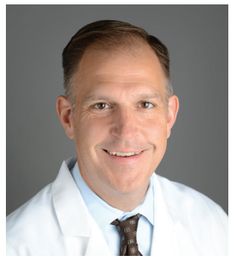
Saad Z. Usmani, MD, FACP

Chief, Plasma Cell Disorders; Director, Clinical Research in Hematologic Malignancies



Peter M. Voorhees, MD

Director, Outreach Services; Plasma Cell Disorders

Manisha Bhutani, MD

Leader, Early Myeloma Program; Plasma Cell Disorders

Reed Friend, MD

Plasma Cell Disorders

Advancing PCD Research and Care

- One of 17 Multiple Myeloma Research Consortium (MMRC) leading early drug development and clinical trials (https://www.themmrf.org/research-partners/clinic/about-the-mmrc/member-institutions/)
- One of the 40 Internal Myeloma Foundation Black Swan Research Initiative (IMF BSRI) sites collaborating for a curative strategy in multiple myeloma (http://bsri.myeloma.org/bsri-team/)
- Internationally recognized clinical and translational research program with >20% trial enrollments comprising minorities and >100 research manuscripts/abstracts published since 2013
- More than 1,000 active patients being followed in clinic cared for by a multi-disciplinary team (Pain Management, Orthopedics, Radiation Oncology, Nephrology, Cardio-Oncology, Infectious Diseases, etc.)

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PROGRESS IN PLASMA CELL DISORDERS

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Shifting Paradigms in Myeloma Care

by Saad Z. Usmani, MD, FACP (Chief, Plasma Cell Disorders Division)

The management of multiple myeloma (MM) has seen a drastic change over the last 15 years, where the median survival for an average MM patient has improved from less than 2 years to seven to 10 years. MM represents a malignant clonal expansion of transformed plasma cells that eventually undergo clonal evolution and heterogeneity that is believed to be the basis of drug resistance with sequencing therapy. This makes MM a complex, multi-hit malignancy with a prognosis and outcome that is extremely variable even in the era of novel agents.

The initial MM prognostic models were developed based on clinical observations and routine laboratory findings. The most commonly used systems are International Staging System (ISS) and Durie-Salmon Staging (DSS), which include data on the presence of bone lytic lesions, Beta-2, serum levels of monoclonal proteins, calcium, creatinine, albumin, -2 microglobulin and hemoglobin concentration. Both these models provide an estimation of burden of disease and also capture host factors/morbidity, but do not account for the biologic heterogeneity of MM. Several techniques using comprehensive evaluation of bone marrow samples (metaphase cytogenetics, fluorescent in situ hybridization, gene expression profiling) have helped us identify the biologic bad actors in MM.

The eventual goal of prognostication for any human disease is to provide for a risk-adaptive therapeutic strategy. Clinicians and cancer researchers now recognize that such prognostication needs to include the host factors (age, co-morbidities and performance status), disease burden (ISS and/or DSS) and disease biology. The MM researchers recognize that our ability to assess the depth of response, by way of following serum M proteins and/or bone marrow examinations, is inadequate. Inclusion of novel imaging (PET/CT, WB-MRI) and specialized lab tests (DNA PCR and/or Flow cytometry) to assess minimal residual disease are being included to assess better depth of response in clinical trials. We also recognize that we need to find a better answer for the “high-risk” MM patients and develop new drug classes that can improve their outcomes.

Levine Cancer Institute’s Plasma Cell Disorders (PCD) program opened its doors to patients in 2013 at its administrative and research headquarters in Charlotte, NC. The program has brought these advances in management to the MM patients being cared for in the Charlotte metro area and intends to expand its reach throughout Carolinas HealthCare System.

The Institute’s PCD program has established uniform practice guidelines that help oncologists across the Institute’s vast network in treating MM patients by having readily available access to an expert opinion. It has also brought value to communities across the Carolinas by offering many clinical trials with novel treatments for both newly diagnosed and previously treated MM patients. In a short span of time, the program has established an international reputation for excellence in clinical care and research.

The Bone Marrow Transplant, established in 2014, has now performed more than 100 stem cell transplants for multiple myeloma and amyloidosis. (SEE PAGE 4)

Early Myeloma Program

by Manisha Bhutani, MD

The comprehensive plasma cell disorders program at Levine Cancer Institute under the leadership of Dr. Saad Usmani has pioneered the initiative of opening an Early Myeloma Program. The program will be directed by Dr. Manisha Bhutani.

The mission of the program is to foster translational research leading to the development of blood tests and molecular imaging approaches to detect cases of monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma at high risk of progression to multiple myeloma (MM), and to offer state-of-the-art clinical trials to patients with smoldering MM and patients with MGUS-related neurologic, hematologic, immunologic or renal disorders. These initiatives will have extensive collaborative links to other facilities of the Institute within the area.

One major focus of the program will be on the African-American population, which has an increased incidence of MGUS and MM and whose cancer education, diagnostic and treatment needs often go undetected or unaddressed for a variety of socioeconomic reasons. Early detection of MM and other plasma cell disorders is difficult because symptoms are non-specific, and patients may be evaluated by a number of practitioners for seemingly unrelated symptoms.

Multiple myeloma might cause indistinct symptoms that mimic many other conditions. Sometimes, however, multiple myeloma or MGUS may be detected based on routine blood tests showing an unusually high level of protein in blood or urine. Often MM is not detected at all until it progresses into advanced stages with such symptoms as anemia, bone pain, renal failure or hypercalcemia.

This program will reach out to regional communities to offer educational programs to increase awareness regarding plasma cell disorders.

Nurse Navigation for PCD

by Patty Fredenburgh, RN

Levine Cancer Institute has a well-developed Nurse Navigation Program. The purpose of a nurse navigator is to answer questions, address patient concerns and provide a better patient experience. The Institute's Multiple Myeloma Program has a designated nurse navigator who is an integral part of the team.

Multiple myeloma can be a very complicated disease. The nurse navigator is there to explain the disease and make things less confusing. The navigator contacts new patients before their appointment and prepares the patient for their clinic visit. She or he can reduce anxiety by addressing any questions or concerns. The navigator will talk with the patient about any needs they may have and help provide resources to meet those needs, such as access to financial assistance, community resources or other support services. The nurse navigator is able to help improve communication between the patient/caregivers and the healthcare team. She or he will work with the referring offices to ensure that the transition of care is smooth and uneventful for patients and their caregivers.

If you have any questions or would like to get in touch with our nurse navigators, please call 980-442-2021.

Active and Upcoming Clinical Trials

Smoldering Multiple Myeloma

- Phase III study of Daratumumab versus observation for Smoldering MM
- Phase II study of Nivolumab, Lenalidomide and Dexamethasone for Smoldering MM
- Phase II study ASCENT (Aggressive Smoldering Cure Evaluating Novel Rx Transplant) for high risk Smoldering MM

Newly Diagnosed Multiple Myeloma

- Phase Ib study of Carfilzomib, Lenalidomide, Dexamethasone and Daratumumab for newly diagnosed transplant eligible Multiple Myeloma
- A Phase III study comparing Daratumumab, Lenalidomide and Dexamethasone (DRd) vs Lenalidomide and Dexamethasone (Rd) in subjects with previously untreated transplant ineligible Multiple Myeloma
- A Phase III study of Lenalidomide and low-dose Dexamethasone with or without Pembrolizumab (MK3475) in subjects with previously untreated transplant ineligible Multiple Myeloma
- A randomized Phase I/II Study of Optimal Induction Therapy of Bortezomib, Dexamethasone and Lenalidomide with or without Elotuzumab (NSC-764479) for Newly Diagnosed High Risk Multiple Myeloma (HRMM)
- Phase II study comparing Daratumumab, Lenalidomide, Bortezomib, and Dexamethasone (D-RVd) versus Lenalidomide, Bortezomib, and Dexamethasone (RVd) in subjects with newly diagnosed Multiple Myeloma

Relapsed/Refractory Multiple Myeloma

- A Phase 1b study of SAR650984 (Anti-CD38 mAb) in combination with Pomalidomide and Dexamethasone for the treatment of relapsed/ refractory multiple myeloma
- An Open-label, Multicenter, Dose Escalation Phase 1b study to assess the safety and pharmacokinetics of subcutaneous delivery of Daratumumab with the addition of Recombinant Human Hyaluronidase (rHuPH20)
- A Phase 1b Multicenter, Open-Label study to determine the recommended dose and regimen of Durvalumab (MEDI4736) either as monotherapy or in combination with Pomalidomide (POM) with or without low dose Dexamethasone (DEX)
- The Targeted Agent and Profiling Utilization Registry (TAPUR) study
- Phase I/II trial of Carfilzomib, Ruxolitinib and Dexamtheasone for Carfilzomib-Refractory Multiple Myeloma
- Phase II study of Daratumumab and Pembrolizumab for Relapsed/Refractory MM
- Phase II study of Daratumumab, Pomalidomide, Dexamethasone and Pembrolizumab for Relapsed/Refractory MM
- Phase I/II study of Ixazomib, Pomalidomide and Dexamethasone for Relapsed/Refractory MM
- Randomized Phase II study of Pomalidomide and Dexamethasone with or without Elotuzumab for Relapsed Multiple Myeloma

Newly Diagnosed Systemic AL Amyloidosis

- Phase 3, Randomized, Multicenter, Double-Blind, Placebo-Controlled, 2-Arm, Efficacy and Safety Study of NEOD001 Plus Standard of Care versus Placebo Plus Standard of Care in Subjects with Light Chain (AL) Amyloidosis