Precision Medicine Initiative (PMI) Committee Meeting

May 31, 2023

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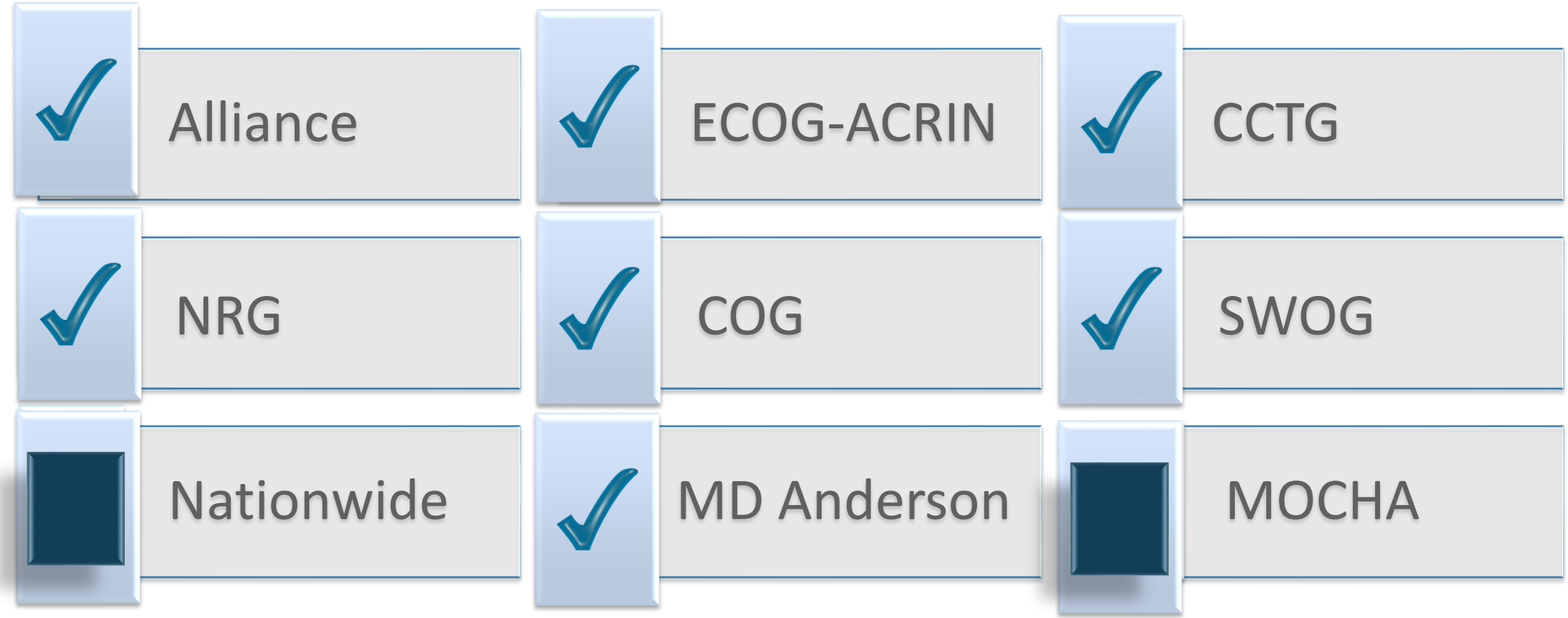
Agenda

- Role Call
- Project Status Updates
- Group Project Status Updates
- Project Discussion Items
- Review FAQs
- Next Steps

Stakeholder Representation



Project Status Updates

Project Updates

- Prioritizing project tasks
- Working on deliverable due dates
- Performing compliance reviews for mapping activities

Project Tasks
Re-Screening: Combo
Re-Screening- Myelo
STMF
Screening Protocol ALS v2.0
Designated Labs for Combo
MyeloMATCH Tx Protocol Crossover (for S01, CTG01 and EA02)
Cohort Migration

Group Project Status Updates

oup	EC Template			Central Study ALS		Screening Protocol ALS		Treatment Protocol ALS		Screening/Treatment Test Cases (%do		
	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 Complet Date
OG-RIN	Screening (Y) Treatment (Y)	Current Version (Y) Screening New Version (Y) Treatment New Version (N)	Both Completed as of 1/27/23	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 (100%) Treatment (100%)	Screeni 2/01/202 Treatme 2/01/202
OG	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%	Not able to move forward without more info	Combo – Ready MM – Pending	Combo done, finishing internal testing and will copy the standard forms into MM	Screening (N) Treatment (Complete for Combo)	Screening () Treatment (Complete for Combo)	Screeni Treatme (Complete Combo
RG	Treatment (Y)	N4 - In Progress N2 – In Progress	1/27/2023 1/31/2023	v1.0- Yes v1.0.1.0 - Yes	1/25/2023	N/A	N/A	Completed		Treatment (Y)	Treatment N2 100% N4 100%	Treatme 2/2/202 2/2/202
nce	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 (100%)	Treatme (3/1/202
TG	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%)	Treatme TBD
OG	Treatment (N)	New Version (N)	2/24/2023	v1.0- Yes v1.0.1.0 –Yes	2/01/2023	N/A	N/A	Completed		Treatment (N)	Treatment (0%)	Treatme 03/31/202

CM/MM Group Testing Updates

Group	Internal UAT	Prod Screening Protocol ALS		Prod Treatment Protocol ALS	
	Progress (% Complete)	*Completed Upload (Y/N)*	*Target Completion Date*	*Completed Upload (Y/N)*	*Target Completion Date*
ECOG-ACRIN	95% 80%	Ran a diff report, used existing version and matched production version (Y)		Imported Central Study, Ran a diff report, used existing version and matched production version (Y)	
SWOG	100% For MM - Waiting on new EC Template			Imported Central Study, Used diff report, used existing version and matched production version (Y)	
NRG	N4 - 100% N4 – 100%	N/A	N/A	Imported Central Study, Used diff report, used existing version and matched production version (Y)	
Alliance	100% (CM) *Will need to retest based on new workflow	N/A	N/A	Imported Central Study, Used diff report, used existing version and matched production version (Y)	
CCTG	100% *have not done OPEN integration Testing for MM – Need Patients – Pending MSRP Build (v2 of EC Template will follow up online)	N/A	N/A		
COG		N/A	N/A		

ComboMATCH/MM FFP Testing Updates

Group	Enrollment Forms
Finalized Enrollment Forms (EC forms and Rave Treatment forms)	
ECOG-ACRIN	Screening: OPEN checklist has a change Working on language to populate instructions field on 15 min delay for uploading Path and CLIA reports Treatment: Complete Screening: Rave Forms – Forms are set Treatment: Forms are set but could be minor changes due to validation checks.
SWOG	Treatment: Completed but had to add consent questions outside of PMI Integrations, should be done by today.
NRG	Treatment: entry forms are finalized in OPEN and Rave. Other forms are also built; still running validation checks.
Alliance	Waiting to hear back from sites
CCTG	N/A
COG	N/A

Group Roadblocks

Group	Roadblock
ECOG-ACRIN	***5/31/2023*** • *Study build portion of E5 is on hold pending language on Cohort Migration; will wait to activate once Cohort Migration is implemented* • *MM Treatment Trial – Need the Treatment Assignments will work*
SWOG	***5/31/2023*** • *EC v2 template; keeping MSRP on hold* • *MM Treatment Trial – Need the Treatment Assignments will work*
NRG	***5/31/2023*** • *N2 Study will require an update from Cohort Migration – How will this impact the current study..need the final language*
Alliance	***5/31/2023*** • *A2 and A3 need Cohort Migration* • *A6 does not need Cohort Migration so we can move forward on this study*
CCTG	***5/31/2023*** • *EC v2 template; keeping MSRP on hold* • *Need patients for UAT testing*
COG	***5/31/2023*** • *No roadblocks*

PMI Project Discussion Items

MM Treatment Workflow for Stratification

Group Consensus = Approach 3B

- Pros
  - There will be a validation with information in MATCHBox
  - Minimizes User Error
- Cons
  - Requires development work to create the needed validation
  - Stratification factors have to be included in the assignment reason information returned back to OPEN
- Potential Impacts to Groups
  - Groups manage CDE curation activities via NCI CBIIT curation team for stratification factor questions

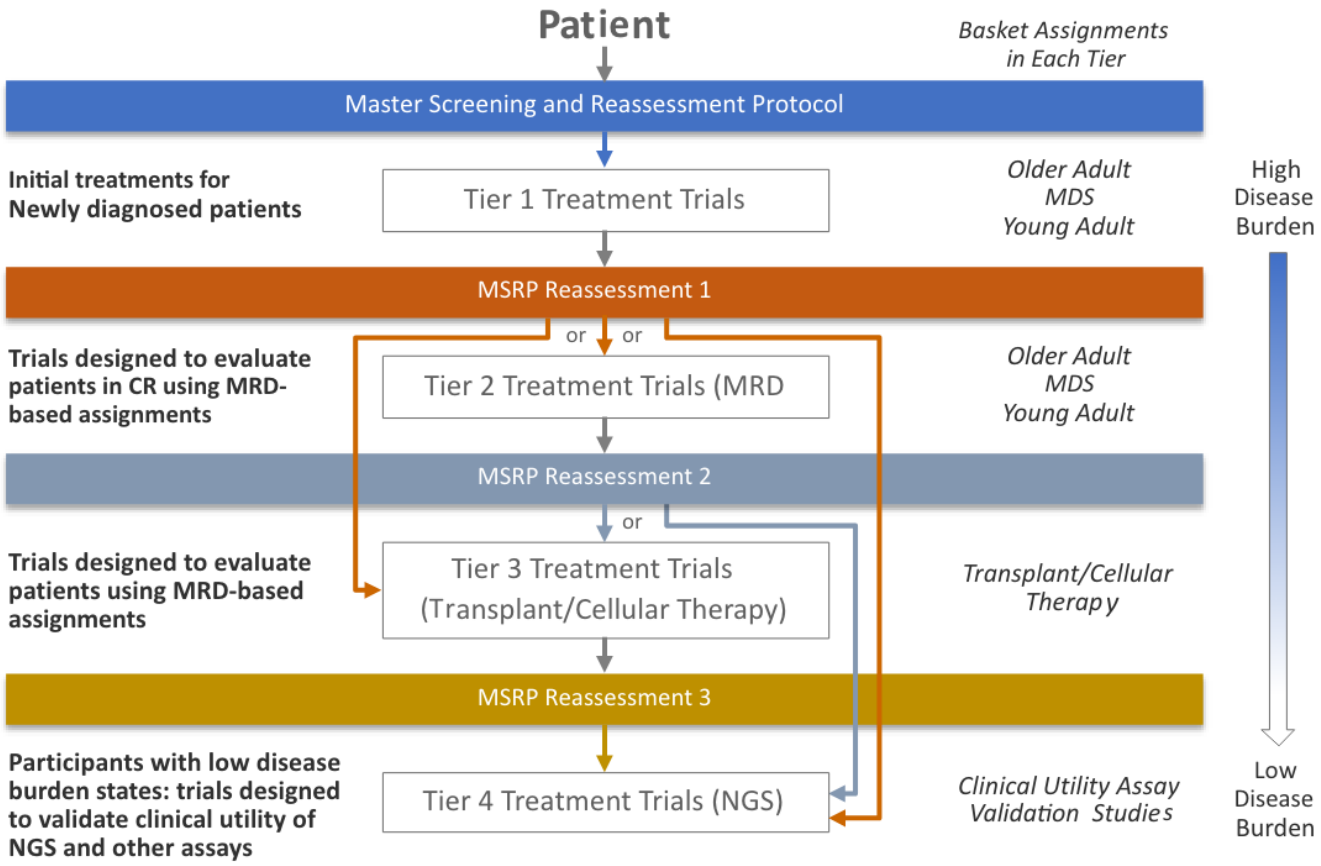
Approach 3B: Use OPEN EC Form with Validations

Stratification factors are questions on the OPEN enrollment EC form for sites to complete

Validation check in OPEN that checks the responses to the stratification questions against the Assignment Reason returned from MATCHBox.

CM and MM Step 2 Enrollment

MyeloMATCH MSRP Schema



MM Step 2 Enrollment

EC Fields on Step 1	Needed On Re-reg?	Comments
ICD-O-3 Disease fields *(histology & behavior code only)*	No	Can the disease be different from step 1 for Myelo?
Prior Drugs	Yes	Required so that drugs taken on TAP can be entered. Only for MM.
ECOG Perf Score	Pending Answer	Not needed unless this is something that may be different than what was entered at Step 1 enrollment.
Is the patient fit for intensive chemotherapy?	No	Only applicable to MM, only on initial.

- MM requires a field on re-registration for the enrolling site to indicate which tier they believe is appropriate for their patient.
- Potential Options after completing by tier:
  - Tier 1: Consolidation (T2), Transplant (T3) or Maintenance (T4)
  - Tier 2: Transplant (T3) or Maintenance (T4)
  - Tier 3: Maintenance (T4)
    - This is on the MSRP
    - Tiers will be managed in MATCH but steps are in OPEN. Register to treatment trial then they will be assigned to one of the tiers.
    - Steps -> Reassessment
    - Provide the

Tier maps to induction, consolidation, transplant or maintenance

Reassessment vs Tier

Review FAQs

PMI Committee Questions

Question	Response
How do we go about getting access to the Matchbox dashboard?	It would be a request to the service desk, CM support. combo-match-support@nih.gov

PMI Committee Questions for Option 3B

Question	Response
How would this validation check work? Would it be written as an edit check or validated when the enrollment is submitted?	This would be written as an edit check and applied to the EC form in OPEN.
Who would develop this, and would it impact the group randonode?	The NCI Project Team would develop this edit check, it should not impact your randonode.
Would it be study-specific, or a general validation process used across studies?	It would be a general edit check that can be applied across different treatment studies.
The slide mentioned that stratification factors would need to be included in the assignment reason information returned to OPEN – is this referring to the screening trial or the treatment trial?	This would apply to the screening trial, specifically the treatment assignment reason that is returned back to OPEN from MATCHBox.

Open Discussion

Next Steps

Next Steps

Next meeting will be on 6/14/2023 at 1:00pm EST

Agenda

- Role Call
- Project Status Update
- Group Status Update
- Review FAQs
- Future Demos/Workflows

Communication

Contact the PMI Mailbox for any PMI related questions & comments

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

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www.cancer.gov

www.cancer.gov/espanol

Appendix

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

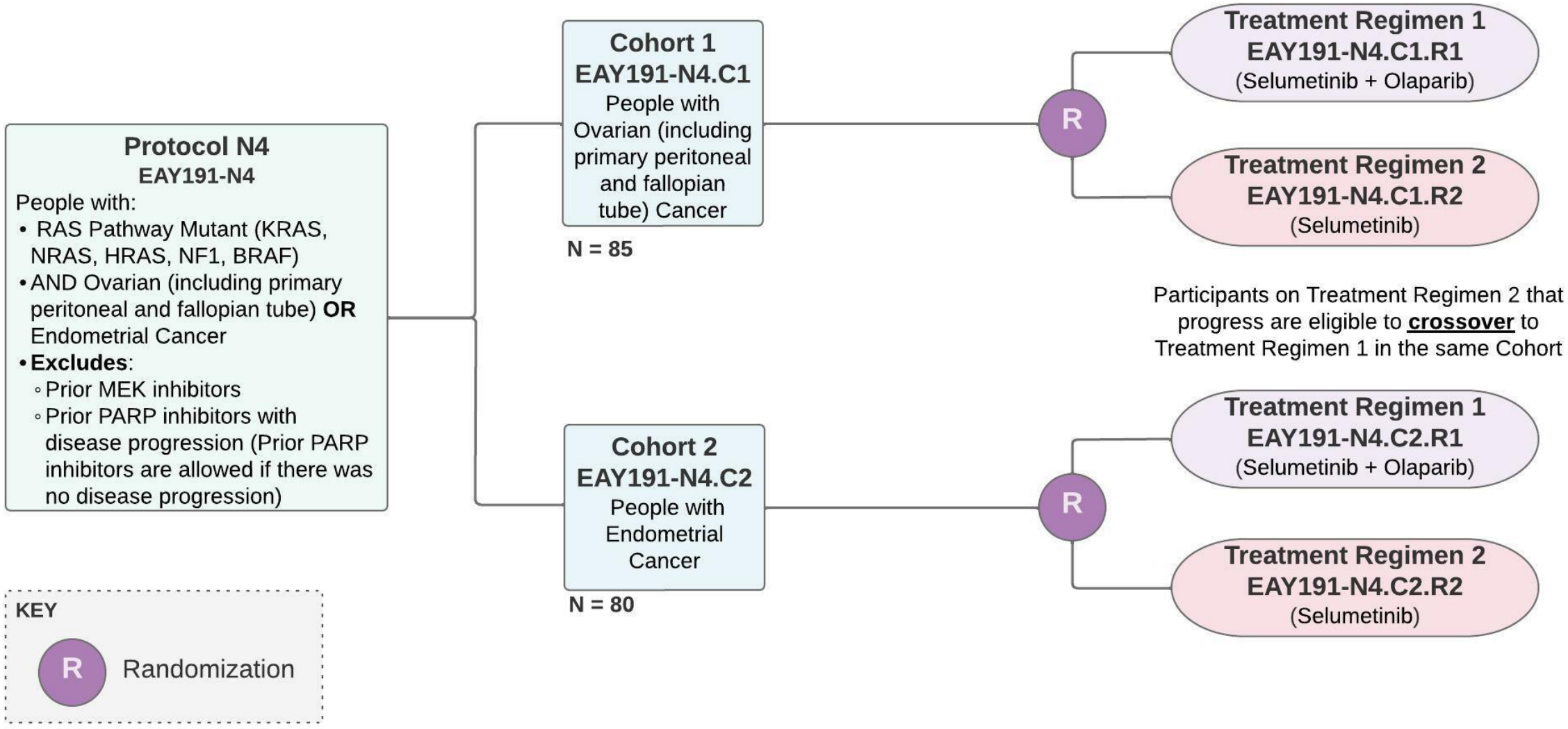
Study #	Document Number	Document Title	Group	Current Status	Next Steps
1	MYELOMATCH	Master Screening and Reassessment Protocol (MSRP) for the NCI MyeloMATCH Clinical Trials	SWOG	11/12/2021: Approval on Hold	CIRB Reviewed on 9/15, version with stips under CTEP review now.
2	MM1YA-S01	A Randomized Phase 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

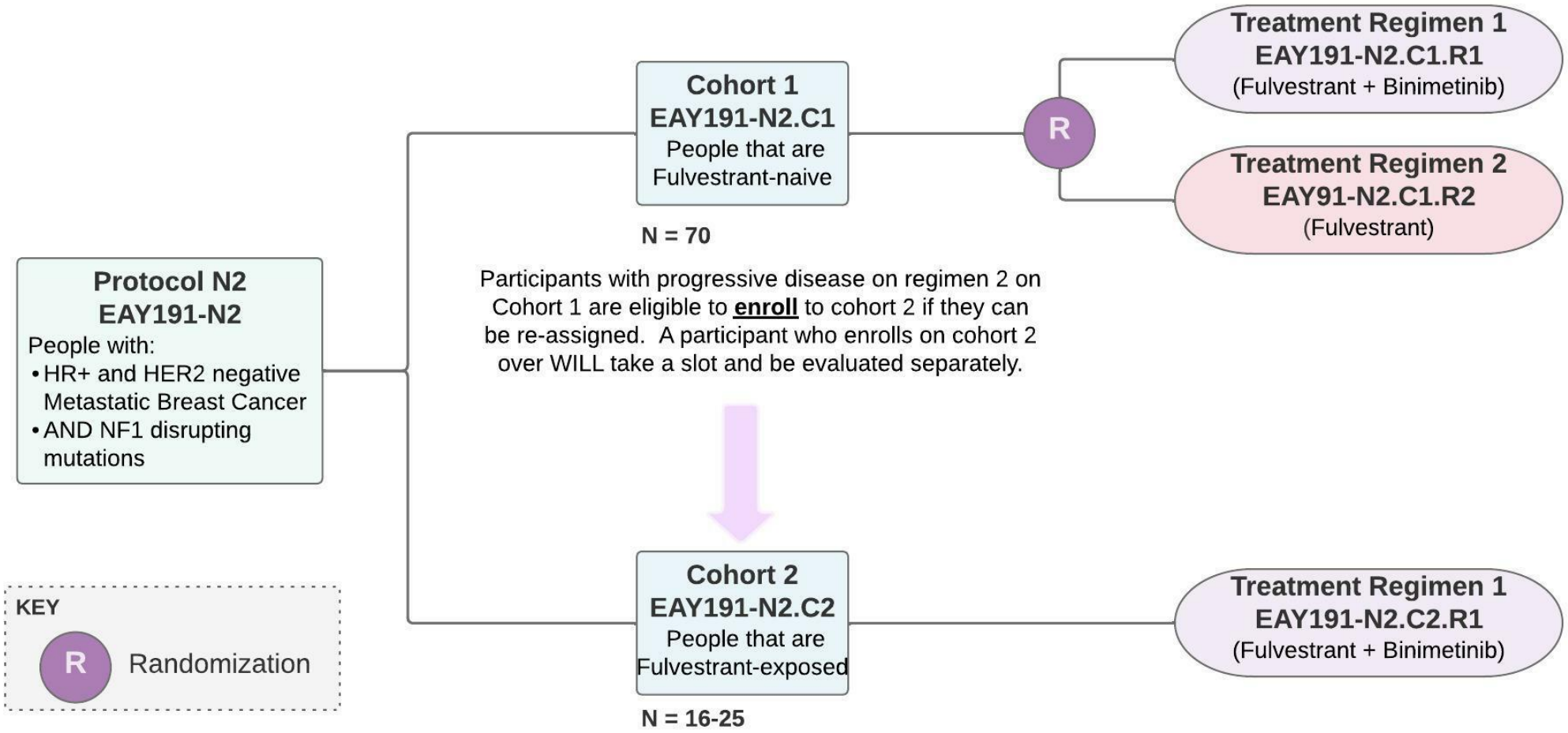
EAY191-N4


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

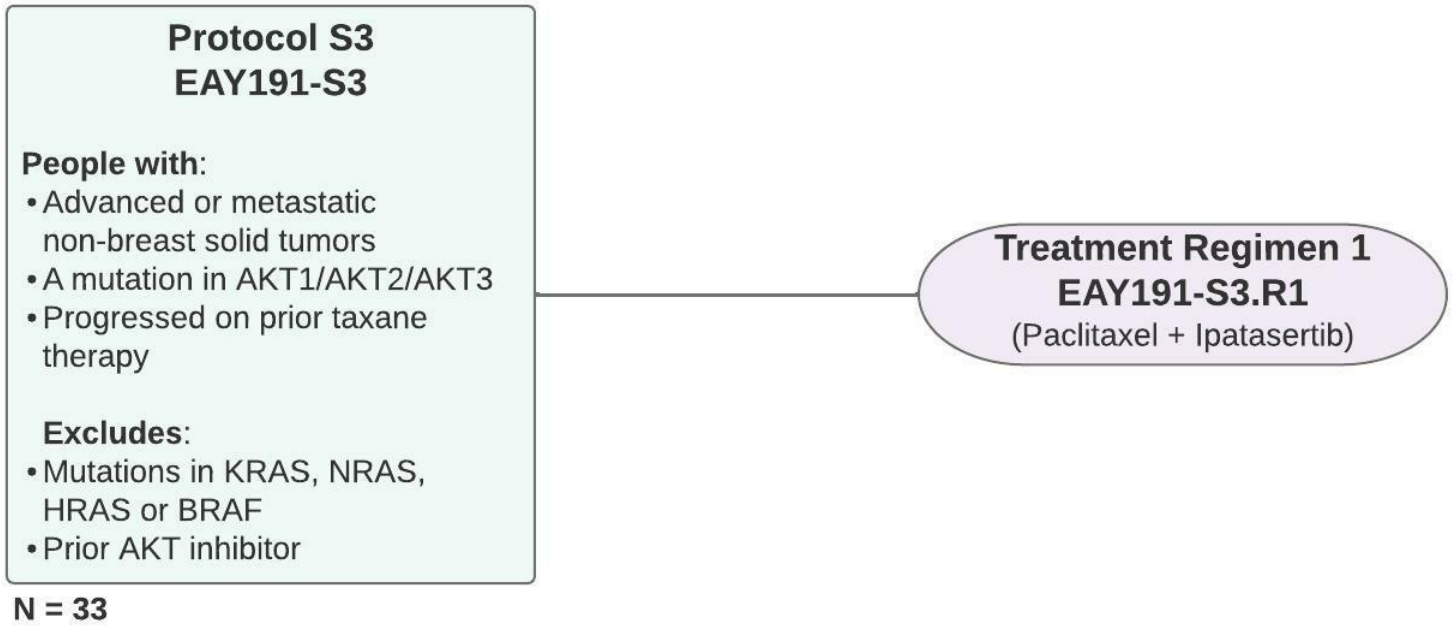
EAY191-E4


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