Precision Medicine Initiative (PMI) Committee Meeting

December 14, 2022

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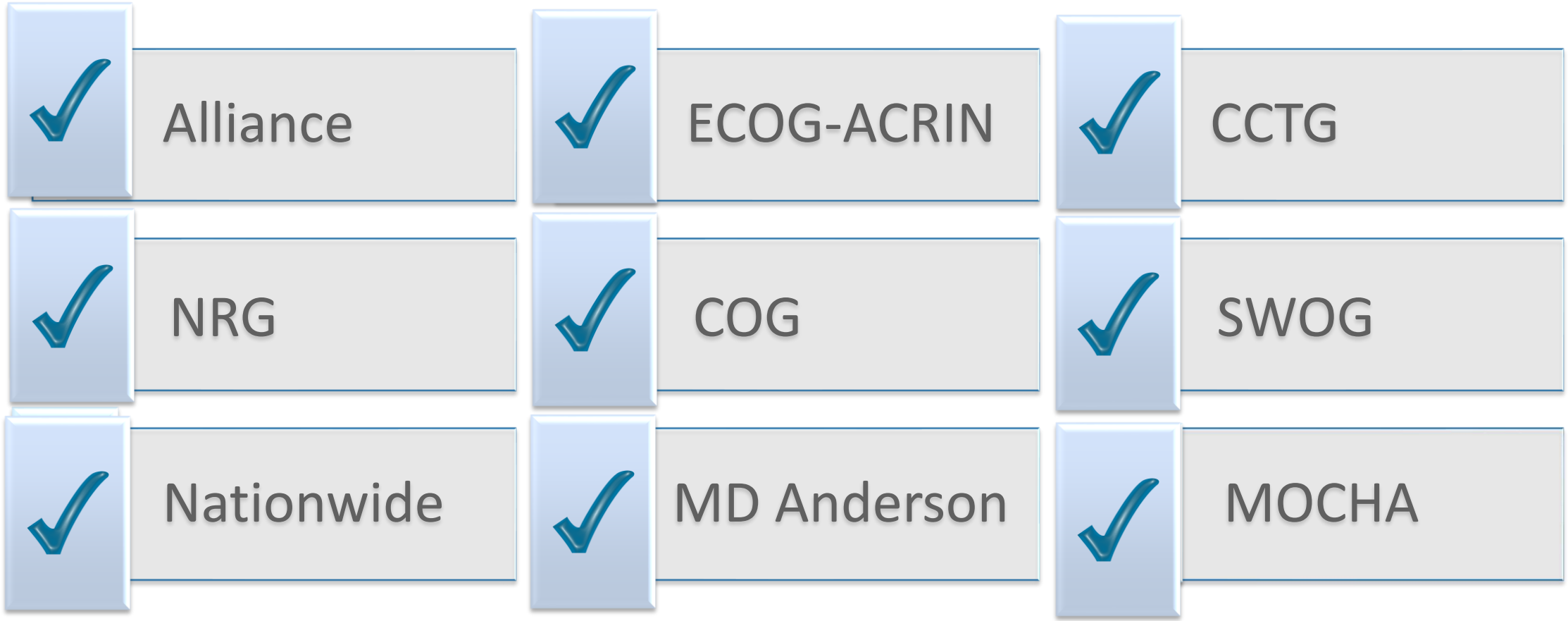
Agenda

- Role Call
- Project Status Updates
- Project Deliverables for Beta Release
- RSS Application
- Review Beta PMI CDISC Eligibility Checklist Fact Sheet
- Next Steps

Stakeholder Representation



Project Status Updates

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PMI Screening Protocol ALS v1.0

Beta Release Screening Protocol ALS v1.0

Target Date: December 16, 2022

Production Release Screening Protocol ALS v1.0

Target Date: January 31, 2023

Form/Deliverable	Completed	In Progress	Not Started
PMI CDISC Step Information Form	Created beta form/field listing for Groups Performed Rave study build and edit check updates Updated custom functions Compliance Review	**Perform additional testing**	
PMI CDISC Treatment Assignment Form	Created beta form/field listing for Groups Performed Rave study build and edit check updates Updated custom functions Compliance Review	**Perform additional testing**	
PMI CDISC Off Study Form	Documented use cases Created beta form/field listing for Groups Performed Rave study build and edit check updates Updated custom functions Compliance Review Deliver beta form/field listing for Groups **Integration + QA testing for ComboMATCH**	**Integration + QA testing for MyeloMATCH**	
PMI CDSIC Consent Withdrawal Form	Documented use cases Created beta form/field listing Performed Rave study build and edit check updates Compliance review Deliver beta form/field listing for Groups Custom functions **Integration + QA testing for ComboMATCH**	**Integration + QA testing for MyeloMATCH**	
Beta Release Screening Protocol ALS v1.0	**Integration + QA testing** **Final compliance review** **Update release notes**		Release Beta ALS for UAT

PMI Treatment Protocol ALS

Beta Release Treatment Protocol ALS v1.0

Target Date: December 16, 2022

Production Release Treatment Protocol ALS v1.0

Target Date: January 31, 2023

Form/Deliverable	Completed		Pending
PMI CDISC Off Treatment Form	Documented use cases Created beta form/field listing for Groups Performed Rave study build and edit check updates Updated custom functions Compliance Review Deliver beta form/field listing for Groups **Integration + QA testing for ComboMATCH**	**Integration + QA testing for MyeloMATCH**	
PMI CDSIC Consent Withdrawal Form	Documented use cases Created beta form/field listing for Groups Performed Rave study build and edit check updates Updated custom functions Compliance Review Deliver beta form/field listing for Groups **Integration + QA testing for ComboMATCH**	**Integration + QA testing for MyeloMATCH**	
Beta Release Treatment Protocol ALS v1.0	**Integration + QA testing** **Final compliance review** **Update release notes**		Release Beta ALS for UAT

PMI Central Study ALS v1.0

Beta Release Central Study ALS v1.0
Target Date: December 16, 2022

Production Release Central Study ALS v1.0
Target Date: January 31, 2023

Tasks	Completed	Pending
Integration Testing	X	
Release Beta ALS to Groups		X

PMI CDISC Eligibility Checklist Template v1.0

Target Date: December 16, 2022

Tasks	Completed	In Progress	Pending
Identify cohort and stratum CDEs	X		
Create custom edit checks in OPEN	X		
Harmonize and curate new EC CDEs	X		
Create beta form/field listing for Groups	X		
Rave form build activity for testing	X		
End to end integration testing + QA testing		X	
EC Template Use Fact Card	X		
Release PMI CDISC Eligibility Checklist Template v1.0 in caDSR II			X
Support Groups as needed			X
Retest integrations as needed			X

PMI Drug and Disease Service Integration

Target Date: December 16, 2022

Tasks	Completed	In Progress	Pending
End to end integration + QA testing		X	
Deploy OPEN updates to UAT/Production			X
Release Drug & Disease CDE's in caDSR			X
Support Groups as needed			X
Retested integrations as needed			X

PMI MyeloMATCH Patient Fitness Integration (OPEN/MATCHbox)

Target Date: December 16, 2022

Tasks	Completed	In Progress	Pending
Finalize requirements	X		
Content + CDISC Review	X		
CDE Curation	X		
Integration + QA Testing		X	

CTSU Protocol Application (RSS) Requirements

Target Date: January 30, 2023

Tasks	Completed	In Progress	Pending
Review rules for protocol status changes	X		
Verify required field population logic	X		
Review target and count validations	X		
Create RSS User Guide		X	
Deploy to UAT			X
Deploy RSS updates to Production			X
Release updated RSS User Guide			X

OPEN-Pathology/CLIA Upload/Download

Target Date: January 30, 2023

Tasks	Completed	In Progress	Pending
Verify integration	X		X
Manage end to end testing		X	
Deployment to UAT/PROD			X

UAT Environments

ComboMATCH Date: Dec 16, 2022
MyeloMATCH Date: Dec 16, 2022 (Potential risk to run a week or two late)

Tasks	Completed	In Progress	Pending
Deploy ComboMATCH UAT Environment		X	
Deploy MM UAT Environment		X	

Group Specific Activities

Tasks	Dates
Develop Study Specific CRFs	November to 12/16/2022
UAT Testing	12/16/2022 to 1/30/2023

PMI Project Discussion Items

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TAC/TAD

- ***NRG**: Confirmed that in NRG randonode Treatment arm that needs to match assignment from the schema is independent of TAC and TAD. It is just that historically we kept it the same. List of codes is not an issue.*

- ***Alliance**: Our concern was just related to the fact that we often get our coding letters communicating TAC/TADs very late in the process and sometimes these letters and requests from CTEP have implications for our trial schema so we will need to all be on the same page about the schemas (Alliance SDMC, PMI Infrastructure, CTEP) and early on in the trial activation process.*

PMI Beta Release Deliverables

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PMI Beta Release Deliverables

1. Beta PMI CDISC Screening Protocol ALS v1.0
2. Beta PMI Screening Protocol Release Notes v1.0
3. Beta PMI CDISC Treatment Protocol ALS v1.0
4. Beta PMI Treatment Protocol Release Notes v1.0
5. Beta PMI Central Study ALS v1.0
6. Beta PMI CDISC Eligibility Checklist Template Listing v1.0
7. Beta PMI CDISC Eligibility Checklist Fact Sheet
8. Beta PMI Randonode Setup Document
9. Beta Protocol Application User Guide

PMI Beta Release Deliverables

- All files will be posted on the **PMI Wiki** under Announcements and PMI Committee Documentation

- All files will be emailed in a zip file to the PMI Committee Members.

  *Note files are large so it may not come through your mailboxes in a timely manner

  *Instructions on how to send over UAT feedback will be included in the email

- To meet our 1/31/2023 Deadline, the PMI project team will review and prioritize UAT findings.
  - High priority items (show stoppers) will be addressed for the first release

RSS Application: Web Services

RSS Application – Group Response

Group	Response
Alliance	Alliance is interested in using the web service. Within the slides it indicates CTSU will provide tech specs if needed – is that something you can provide? Or who at CTSU should I contact for those?
COG	COG is interesting in using a CEWS service to push from our group's database , as that would be more reliable than manual entry.
SWOG	SWOG would be interested in discussing this option further. Seems like making it automated is the best way to ensure that the data that's being used for assignment is as up to date as possible.

Next Steps

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Next Steps

- Next meeting will be on 12/21/2022 at 1:00pm EST
- Agenda
  - Role Call
  - Project Status Update
  - Review UAT Test Plan
  - Future Demos/Workflows
    - Step Information and Treatment Assignment Form in workflow
    - MM Demo

Communication

- Contact PMI Mailbox for any PMI related questions
  - ncipmistandards@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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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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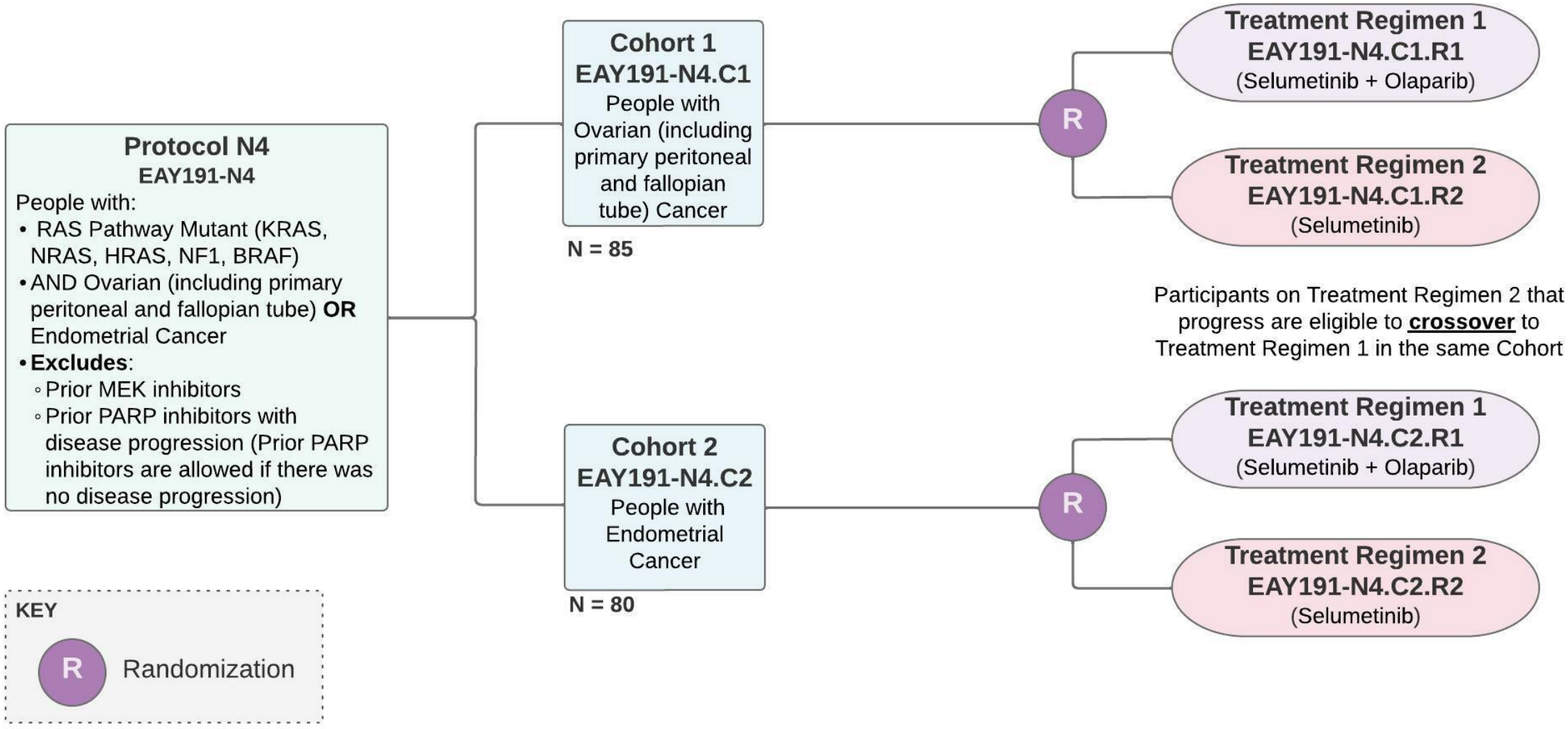
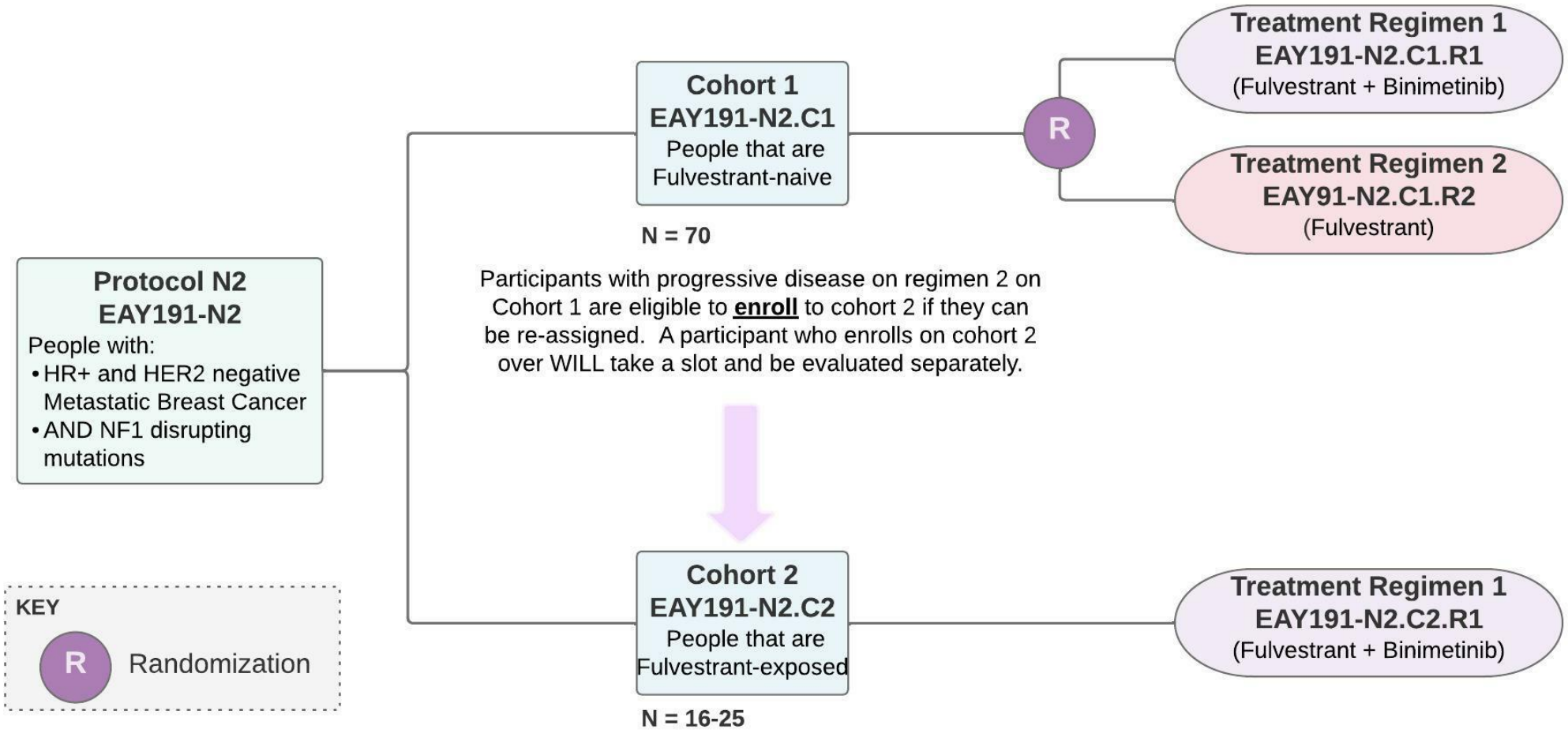
EAY191-N4


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

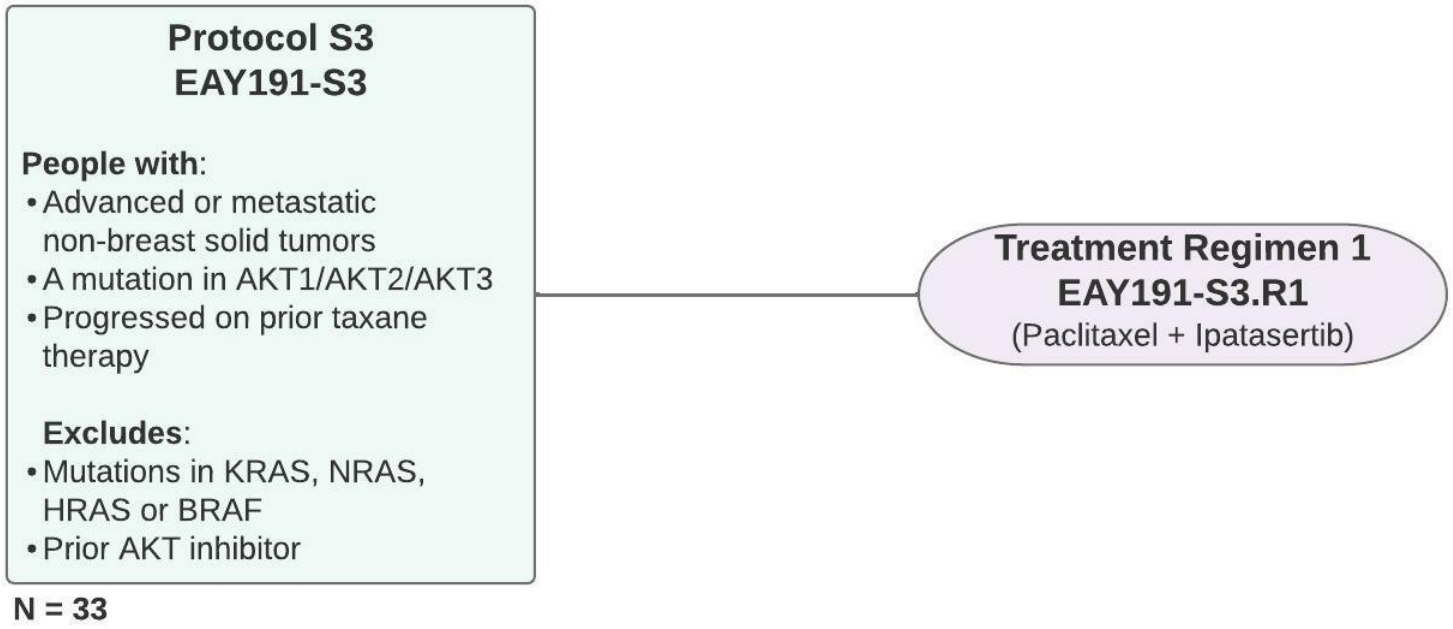
EAY191-E4


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