Precision Medicine Initiative (PMI) Committee Meeting

Jan 25, 2023

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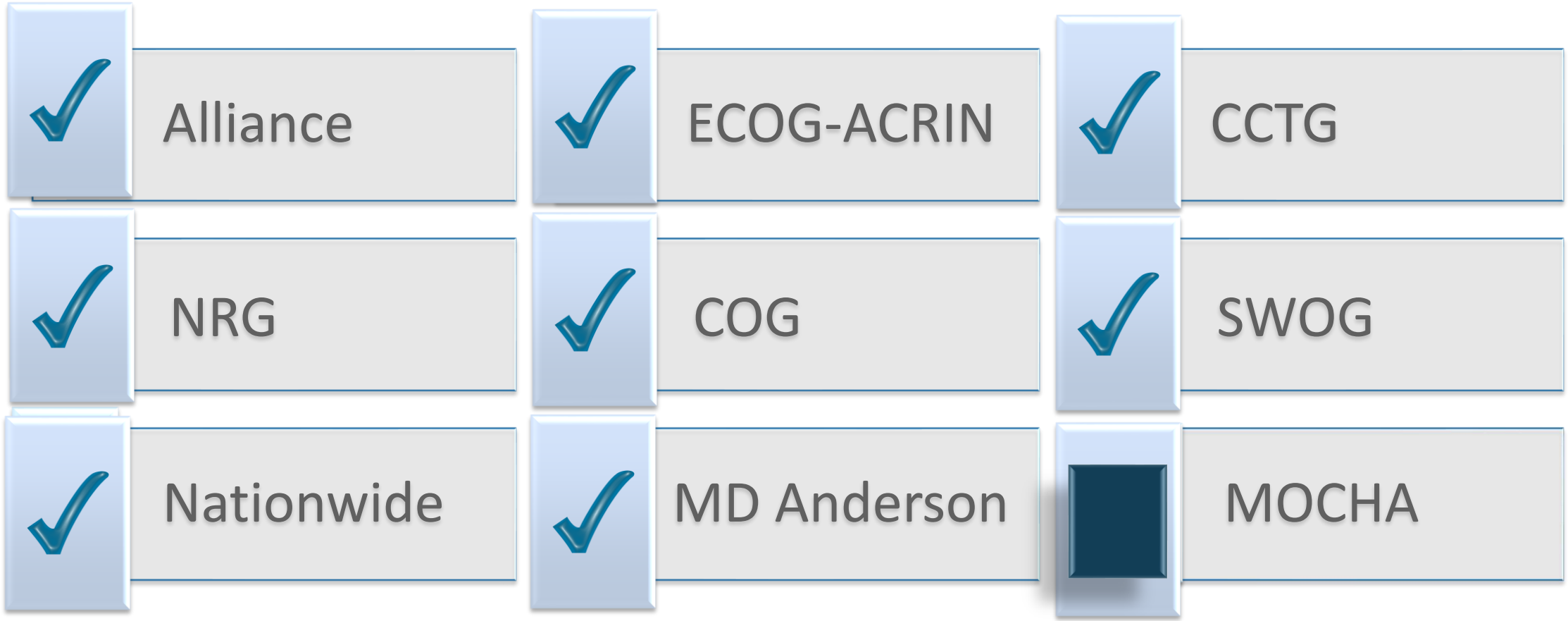
Agenda

- Role Call
- Project Status Updates
- Group Project Status Updates
- Review FAQs
- FFP Testing
- Open Discussion
- Next Steps

Stakeholder Representation



Project Status Updates

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Project Updates

- Released Screening and Treatment Test Cases
- Released the PMI OS-OT-CW Forms: PT Status PV/PVM Reqs listing
- Addressing UAT findings as reported by groups

Group Project Status Updates

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Group	EC Template			Beta Central Study ALS		Beta Screening Protocol ALS		Beta Treatment Protocol ALS		Screening/Treatment Test Cases (%done)		
	caDSR II (Y/N)	EC Build in Rave (Y/N)	Target Completion Date	Completed Upload (Y/N)	Target Completion Date	Completed Upload (Y/N)	Target Completion Date	Completed Upload (Y/N)	Target Completion Date	Initiated Beta UAT (Y/N)	Group Test Cases (%)	Target Completion Date
ECOG-ACRIN	Screening (Y) Treatment (Y)	Current Version (Y) Screening New Version (Y) Treatment New Version (N)	Treatment: 1/26/2023	v1.0- Yes v1.0.1.0 - Yes	1/20/2023	100%	1/18/2023	100%	1/18/2023	Screening (Y) Treatment (In Progress)	Screening (30%) Treatment (30%)	Screening (1/31/2023) Treatment
SWOG	Screening (Y) Treatment (Y)	Current Version (Y) Screening New Version (Y) Treatment New Version (Y)	1/20/2023	v1.0- Yes v1.0.1.0 - Yes	1/20/2023	50%	1/13/2023	Combo – Ready MM – Pending		Screening (N) Treatment (In Progress)	Screening () Treatment (50%)	Screening Treatment (1/31/2023)
NRG	Treatment (Y)	N4 - In Progress N2 – In Progress	1/27/2023	v1.0- Yes v1.0.1.0 - Yes	1/25/2023	N/A	N/A	Completed		Treatment (Y)	Treatment (N2 0%) (N4 15%)	Treatment (N2 –) 2/15/2023) (N4 - 2/8/2023)
Alliance	Treatment (Y)	Treatment (Y)	1/25/2023 Starting with A3 first	v1.0- Yes v1.0.1.0 - Yes	1/25/2023	N/A	N/A	Completed		Treatment (Y)	Treatment (15%)	Treatment (3/1/2023)
CCTG	Treatment (Y)	Current Version (Y) New Version (N)	1/30/2023	v1.0- Yes v1.0.1.0 - Yes	1/25/2023	N/A	N/A	Completed		Treatment (N)	Treatment (0%)	Treatment
COG	Treatment (N)	New Version (N)	Feb	v1.0.1.0 – No	Feb/March	N/A	N/A	N		Treatment	Treatment	Treatment

Group Testing Roadblocks

Group	Roadblock
ECOG-ACRIN	***11/25/2023*** • *Working to get the checklist data from OPEN to Rave on the screening protocol* • *Not prepared for Step 2 Registration either in OPEN or in Rave*
SWOG	***1/12/2023*** • *1/11/2023 – Need list of final Off Study Lists, as well as Off Treatment Reasons – Need clarifications on the PVs…Ginger to send clarification* ***1/25/2023*** • *Need to remove cohort and stratum* • *Need MM Meeting with NCI to continue builds/UAT* • *R codes and names for MM substudy and will discuss in meeting with NCI*
NRG	***1/25/2023*** • *Protocol change requires a change to update the EC template* • *Changing protocols making it difficult to finalize builds*
Alliance	***1/12/2023*** • *Need to do additional work to build the EC Template in Rave, need to build an integration in Rave; IT group working on push into Rave; will manually do it until IT is done* ***1/25/2023*** • *Using same testing plan for Alliance Off Treatment, will do 2 rounds of testing with derivations on the 2nd round*
CCTG	***1/12/2023*** ***1/25/2023*** • *May have to remove cohort/strata from the EC Template*
COG	***1/25/2023*** • *Received comments on protocol from CTEP as well as the schema*

Review FAQs

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PMI Committee Questions

Question	Response
Why are the topography, morphology, and grade fields all required? They are mostly not applicable to the disease for this trial, especially grade. Seems like that would be “N/A” for all patients. If they must enter topography and morphology, can we at least narrow down the lists to the few things that are applicable?	SWOG can decide if they want to collect these questions on their MM Screening Protocol EC form in the caDSR II during form build activities. The grade and topography fields will be marked as optional in OPEN: if data is present, it will be pushed. The 'Morphology' field is required for the MyeloMATCH protocols, specifically "9860/3"; SWOG can default the value for this field in OPEN.
Why are prior treatment fields included for this trial when these are all treatment naive patients? Are you expecting them to enter prior treatment for other cancers if they’ve had any?	On Tier 1, all participants must be treatment naïve. For Tier 1, patients can have taken some therapy as long as it’s a minimal dose.
What data will be entered in OPEN for a new assignment? How will we get that data into Rave? I assume there’s a template form that we’ll need to build out so the data can be pushed into our Rave instance.	The PMI Project team will address reassignment questions at a future meeting since reassignment was not part of the Phase 1 release.

PMI Committee Questions

Question	Response
How is the step information form going to look for a reassessment vs a new assignment? Will a logline still be added showing that specimens were analyzed but that the decision was that they should stay on their current treatment trial? Is a logline added every time they submit something in OPEN or only in some cases?	A notification will be sent that a treatment is complete, and the patient is eligible for a new tier assignment. Every new step in OPEN will result in a log line in Rave. If they get reassigned, they have a log line added. No additional new log lines based on updates or events, only mapped with STEP.
In the A3 schema there is an indication that there should be a max of 6 pts enrolled to cohort 4 for a given histology. How will this be handled in the screening trial and in terms of managing/capping enrollment to cohort 4?	This will be handled in MATCHbox. No assignments will be generated for Histology once maximum is reached.
What happens/what is the process when the site leaves the DLAP Scenario ID blank? What happens/what is the process when there's a blank DLAP Scenario ID under Physician's choice?	The site user may not have a scenario ID, so they do not have to populate it. This field is required on the EC form but may be left blank by the site if the data has not yet been entered and confirmed in DLAP. There is no correlation between Physicians choice or DLAP.

PMI Committee Questions

Question	Response
Is it correct that two Off Treatment forms are not needed for crossover?	The Off Treatment from does not need to be completed for a Crossover.
We are in the process of writing specifications for folder rollout for the ComboMATCH Screening protocol in Rave. The assumption is that we need to build multiple Steps into Rave. I have reviewed all the materials, including the test plans and instructions for generating OPEN Checklists, and it appears that there is no plan to have the ability to enter Step 2 registrations in the Screening Study at Go Live. Is this correct?	Yes, this is correct. Step 2 is only for re-registration.
Will data management staff have access to the EAY191 Source Documents being uploaded to OPEN? Typically, we have sites upload Path Reports into Rave, however if EA will have access to the Path Reports uploaded to OPEN we could reduce burden on sites and eliminate duplicate data entry.	Access can be given in OPEN to view the reports, however you will need to view the report patient by patient.

PMI Committee Questions

Question	Response
After the initial paper-based process, it sounds like there will be Precision Medicine Specimen Tracking Forms and the other specimen-related forms submitted via Rave (listed below). Should these forms be part of our study build or will they exist in a different Rave “instance”? • Samples Tracking and Manifest Form • Local Pathology Group Information Form • CLIA Laboratory Specimen Submission Form • MyeloMATCH Generic Specimen Submission form • Pathology Group Form	MM Generic Specimen submission form will not be part of the Rave study build; this is a placeholder paper form for the STMF which will be part of the study build in the future. The below forms are targeted to be added to the PMI Screening Protocol ALS as part of Phase II activities. • PMI STMF • PMI Pathology Group Form • PMI CLIA Submission Form
We are finishing out study builds for our ComboMATCH treatment trial (EAY191-S3) and our MyeloMATCH treatment trial (MM1YA-S01) and I would like to confirm the correct arm names and/or Treatment Assignment Codes. Can you please provide the correct names and codes for these two trials? How is our RandoNode is supposed to push into OPEN?	MATCHBox the IDs are below, and they give both stratification and randomization. List of codes has been sent. • EAY191-S3 • MM1YA-S01 A Randonode setup document was provided to explain how RandoNode is supposed to push into OPEN with the initial release.

PMI Committee Questions

Question	Response
The CDE 10948385 is being used to capture the ICD code for Screening and is a text string. Would 6154743 be better as that has a dictionary associated with it that represents the ICD-O-3 topography codes you mentioned? We are asking so we don't collect a different data element on the treatment form then what is being collected on the screening form and this would allow Alliance to monitor the rates as well and if we need to do some collapsing of a set of codes to a broader class of "histologies/type of cancer" we would be able to evaluate that as we go.	The fields on the screening protocol are integrated with the disease service. We will consider this option at a future timepoint, but you will have access in MATCHbox to view this data in real-time and export that data.

PMI Committee Questions

Question	Response
I was told a subset of the pre-randomization nodes will be used on the drop-down option for when they go into Open. But, they will only have 1 option in the drop down menu, so it is there as a “double-check”. I was told the sites will never need to enter that code or to select from among a list of similar looking codes. I asked if we could revise the codes to use text that sites could read without having to refer to the schema or another document. I was told they were not sure what was in the demo yet, but it may be the case. So, the current plan – if they use those not-super-user-friendly (in my opinion) in the drop-down menu, we will create a table in the protocol that maps the codes to words (“TP53 mutated and age 18-39” for example)and I was told this was fine. Since OPEN won’t be using the codes at the end of the branches/trees, I think the schema will be challenging for sites to navigate.	You must select from the drop down and this is a double check. Only the cohort and stratum assigned to that particular patient will be in the dropdown. No other values will be in the dropdown.

Fit For Purpose Testing

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What is FFP Testing?

- Fit-for-Purpose (FFP) testing is a ‘dress rehearsal’ to make sure all components that make up the precision medicine trial are ready and capable of meeting its objectives
- Allows NCI and external sites to check software and physical processes work according to expectations
- Will be testing scenario of least-restraint (happy path) as well as potentially other scenarios

Oncology Group Involvement

- Review list of task items in FFP script
- Send contact info of responsible individual to PMIStandards@nih.gov by ***27 Jan***
- Understand each task request is urgent
- Pre-task reminders and nudges will be sent
- Each task should only take as long as it should when trials are in production

Schedule

- Identification of key individuals: Jan 27
- Distribution of draft scripts: Jan 30
- Kickoff call: TBD
- Testing Period: TBD (4 weeks duration)

PMI Project Discussion Items

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Open Discussion

- Questions

Next Steps

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Next Steps

- Next meeting will be on 2/08/2023 at 1:00pm EST
- Agenda
  - Role Call
  - Project Status Update
  - Group Status Update
  - Review FAQs
  - Future Demos/Workflows
    - MM Demo – March 1, 2023 at 1:00pm EST

Communication

- Contact PMI Mailbox for any PMI related questions
  - pmistandards@nih.gov
  - The project team will respond within 48 hours with a response or a follow up

- PMI Wiki
  - https://wiki.nci.nih.gov/display/CDISC/Precision+Medicine+Initiative
  - All presentations, recordings, minutes, project documents and releases will be posted on this wiki

Appendix

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Testing Date Extensions

- February 10, 2023
  - Groups last day to provide any showstopper findings
- February Feb 17, 2023
  - Release Production Files
- March 3, 2023
  - Study Activation for Priority 1

****Assumption that there are no showstopper findings towards the end of the testing period*

Testing Date Extensions

- February 10, 2023
  - Groups last day to provide any showstopper findings
- February Feb 24, 2023
  - Release Production Files
- March 10, 2023
  - Study Activation for Priority 1

****Assumption that there are showstopper findings towards the end of the testing period*

Target Timeline

Nov – Mid Dec 2022

Group Activities
- Develop Study-specific Rave CRFs

NCI Activities
- ComboMATCH UAT Matchbox Environment
- MyeloMATCH UAT Matchbox Environment
- MATCHBox & OPEN Integrations for UAT
- Prepare Beta Screening & Treatment ALS files

Mid Dec 2022

NCI Activities
- Release EC Templatev1
- Release Beta Screening Protocol ALS
- Release Beta Treatment Protocol ALS
- aMOI List Approval and MATCHBox Upload

Mid Dec to Jan 30, 2023

Group Activities
- UAT Testing

NCI Activities
- Iterative updates to test findings (show-stoppers)

Target Timeline

Jan 31, 2023

NCI Activities
- Release EC Template v1
- Release Prod Screening Protocol ALS
- Release Prod Treatment Protocol ALS
- Release Prod Central Study ALS
- Release NCI OPEN Integrations for Prod
- Release NCI Genexus Installation (MyeloMATCH)

Jan 31 to Feb 14, 2023

NCI + Group Activities
- Support Group Study Builds

Feb 14, 2023

NCI + Group Activities
- Launch BOTH Initiatives

Spring 2023

NCI Activities
- Release Additional ALS(s)

ComboMATCH Priority 1 List

Study #	Document Number	Document Title	Group	Current Status	Next Steps	Primary Agent Name (P) Other Agent Name (O)
1	EAY191	Molecular Analysis for Combination Therapy Choice (ComboMATCH)	ECOG-ACRIN	8/15/2022 Approval on Hold	Revision 3 back from CIRB with approval. On hold for DTL, funding sheet and IND filing.	
2	EAY191-N4	Molecular Analysis for Combination Therapy Choice (ComboMATCH) EAY191-N4: A Randomized Trial of Selumetinib and Olaparib or Selumetinib Alone in Patients with Recurrent or Persistent RAS Pathway Mutant Ovarian and Endometrial Cancers A ComboMATCH Treatment Trial	NRG	8/15/2022 Approval on Hold	Revision 4 back from CIRB with approval. On hold for DTL, funding sheet and IND filing.	(P) Olaparib (AZD2281) (747856) (O) Selumetinib (AZD6244 hydrogen sulfate) (748727)
3	EAY191-E4	A ComboMATCH Treatment Trial ComboMATCH Treatment Trial E4: Nilotinib and Paclitaxel in Patients with Prior Taxane-Treated Solid Tumors	ECOG-ACRIN	8/26/2022 Approval on Hold	Revision 3 back from CIRB with approval. On hold for DTL, funding sheet and IND filing.	(P) Nilotinib (747599) (O) Paclitaxel (Taxol) (673089)
4	EAY191-N2	A ComboMATCH Treatment Trial EAY191-N2: Phase 2 Trial of Fulvestrant and Binimetinib in Patients with Hormone Receptor-Positive Metastatic Breast Cancer with a Frameshift or Nonsense Mutation or Genomic Deletion in NF1	NRG	8/26/2022 Approval on Hold	Revision 3 back from CIRB with approval. On hold for DTL, funding sheet and IND filing.	(P) Binimetinib (788187) (O) Fulvestrant (Faslodex) (719276)
5	EAY191-S3	Phase 2 Study of Paclitaxel + Ipatasertib in Taxane-Refractory Participants with AKT-Altered Advanced Non-Breast Solid Tumors	SWOG	8/29/2022 Approval on Hold	Revision 4 back from CIRB with approval. On hold for DTL, funding sheet and IND filing.	(P) Ipatasertib (781451) (O) Paclitaxel (Taxol) (673089)

ComboMATCH Priority 2 List

Study #	Document Number	Document Title	Group	Current Status	Next Steps	Primary Agent Name (P) Other Agent Name (O)
6	EAY191-A6	A ComboMATCH Treatment Trial: FOLFOX in Combination with Binimetinib as 2nd Line Therapy for Patients with Advanced Biliary Tract Cancers with MAPK Pathway Alterations	Alliance	Approval on Hold 9/14/2022	Rev 4 approved by CIRB on 10/24. CTEP currently reviewing stips.	(P) Binimetinib (788187) (O) OXALIplatin (Eloxatin) (266046) (O) 5-Fluorouracil (5-FU) (19893) (O)Leucovorin calcium (3590)
7	EAY191-A3	Palbociclib and Binimetinib in RAS-Mutant Cancers	Alliance	Approval on Hold 8/26/2022	Rev 2 sent to CIRB . Reviewed on 10/6, study team responding to stips	(P) Palbociclib (PD-0332991) (772256) (O) Binimetinib (788187)

ComboMATCH Priority 3 List

Study #	Document Number	Document Title	Group	Current Status	Next Steps	Primary Agent Name (P) Other Agent Name (O)
8	EAY191-A2	Olaparib Plus Low-Dose Alpelisib for Breast Cancer	Alliance	In Review 4/4/2022	Rev 3 recv;d 10/19, currently with LR. Looks like it'll be another disapproval. Not yet sent to CIRB for initial review.	(P) Olaparib (AZD2281) (747856) (O) Alpelisib (BYL719) (801658)
9	EAY191-C1	Phase 2 Subprotocol of the Combination of a MEK Inhibitor and a Pan-RAF Inhibitor in Patients with Relapsed/Refractory Tumors Harboring Activating MAPK Pathway Mutations	COG	In Review 9/29/2022	Protocol reviewed at PRC 10/20; CR is being put together	(P) Selumetinib (AZD6244 hydrogen sulfate) (748727) (O) DAY101 (TAK-580, MLN-2480) (800798)
10	EAY191-E5	ComboMATCH Treatment Trial E5: A Randomized Phase II Study of AMG 510 (Sotorasib) with or Without Panitumumab in Advanced Solid Tumors	ECOG-ACRIN	In Review 2/22/2022	Waiting for revision 2 since 9/28; reminder was sent to EA 10/24	(P) AMG 510 (Sotorasib) (825510) (O) Panitumumab (742319)
11	EAY191-N5	Molecular Analysis for Combination Therapy Choice (ComboMATCH) EAY191-N5: A Randomized Trial of Neratinib, A Pan-ERBB Inhibitor, Alone or in Combination with Palbociclib, a CDK4/6 Inhibitor, in Patients with HER2+ Gynecologic Cancers and Other Solid Tumors A ComboMATCH Treatment Trial	NRG	In Review 11/22/2021	Rev 3 disapproval sent 10/15; waiting for Rev 4	(P) Neratinib (783782) (O) Palbociclib (PD-0332991) (772256)

MyeloMATCH Priority 1 List

Study #	Document Number	Document Title	Group	Current Status	Next Steps
1	MYELOMATCH	Master Screening and Reassessment Protocol (MSRP) for the NCI MyeloMATCH Clinical Trials	SWOG	11/12/2021: Approval on Hold	CIRB Reviewed on 9/15, version with stips under CTEP review now.
2	MM1YA-S01	A Randomized Phase II Study Comparing Cytarabine + Daunorubicin (7 + 3) to (Daunorubicin and Cytarabine) Liposome, Cytarabine + Daunorubicin + Venetoclax, and Azacitidine + Venetoclax in Patients Aged 59 or Younger with High-Risk (Adverse) Acute Myeloid Leukemia; A MYELOMATCH Clinical Trial	SWOG	9/2/2022: Approval on Hold	CIRB Reviewed on 9/15, version with stips under CTEP review now.
3	MM1YA-CTG01	A Measurable Residual Disease (MRD) Driven, Phase II Study of Venetoclax Plus Chemotherapy for Newly Diagnosed Younger Patients with Intermediate Risk Acute Myeloid Leukemia: A Tier 1 MYELOMATCH Clinical Trial	CCTG	9/2/2022: Approval on Hold	CIRB Review Oct 6, responding to stips
6	MM1OA-EA02 (Concept)	A Randomized Phase II Study of HMA-Based Therapies for the Treatment of Older Adults with Newly Diagnosed FLT3-Mutated Acute Myeloid Leukemia: A myeloMATCH Treatment Trial	ECOG-ACRIN	8/29/2022: Approved, no protocol yet	Waiting for protocol

MyeloMATCH Priority 2 List

Study #	Document Number	Document Title	Group	Current Status	Next Steps
4	MM2YA-EA01	Eradicating Measurable Residual Disease in Patients with Acute Myeloid Leukemia (AML) Prior to StEm Cell Transplantation (ERASE): A MyeloMATCH Treatment Trial	ECOG-ACRIN	1/21/2022: In Review	Reviewed by CIRB, responding to stips
5	MM1OA-S02	A Randomized Phase II Study of Targeted Agents with the Oral DNMT1 Inhibitor Cedazuridine-Decitabine (ASTX727) for the Treatment of Newly Diagnosed TP53-Mutated Acute Myeloid Leukemia in Older Patients: A myeloMATCH Treatment Trial	SWOG	10/17/2022: In Review	Scheduled for PRC 11/4
7	MM1MDS-EA03 (Concept	ERADICATE MDS with TP53 Study: Efficacy of taRgeted Agents Combinations with Oral DNMT1 Inhibitor C-DEC (ASTX727) for TrEatment of Higher Risk myElodysplastic Syndromes with TP53 Mutations: A Non-Comparative, Parallel, Multi-Arm Phase 2 Study	ECOG-ACRIN	8/12/2022: Approval on hold, waiting for drug commitment	W+A6:G8aiting for Astex commitment, Genentech has provided commitment on 10/20

Review Schemas

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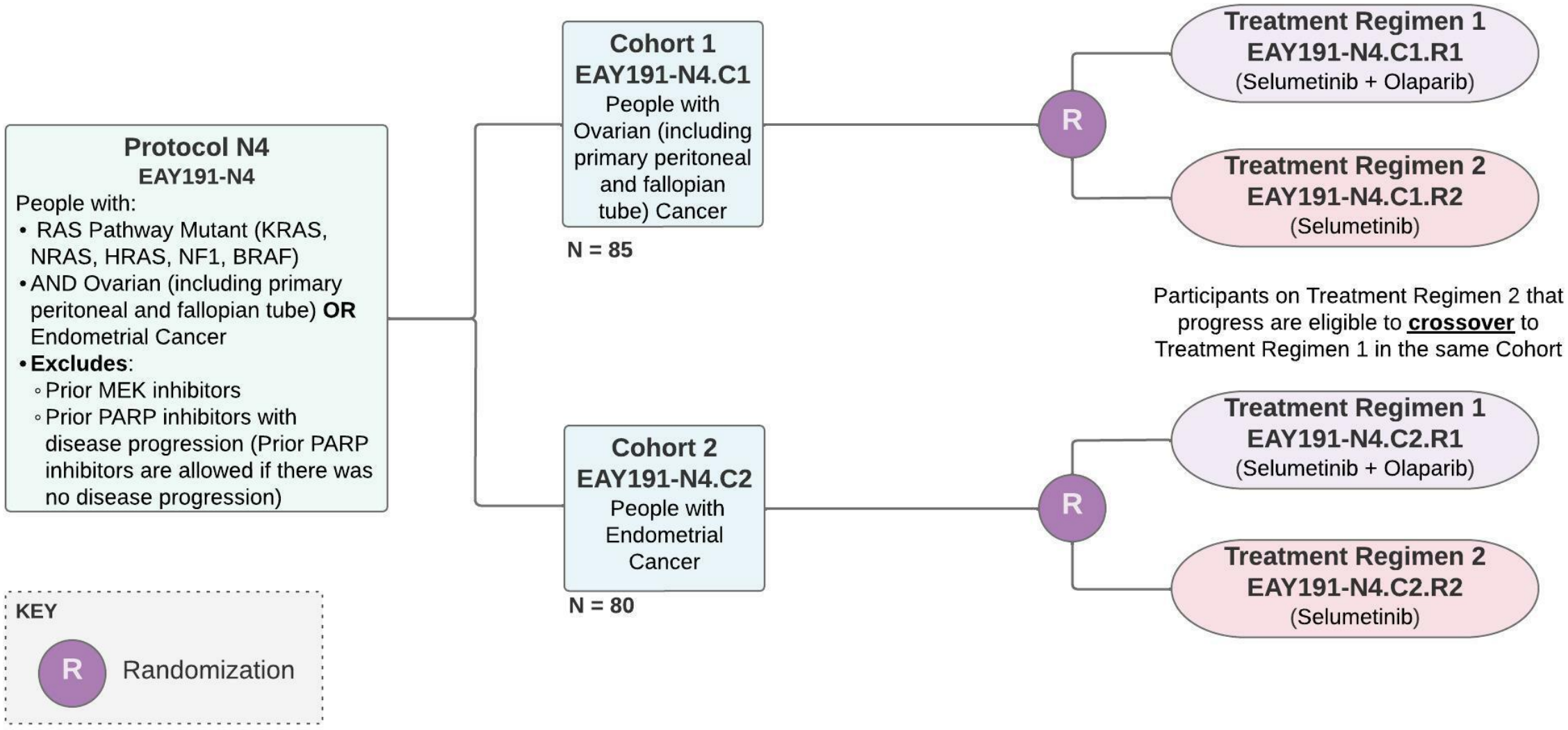
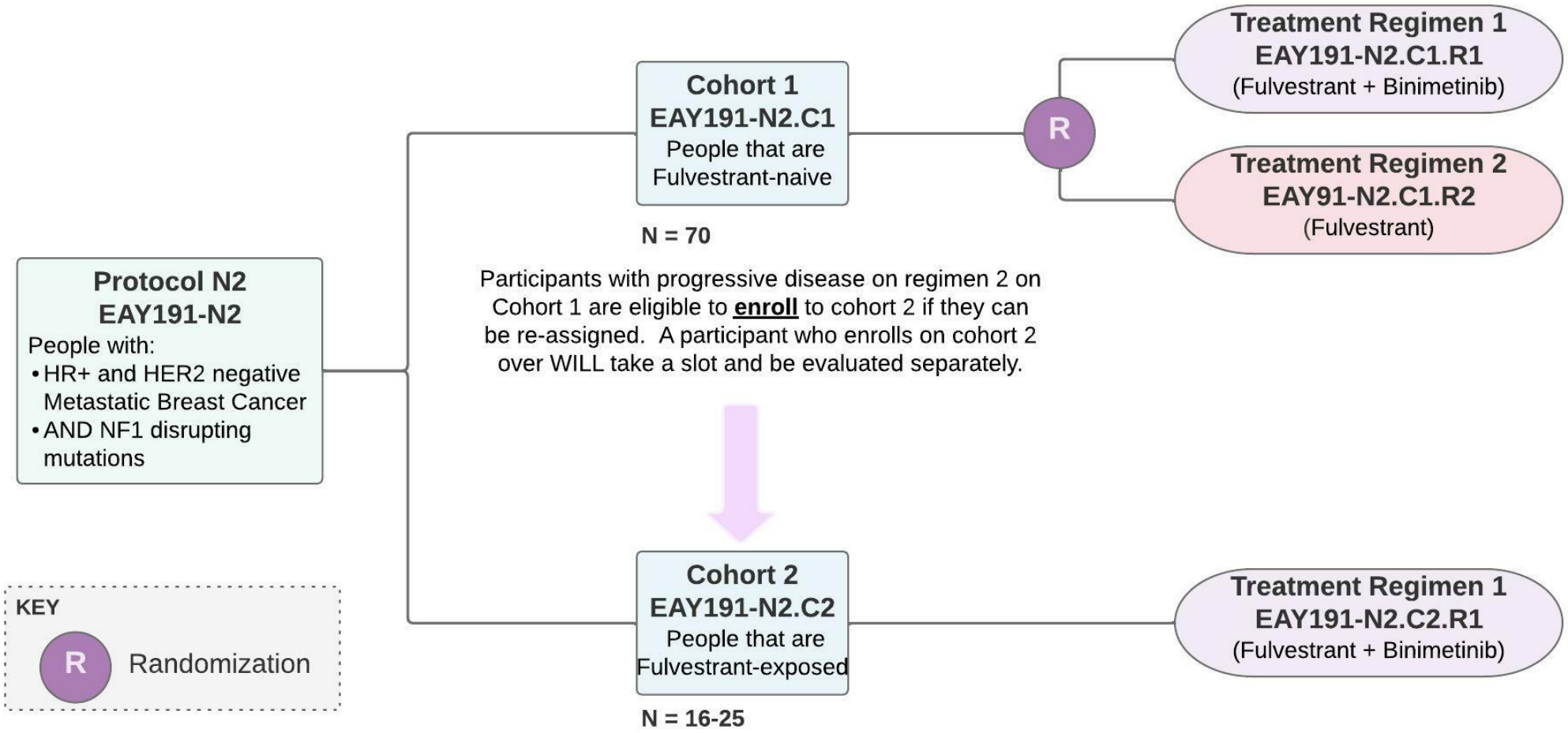
EAY191-N4


Protocol N4
EAY191-N4
People with:
• RAS Pathway Mutant (KRAS, NRAS, HRAS, NF1, BRAF)
• AND Ovarian (including primary peritoneal and fallopian tube) OR Endometrial Cancer
• Excludes:
◦ Prior MEK inhibitors
◦ Prior PARP inhibitors with disease progression (Prior PARP inhibitors are allowed if there was no disease progression)
Cohort 1
EAY191-N4.C1
People with Ovarian (including primary peritoneal and fallopian tube) Cancer
N = 85
Cohort 2
EAY191-N4.C2
People with Endometrial Cancer
N = 80
R
R
Treatment Regimen 1
EAY191-N4.C1.R1
(Selumetinib + Olaparib)
Treatment Regimen 2
EAY191-N4.C1.R2
(Selumetinib)
Participants on Treatment Regimen 2 that progress are eligible to crossover to Treatment Regimen 1 in the same Cohort
Treatment Regimen 1
EAY191-N4.C2.R1
(Selumetinib + Olaparib)
Treatment Regimen 2
EAY191-N4.C2.R2
(Selumetinib)
KEY
R
Randomization

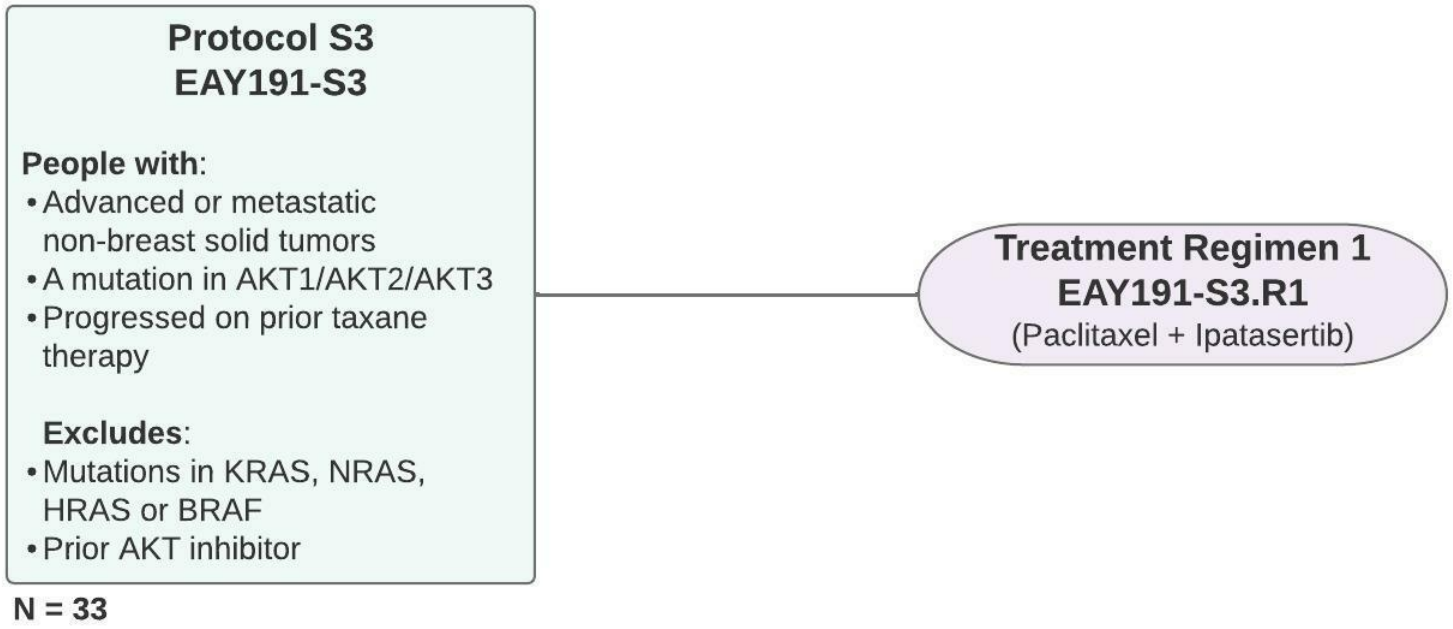
EAY191-E4


Protocol E4
EAY191-E4
People with:
• Previous taxane therapy (metastatic setting)
• Excludes:
◦ Platinum-resistant epithelial serous ovarian cancer
◦ cKIT variants
◦ PDGFRA D842V variants
N = 40
Treatment Regimen 1
EAY191-E4.R1
(Nilotinib + Paclitaxel)

EAY191-N2- Draft



EAY191-S3


Protocol S3
EAY191-S3
People with:
• Advanced or metastatic non-breast solid tumors
• A mutation in AKT1/AKT2/AKT3
• Progressed on prior taxane therapy
Excludes:
• Mutations in KRAS, NRAS, HRAS or BRAF
• Prior AKT inhibitor
N = 33
Treatment Regimen 1
EAY191-S3.R1
(Paclitaxel + Ipatasertib)

MMIYA-CTG01 Draft