonadal germ cell tumors	1
Endocrine carcinoma of pancreas and digestive tract	1
Neuroendocrine carcinoma including carcinoid of the lung	1
Cancer of Unknown Primary	3
Other	3

# Innovation: S1602: PRIME

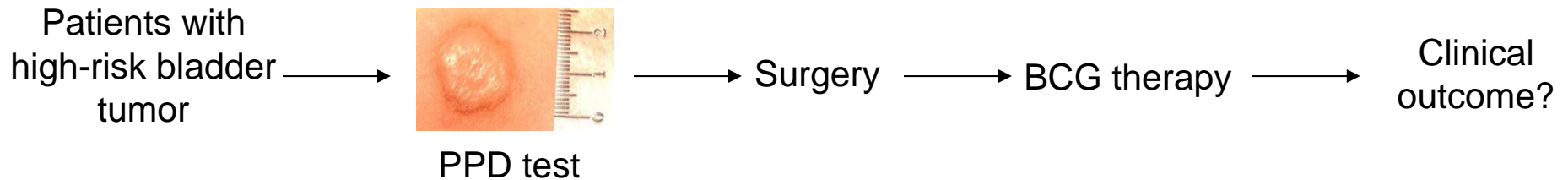
A Phase III Randomized Trial to Evaluate the  
Influence of BCG Strain Differences and T-Cell  
Priming with Intradermal BCG Before Intravesical  
Therapy for BCG-Naïve High-Grade Non-Muscle  
Invasive Bladder Cancer

Robert S. Svatek, MD  
UT San Antonio

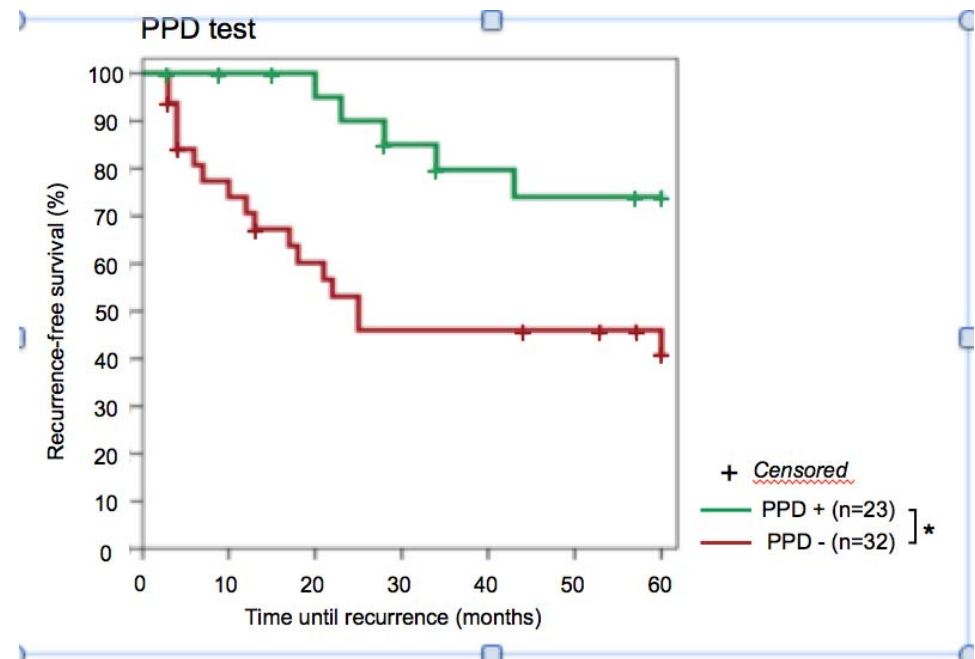




# Pre-existing BCG-specific immunity improves outcomes for patients undergoing intravesical BCG



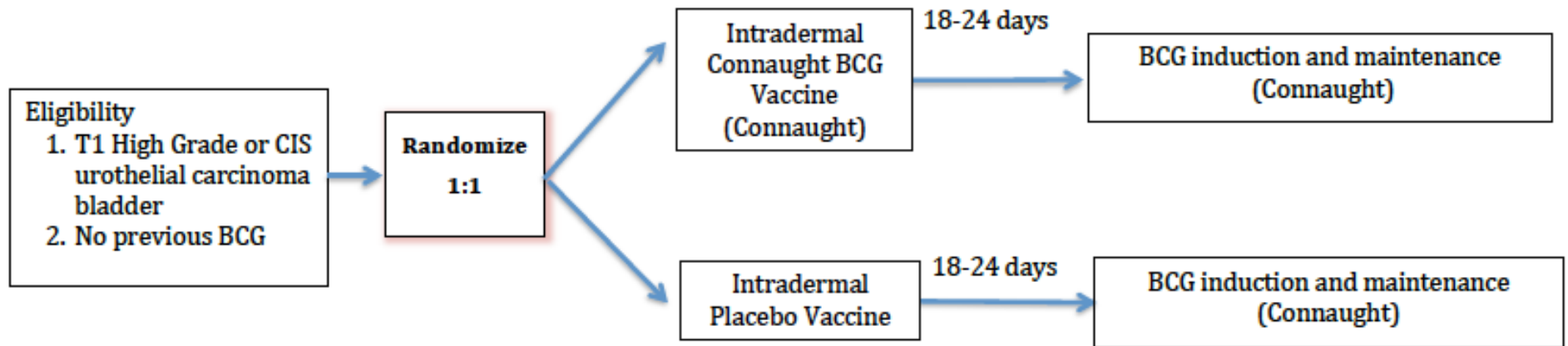
- In preliminary studies, “priming” with intradermal BCG improved the response to intravesical BCG



# PRIME :

## Original Trial Design

Test the ability of T-cell priming to boost response to BCG therapy.



# Bacillus Calmette-Guérin (BCG)

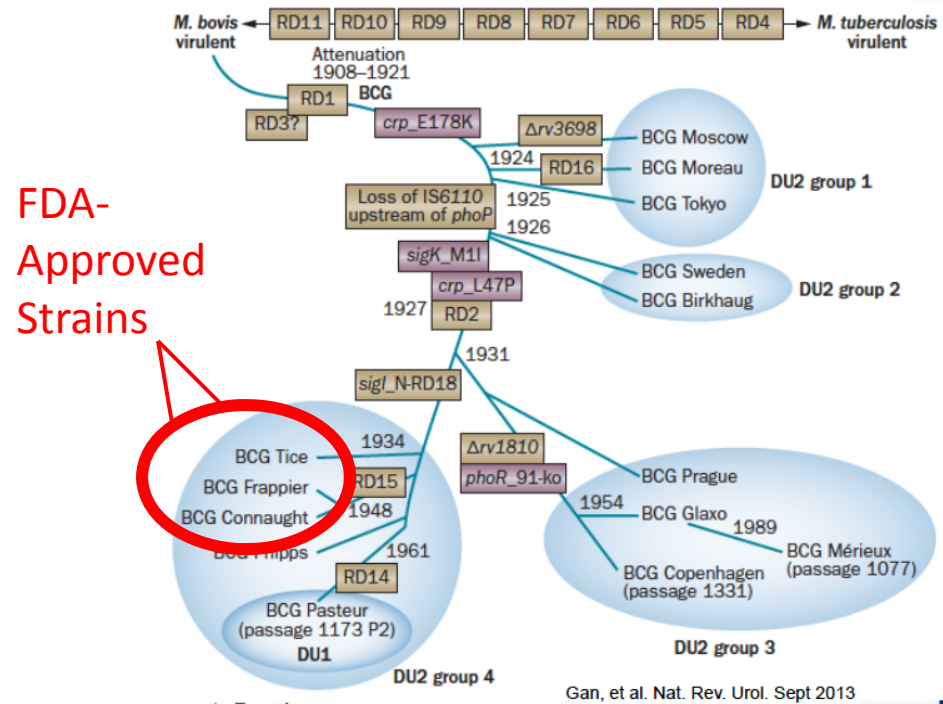
- All strains derive from original *M. bovis* parent strain @ Pasteur Institute



Albert Calmette and Camille Guérin

- Distinct genetic substrains have evolved during global dissemination and manufacturing

## Genealogy of BCG Strains



# Connaught Laboratories

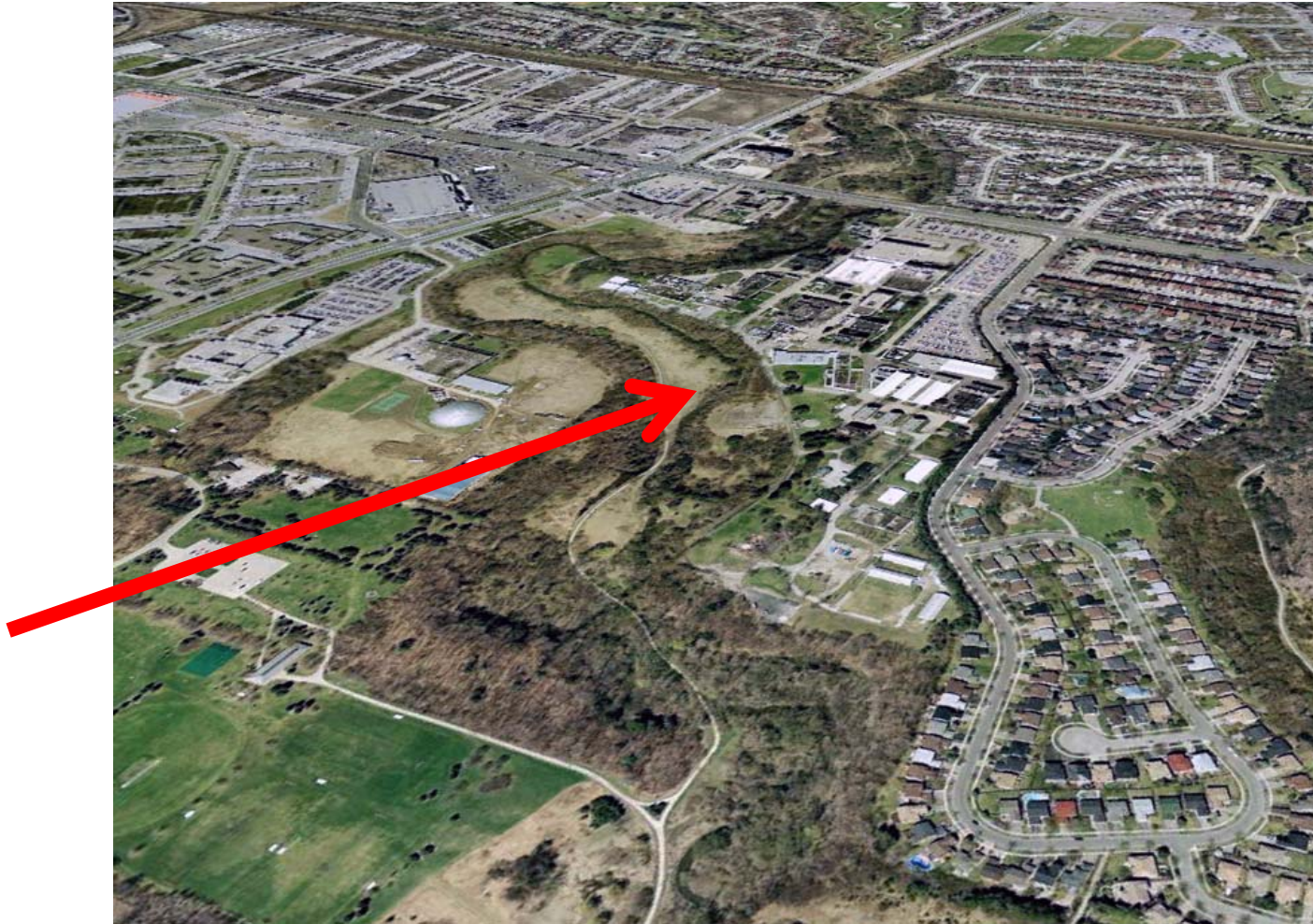
Toronto, Ontario

- Contributed to development of Salk's polio vaccine
- Founded due to shortage of tetanus antitoxin during WWI





# Sanofi Pasteur Connaught Lab



Regulatory

## UPDATED: FDA ravages Sanofi vaccine sterility process in warning letter

by *Eric Palmer* | Jul 24, 2012 4:18pm

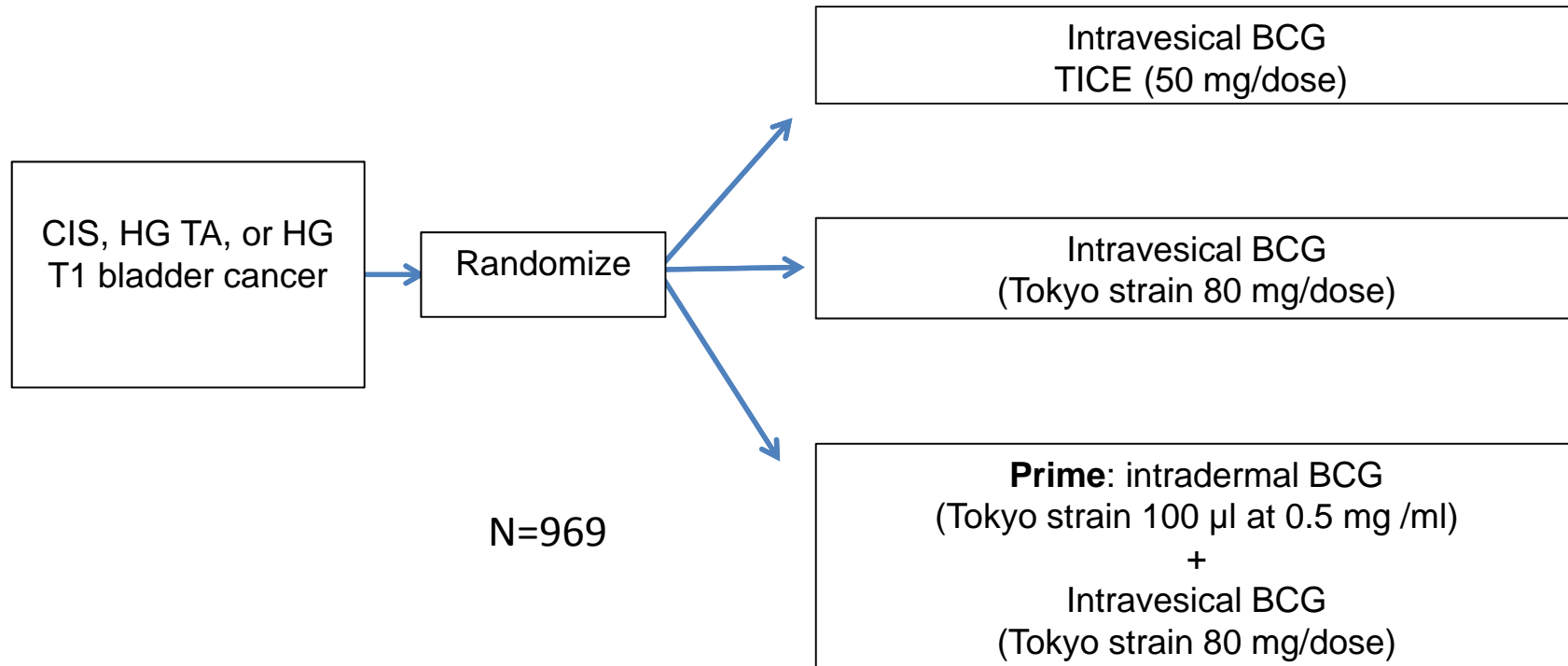
- 2012 – large scale BCG shortage
- 2016 – Sanofi announces it will cease production of Connaught BCG

# Innovation: *Modernization*

## S1602: PRIME

- S1602 redesigned to address drug shortage
- Tokyo-172 strain
  - Japan BCG Laboratory

# PRIME (S1602) Trial Schema



## Primary Objectives

- Compare time to high-grade recurrence between Tokyo and TICE
- Compare time to high-grade recurrence in Tokyo +/- priming

# Innovation:

## S1602: PRIME

- Investigating simple and readily accessible method of immunologic priming
- Adaptation of trial design to real world catastrophe
  - Results could potentially lead to availability of another BCG strain in the U.S.

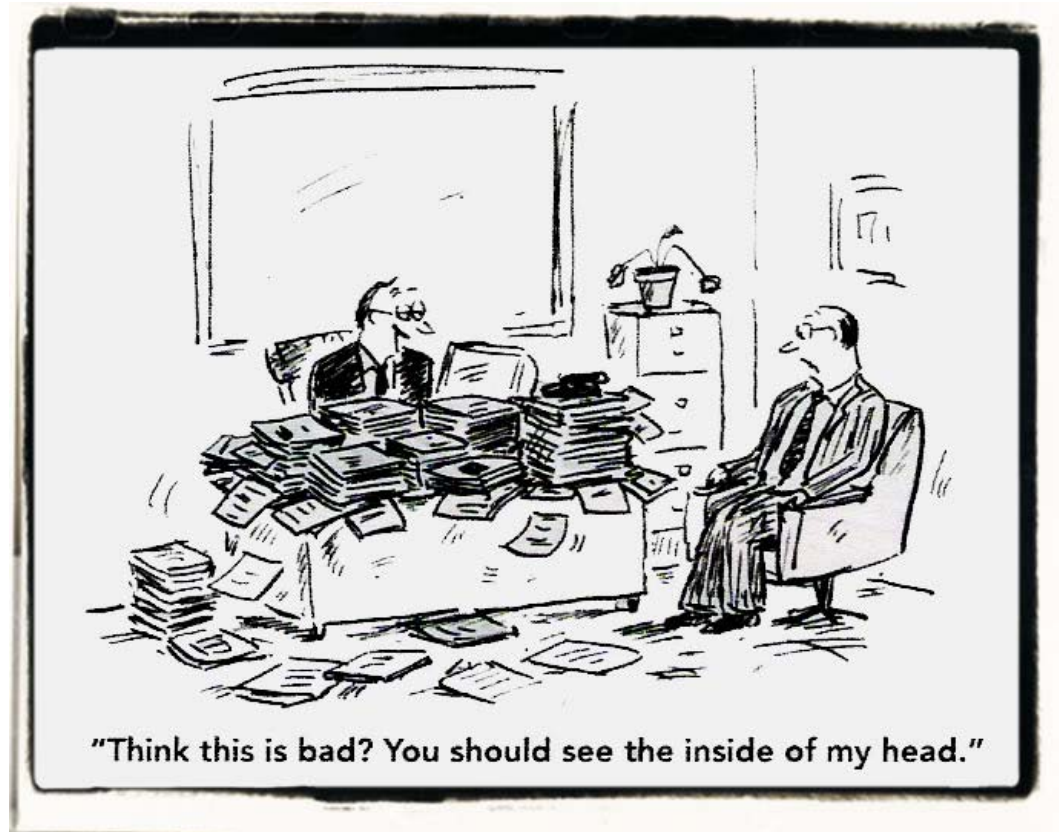
# SWOG Policy #13

## PROTOCOL GUIDELINES

“The goal of centralized protocol development in SWOG is to speed development and standardize quality and format *of the most important studies* in the judgment of the Committee Chair within every research committee of the Group”

# Protocol Development

- How are "the most important" studies chosen?
- Operations Office and Statistical Center are limited resources





# GU Committee “Priority” List 2012

Priority	Prot #	Organ Site	Title	Status	Activation Deadline Date
1.	S1216	Prostate – Adv	Ph III TAK 700 SC: Agarwal	8/27/12: Protocol submitted to CTEP. Tentatively scheduled for CTEP PRC on 9/20/12.	Target Activation: 12/25/12 OEWG Drop Dead: 2/28/14
2.	S1XXX	Bladder	Transformative Trial w/ COXEN. SC: Flaig		
3.	S1XXX	Renal – Adv	Ph III Biomarker Trial to Examine Benefit of Plasma Cytokine & Angiogenic Factors to Predict Response to Targeted Therapy in Frontline Tx of Met RCC.		
4.	S1XXX	Bladder – Adv	Ph III Gem/Paclitaxel/Doxorubicin vs Gem/Carbo for Metastatic or Unresectable		
5.	S1XXX	Bladder – Local	S0337 Follow Up Trial - Assuming S0337 positive: two arm ph III periop gem +/- Cysview powered for a 15% improvement in RFS. Estimate 180-280 per group depending on power. If 0337 negative could do with MMC.		
6.	S1XXX	Bladder - Adv	Rand Ph II: OGX 427 in 2 <sup>nd</sup> Line Bladder		
7.	SXXXX	Prostate – Adv	Transformative Trial		
8.	SXXXX	Prostate – Local	Salvage Protocol		
9.	SXXXX	Renal – Adv	RP2-XL184 in 2 <sup>nd</sup> Line		
10.	SXXXX	Prostate – Adv	OGX-011 MDV 3011		
11.	SXXXX	Prostate – Local	Rand Ph II/III Dutasteride +/- Pulsatile MDV 3100 in Low to Intermediate Risk PCa	7/27/12: Proposal accepted for YIWS.	



# Innovation: *Change*

## GU Committee Protocol Development

- Formal RFA process instituted in 2013
- Applications accepted every ~12-18 months

### **SWOG GU Committee Study Submission Format**

- **Background and significance**
- **Scientific hypothesis**
- **Endpoints**
- **Study design**
- **Magnitude of targeted treatment effect**
- **Eligibility Criteria**
- **Statistical considerations**
- **Letters of support from SWOG investigators**
- **Planned financial support**
- **References**

# Innovation: *Change*

## GU Committee Protocol Development

- Applications reviewed by GU Executive Committee
- Formal scores assigned using NIH system (1-9)
  - Clinical relevance
  - Accrual potential
  - Portfolio “fit”
  - Transformative correlative science
  - Leadership team ability
- Teleconference to finalize selection of top 2-3 concepts

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# GU Committee Priority List 2017

## UPDATE – PROPOSED SWOG-COORDINATED STUDIES

Priority	Prot #	Organ Site	Title	Status	Activation Deadline Date
1.		Prostate	A Multicenter, Phase III Trial of Standard Systemic Therapy (SST) vs SST Plus Surgical Excision of the Primary in Metastatic (M1) Prostate Cancer. SC: Chapin	Received favorable re-review at prostate task force meeting in Nov. Need to expand QOL and TM plans and submit full capsule to triage and then GUSC. QOL call planned for early Jan?	Too early to project.
2.		Bladder	Bladder sparing trial: SC: Singh	Planning meeting at GU-ASCO, stats provided some design considerations	Too early to project

# Innovation: *Change*

## GU Committee Protocol Development

- Improved efficiency of study development
- Improved communication re: workload
- Improved transparency
- Reduced frustration

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noun: innovation

the action or process of innovating.

*synonyms:* change, alteration, revolution, upheaval, transformation, metamorphosis, breakthrough; new measures, new methods, modernization, novelty, newness; creativity, originality, ingenuity, inspiration, inventiveness

a new method, idea, product, etc.

- Metamorphosis – ET/RC committee
- Ingenuity – DART trial symbiosis
- Modernization – PRIME trial adaptation
- Change – GU Committee RFA process

# Other Innovative Studies

- Gastrointestinal Committee
  - **S1513**, Randomized Phase II Study of 2nd Line Therapy with FOLFIRI and PARPi ABT888 in Metastatic Pancreatic Cancer. Dr. Chiorean
- Melanoma Committee
  - **S1607**, A Phase II Study of Combining T-VEC and PD-1 Blockade With Pembrolizumab In Patients With Advanced Melanoma Who Have Progressed On Anti-PD1 Therapy. Dr. Hu-Lieskovan.

Thank You