The role of big data analytics in the evolution of clinical trials

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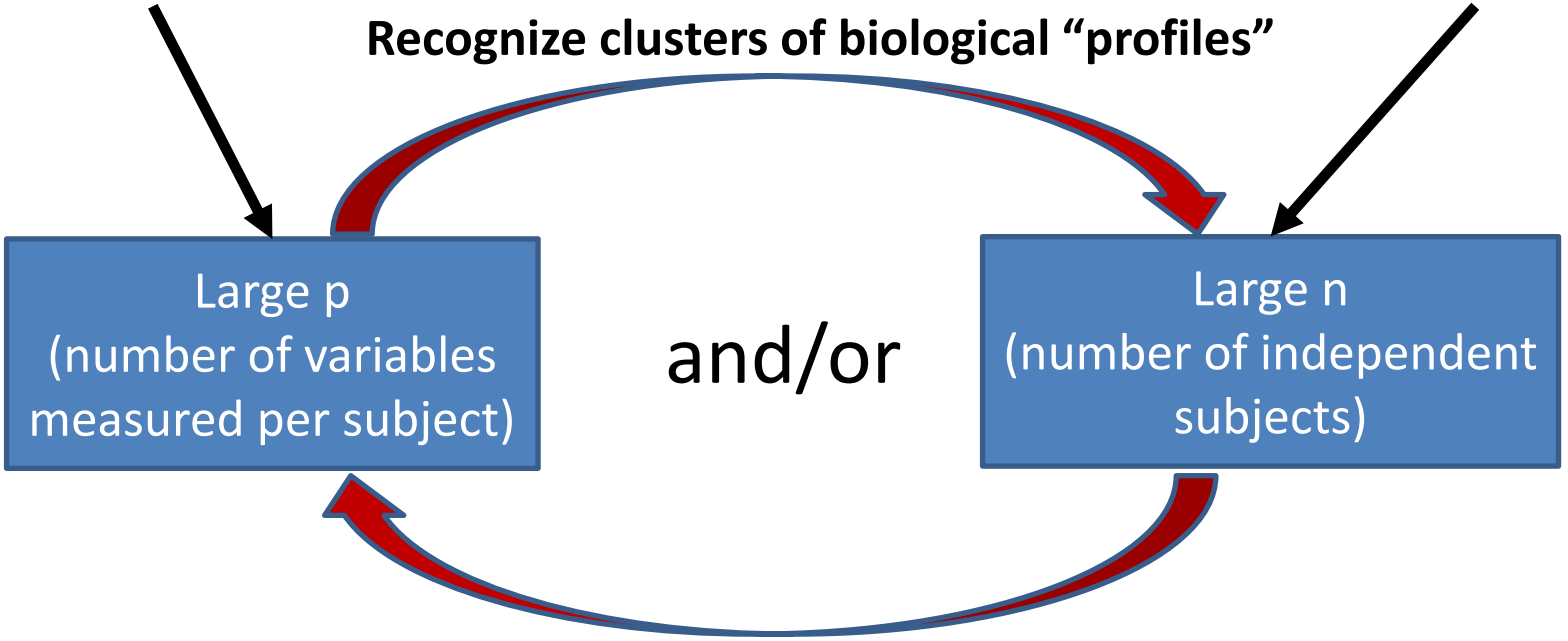
Precision ("personalized") medicine transforms some diseases into a collection of rare diseases

New technologies producing comprehensive sets of measurements (e.g., omics*)

BIG DATA

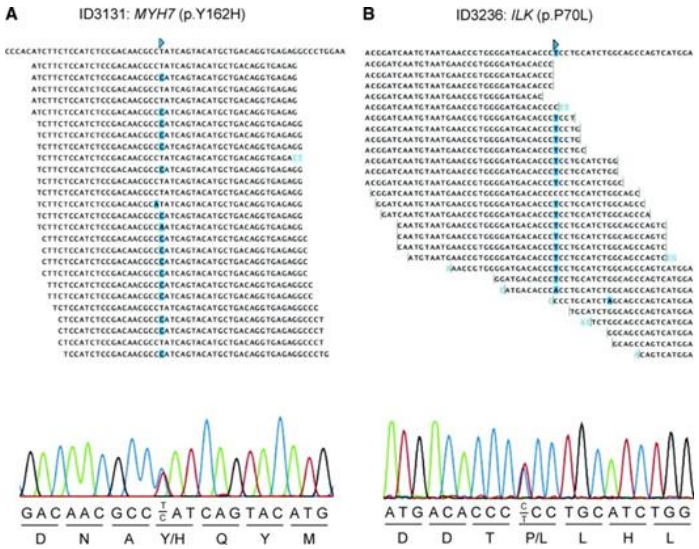
Increasing study size and combining across studies

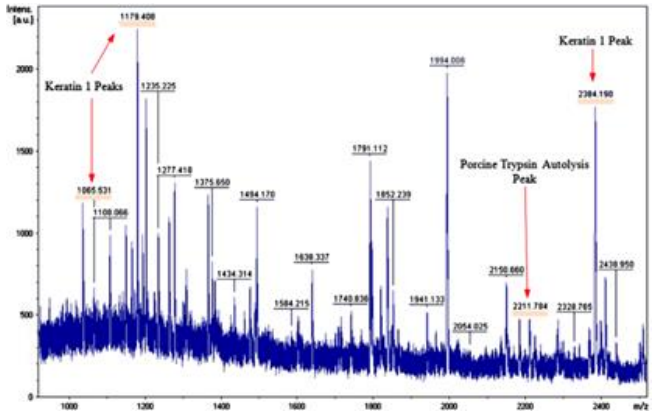


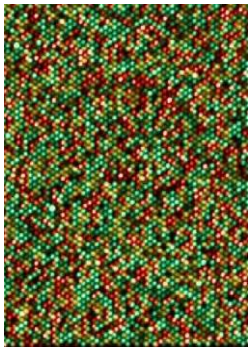
*A term encompassing multiple molecular disciplines, which involve the characterization of global sets of biological molecules such as DNAs, RNAs, proteins, and metabolites

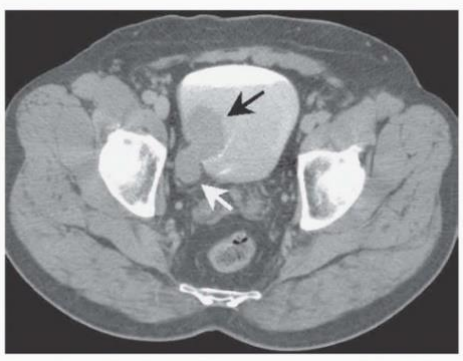
http://www.iom.edu/Reports/2012/Evolution-of-Translational-Omics.aspx

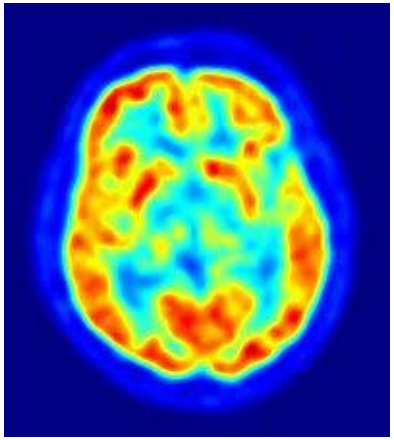
Molecular ("omics") & imaging technologies and wearable devices generate "big data" to characterize disease and host to support precision medicine

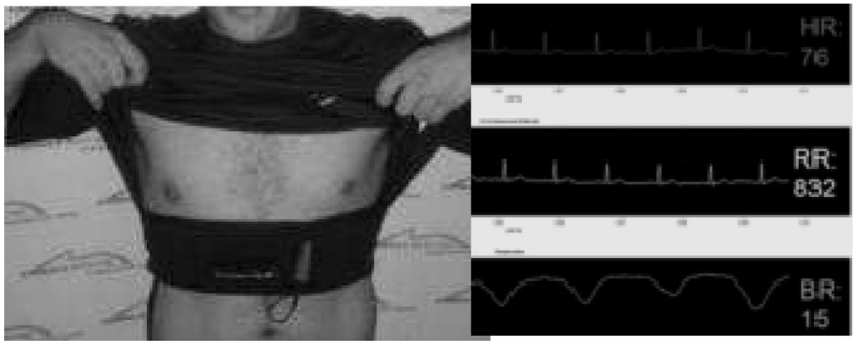




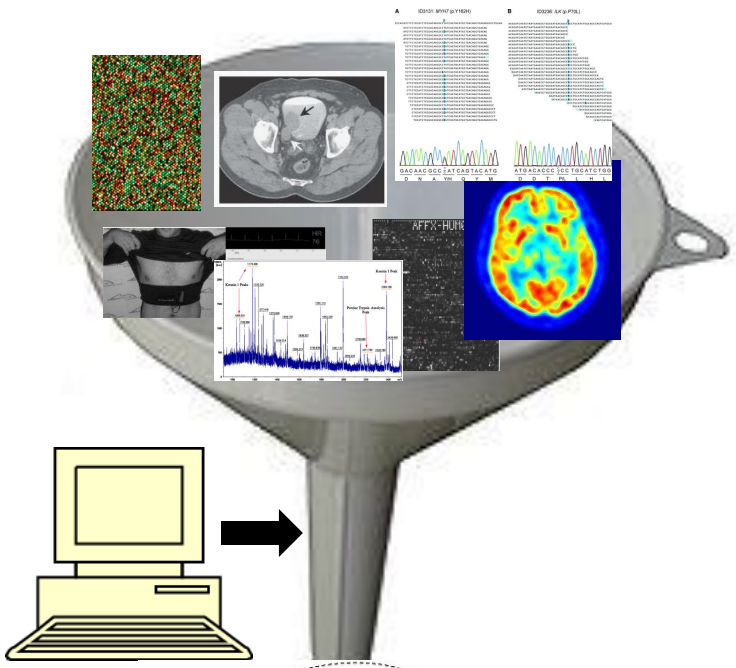


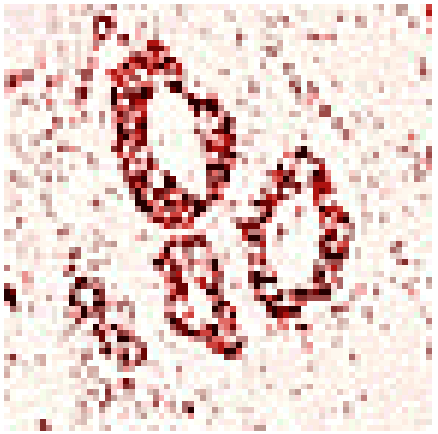


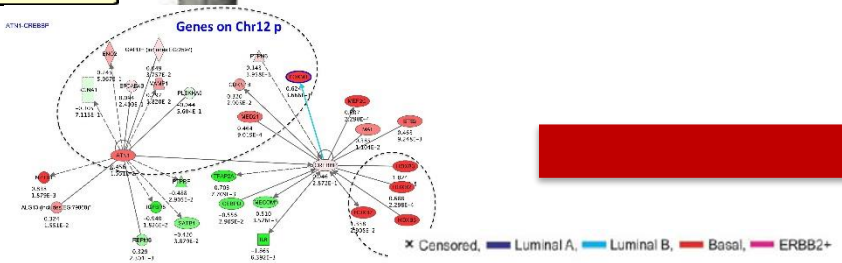


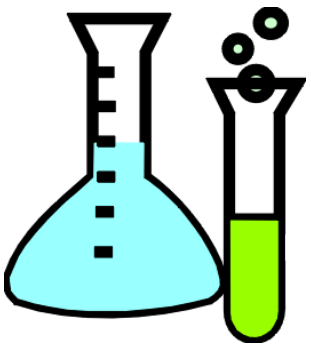


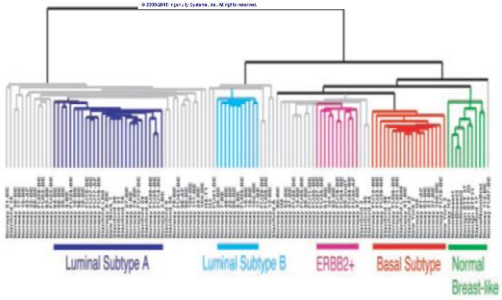
Computational biology and prediction modeling to develop precision medicine approaches

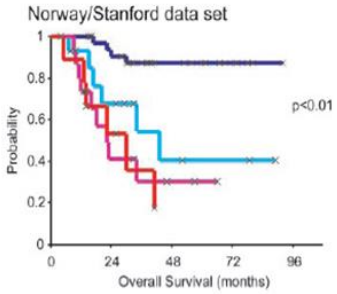












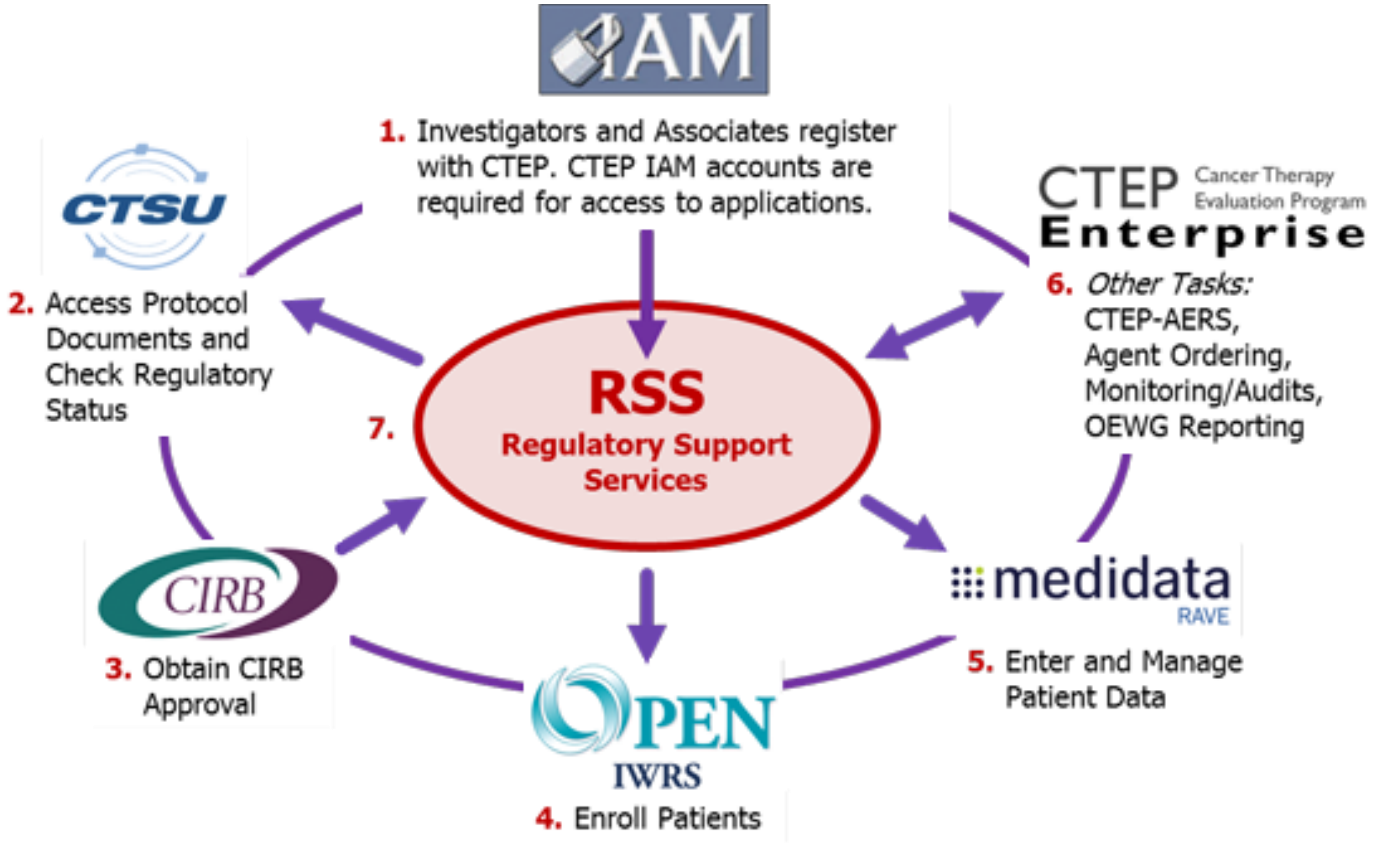
Develop new treatment and prevention approaches

Big data have transformed oncology clinical trials
The U.S. National Cancer Institute experience

- Informatics-enabled NCI clinical trials networks
  - NCI Experimental Therapeutics Clinical Trials Network (ETCTN)
  - NCI National Clinical Trials Network (NCTN)
- Some major omics-based clinical trials involving NCI support
  - Next generation sequencing (large panels)
    - NCI Molecular Analysis for Therapy Choice (NCI-MATCH)
    - Lung-MAP
  - Omics "signatures" (multivariable prediction models or algorithms)
    - Oncotype DX – a success story
    - Cautionary note on common failures
- Exceptional Responder Initiative
- NCTN Data Archive
- NCI NCTN Specimen Navigator
- Summary remarks

U.S. National Cancer Institute Clinical Trials System

Informatics systems are critical to the re-designed NCI clinical trials enterprise



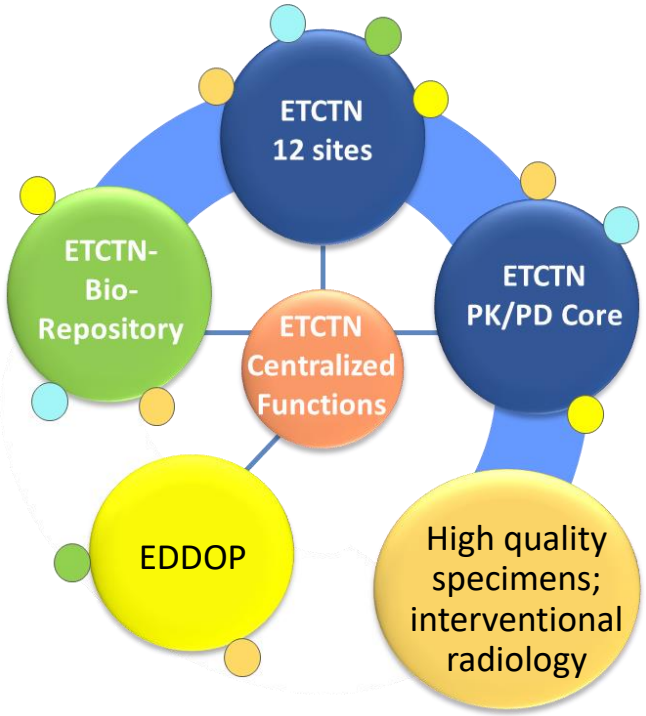
https://ctep.cancer.gov/initiativesPrograms/etctn.htm

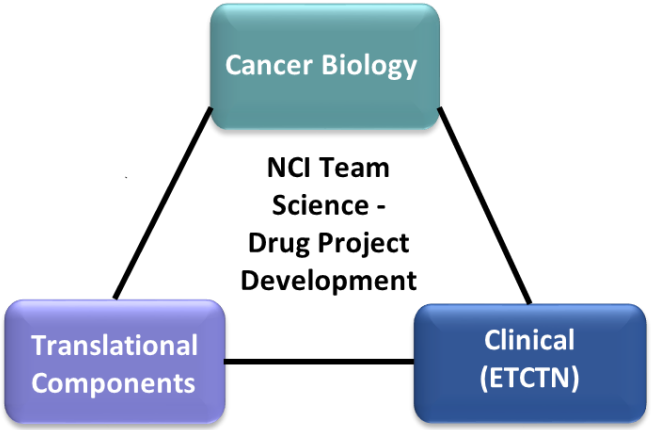
U.S. National Cancer Institute Clinical Trials System

NCI Experimental Therapeutics Clinical Trials Network (ETCTN)

Phase I and some phase II trials (often nonrandomized, fairly small)

- Affiliated organizations
- Centralized functions for operational efficiencies & optimized use of scientific innovations
- 1 biorepository (U24)
- Early drug development opportunities programs in NCI CCs (EDDOP) for accrual and leadership



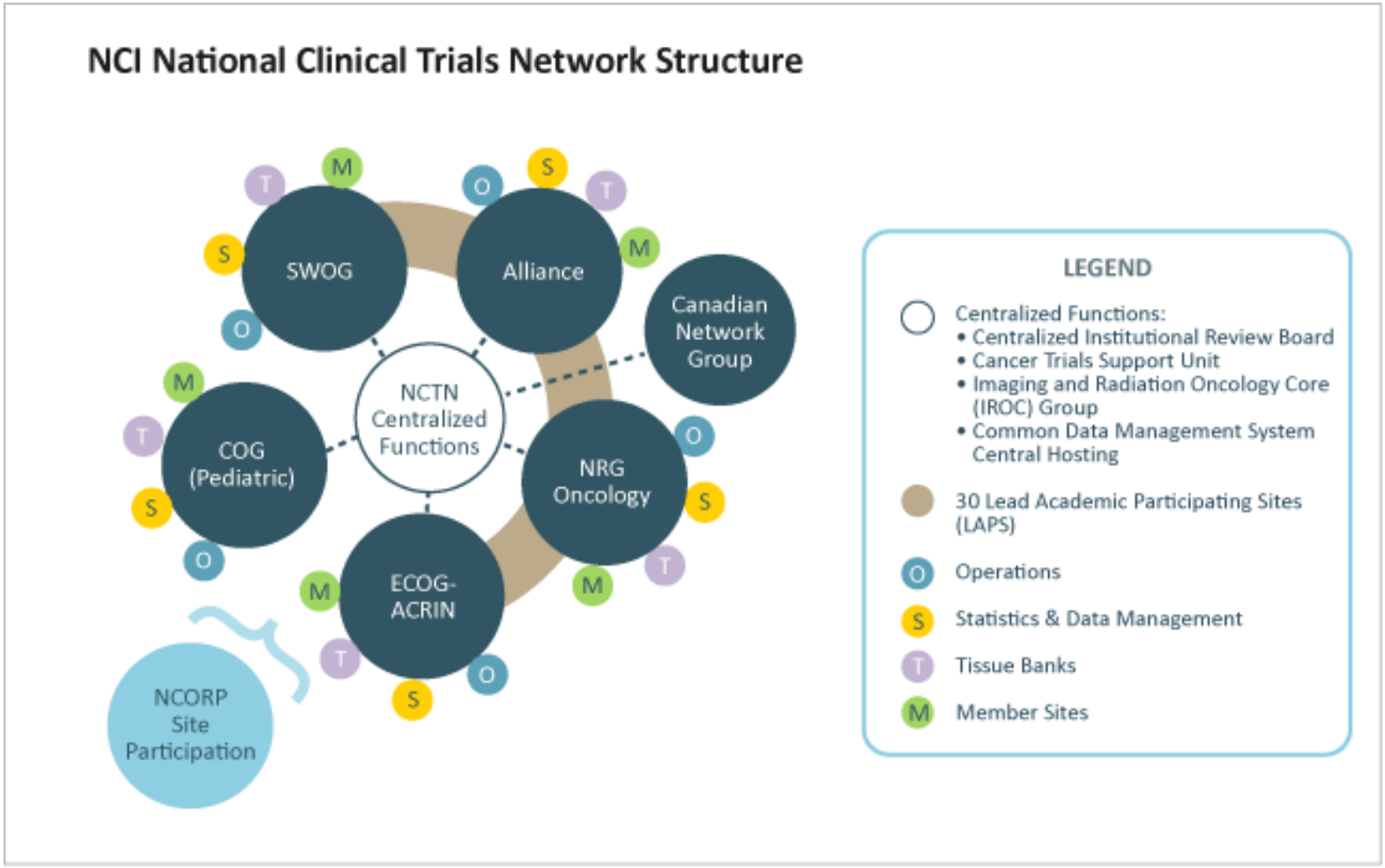


https://ctep.cancer.gov/initiativesPrograms/etctn.htm

U.S. National Cancer Institute Clinical Trials System

NCI National Clinical Trials Network (NCTN)

Phase III and some phase II (mostly randomized, generally large)



https://www.cancer.gov/research/areas/clinical-trials/nctn

NCI-MATCH trial

A multi-histology umbrella basket trial

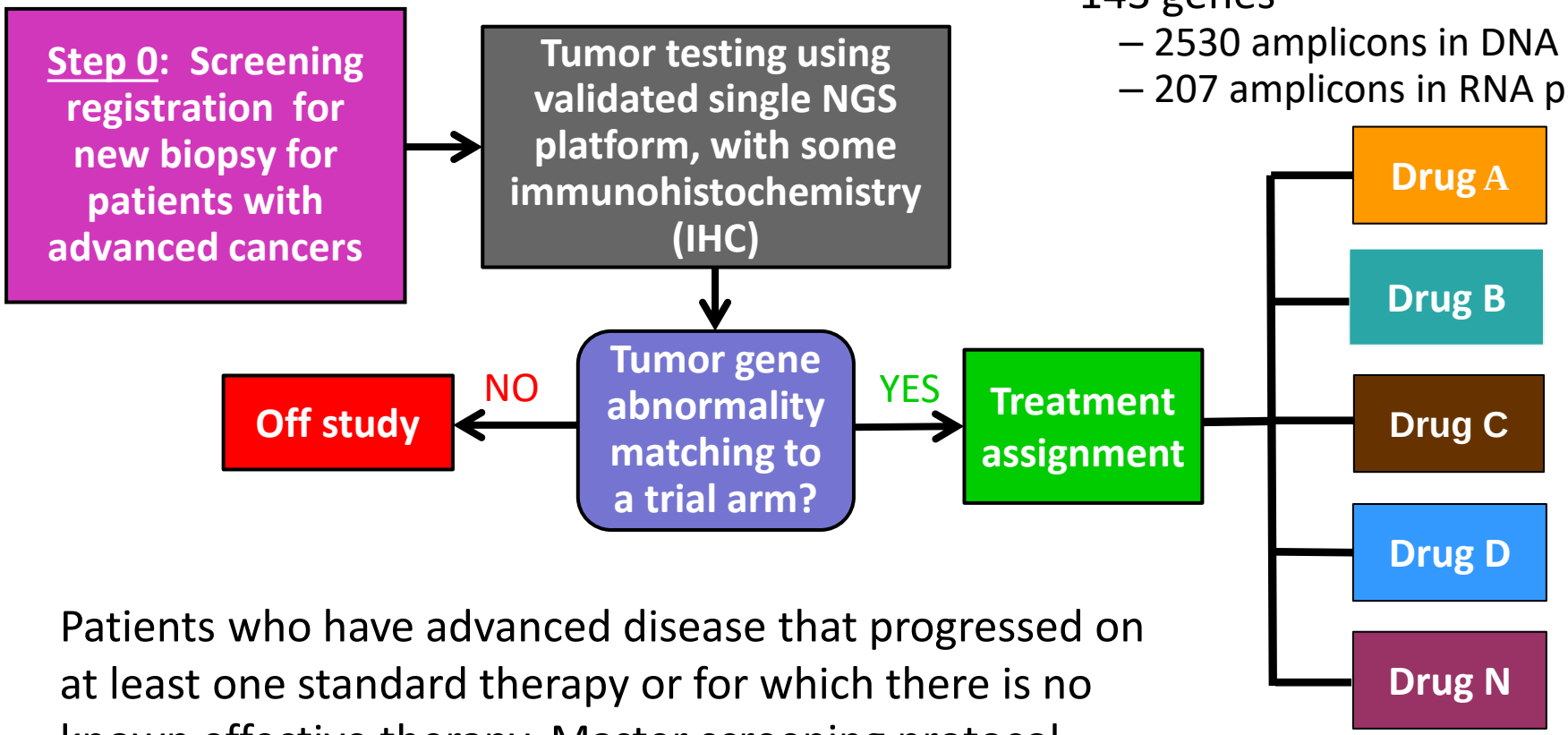
Objectives

- To determine whether matching certain drugs or drug combinations in adults whose tumors have specific gene abnormalities will effectively treat their cancer, regardless of the cancer type
- **This is a signal-finding trial;** treatments that show promise can advance to larger, more definitive trials

NCI-MATCH trial

Led by ECOG-ACRIN for NCI National Clinical Trials Network (NCTN)

Overarching Screening Protocol



NGS Assay (version 1)

- 143 genes
  - 2530 amplicons in DNA panel
  - 207 amplicons in RNA panel

Patients who have advanced disease that progressed on at least one standard therapy or for which there is no known effective therapy. Master screening protocol directing to multiple biomarker-based mixed histology single arm phase II trial sub-protocols.

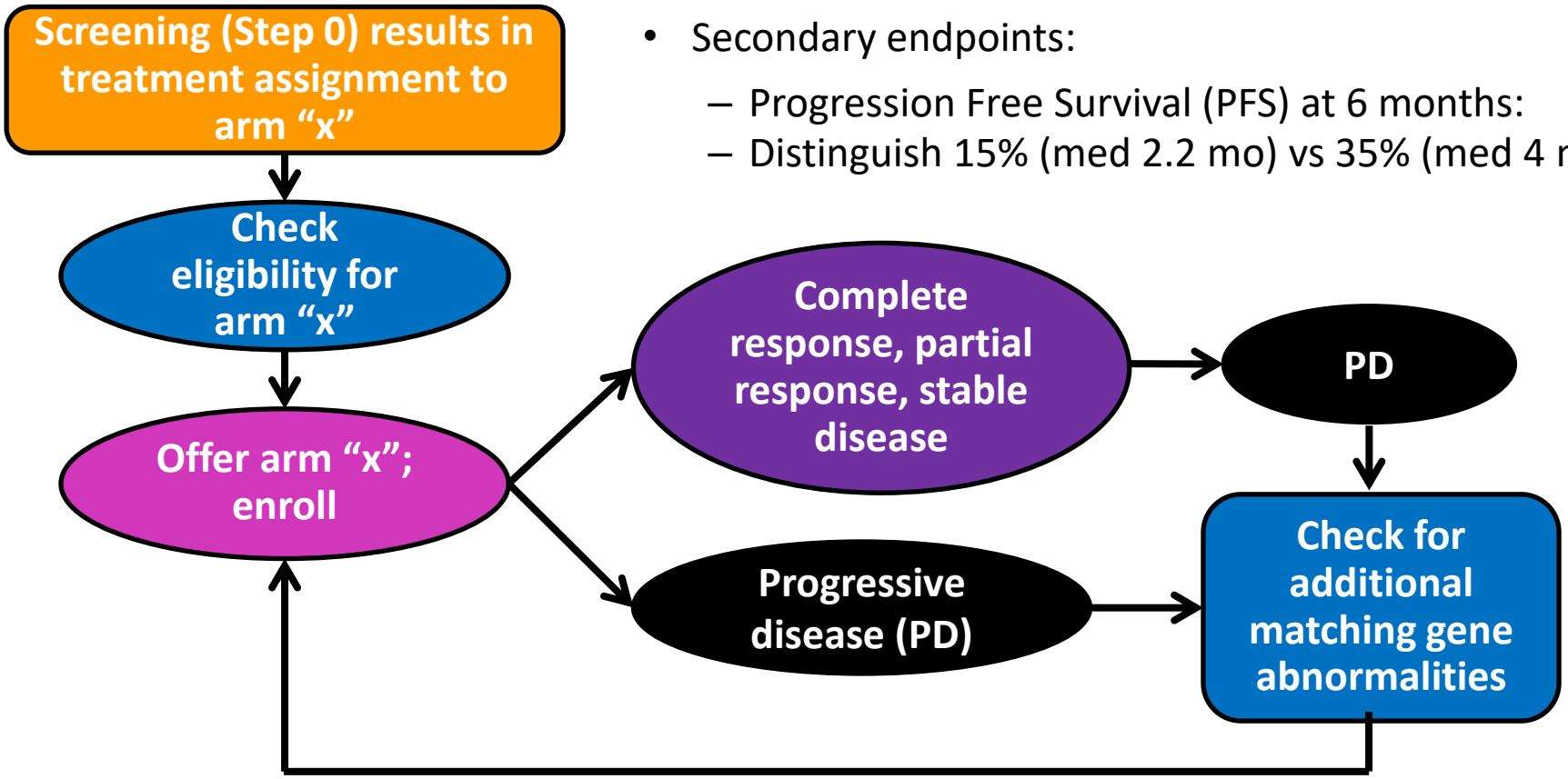
NCI-MATCH trial specific aims

- **Primary:** To evaluate the proportion of patients with objective response (OR) to targeted study agent(s)
- **Secondary:** To evaluate the proportion of patients with PFS >= 6 months of treatment with targeted study agent(s), time to progression (TTP), toxicity
- **Exploratory:**
  - Frequency of a wide array of actionable mutations in refractory cancer patients, across tumor histologies
  - Plan for whole exome sequencing and RNA sequencing on specimens from patients who enrolled on a treatment arm
    - Potentially, influence of co-mutations and activations of other molecular pathways on response/six-month PFS
    - Tumor mutation burden
  - Potentially, influence of immune response

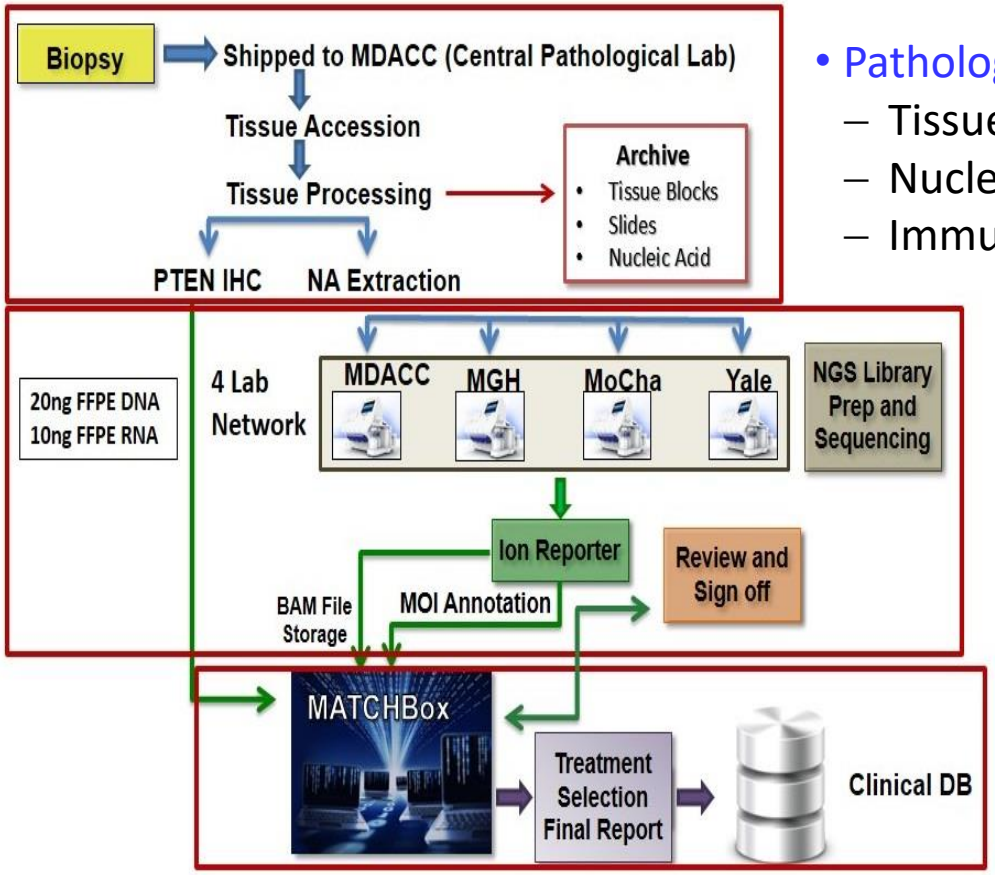
NCI-MATCH design for each treatment arm
(Single-Arm, single stage Phase II)

- N=35 per arm (expect 31 eligible)
- Minimum 8 months follow-up per patient

- Primary endpoint: ORR, H_0: ≤5% vs H_a: 25%
  - Reject H_0 if >= 5/31 responses (~16%)
  - Type I error 1.8% / arm (one-sided)
  - Power 92%
- Secondary endpoints:
  - Progression Free Survival (PFS) at 6 months:
  - Distinguish 15% (med 2.2 mo) vs 35% (med 4 mo)



NCI-MATCH assay workflow



- Pathology
  - Tissue accession & processing
  - Nucleic acid extraction
  - Immunohistochemical (IHC) assays (e.g., PTEN)
- Next generation sequencing assay (vers. 1)*
  - 4-laboratory network - identical & reproducible methods
  - 143 genes
  - 2530 amplicons in DNA panel
  - 207 amplicons in RNA panel

*Now on assay vers. 3

- Bioinformatic and clinicopathologic data review
  - Identify MOIs & aMOIs
  - Apply genomic treatment arm assignment rules
  - Apply arm-specific clinico-pathologic inclusion & exclusion criteria
  - Treatment arm assignment & enrollment (if consent)

MOI = Mutation of Interest
aMOI = actionable MOI (targeting treatment arm available in MATCH)

MATCH bioinformatics: "MATCHBox"

Centrally hosted informatics system* developed for trial

- Enable examination of genomic results along with clinical data in order to make treatment assignments
  - Receive VCF (variant) files uploaded by laboratories
  - Filter variants down to MOIs (mutations of interest in MATCH Oncomine® Cancer Panel & other)
  - Send MOI list back to CLIA laboratory for review and sign-off
  - Identify *tentative* treatment eligibility based on actionable MOIs (aMOIs) and preliminary clinical & pathologic data
    - Apply tiebreaker rules if needed (using LOE for aMOIs & other arm criteria)
- CLIA report of MOIs sent to enrolling clinician
- Final eligibility for selected treatment arm determined
- Enroll patient on treatment arm (if consent)

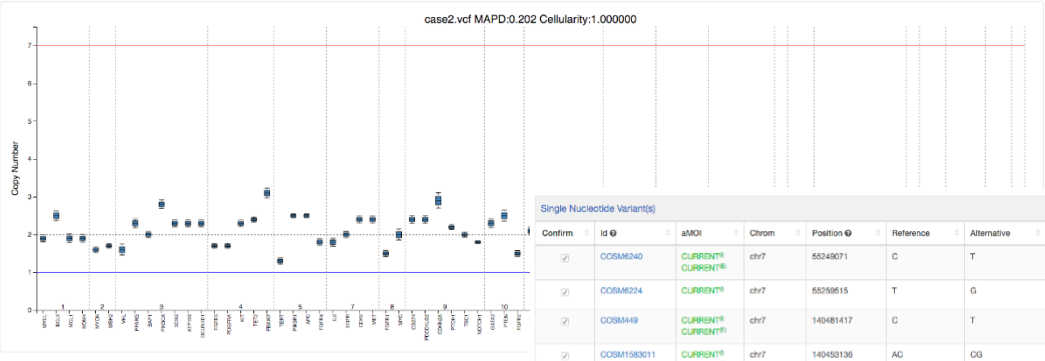
*NCI Center for Bioinformatics & Information Technology (CBIIT)

MATCHBox processing

Variant (vcf) file

#CHROM POS ID REF ALT QUAL FILTER INFO FORMAT
Mock-rep1-DNAchr1 11184539 . C <CNV> 100.0 PASS
PRECISE=FALSE;SVTYPE=CNV;END=65312407;LEN=54127868;NUMTILES=26;CDF_MAPD=0.025000:1.811614,0.050000:1.825542,0.100000:1.841732,0.200000:1.861530,0.250000:1.869107,0.500000:1.900000,0.750000:1.931404,0.800000:1.939265,0.900000:1.960111,0.950000:1.977495,0.975000:1.992698;CDF_LD=0.025000:1.851119,0.050000:1.854235,0.100000:1.860468,0.200000:1.872932,0.250000:1.879164,0.500000:1.910325,0.750000:1.941485,0.800000:1.947717,0.900000:1.995053,0.950000:2.022631,0.975000:2.036420;REF_CN=2;CI=0.05:1.82554,0.95:2.02263;RAW_CN=1.9 GT:GQ:CN ./.:0:1.9chr1 11184568 MCH4 G A 201.94 PASS
AF=0;AO=0;DP=1542;FAO=0;FDP=1534;FR=.,REALIGNEDx0.01361;FRO=1534;FSAF=0;FSAR=0;FSRF=1006;FSRR=528;FWDB=-9.64204E-4;FXX=0.00583276;HRUN=1;HS;LEN=1;MLLD=202.909;QD=0.526561;RBI=0.00632446;REFB=-3.87243E-7;REVB=-0.00625053;RO=1535;SAF=0;SAR=0;SRF=1001;SRR=534;SSEN=0;SSEP=0;SSSB=0;STB=0.5;STBP=1;TYPE=snp;VARB=0;OID=MCH4;OPOS=11184568;OREF=G;OALT=A;OMAPALT=A;FUNC=[{'transcript':'NM_004958.3','gene':'MTOR','location':'exonic','exon':'47'}] GT:GQ:DP:FDP:RO:FRO:AO:FAO:AF:SAR:SAF:SRF:SRR:FSAR:FSAF:FSRF:FSRR
0/0:99:1542:1534:1535:1534:0:0:0:0:0:1001:534:0:0:1006:528chr1 11184570 COSM3965698 A G
187.65999999999997 PASS

Copy number variants (CNVs)



Variant report

Single Nucleotide Variant(s)

Confirm	Id	aMOI	Chrom	Position	Reference	Alternative	Allele Freq	Func Gene	Oncomine Variant Class	Exon	Function	HGVS	Read Depth	Transcript	Protein
☑	COSM6240	CURRENT[1] CURRENT[2]	chr7	55249071	C	T	0.1968	EGFR	-	2	-	-	862	NR_047551.1	-
☑	COSM6224	CURRENT[1]	chr7	55259515	T	G	0.8412	EGFR	-	21	-	-	2198	NM_005228.3	-
☑	COSM449	CURRENT[1] CURRENT[2]	chr7	140481417	C	T	0.7732	BRAF	-	11	-	-	2200	NM_004333.4	-
☑	COSM1583011	CURRENT[1] CURRENT[2]	chr7	140453136	AC	CG	0.2268	BRAF	-	15	-	-	500	NM_004333.4	-

Indel(s)

Confirm	Id	aMOI	Chrom	Position	Reference	Alternative	Allele Freq	Func Gene	Oncomine Variant Class	Exon	Function	HGVS	Read Depth	Transcript	Protein
☑	COSM21599	-	chr17	7578505	GGGCAGGTCTTG	-	0.7294	ERBB2	-	5	-	-	845	NM_000546.5	-
☑	COSM22189	CURRENT[1] CURRENT[2]	chr22	30035190	TTC	-	0.2000	NF2	deleterious	-	-	-	1695	-	-

Copy Number Variant(s)

Confirm	Id	aMOI	Chrom	Position	Raw CN	CN	CI 5%	CI 95%
☑	ERBB2	CURRENT[1]	chr17	37845133	7.5	7.5	1.44331	1.55891

Gene Fusion(s)

Confirm	Id	aMOI	Gene 2	Gene 2 Count	Gene 1	Gene 1 Count	Annotation
☑	SDC4-ROS1.S4R34.COSF1280	CURRENT[1]	ROS1	120	SDC4	120	COSF1280

MATCHBox Processing

Treatment assignment report

Patient Sequence Number	10370
Patient Status	ON_TREATMENT_ARM
Patient Step Number	1
Biopsy Sequence Number	N-15-00005
Molecular Sequence Number	10370_1000_N-15-00005
Analysis Id	testjob1
Assignment Generation Date	August 4, 2015 4:49 PM GMT
Assignment Confirmation Date	August 4, 2015 4:59 PM GMT
Assignment Sent to ECOG Date	-
Assignment Received from ECOG Date	-
Variant Report	Variant Report
Patient Concordance	YES
Variant Report aMOI(s)	COSM6240, COSM6224, COSM449, COSM1583011, COSM22189, ERBB2, SDC4-ROS1.S4R34.COSF1280

Selected Treatment Arm: EAY131-G (2015-08-06)

The patient and treatment arm match on variant identifier [SDC4-ROS1.S4R34.COSF1280]. The variant's level of evidence for the treatment arm is 2. The patient was selected for this treatment arm because it has the highest level of evidence of 2.

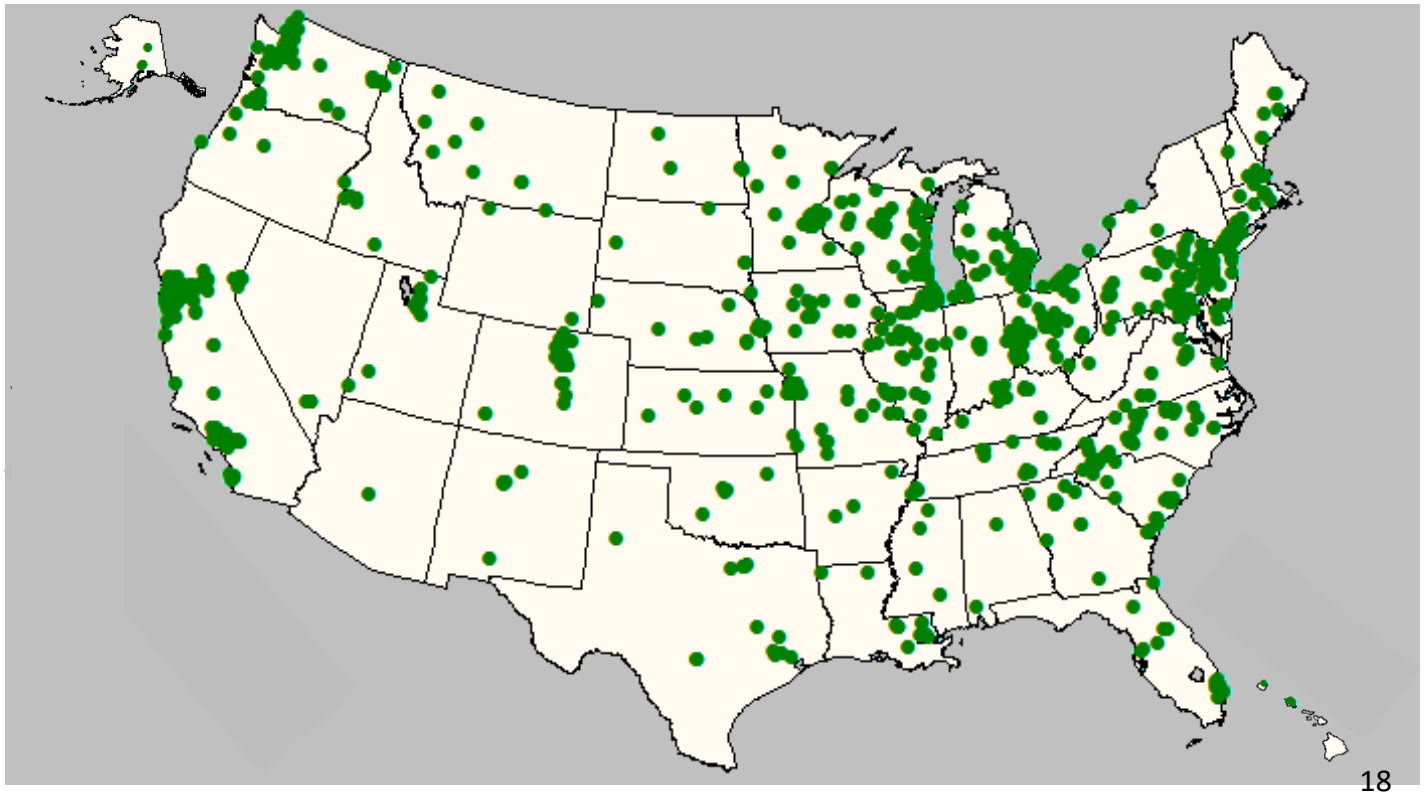
Treatment Arm	Reason
1 - NO VARIANT MATCH	
EAY131-F (2015-08-06)	The patient contains no matching variant.
EAY131-V (2015-08-06)	The patient contains no matching variant.
2 - RECORD BASED EXCLUSION	
EAY131-Q (2015-08-06)	The patient is excluded from this treatment arm because the patient has disease(s) Adenocarcinoma - esophagus.
EAY131-H (2015-08-06)	The patient is excluded from this treatment arm because the patient has taken drug(s) [["Name: Dabrafenib Mesylate(Tafinlar) ID: 763760"]].
EAY131-A (2015-08-06)	The patient is excluded from this treatment arm because the patient has taken drug(s) [["Name: Afatinib\r(BIBW2992) ID: 750691"]].
EAY131-B (2015-08-06)	The patient is excluded from this treatment arm because the patient has taken drug(s) [["Name: Afatinib\r(BIBW2992) ID: 750691"]].
3 - NOT ELIGIBLE	
EAY131-E (2015-08-06)	The patient is excluded from this treatment arm because the patient is not eligible.
4 - LEVEL OF EVIDENCE TIE BREAKER	
EAY131-U (2015-08-06)	The patient and treatment arm match on non-hotspot variant [(ID: COSM22189,GENE: NF2,OVA: deleterious,EXON: -,FUNC: -,PROTEIN: -)]. The variant's level of evidence for the treatment arm is 3. The patient was not selected for this treatment arm because its level of evidence is 3 and is lower than the one chosen.
EAY131-R (2015-08-06)	The patient and treatment arm match on variant identifier [COSM449]. The variant's level of evidence for the treatment arm is 3. The patient was not selected for this treatment arm because its level of evidence is 3 and is lower than the one chosen.
5 - SELECTED	
EAY131-G (2015-08-06)	The patient and treatment arm match on variant identifier [SDC4-ROS1.S4R34.COSF1280]. The variant's level of evidence for the treatment arm is 2. The patient was selected for this treatment arm because it has the highest level of evidence of 2.

Brief history of NCI-MATCH

12 Aug 2015	Opened with 10 treatment arms; goal to screen 3000 patients	
Nov 2015	Pause in enrollment for pre-planned feasibility assessment at ~500 patients screened; 795 patients screened in 3 months	Accrual reached nearly 150 patients *per week*; expected 50 *per month*!
May 2016	Reopen with 24 treatment arms and expanded laboratory capacity	
Late 2016	Increased screening goal to 6000 patients; expanded eligibility to include myeloma	
March 2017	Expanded to 30 treatment arms	
Spring 2017	Began transition to referrals from outside laboratories	
July 2017	Completed central screening of ~6000 patients	Maximum accrual reached nearly 2 years ahead of schedule!
Present	Continue accrual to “rare variant” arms with referrals from 4 outside laboratories	Approximately 30 outside laboratories have expressed interest to join

NCI-MATCH success in bringing genomics to the community

- The pace of accrual, and the trial's availability at over 1100 sites, reflects the broad interest in the promise of genomics and the ability of such a trial to deliver on that promise
- At least one patient was screened in every state, the District of Columbia, and Puerto Rico



NCI-MATCH 30 treatment arms

By prevalence rate of gene abnormality

Arm	Variant	Prevalence Rate %	Drug
I	PIK3CA	3.47	Taselisib
W	FGFR	2.86	AZD4547
Z1I	BRCA1 or BRCA2	2.79	AZD1775
P	PTEN loss	1.93	GSK2636771
Z1A	NRAS	1.90	Binimetinib
S1	NF1	1.77	Mekinist™
N	PTEN	1.75	GSK2636771
Z1D	dMMR status	1.51	Opdivo®
Q	HER2 amplif.	1.49	Kadcyla®
J	HER2 amplif.	1.49	Herceptin® Perjeta®
Z1C	CDK4 or CDK6	1.36	Ibrance®
M	TSC1 or TSC2	1.11	TAK-228
B	HER2 activating	1.04	Gilotrif®
Z1B	CCND1/2/3	0.84	Ibrance®
R	BRAF fusions	0.80	Mekinist™

Arm	Variant	Prevalence Rate %	Drug
Y	AKT	0.77	AZD5363
H	BRAF V600 E/K	0.69	Taflinar® Mekinist™
U	NF2 loss	0.69	Defactinib (VS-6063)
C2	MET exon 14	0.61	Xalkori®
C1	MET amplif.	0.51	Xalkori®
T	SMO/PTCH1	0.42	Erivedge®
L	mTOR	0.31	TAK-228
S2	GNAQ/GNA11	0.16	Mekinist™
E	EGFR T790M	0.11	AZD9291
V	cKIT	0.11	Sutent®
Z1E	NTRK	0.10	Larotrectinib
G	ROS1	0.05	Xalkori®
A	EGFR activating	0.05	Gilotrif®
F	ALK	0.03	Xalkori®
X	DDR2	0.00	Sprycel®

Highlighted in yellow are “rare variant” arms (prevalence ≤ 1.5%)

NCI-MATCH central screening by cancer type

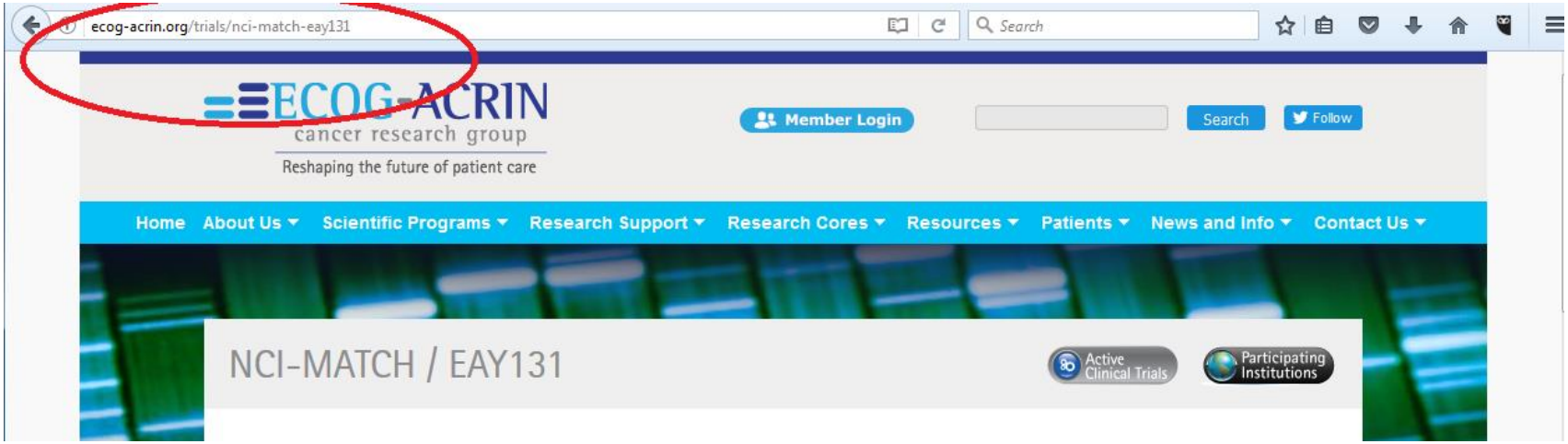
Less Common Disease Type	% of Total Screened (N=5560)
Ovarian	9.5
Uterine	6.2
Pancreas	6.1
Sarcoma	4.6
Head and Neck	3.9
Neuroendocrine	3.3
Gastroesophageal	3.2
Cholangiocarcinoma	2.8
Liver and Hepatobiliary w/o Cholangio.	1.9
Central Nervous System	1.7
Bladder/Urinary Tract	1.6
Cervical	1.6
Small Cell Lung	1.4
Melanoma	1.4
Kidney	1.2
Anal	0.8
Mesothelioma	0.8
Lymphoma	0.7
Myeloma	0
Other	9.7
Less Common Cancers	**62.5%**

Common Disease Type	% of Total Screened (N=5560)
Colorectal	15.3
Breast	12.4
Non-Small cell lung	7.3
Prostate	2.5
Common Cancers	**37.5%**

Coordinated recruitment/referral with **DART**: **D**ual **a**nti-CTLA-4 and anti-PD-1 blockage in **r**are **t**umors trial (S1609). Patients with rare tumors registered to NCI-MATCH but not qualifying for one its subarms (non-match) or who qualified and progressed on matched therapy, were referred to DART.

Goal of 25% *FAR EXCEEDED*

NCI-MATCH accrual per arm is posted publicly



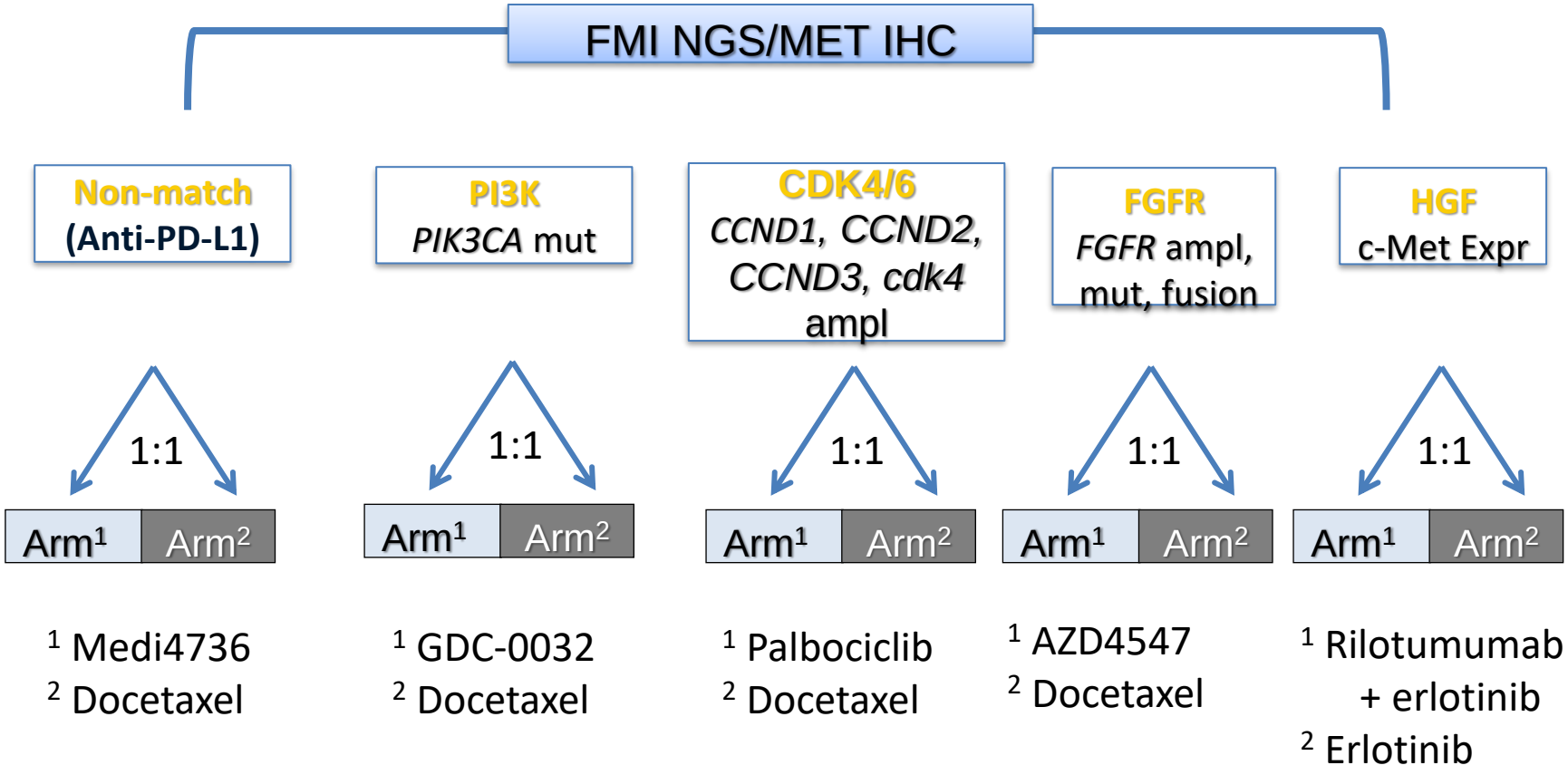
Study/ID	Description	Accrual Goal (Actual)	Date Activated
EAY131-H	Taflinar® (dabrafenib) and Mekinist™(trametinib) BRAF V600E or V600K mutations (0.69% frequency) Disease Exceptions: colorectal cancer, melanoma, thyroid cancer, hepatitis b (HBV) or C (HCV), or history of interstitial lung disease	35 (25)	08/12/2015

ecog-acrin.org/trials/nci-match-eay131

(also the source of many of the slides in this presentation)

Lung-MAP: Version 1

Lung-MAP (SWOG S1400) is a multi-drug, multi-sub-study, biomarker-driven squamous cell lung cancer clinical trial that uses state-of-the-art genomic profiling (Foundation Medicine) to match patients to sub-studies testing investigational treatments that may target the genomic alterations, or mutations, found to be driving the growth of their cancer. (https://www.lung-map.org)

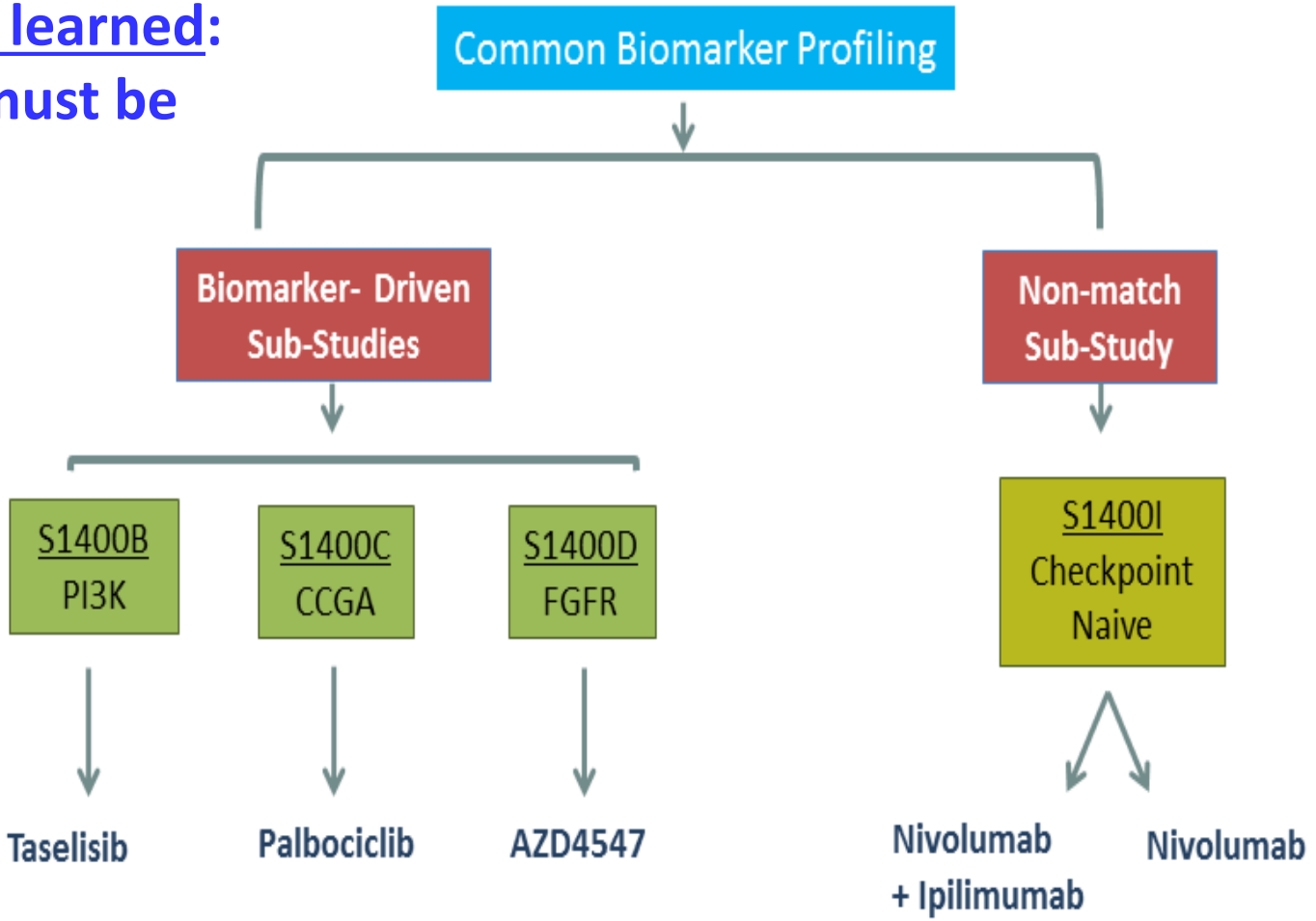


Each sub-study is a randomized phase II/III trial

Lung-MAP TRIAL – Version 2

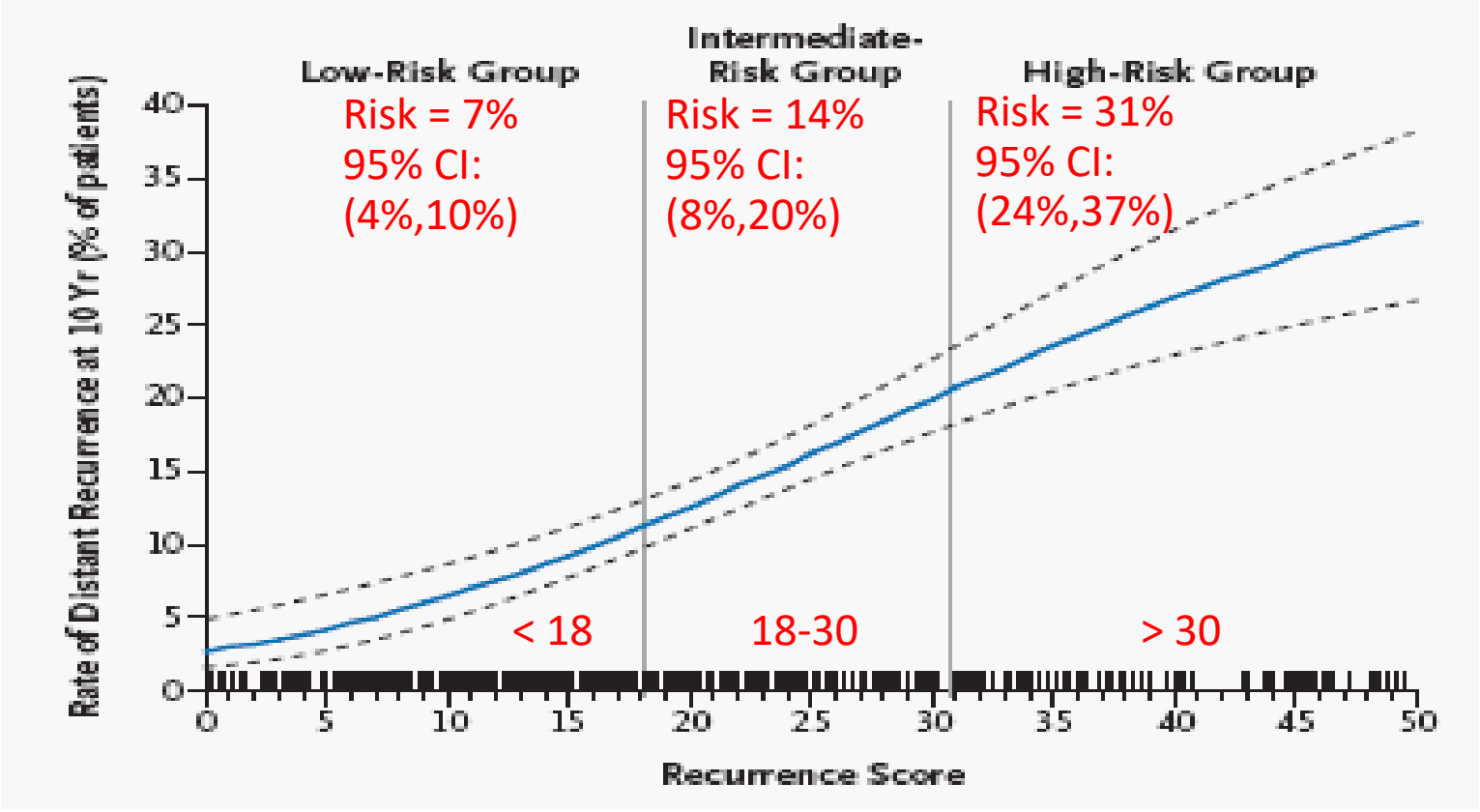
Design change required after approval of nivolumab changed standard of care for advanced squamous NSCLC. Arms are being added as new investigational targeted agents become available for this patient population.

Lesson learned: Trials must be agile!



Oncotype DX recurrence score (RS) is prognostic in tamoxifen treated ER+ breast cancer

Validation* of RS on NSABP B-14 Tamoxifen Arm



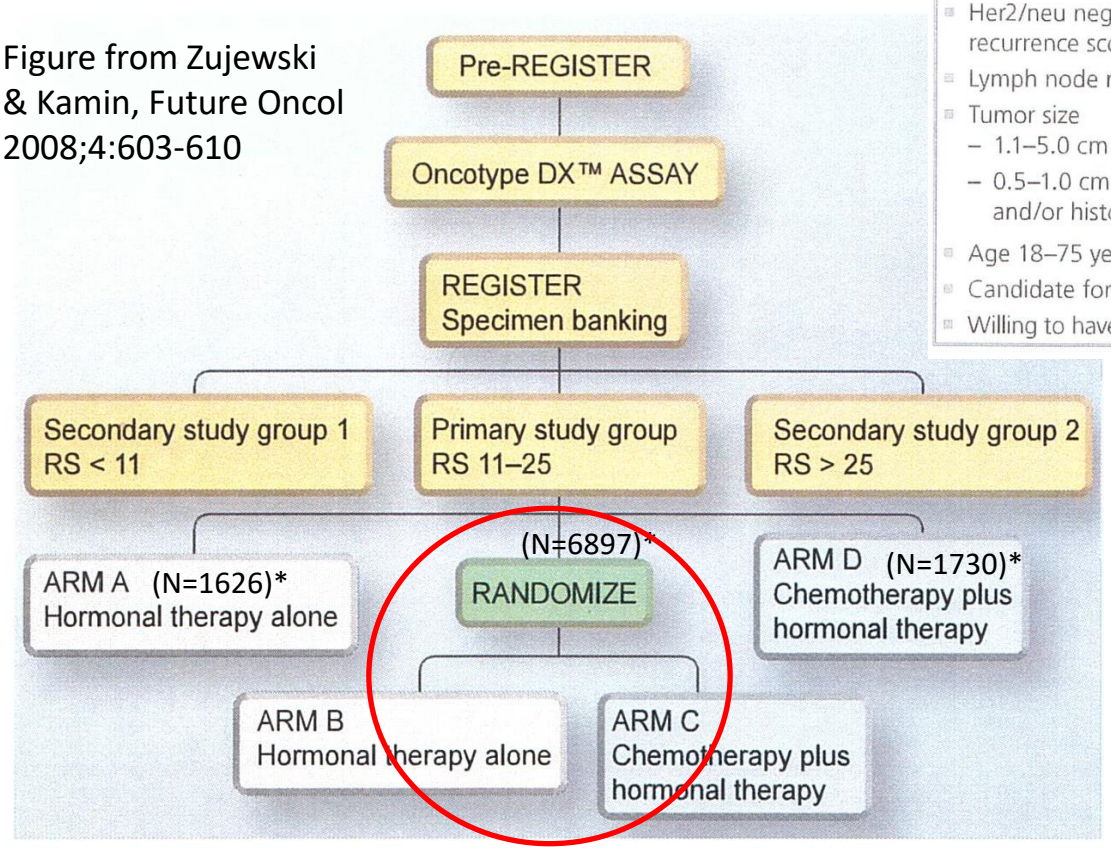
- 21-gene RT-PCR based gene expression assay
- FFPE tissues

Figure 4 from Paik et al., *N Engl J Med* 2004;351:2817-26

*Conducted using stored specimens but following a rigorous prospective-retrospective study design and analysis plan

TAILORx TRIAL

Figure from Zujewski & Kamin, Future Oncol 2008;4:603-610



Box 1. Patient eligibility criteria.

- Estrogen-receptor- and/or progesterone-positive breast cancer
- Her2/neu negative (re: most Her2-positive disease associated with high recurrence score)
- Lymph node negative (by sentinel node or axillary dissection)
- Tumor size
  - 1.1–5.0 cm
  - 0.5–1.0 cm plus unfavorable histologic features (intermediate or poor nuclear and/or histologic grade, or lymphovascular invasion)
- Age 18–75 years
- Candidate for systemic chemotherapy
- Willing to have treatment assigned or to be randomized based upon Oncotype DX™

Low Risk Group Results

N=1626*

5-year rates (95% CI):

Inv DFS = 93.8% (92.4-94.9)

Free of Dist Rec = 99.3% (98.7-99.6)

Free of any Rec = 98.7% (97.9-99.2)

Overall Surv = 98.0% (97.1-98.6)

*N = no. eligible of 10253 total eligible

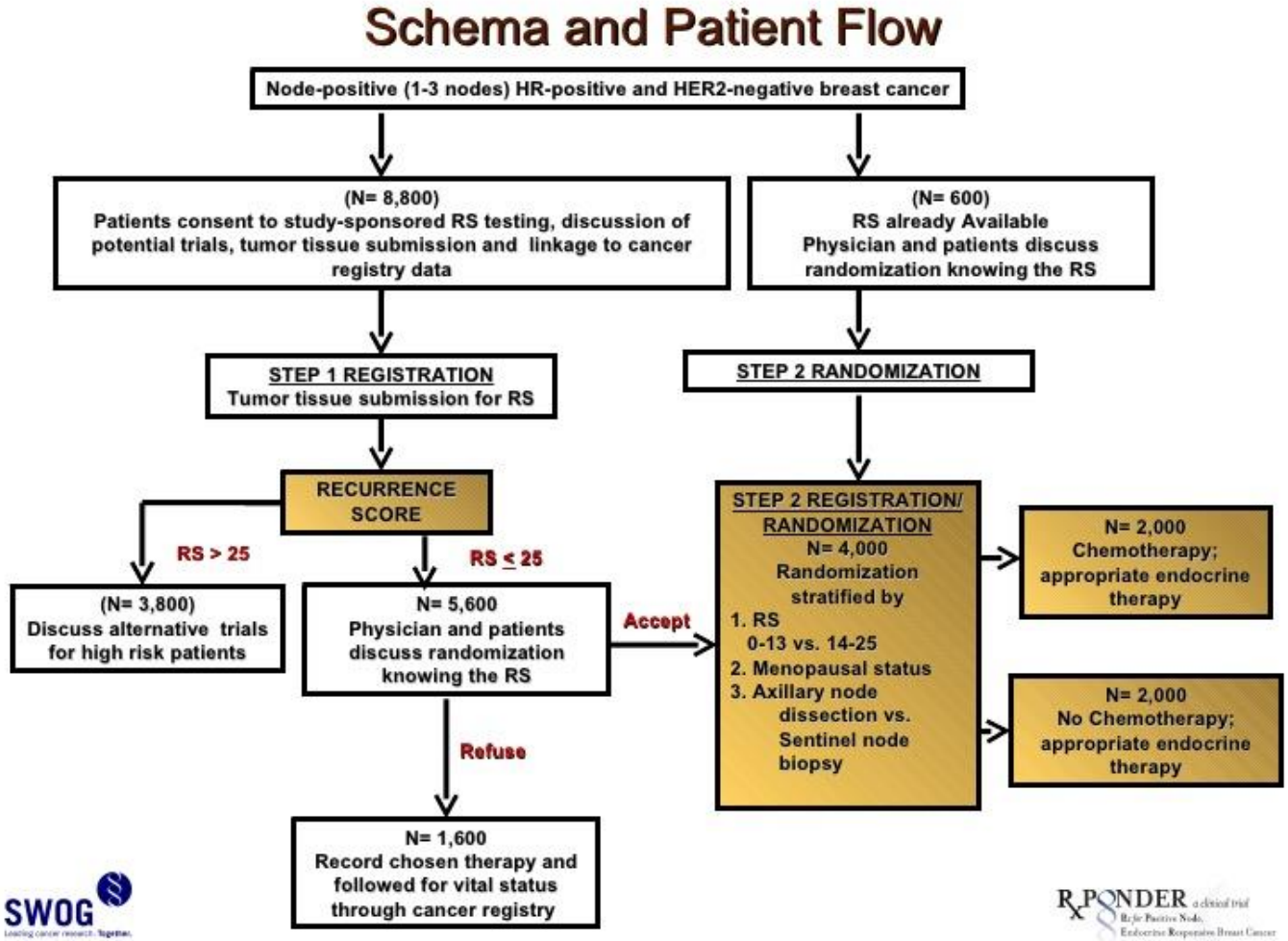
Sparano et al., *N Engl J Med* 2015;373:2005-2014

The TAILORx trial will establish whether Oncotype DX has clinical utility for selection of which patients with node negative hormone receptor-positive breast cancer benefit from receiving chemotherapy in addition to endocrine therapy (predictive ability).

Awaiting results from randomized patients

RxPONDER trial

Evaluation of Oncotype DX RS in patients who have node positive (1-3 nodes), hormone receptor-positive, HER2-neg breast cancer



> 9000 patients registered

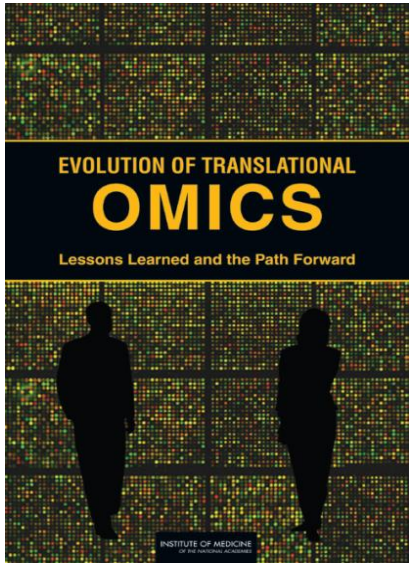
https://www.swog.org/clinical-trials/s1007

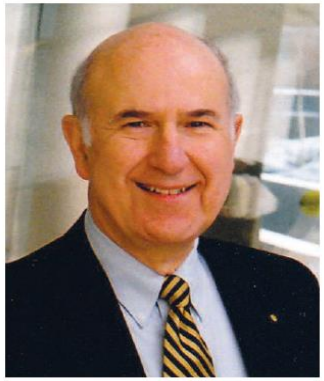
Primary Objective

To determine the effect of chemotherapy in patients with node positive breast cancer who do not have high RS by Oncotype DX®.

- Patients with 1-3 positive nodes, and HR+ and HER2- breast cancer with RS ≤ 25
- DFS for patients treated with chemotherapy compared to no chemotherapy and dependence on the magnitude of RS.
- Determine the optimal cutpoint for recommending chemotherapy or not.

Cautionary note: Many omics signatures have not been successful





"There are a lot of lessons here that surely apply to other places."

—GILBERT S. OMENN, UNIVERSITY OF MICHIGAN, ANN ARBOR

U.S. Institute of Medicine review of field of translational omics: "There are a lot of lessons here that surely apply to other places."

http://www.iom.edu/Reports/2012/Evolution-of-Translational-Omics.aspx

NCI criteria for the use of omics-based predictors in clinical trials

McShane et al., *Nature* 2013;502:317-320 (checklist)
McShane et al., *BMC Medicine* 2013;11:220 (explanation & elaboration)

NCI Exceptional Responders Initiative: Rationale

- Up to 10% of patients respond 'exceptionally well' to drugs that do not go on to receive FDA approval for that indication
- Certain agents deemed 'inactive' are actually active in a subset of patients
- Specific genomic lesions or patterns of expression might explain these "exceptional responses"
- Identification of these molecular changes could lead to development of predictive assays
- Improved biologic understanding of 'exceptional response' may point to new diagnostic/therapeutic avenues

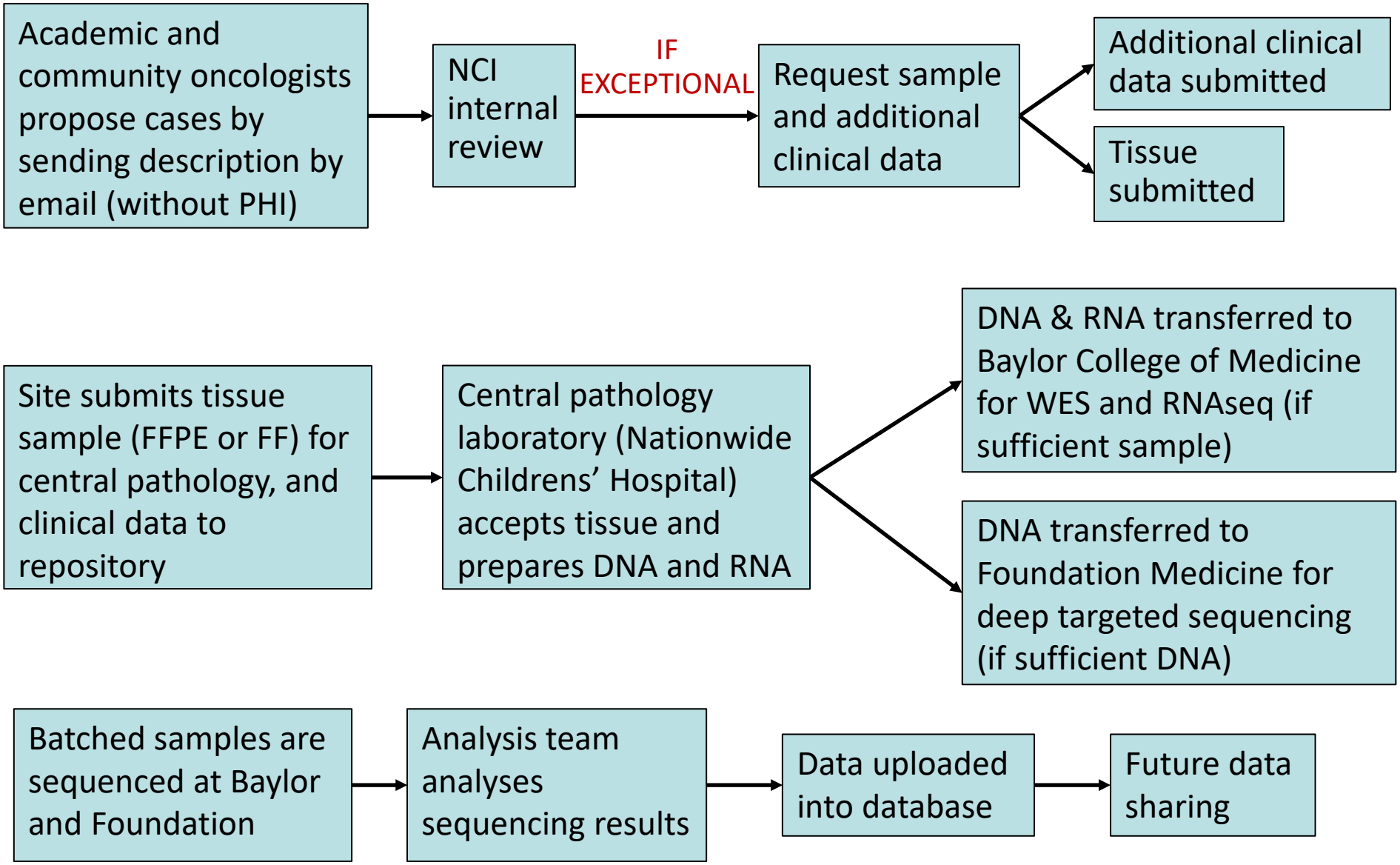
NCI Exceptional Responders Initiative

- Definition of an "exceptional response"
  - Cancer (evaluable for response) showing complete response (CR), or partial response (PR) lasting at least 6 months
  - Drug showed insufficient activity in disease setting to gain regulatory approval
  - Standard therapy not expected to produce CR or PR > 6 months in at least 10% of patients
  - Standard treatment with response lasting 3X longer than the median response duration seen in clinical trials

Search of NCI phase II clinical trial database identified about 100 hundred cases meeting "exceptional response" criteria

https://www.cancer.gov/about-cancer/treatment/research/exceptional-responders-initiative-qa

NCI Exceptional Responders Initiative workflow



Exceptional Responders status update as of December 2017

Accrual and assay status

Cases proposed:	522
Conditionally accepted:	221
Cases on a clinical trial:	78
Tumors received:	108

Unexpected findings

- Most patients are living (209 of 221)
- Most cases are ‘standard’ treatment (not investigational therapy)

NCI Exceptional Responders Initiative

Tumor types

Tumor type	# of cases
Adnexal Carcinoma	1
Ampulla of vater	1
Bladder	4
Blood	7
Brain	13
Breast	24
Ca unk primary (CUP)	3
Cervical	2
Colon	25
Endometrial	3
Fallopian tube	1
Gastroesophageal	34
Head and neck	5
Kidney	2
Leiomyosarcoma	1

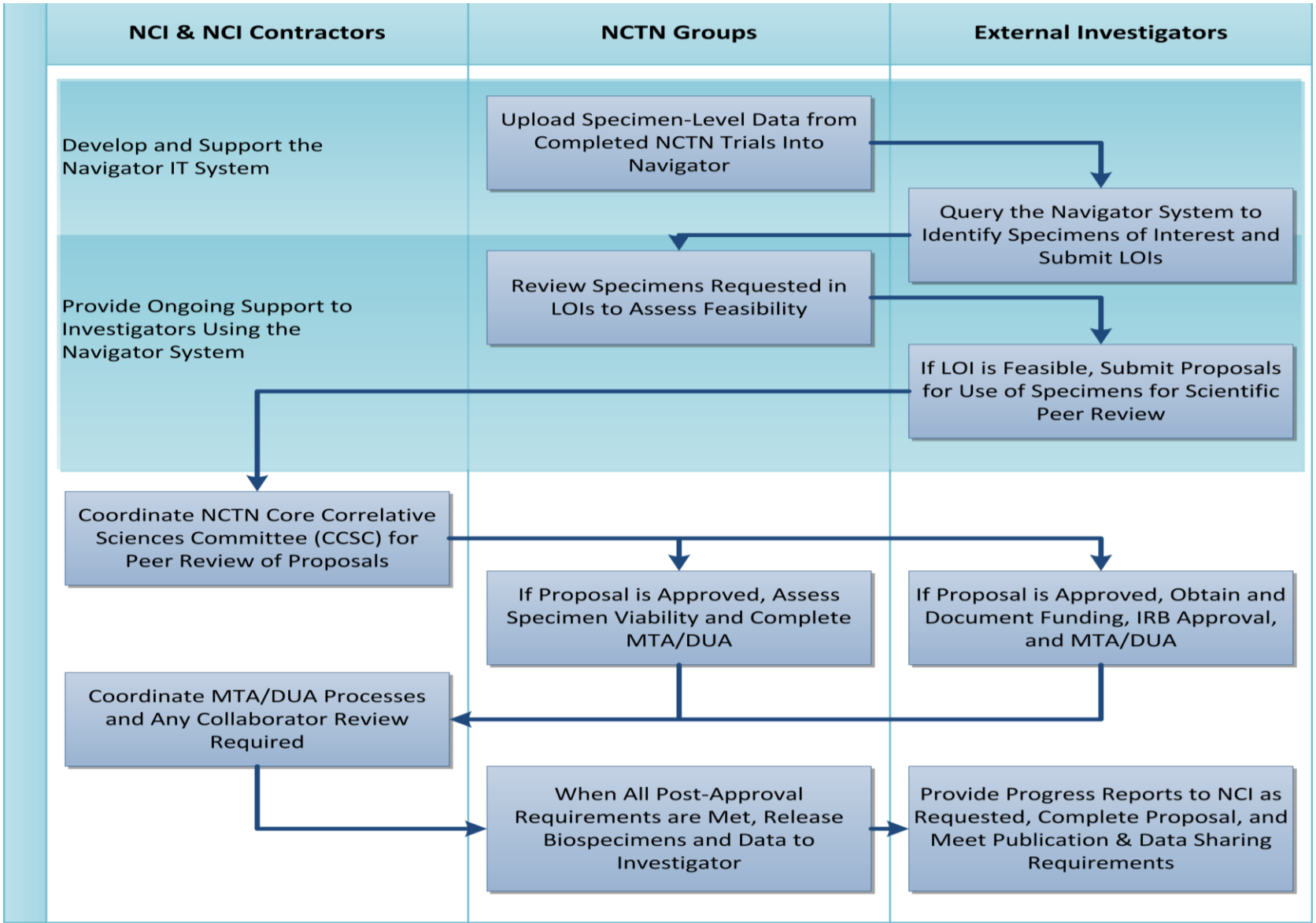
Tumor type	# of cases
Liver	5
Lung	32
Melanoma	8
Mesothelioma	1
Myeloma	1
Neuroendocrine	2
Ovarian	14
Pancreas	10
Prostate	4
Rectal	1
Renal	4
Sarcoma	4
Skin	2
Thyroid	2
Uterus	5

Analysis: A few preliminary interesting cases

Tumor type	Treatment	Response	Duration	Explanatory aberration?
Metastatic adenocarcinoma of GE junction	FOLFOX + Herceptin	PR	26mo	yes
Bilateral metastatic breast cancer	Carboplatin + docetaxel + Herceptin	CR	84mo	yes
Metastatic small cell cancer of the colon	Cisplatin + etoposide	CR	72mo	yes
Metastatic melanoma	Ipilimumab	CR	8 mo	yes
Small cell lung cancer	Etoposide + cisplatin	PR	24mo	yes
Merkel cell	Topotecan	PR	36mo	yes
Metastatic NSCLC	Afatinib	CR	6mo	yes
Stage IV colon cancer	FOLFOX + bevacizumab	CR	42mo	yes

NCTN Navigator

System for external investigators to query, submit proposals for, & obtain specimens from NCTN trials



NCTN Data Archive (launched Feb. 6, 2017)

Database of data sets from published NCTN trials

- Will prospectively contain individual, de-identified patient-level clinical data from phase III and phase II/III clinical trials conducted by NCI's National Clinical Trials Network (NCTN) and NCI's Community Oncology Research Program (NCORP) (published after Jan. 1, 2015)
  - Legacy trials (those published before January 01, 2015) will be included in the Archive on a case-by-case basis
- Complements other NCI data sharing activities which focus on genomic (NCI Genomic Data Commons; https://gdc.cancer.gov/) or imaging data (The Cancer Image Archive; http://www.cancerimagingarchive.net/) and specimen sharing
- In future, subsequent publications from trials (e.g., ancillary biology studies) will be included as well.
- Current inventory includes data from 32 trials (13 cancer types)

http://nctn-data-archive.nci.nih.gov/

Summary remarks

- Successful development of precision medicine approaches will require
  - Greater sharing of existing and future data and specimens
  - Inter-operative informatics tools
  - Larger and/or more connected and agile clinical trials and data systems
  - Continued development of analytical tools (computational, bioinformatics, and statistical) to optimally extract knowledge from data
- Although the goal of precision medicine is to find therapeutic approaches that produce large benefits in carefully defined (sometime small) groups of patients, major resources will be required to develop these approaches

THANK YOU

for your attention

Thanks to those who contributed graphics or slides:

NCI Exceptional Responders Initiative team

NCI MATCH Trial team

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