Precision Medicine Initiative (PMI) Committee Meeting

October 4, 2023

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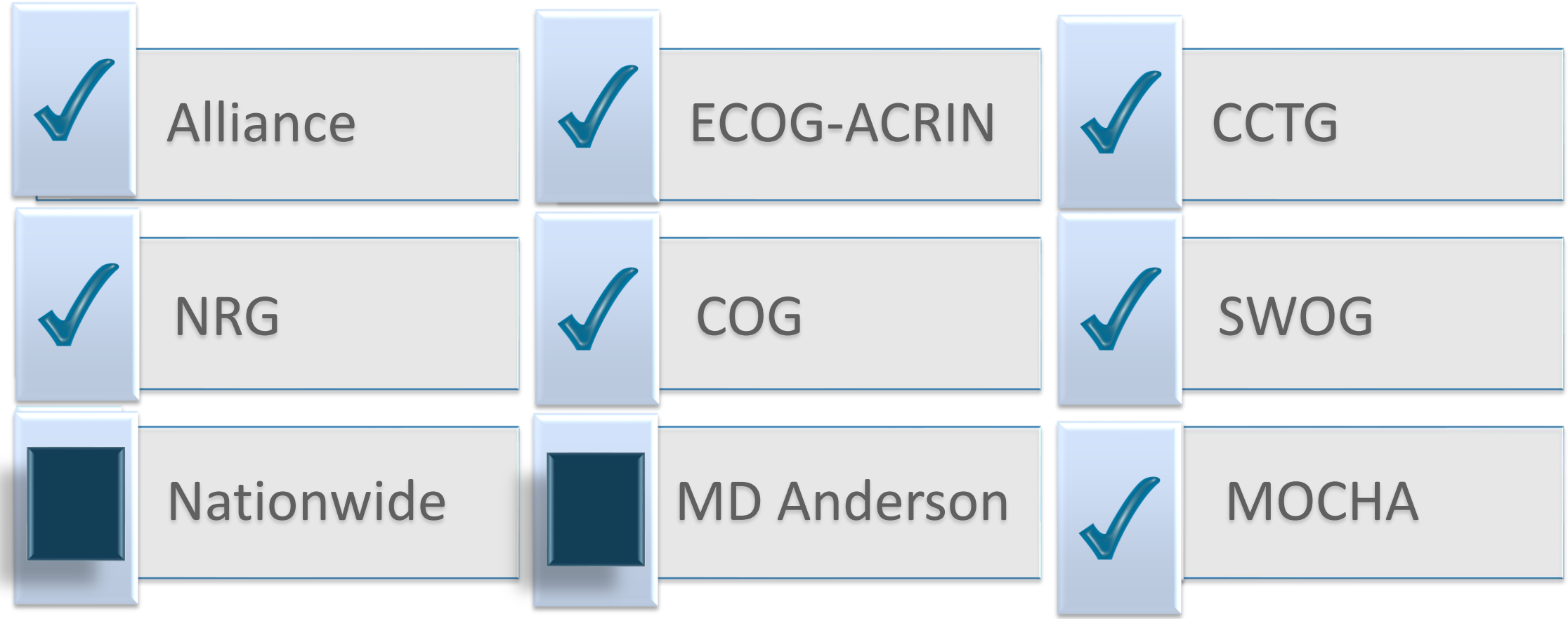
Agenda

- Role Call
- Project Status Updates
- Project Discussion Items
- Next Steps

Stakeholder Representation



Project Status Updates

Project Updates – PMI Deliverables

	Deliverable	Target Release Date	Target Release Vehicle
☑	**ComboMATCH changes** (Disease fields, histology, behavior field code)	**PROD Released: July 17, 2023**	**Screening Protocol EC Template v2.0**
☑	**Designated Labs for Combo**	**PROD Released: Sept 6, 2023**	**Screening Protocol EC Template v3.0** *(UAT Release w/EA – 07/27/2023)*
☑	**Re-Screening ComboMATCH**	**PROD Release: Sept 27, 2023**	**MSRP Re-Screening EC Template v1.0** *(UAT Release w/EA – 07/27/2023)*
☐	**Cohort Migration**	**PROD OPEN Release: Sept 28, 2023** *PROD EC Temp v1.0: Oct tbd, 2023*	**Treatment Protocol Cohort Migration EC Template v1.0** *(UAT Release w/TX Groups – 09/15/2023; updated UAT Fact Sheet v1.1 to be released to TX Groups – 10/04/2023; PROD EC Template v1.0 date TBD)*
☑	**MyeloMATCH Tx Protocol Crossover** (for S01, CTG01 and EA02)	*n/a*	Part of the existing Treatment Protocol workflow; no PRODUCTION OPEN Release required; the Westat team is prepared to support this workflow as Groups begin using it.
☐	**Re-Screening MM**	*n/a* *PROD RS EC Temp v2.0: Oct tbd, 2023*	No PRODUCTION OPEN Release is required for MM Re-Screening activities; the Westat team is prepared to support this workflow as Groups begin using it. **MSRP Re-Screening EC Template v2.0** *(UAT Release w/SWOG TBD – 10/xx/2023; PROD RS EC Template v2.0 date TBD)*
☐	**MyeloMATCH Stratification**	*PROD OPEN Release: Nov 15, 2023*	Part of existing Treatment Protocol Workflow.
☐	**BETA PMI Screening Protocol ALS v2.0** *New Forms: STMF, CLIA, PATH GROUP*	*BETA Release: Dec 22, 2023*	Target date for BETA Release for Groups to initiate UAT activities. *(accompanied by BETA Screening Protocol Central Study ALS v2.0)*
☐	**PROD PMI Screening Protocol ALS v2.0** *New Forms: STMF, CLIA, PATH GROUP*	*PROD Release: Feb 26, 2024*	Target date for PRODUCTION Release for Groups to initiate implementation activities. *(accompanied by PROD Screening Protocol Central Study ALS v2.0)*

Project Updates - EC Template Release Schedule

Template	Version	UAT Release Date	PROD Release Date	Details
☑ **PMI Screening Protocol EC Template**	V1.0	Released: 12/16/2022	**Released: 02/15/2023**	
☑ PMI Screening Protocol EC Template	V2.0	Released: 05/01/2023	**Released: 07/17/2023**	Includes CM changes (Disease fields, histology, behavior field code)
☑ PMI Screening Protocol EC Template	V3.0	Released: 07/27/2023	**Released: 09/06/2023**	Includes updates for Designated Labs (DLAP fields)
PMI Screening Protocol EC Template Fact Sheet	*v3.1*	*n/a*	*Target: 10/6/2023*	Administrative version/release of the Fact Sheet to capture MyeloMATCH Field Help/Instructional Text for the 'Prior therapy name' field; to be used in conjunction with the PMI Screening Protocol EC Template v3.0.
☑ **PMI Treatment Protocol EC Template**	V1.0	Released: 12/16/2022	**Released: 02/15/2023**	
☑ **PMI MSRP Re-Screening EC Template**	V1.0	Released: 07/27/2023	**Released: 09/27/2023**	Supports ComboMATCH MSRP.
☐ PMI MSRP Re-Screening EC Template	*V2.0*	*Target: 10/xx/2023*	*Target: 10/xx/2023*	*Supports MyeloMATCH MSRP; UAT date pending discussion with SWOG; PROD release date to be determined.*
☐ **PMI Treatment Protocol Cohort Migration EC Template**	*V1.0*	Released: 09/18/2023	*Target: 10/xx/2023*	*Supports cohort migration activities for ComboMATCH; PROD release date to be determined.*
PMI Treatment Protocol Cohort Migration EC Template Fact Sheet	*v1.1*	*Re-Release Target: 10/4/2023* Released: 09/18/2023	*n/a*	Administrative version/re-release of the UAT Fact Sheet to capture updated Field Help/Instructional Text for the 'Cohort migration assignment' field; to be used in conjunction with the UAT PMI Treatment Protocol Cohort Migration EC Template v1.0.

ComboMATCH Priority 1 List

#	Protocol #	Protocol Title	Group	Activated	Current Status
1	EAY191	Molecular Analysis for Combination Therapy Choice (ComboMATCH)	ECOG-ACRIN	**Yes**	***9/20:*** CTEP requested an amendment for EAY191 to remove SSN and Hospital Number. We anticipate activating this and another amendment on 9/27. Plan to combine these updates to OPEN with the addition of "Reassignment/Step 2" functionality on 9/27/2023. **10/4: Completed and no other updates**
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	**Yes**	***9/20:*** Working with CTSU on incorporating ineligibility requirements **10/4: Still waiting on the edit check with CTSU, Randonode was updated; Westat is doing internal testing**
3	EAY191-E4	A ComboMATCH Treatment Trial ComboMATCH Treatment Trial E4: Nilotinib and Paclitaxel in Patients with Prior Taxane-Treated Solid Tumors	ECOG-ACRIN	**Yes**	***9/20:*** Need to incorporate ineligibility **10/4: Working on** incorporating ineligibility requirements
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	**Yes**	***9/20:*** Need to incorporate ineligibility and cohort migration **10/4: Submitted OPEN request forms and new forms for STEP 1 and 2 are in OPEN. CSTU added a widget on Treatment model Step 2. Need patients but need to update Rave.**
5	EAY191-S3	Phase 2 Study of Paclitaxel + Ipatasertib in Taxane-Refractory Participants with AKT-Altered Advanced Non-Breast Solid Tumors	**SWOG**	**Yes**	9/20: Need to incorporate ineligibility ****Project team to send over additional information for implementation** **10/4: Westat will send over additional documentation for ineligibility implementation and will remove SSN.**

ComboMATCH Priority 2 List

#	Protocol #	Protocol Title	Group	Activated	Current Status
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	**Yes**	***9/20***: Need to incorporate ineligibility **10/4: No Update**
7	EAY191-A3	Palbociclib and Binimetinib in RAS-Mutant Cancers	Alliance	No	***9/20***: Need to incorporate ineligibility and cohort migration **10/4: Target Activated by 11/1, working on cohort migration**

ComboMATCH Priority 3 List

#	Protocol #	Protocol Title	Group	Current Status
8	EAY191-A2	Olaparib Plus Low-Dose Alpelisib for Breast Cancer	Alliance	***9/20:*** Dropped **10/4:**
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	***9/20:*** No attendance at meeting **10/4: Waiting on finalized protocol**
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	***9/20:*** Working on new Cohort Migration EC template; having interactive review for study build today **10/4: Working on OPEN setup**
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	***9/20:*** Protocol was submitted on 9/15 to PIO; starting study build but hoping for an extension; date is Oct 23rd – No cohort migration, just a crossover David will follow up with NRG and the Pis; cannot verify copy number loss; my require a protocol update David will send Rich the language to send to the sites to update **10/4: David will response on 10/5**

MyeloMATCH Priority 1 List

#	Protocol #	Protocol Title	Group	Current Status
1	MYELOMATCH	Master Screening and Reassessment Protocol (MSRP) for the NCI MyeloMATCH Clinical Trials	SWOG	***9/20:*** Need to know which version of the ALS should be used; which version of the EC template and which features do you expect to activate with? SWOG should proceed with Screening Protocol ALS v1.0 and PMI Screening Protocol EC Template v3.0 Step 2 Rescreening will not be required for the initial build No Specimen forms needed for initial activation **10/4: Started work on this again, target to finish is end of the month; SWOG can perform internal testing in OPEN UAT, that is okay to do that.**
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	***9/20:*** Will provide an update next meeting; is using an old EC template. **10/4: Started work, but focusing on Screening as a priority**
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	***9/20:*** No updates **10/4: No Updates**
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	***9/20:*** Started looking at study build, no OPEN work started yet **10/4: No Updates**

MyeloMATCH Priority 2 List

#	Protocol #	Protocol Title	Group	Current Status
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	**9/20** – No Updates **10/4: No Updates**
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	**9/20** – Will work on this after S01 is tested and completed to copy functionality **10/4: No Updates**
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	**9/20** – No Updates **10/4: No Updates**

MM Activation Update

- Rich had an IDE meeting, came to an agreement to respond to confirms, if they resubmit IDE, would be able to approve it.
- There will be a 30-day review day period. Hoping to get the IDE and IND applications by next week.
- Looking to activation mid to end of November.

PMI Project Discussion Items

Ineligibility Workflow

Open Discussion

Next Steps

Next Steps

Next meeting will be on 10/18/2023 at 1:00pm EST

Agenda

- Role Call
- Project Status Update
- Group Status Update
- Review FAQs

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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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

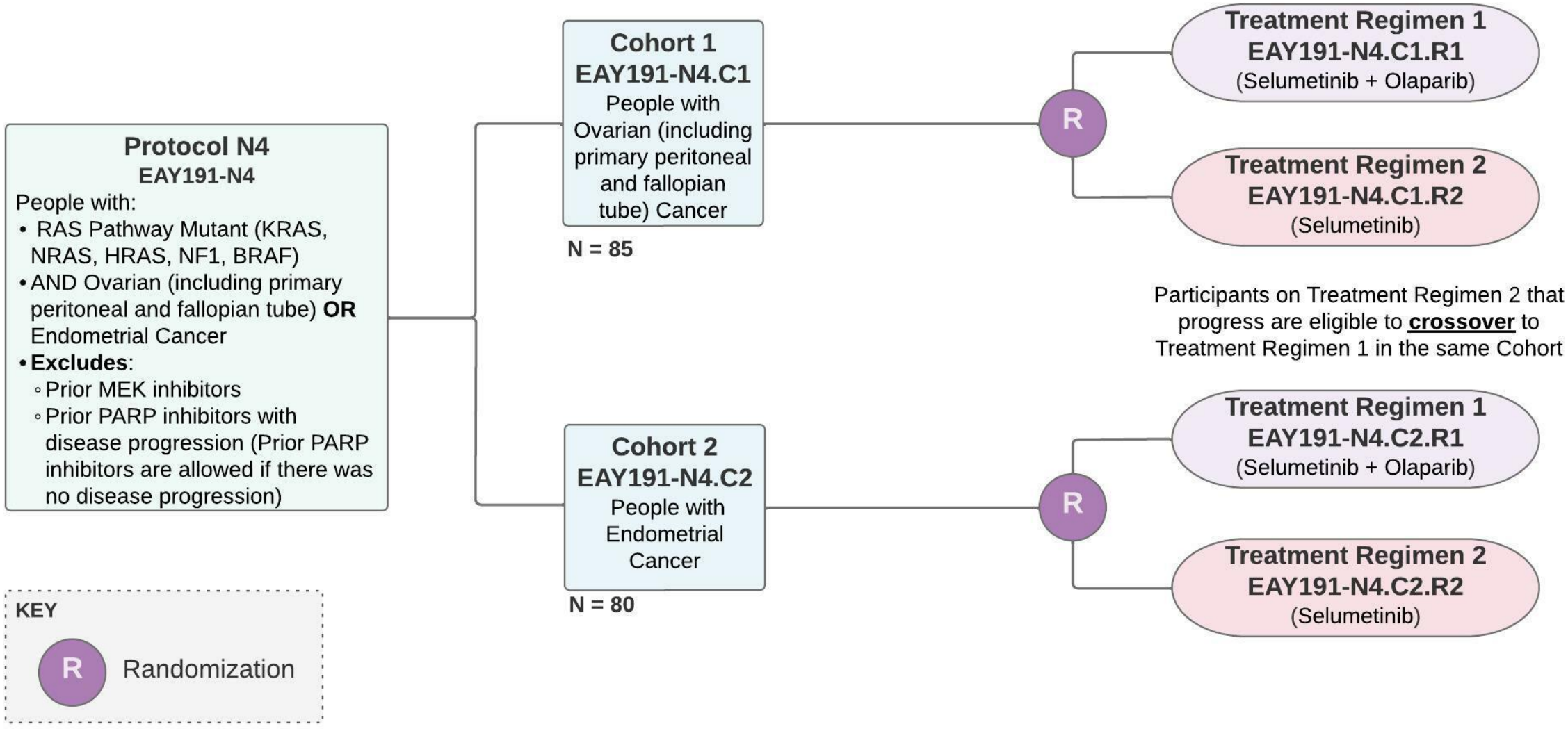
Study #	Document Number	Document Title	Group	Current Status	Next Steps
1	MYELOMATCH	Master Screening and Reassessment Protocol (MSRP) for the NCI MyeloMATCH Clinical Trials	SWOG	11/12/2021: Approval on Hold	CIRB Reviewed on 9/15, version with stips under CTEP review now.
2	MM1YA-S01	A Randomized Phase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

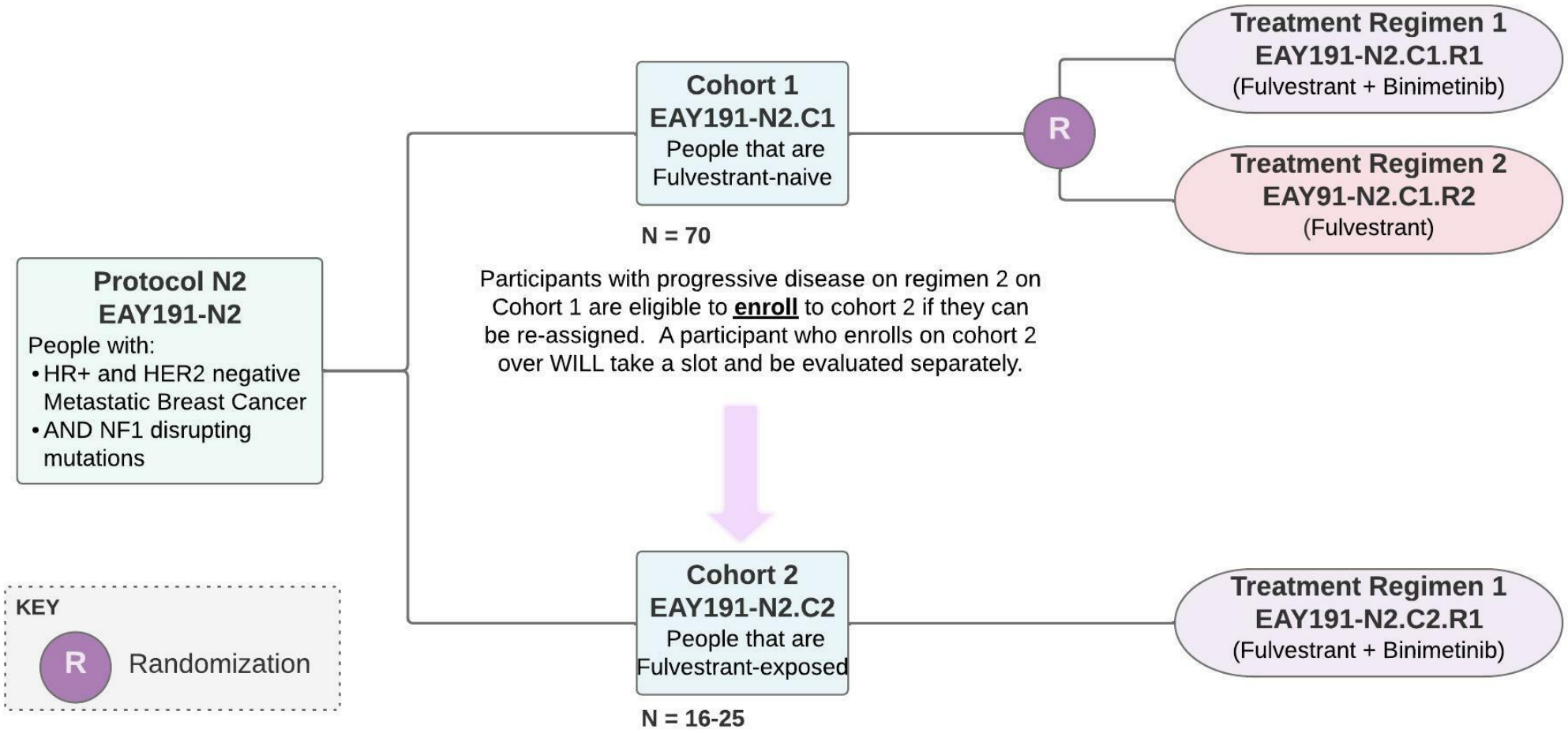
EAY191-N4


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

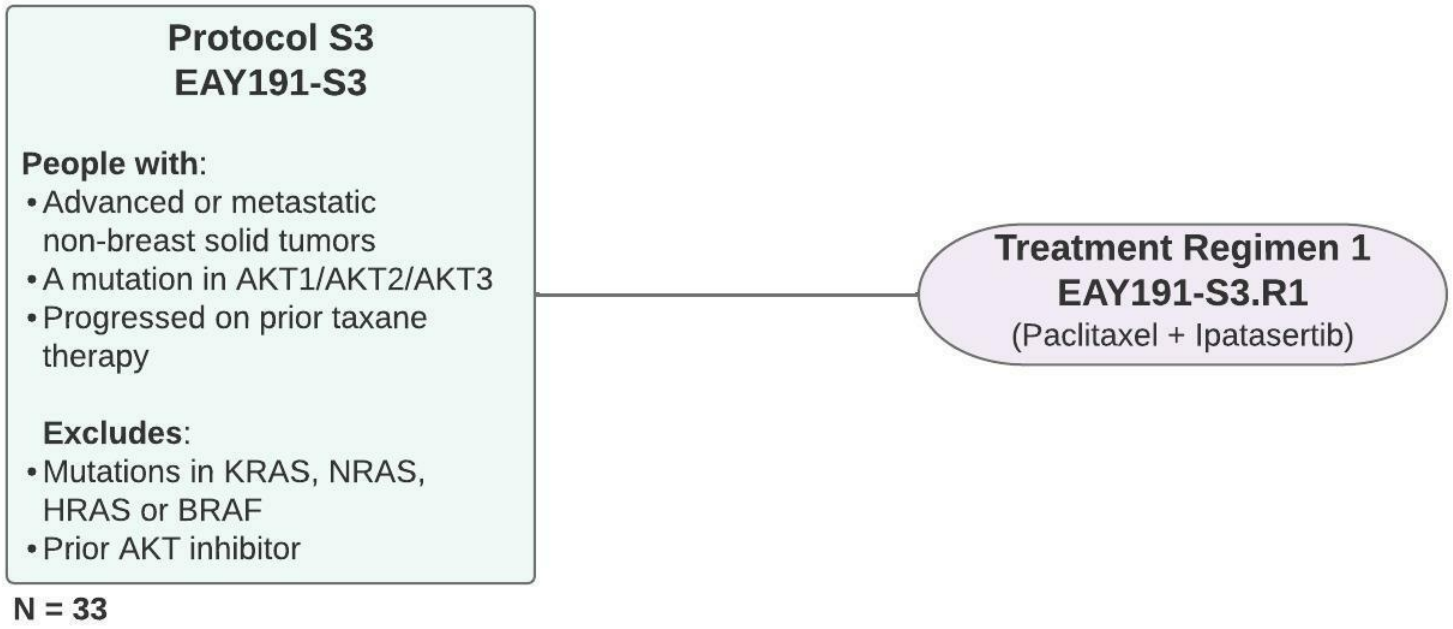
EAY191-E4


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