Highlights from the NCCN 10th Annual Congress: Hematologic Malignancies

On Friday, October 16, and Saturday, October 17, 2015, NCCN hosted its 10th Annual Congress: Hematologic Malignancies.

This year's event was moderated by Andrew D. Zelenetz, MD, PhD, Memorial Sloan Kettering Cancer Center, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Panel Chair for Non-Hodgkin's Lymphomas (NHL), and Dr. Ranjana Advani, MD, Stanford Cancer Institute, Member of the NCCN Guidelines Panel for NHL. More than 540 oncology professionals attended the event, which featured expert speakers from the NCCN Member Institutions.

The presentations focused on a wide range of topics in hematologic malignancies, including chronic lymphocytic leukemia (CLL), NHL, acute myeloid leukemia (AML), myelodysplastic syndromes (MDS), acute lymphoblastic leukemia (ALL), multiple myeloma (MM), Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma (WM/LPL), Castleman disease, classical Hodgkin lymphoma (CHL), and survivorship issues. In addition, 9 patient case studies were presented in 3 interactive panel discussions.

Friday's session commenced with opening remarks from Dr. Zelenetz followed by patient case study presentations involving different subtypes of NHLs and discussion by panelists, Jeremy S. Abramson, MD, Massachusetts General Hospital Cancer Center; Dr. Advani; and Dr. Zelenetz. This interactive session underscored the importance of accurate diagnosis and individualizing treatment options (depending on patient's age, performance status, and comorbidities) in the management of mantle cell lymphoma, ALK-negative anaplastic large cell lymphoma, and double-hit diffuse large B-cell lymphoma.

William G. Wierda, MD, PhD, The University of Texas MD Anderson Cancer Center, summarized data from clinical trials that led to the approval of ibrutinib and idelalisib (small molecule inhibitors of B-cell receptor signalling pathways) for the management of heavily pretreated relapsed/refractory CLL with del (17p) and del (11q). Ibrutinib is also approved for first-line therapy for CLL with del (17p). Venetoclax is an oral Bcl-2 inhibitor with potent monotherapy activity in high-risk relapsed/refractory CLL which may be approved in the near future for the treatment of relapsed/refractory CLL, Dr. Wierda acknowledged.

In the next presentation, Dr. Zelenetz explained the need for new treatment strategies for the management of follicular lymphoma (FL) and provided a comprehensive overview of clinical trials evaluating a variety of emerging treatment options for first-line therapy and relapsed/refractory FL. He also alluded to the new clinicogenomic risk model (M7-FLIPI) that improves risk stratification with the integration of mutational status of 7 genes (*EP300*, *FOXO1*, CREBBP, *CARD11*, *MEF2B*, *ARID1A*, and *EZH2*), FLIPI and ECOG performance status. M7-FLIPI may help to identify high-risk patients at diagnosis who would be candidates for novel treatments, Dr. Zelenetz noted.

Friday's session concluded with the presentation on the management of HIV-associated NHLs. Lawrence D. Kaplan, MD, UCSF Helen Diller Family Comprehensive Cancer Center, highlighted the special considerations for the treatment of aggressive NHLs in patients with HIV-infection. Rituximab should be included with frontline chemotherapy regimens for most patients with the exception of those with CD4 count less than 50, he pointed out. Antiretroviral therapy, when administered with chemotherapy, achieves better control of HIV replication. Most importantly, communication between the oncologist and HIV-treating physician is critical, Dr. Kaplan emphasized.

Saturday morning opened with 3 case studies involving myeloproliferative neoplasms (MPNs) and hemophagocytic lymphohistiocytosis (HLH) presented by Peter L. Greenberg, MD, Stanford Cancer Institute; Jessica Altman, MD, Robert H. Lurie Comprehensive Cancer Center of Northwestern University; and Joseph C. Alvarnas, MD, City of Hope Comprehensive Cancer Center. Dr. Greenberg discussed distinctions among classical MPNs, less common MPNs, and MDS/MPNs. Treatment of MPNs is complicated by

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phenotypic mimicry, determinants of thrombotic risk, and molecular markers; however, risk prognostication tools are available. Dr. Altman elaborated on current and new drugs that target various mutations including *Jak2* and telomerase inhibitors for myelofibrosis in older patients. The next case study presented by Dr. Alvarnas illustrated the diagnosis and management of HLH. Allogeneic hematopoietic cell transplant (HCT) is the treatment for primary HLH, whereas treatment for secondary HLH is based on the underlying disorder.

The case studies segued to 3 talks encompassing AML, MDS, and ALL and the importance of cytogenetics and molecular genetics. Dr. Altman highlighted *FLT3-ITD*, *NPM1*, *CEBPα*, and *C-KIT* as important mutations in AML; future mutations of importance may include *IDH1/2*, *DNMT2A*, *TET2*, and *ASXL1*. Dr. Greenberg also identified molecular mutations in patients with MDS; however, these mutations are also seen in older patients without hematologic abnormalities and therefore must be interpreted with caution. Currently, mutations can guide treatment decisions but are not diagnostic, but mutations resulting in defective DNA damage repair could be targeted in the future, said Dr. Greenberg. Other factors important in treatment include stratification and delineation of treatment-related MDS (t-MDS) and de novo MDS. Patients with t-MDS have a poorer outcome and are less responsive to treatments.

Dr. Alvarnas discussed improved outcomes for ALL including optimization and application of current modalities and the incorporation of newer treatment options. Dr. Alvarnas discussed the broader application of pediatric regiments to other age groups and noted that allogeneic HCT should be considered in older patients who meet the fitness requirements. Finally, the clinical trial data that led to the FDA approval of blinatumomab for relapsed disease was presented and inotuzumab ozogamicin and CAR T-cells were discussed as developing therapies.

With the introduction of new therapeutic options that could result in more curative therapy, late effects remain an important consideration in the growing population of survivors, creating a good segue into the next discussion in which Glen J. Peterson, RN, DNP, ACNP, University of Colorado Cancer Center, addressed the importance of developing a survivorship program for the management of long-term and late effects of curative therapy in lymphoma survivors.

The afternoon session commenced with patient case–based discussions on rare plasma cell disorders by panelists Damian Green, MD, Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance, and Amrita Krishnan, MD, City of Hope Comprehensive Cancer Center. The panelists provided rationale and clinical insights for diagnosis and treatment of amyloidosis, POEMS syndrome, and plasmacytoma.

Next, Steven P. Treon, MD, PhD, Dana-Farber/Brigham and Women's Cancer Center | Massachusetts General Hospital Cancer Center introduced the audience to new findings in the management of WM/LPL. He noted that *MYD88* (L265P) mutations are present in greater than 95% to 97% of patients with WM and allele-specific polymerase chain reaction for MYD88 (L265P) has been adopted as an essential test in differentiating WM from other entities that secrete IgM. He also discussed clinical data on currently available combination therapies and on the newer therapeutic options for WM/LPL. In closing, Dr. Treon shared how genomics (mutations in *MYD88* and *CXCR4*) helps identify patients who may benefit with ibrutinib treatment using a recently published study (Treon et al, N Engl J Med 2015;372:1430–1440) as an example.

Dr. Green provided an overview of the management of MM, pointing out that the rapid changes in the treatment landscape have contributed to dramatic improvement in survival rates of patients with MM. He discussed the updated diagnostic criteria by the IMWG, which include imaging, bone marrow assessment, and free light chain ratio existing requirements of CRAB features and how it redefines the subset of patients with smoldering myeloma requiring active treatment. Dr. Green also noted that patients with newly diagnosed disease are best served with a triplet regimen and treatment based on cytogenetic risk assessment may improve outcomes for individuals with high risk features. Autologous HCT remains the standard of care in transplant eligible patients. Dr.

Green concluded his talk noting that new targets, immunotherapies, and other novel approaches may be approved for MM treatment in the near future.

Bone-related morbidity is a debilitating side effect of MM, and Dr. Krishnan discussed the strategies for the management of bone health in patients, including surgical options and bisphosphonates. She provided an overview of clinical trial data showing the equivalence of pamidronate versus zoledronic acid, discussed data showing the survival advantage with zoledronic acid compared with clodronate, and talked about the potential role of denosumab in this setting. In conclusion, Dr. Krishnan presented novel approaches that are under clinical investigation for management of MM bone disease.

Dr. Abramson discussed the classification, clinical presentation, and management of Castleman's disease, a rare heterogeneous non-malignant lymphoproliferative disease. Unicentric Castleman's disease is managed with surgical excision. Systemic therapy is reserved for unresectable and relapsed/refractory disease. Multicentric Castleman's disease (MCD) is a relapsing remitting disease and treatment is indicated when active disease is present. Siltuximab, an anti–IL-6 antibody, has a role in the treatment of MCD in HHV8/HIV-negative patients, Dr. Abramson concluded.

The final presentations focused on CHL. Dr. Advani reviewed risk-adapted strategies for optimizing frontline therapy for advanced stage CHL, emphasizing the need to use the Deauville criteria (5-point scale based on the assessment of uptake in the liver and mediastinum) for the interpretation of PET/CT. A dialog between the medical oncologist and nuclear medicine physician is critical to appropriately implement the new response criteria to optimize treatment of advanced stage CHL, she explained. Weiyun Z. Ai, MD, PhD, UCSF Helen Diller Family Comprehensive Cancer Center, discussed the results of the pivotal clinical studies that formed the basis for the approval of brentuximab vedotin for relapsed/refractory CHL and as maintenance therapy after autologous HCT in patients at high risk of relapse. Dr. Ai concluded her presentation mentioning that PD-1 blockade with nivolumab and pembrolizumab looks promising as a potential treatment option for heavily pretreated relapsed/refractory HL.

The congress concluded with closing remarks from Dr. Zelenetz and Dr. Advani.

For more information about the NCCN Annual Congress: Hematologic Malignancies, visit NCCN.org/HEM.

Dr. Robert C. Young Joins NCCN Leadership Team

NCCN has appointed Robert C. Young, MD, as Interim Vice President of the NCCN Oncology Research Program (ORP).

Dr. Young brings to NCCN more than 45 years of oncology experience. Dr. Young is President of RCY Medicine, a consulting service focused on cancer center productivity, health care quality, and health policy. He served as President and Chief Executive Officer of Fox Chase Cancer Center—one of the original NCCN Member Institutions—for 18 years, following which he served 2 years as Chancellor. Dr. Young is internationally known for his treatment of lymphoma and ovarian cancer.

"We are pleased to welcome Dr. Young as Interim Vice President of ORP," said Robert W. Carlson, MD, Chief Executive Officer, NCCN. "As an original member and leader of NCCN, Dr. Young indeed was instrumental in initiating the practices and policies that have led to more than 20 years of success for the organization. We are sure his expertise will further enhance ORP's position in the oncology community."

As Interim Vice President, Dr. Young will be responsible for developing and managing NCCN's centralized, standardized infrastructure for the conduct of clinical trials among its 26 NCCN Member Institutions and their community affiliates. The ORP fosters collaboration among NCCN Member Institutions and pharmaceutical and biotechnology companies to bring promising and effective new treatments to patients with cancer. In addition to providing funding for groundbreaking clinical research, ORP publishes important resources for clinical investigators, including but not limited to

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the Informed Consent Language Database and Points to Consider on the Best Practices for Biorepositories, Registries, and Databases.

"I am very pleased to be working with NCCN again in this new capacity as Interim Vice President of the ORP," said Dr. Young. "It's exciting to be part of the team that brings new novel therapies to researchers at NCCN Member Institutions so that our patients can benefit from early access to these new medicines."

Among his national leadership positions in oncology, Dr. Young served as President of ASCO, the American Cancer Society, and the International Gynecological Cancer Society, as well as Chairman of the NCCN Board of Directors and Chair of the NCI Board of Scientific Advisors. He also served as a member of the National Cancer Policy Board of the Institute of Medicine. Dr. Young was a member of the subspecialty board on medical oncology for the American Board of Internal Medicine and on the Experimental Therapeutics study section of NCI. In 1995, he served as Chairman of the General Motors Cancer Research Foundation's Charles F. Kettering Selections Committee.

Since 2010, Dr. Young has been a member of the NCCN Foundation Board of Directors and he currently serves on the Board of Directors of AVEO Pharmaceuticals, Inc. He also serves on the Scientific Advisory Boards of The Ohio State University Comprehensive Cancer – James Cancer Hospital and Solove Research Institute, the University of Kansas Cancer Center, and the University of Oklahoma Cancer Center.

From 1987 to 2001, Dr. Young was an Associate Editor of the *Journal of Clinical Oncology* and currently serves as Chairman of the Editorial Board of *Oncology Times*.

Dr. Young received his Bachelor of Science degree from The Ohio State University and his medical degree from Cornell University Medical College. Following his internship at New York Hospital, he completed a residency at NCI and Yale-New Haven Medical Center. He is board-certified in internal medicine, hematology, and oncology by the American Board of Internal Medicine.

For more information about NCCN ORP, visit NCCN.org/ORP.