Precision Medicine Initiative (PMI) Committee Meeting

Mar 8, 2023

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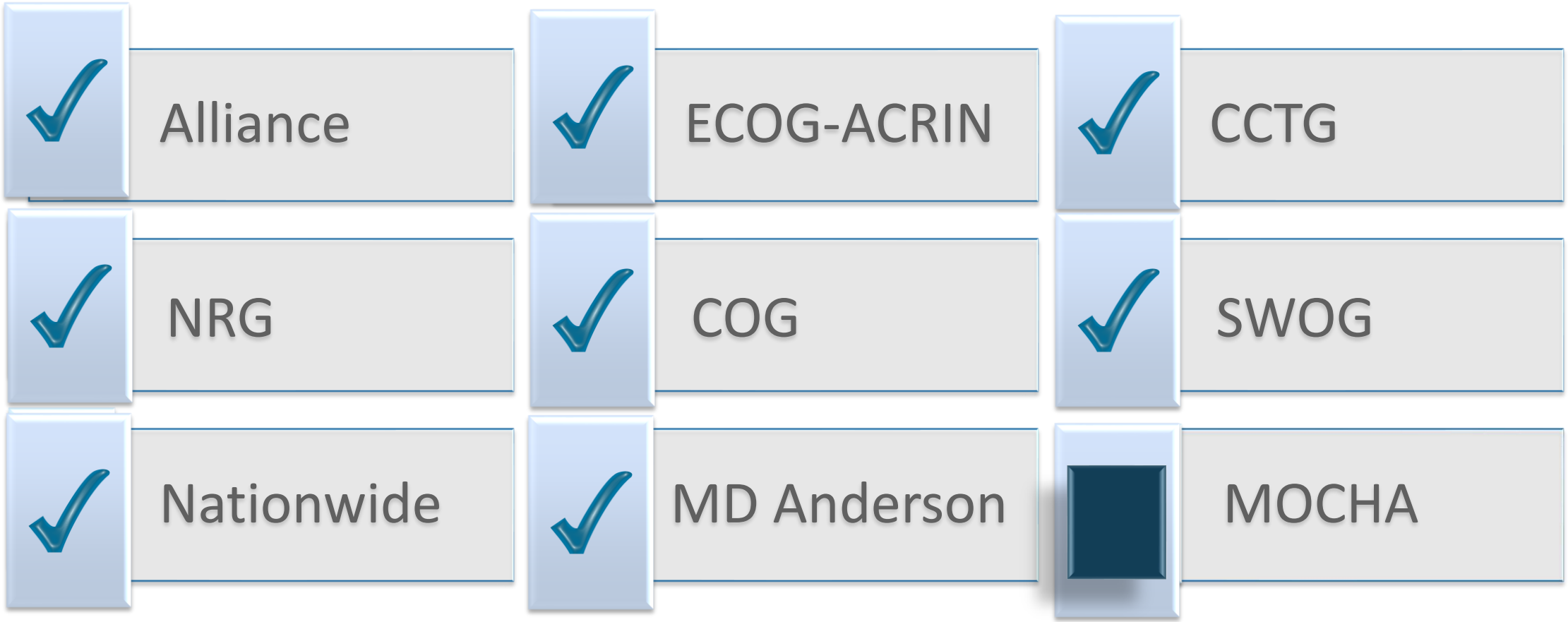
Agenda

- Role Call
- Project Status Updates
- Group Project Status Updates
- Target Project Timelines
- Open Discussion
- Next Steps

Stakeholder Representation



Project Status Updates

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Project Updates

- Completed FFP Testing
- Activated the following studies

Study #	Document Number	Document Title
1	EAY191	Molecular Analysis for Combination Therapy Choice (ComboMATCH)
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
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
5	EAY191-S3	Phase 2 Study of Paclitaxel + Ipatasertib in Taxane-Refractory Participants with AKT-Altered Advanced Non-Breast Solid Tumors

Upcoming Planning

- Post activation functionality for CM Release 1
- Target timeline and milestones for Priority 1 MM
- Target timelines and milestones for Priority 2 CM
- Lessons learned session for Priority 1 activation

Group Project Status Updates

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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
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%)	Screening 2/01/2023 Treatment 2/01/2023
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	100%	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)	Screening Treatment (Complete for Combo)
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%	Treatment 2/2/2023 2/2/2023
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 (95%) A6 (75%)	Treatment (3/17/2023) A6 (TBD)
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 TBD
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%)	Treatment 03/31/2023-C1

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	100% 100%	Ran a diff report, used existing version and matched production version (Y)	Completed	Imported Central Study, Ran a diff report, used existing version and matched production version (Y)	Completed
SWOG	100% 100%		Completed	Imported Central Study, Used diff report, used existing version and matched production version (Y)	Completed
NRG	N4 - 100% N4 – 100%	N/A	N/A	Imported Central Study, Used diff report, used existing version and matched production version (Y)	Completed
Alliance	100%	N/A	N/A	Imported Central Study, Used diff report, used existing version and matched production version (Y)	
CCTG		N/A	N/A		
COG		N/A	N/A		

Group Testing Roadblocks

Group	Roadblock
ECOG-ACRIN	***3/8/2023***
SWOG	***2/22/2023*** • *Consent spec, sending that information to NCI if a bank does not consent to banking* • *Once we move towards electronic, it will be available for tracking. For now we are using a manual process* • *Prior Therapy section for MM – Had particular things to be entered and may not be the same definition for prior therapy. Waiting on instructions* • *Morphology List – Reviewing the list of full items and will have a subset to use for MM; will send those values to the PMI mailbox* ***3/8/2023***
NRG	***3/8/2023***
Alliance	***3/8/2023***
CCTG	***2/22/2023*** • *Test patients pending* ***3/8/2023***
COG	***2/8/2023*** • *Waiting on derivations* ***3/8/2023***

PMI Project Discussion Items

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Open Discussion

- Dani
  - Is the timeline for MM still April
    - Had an IDE meeting with FDA – work that needs to be done to resolve lab assays
    - Demo will be end of March and include TAP protocols
    - Need a better understanding of what will be collected in OPEN and what will be needed in Rave (Specimens and for reassignment)
    - Neesha to schedule a call with SWOG to discuss requirements

Next Steps

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Next Steps

- Next meeting will be on 3/22/2023 at 1:00pm EST
- Agenda
  - Role Call
  - Project Status Update
  - Group Status Update
  - Review FAQs
  - Future Demos/Workflows
    - Target Date for MM Demo – March 29, 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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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

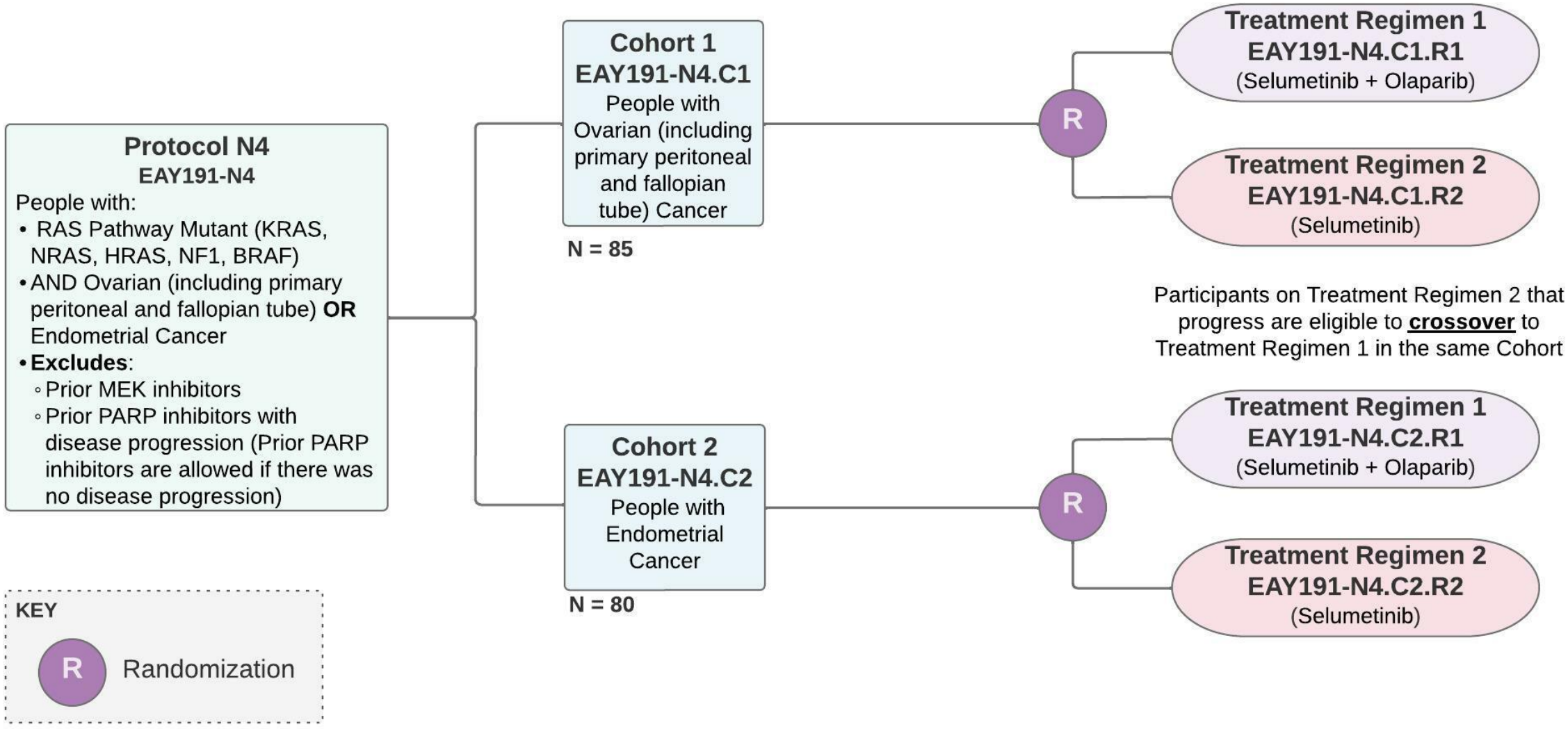
Study #	Document Number	Document Title	Group	Current Status	Next Steps
1	MYELOMATCH	Master Screening and Reassessment Protocol (MSRP) for the NCI MyeloMATCH Clinical Trials	SWOG	11/12/2021: Approval on Hold	CIRB Reviewed on 9/15, version with stips under CTEP review now.
2	MM1YA-S01	A Randomized Phase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

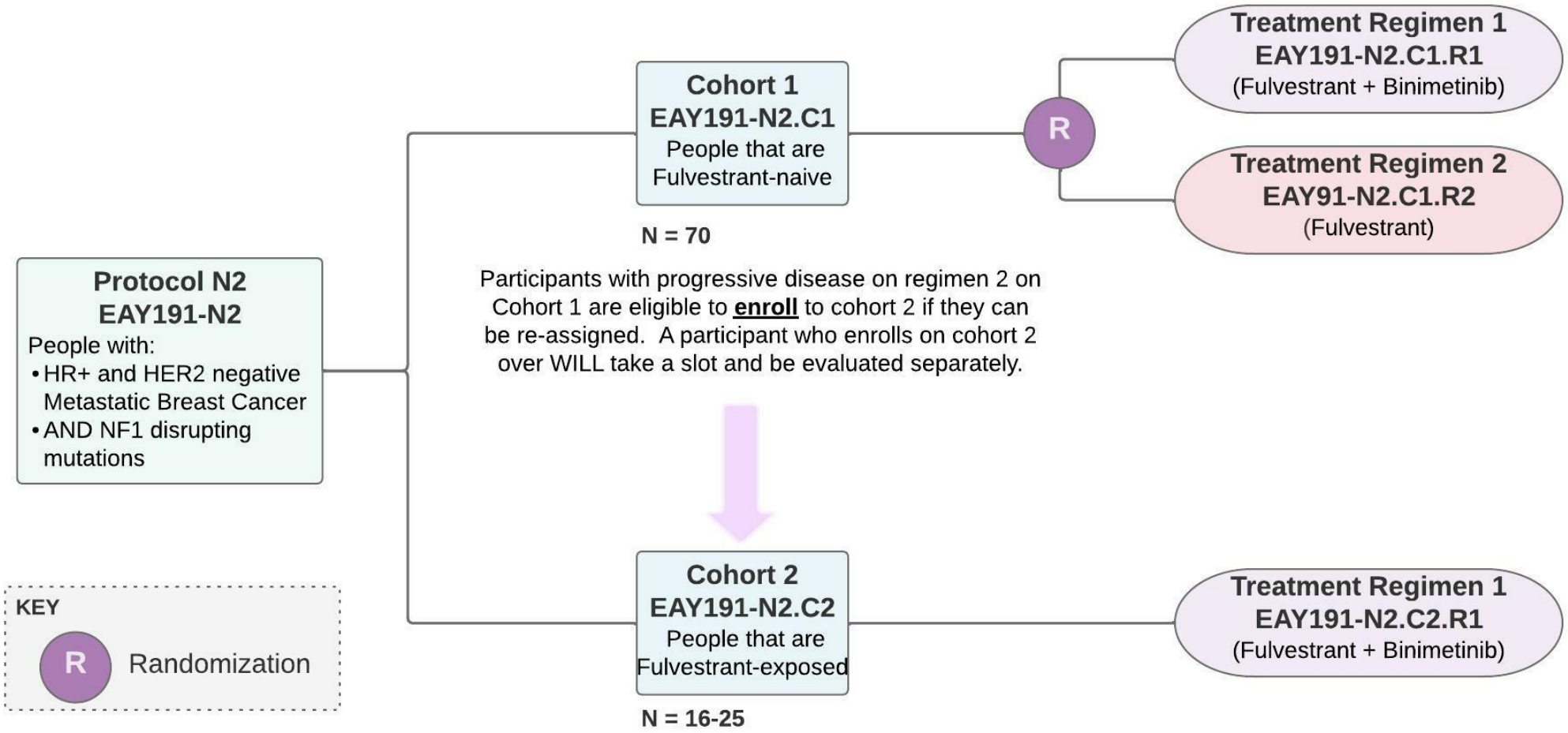
EAY191-N4


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

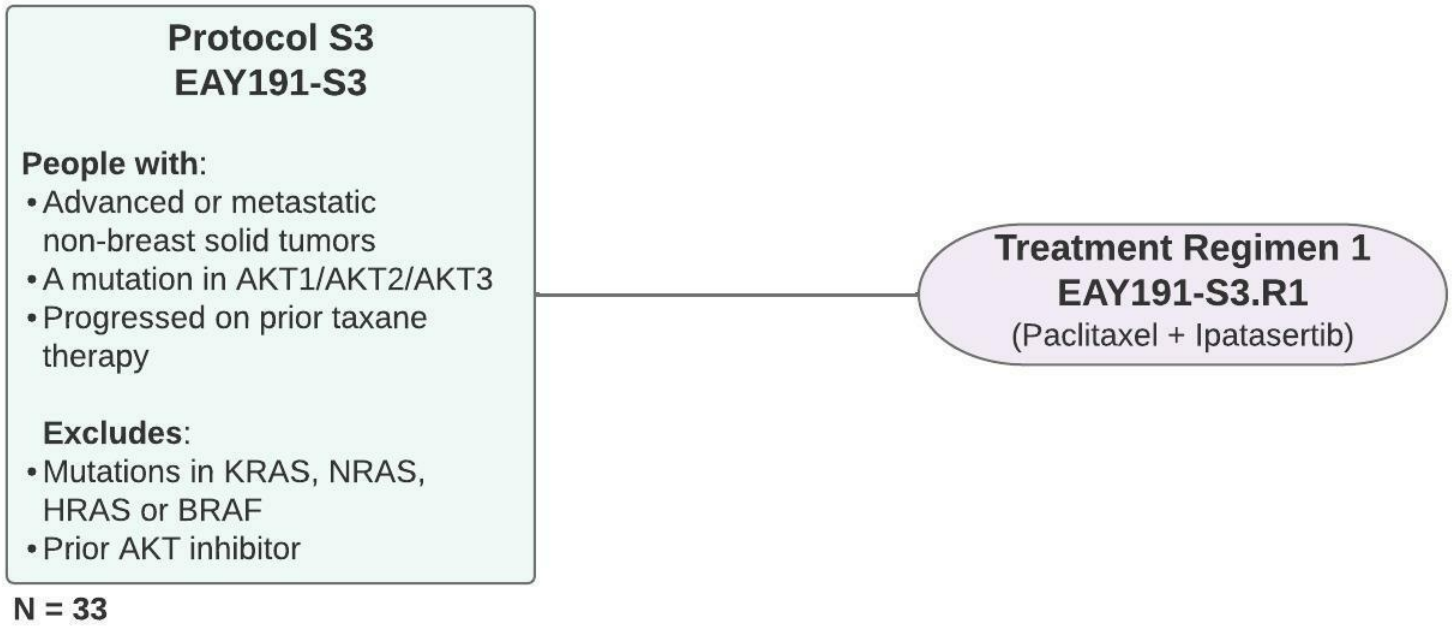
EAY191-E4


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