AVAHO - 2023
VA - SWOG Participation

Awareness
VA members of SWOG disease committee can directly promote trials to VA site investigators

Advantage for VA is regional CBOCs for laboratory assessments to avoid unnecessary travel to enrollment site. VA EMR provides ready access to longitudinal records and test ordering

Disadvantage can be geographically disparate populations in many regions (e.g., VISN 20)
Moving care to a different VA facility

Challenges
Institutional department support (e.g., pathology, pharmacy, radiology) for therapy and/or evaluation

Clarify VA Central Office (VACO) policies on support for enrollment on NCI-Cooperative Group studies.

US Department of Veterans Affairs SWOG Participating Members

US Department of Veterans Affairs SWOG Participating Members

- Tucson VA Medical Center
- Rocky Mountain Regional VA Medical Center
- John L. McClellan Memorial Veterans' Hospital
- West Haven VA Medical Center
- Tibor Rubin VA Medical Center
- Jerry L. Pettis Memorial Veteran's Hospital
- Jennifer Moreno Department of Veterans Affairs Medical Center
- Malcolm Randall Department of Veterans Affairs Medical Center
- Edward Hines, Jr. VA Hospital
- Colmery-O'Neil Veterans' Administration Medical Center
- Robert J. Dole Department of Veterans Affairs Medical Center and Regional Office Center
- Dwight D. Eisenhower Department of Veterans Affairs Medical Center
- Ioannis A. Lougaris Veterans' Administration Medical Center
- North Las Vegas VA Medical Center
- James J. Peters Department of Veterans Affairs Medical Center
- W.G. (Bill) Hefner Salisbury Department of Veterans Affairs Medical Center
- Louis Stokes Cleveland Department of Veterans Affairs Medical Center
- Jamaica Plain VA Medical Center
- LTC Charles S. Kettles VA Medical Center
- Portland VA Medical Center
- Kansas City VA Medical Center
- Corporal Michael J. Crescenz Department of Veterans Affairs Medical Center
- Providence VA Medical Center
- Clement J. Zablocki Veterans' Administration Medical Center
- Ralph H. Johnson Department of Veterans Affairs Medical Center
- Michael E. DeBakey Department of Veterans Affairs Medical Center
- Audie L. Murphy Memorial Veterans' Hospital
- George E. Wahlen Department of Veterans Affairs Medical Center
- White River Junction VA Medical Center
- VA Puget Sound Health Care System – Seattle Division

S2209 (NCT 05561387)

A PHASE III RANDOMIZED TRIAL FOR “FRAIL” OR A SUBSET OF “INTERMEDIATE FIT” **NEWLY DIAGNOSED MULTIPLE MYELOMA (NDMM)** PATIENTS COMPARING UPFRONT THREE-DRUG INDUCTION REGIMENS FOLLOWED BY DOUBLE- OR SINGLE-AGENT MAINTENANCE

Study Chairs:
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Brea Lipe, MD
Krisstina Gowin, D.O. (Quality of Life/PRO)
Thomas Chauncey, M.D., Ph.D. (VA Committee)

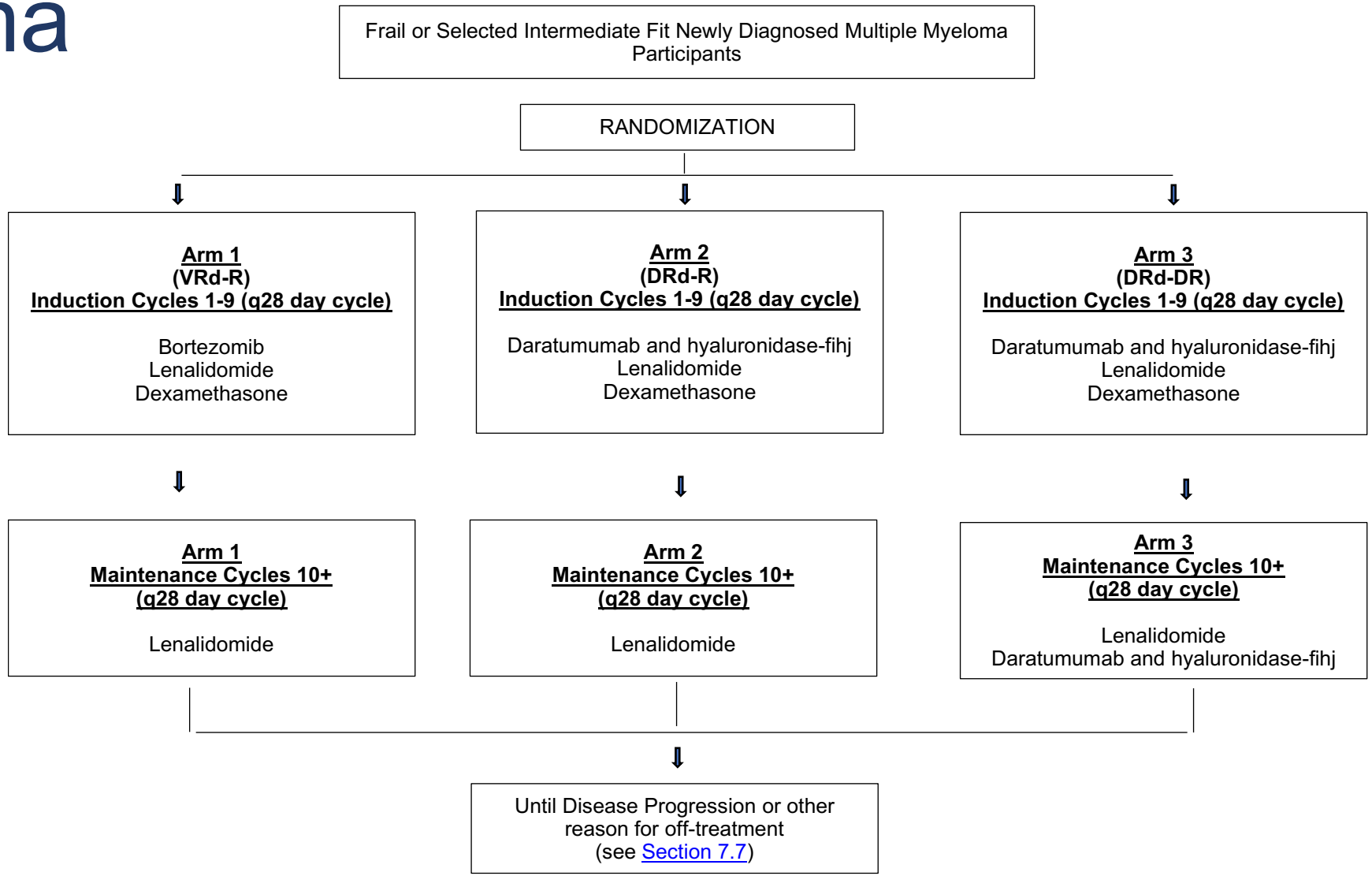
Background/Overview

- Unmet needs in frail and real-world patients with NDMM.
- “VRd-Lite” is a widely accepted regimen before Daratumumab approval (O’Donnell et al, Br J Haematol 2018).
- DaraRd showed better PFS compared with Rd in MAIA trial in transplant ineligible patients (Facon et al, NEJM 2019) and has become a new standard of care in this patient population.
- Patients are often considered ineligible for prospective clinical trials due to strict inclusion criteria.

➢ Introducing practical inclusion criteria to maximize study enrollment from this group and focusing on real-world NDMM patient population

Schema

SCHEMA



Eligibility – Key criteria

- Participants must have documented multiple myeloma satisfying standard International Myeloma Working Group (IMWG) diagnostic criteria (Protocol Section 4.1) and measurable disease within 28 days prior to registration:
  - IgG MM with M spike ≥0.5 g/dL
  - IgA, IgM, IgD, IgE MM with M spike ≥0.2 g/dL
  - Urine M-protein level ≥200 mg/24 hrs
  - Light chain MM with involved free light chains ≥10 mg/dL and abnormal serum free light chain ratio
- Participants must not have received any prior systemic therapy for multiple myeloma with exception of:
  - Emergency use short course of corticosteroids,
  - Up to 1 complete cycle of a non-daratumumab and hyaluronidase-fihj containing anti-myeloma regimen allowed,
  - Localized palliative radiation for multiple myeloma, must be completed at least 3 days prior to starting protocol-directed systemic treatment.

Management Considerations: Fitness Status

IMWG Frailty Score

Variable		HR (CI 95%)	*P*	SCORE
AGE	Age <75 years	1	-	0
	Age 75-80 years	1.37 (0.93-2.03)	.114	1
	Age >80 years	2.75 (1.81-4.18)	<.001	2
CHARLSON INDEX	Charlson ≤1	1	-	0
	Charlson ≥2	1.6 (1.07-2.39)	.021	1
ADL SCORE	ADL >4	1	-	0
	ADL≤4	1.76 (1.14-2.71)	.01	1
IADL SCORE	IADL >5	1	-	0
	IADL≤5	1.53 (1.03-2.27)	.036	1

Additive Total Score	Patient Status
0	FIT
1	UNFIT
≥2	FRAIL

Palumbo A, Bringhen S, Rajkumar SV, et al. *Blood*. 2015;125(13):2068-2074.

Management Considerations: Fitness Status

Additive Total IMWG Frailty Score and Related Rate of OS, PFS At 3 Years

Additive Total Score	Patient Status	No. of Patients (%)	OS (95% CI)	PFS (95% CI)	Cumulative Incidence at 12 mo, %	
					Treatment Discontinuation	Grade 3-4 Nonhematologic AEs
0	Fit	340 (39)	84 (78-89)	48 (41-56)	16	22
1	Intermediate-fitness	269 (31)	76 (67-82)	41 (32-49)	21	26
≥2	Frail	260 (30)	57 (45-68)	33 (25-41)	31	34

Palumbo A, Bringhen S, Rajkumar SV, et al. *Blood*. 2015;125(13):2068-2074.

Study Objectives

Dual Primary Objectives

- To compare progression-free survival (PFS) in frail or selected intermediate fit NDMM participants treated with VRd-Lite induction followed by Len maintenance (Arm 1) versus DRd induction followed by Len maintenance (Arm 2).
- To compare overall survival (OS) in frail or selected intermediate fit NDMM participants treated with VRd-Lite induction followed by Len maintenance (Arm 1) versus DRd induction followed by Dara-Len maintenance (Arm 3).

Study Objectives

QoL Objectives

- To compare patient-reported global health status between treatment arms (Arm 1 versus the combination of Arms 2 and 3) at 9 months after randomization (end of induction therapy) using the European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life Questionnaire (QLQ-C30).
- To compare longitudinal changes in global health status between treatment arms (Arm 1 versus the combination of Arms 2 and 3) from baseline to 9 months after randomization (end of induction therapy).

PRO-CTCAE Objective

- To compare selected patient-reported outcome symptoms using PRO-CTCAE items among the 3 study arms.

Study Objectives

Additional Objectives- MRD Assessment

- To compare the rate of MRD by clonoSEQ® after 9 cycles of induction in Arm 1 vs. Arm 2 and Arm 3, respectively.
- To compare the rate of MRD conversion after 1 year of maintenance in participants who were MRD positive after induction in Arm 1 vs. Arm 2 and Arm 3, respectively.
- To compare the rate of sustained MRD negativity at time points of post-induction and post-1 year maintenance in Arm 1 vs. Arm 2 and Arm 3, respectively.

Additional Objectives- Banking

- To bank specimens for future correlative studies.

Follow-up

- Every 3 months* in Year 1, then
- Every 6 months* in Years 2-3, then
- Annually* for up to 10 years or death, whichever occurs first.

* or more frequently as clinically indicated at provider's discretion

Funding

- The daratumumab and hyaluronidase-fihj medication will be provided by the study.
- Bortezomib, lenalidomide and dexamethasone will be used from the commercial sourcing.
- S2209 available site payments information is included in the table below.

Funding Source and Study Component		Collect Type	Study Specific Notes	Enter Date in Open? (c)	NCTN Funding per Patient (a) Std/HP LAPS	NCORP Funding per Patient (b) Std/HP
Federal	Base Intervention – Standard / High Performance LAPS & NCORP	Mandatory		No	$2,700/$4,300	$2,700/$4,300
Federal	Biospecimen – Bone Marrow Multiple Time Points	Mandatory Request	1	Yes	$300	$300
Federal	Biospecimen – Blood Multiple Time Points	Mandatory Request	1	Yes	$200	$200
Federal	QOL/PRO Questionnaires	Mandatory	2	Yes	$1000	$1000
Total Potential Federal Funds					**$4,200/$5,800**	**$4,200/$5,800**
Total Potential Funds					**$4,200/$5,800**	**$4,200/$5,800**

Study Specific notes:

1. See Protocol Section 15.1-15.3. Federal biospecimen payments will be triggered by submission of information for the first time point for each submission type into the OPEN system.
2. See Protocol Section 15.4. Federal Quality of Life/Patient Reported Outcomes payments will be triggered by submission of information for the first time point into the OPEN system.

National Coverage Determinations (NCD)

Under NCD 310.1, the Medicare program covers "routine costs of qualifying clinical trials … as well as reasonable and necessary times and services used to diagnose and treat complications arising from participation in all clinical trials." The term "routine costs" is a defined term under the Clinical Trial Policy.

NCD 310.1 allows for coverage of routine costs of conventional care. UpToDate article "Multiple Myeloma: Evaluating Response to Treatment" (SV Rajkumar; last updated 07/01/22), "We typically reserve MRD assessment for patients on clinical trials. MRD status is prognostic, and has been proposed as a surrogate marker for progression-free survival (PFS) and overall survival (OS) in clinical trials." Per NCD 90.2, Article ID A56277, the clonoSEQ® Assay was granted de novo designation by the FDA and is the only MRD assessment tool to have received FDA clearance for the measurement of MRD in patients with MM. Effective 03/16/2018, molDX has determined that clonoSEQ® Assay testing is reasonable and necessary when performed on bone marrow specimens in patients with MM. Medicare will pay for a single episode of testing using clonoSEQ® in these patients. For a patient with MM in whom clonoSEQ® is being used according to its FDA cleared indications and clinical guidelines, it is anticipated that an episode of testing will typically require a baseline assay and 3 follow-up assays. This service should be billed at the start of the episode of testing. Medical records must document medical necessity to support billing.

AVAHO - 2023
VA - SWOG Participation

Understand and navigate the challenges in VA site participation

Provide access to NCI-Cooperative Group studies for eligible veterans