University Hospitals

May 2017

Hematology Update

Dear Colleagues:

The treatment of lymphoma has seen significant advances in the last several years, with rapid introduction of new agents, including antibody-based therapies (monoclonal antibodies, bispecific antibodies and antibody-drug conjugates), signaling inhibitors and cellular therapies.

Nationally recognized researchers and clinicians at University Hospitals Seidman Cancer Center are making important strides in the treatment of hematologic malignancies. In this newsletter, we'll specifically discuss lymphoma clinical trials.

Presently, the lymphoid malignancies clinical trial portfolio at UH Seidman Cancer Center is centered around these new therapies:

Our **frontline diffuse large B cell lymphoma studies** are investigating improvements to the R-CHOP backbone. These trials include CASE 3413, investigating the addition of the proteasome inhibitor carfilzomib to R-CHOP, and the upcoming SEGE2416 study of the incorporation of the antibody-drug immunoconjugate denintuzumab mafodotin (targeting CD19) to R-CHOP or R-CHP.

Studies in relapsed lymphoma include a variety of different agents, including the nuclear transport inhibitor selinexor (KARY1414), signaling inhibitors against PI3K and JAK1 inhibitors (INCT1416), antibody-drug immunoconjugates targeting CD19 (ADCT1416) and CD30 (brentuximab) (CASE1415), the monoclonal antibody against PD-1 (REGE1416) as well as the bispecific antibody blinatumomab (AMGN1416).

The broad variety of current and upcoming studies reflects our goal of having a diverse portfolio of clinical trials, including different types of lymphoma and bringing to our patients multiple new agents. Our aim is to have studies and targeted therapies available for the majority of our patients.

Please feel free to contact us with questions or for more information regarding available clinical studies for your lymphoma patients.

Sincerely,

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Open Lymphoma Clinical Trial Highlights

DIFFUSE LARGE B CELL LYMPHOMA

CASE 3413. A Phase I/II Study of Carfilzomib in Combination with R-CHOP (CR-CHOP) for Patients with Diffuse Large B-Cell Lymphoma. clinicaltrials.gov #NCT02073097
Local PI: Paolo Caimi, MD

SEGE 2416. An Open-Label Phase 2 Study of Denintuzumab Mafodotin (SGN-CD19A) in Combination with RCHOP or RCHP Compared with RCHOP Alone as Frontline Therapy in Patients with Diffuse Large B-Cell Lymphoma (DLBCL) or Follicular Lymphoma (FL) Grade 3b (UPCOMING STUDY). clinicaltrials.gov #NCT02855359
Local PI: Paolo Caimi, MD

KARY1414. A Phase 2b Open-label, Randomized Two-arm Study Comparing High and Low Doses of Selinexor (KPT-330) in Patients with Relapsed/Refractory Diffuse Large B-Cell Lymphoma (DLBCL). clinicaltrials.gov #NCT02227251
Local PI: Paolo Caimi, MD

RELAPSED B-CELL LYMPHOMA

REGE1416. A Phase 1 Study to Assess Safety and Tolerability of REGN1979, an Anti-CD20 x Anti-CD3 Bispecific Monoclonal Antibody, and REGN2810, an Anti-Programmed Death-1 Monoclonal Antibody, in Patients with B-Cell Malignancies. clinicaltrials.gov #NCT02651662
Local PI: Paolo Caimi, MD

INCT1416. Phase 1/2, Open-Label, Dose-Escalation, Safety and Tolerability Study of INCB050465 and INCB039110 in Subjects With Previously Treated B-Cell Malignancies. clinicaltrials.gov #NCT02018861

AMGN1416. A Phase 2/3 Multi-center Study to Evaluate the Safety and Efficacy of Blinatumomab in Subjects with Relapsed/Refractory Aggressive B-Cell Non-Hodgkin Lymphoma (UPCOMING STUDY). clinicaltrials.gov #NCT02910063
Local PI: Paolo Caimi, MD

A051301. A Randomized Double-Blind Phase III Study of Ibrutinib During and Following Autologous Stem Cell Transplantation Versus Placebo in Patients With Relapsed or Refractory Diffuse Large B-cell Lymphoma of the Activated B-cell Subtype. clinicaltrials.gov #NCT02443077
Local PI: Paolo Caimi, MD

RELAPSED T CELL LYMPHOMA

CASE1415. A Phase II Study of Single Agent Brentuximab Vedotin in Relapsed/Refractory CD30 Low (<10%) Mature T Cell Lymphoma (TCL). clinicaltrials.gov #NCT02588651
Local PI: Paolo Caimi, MD

EBV-ASSOCIATED LYMPHOMAS

ATARA1416. Multicenter Expanded Access Protocol of Allogeneic Epstein-Barr Virus Cytotoxic T Lymphocytes (EBV-CTLs) for Patients with EBV-Associated Lymphomas and Lymphoproliferative Disorders in Immunocompromised Patients. clinicaltrials.gov #NCT00002663
Local PI: Ben Tomlinson, MD

For additional information, the following publications all focus on the study and treatment of lymphomas. If you would like further information on any of these, or the work currently being conducted at UH Seidman Cancer Center Department of Hematology, contact Dr. Paolo Caimi at Paolo.Caimi@UHhospitals.org or Dr. Marcos de Lima at Marcos.deLima@UHhospitals.org.

Nivolumab before and after allogeneic hematopoietic cell transplantation.
Covut F, Pinto R, Cooper BW, Tomlinson B, Metheny L, Malek E, Lazarus HM, de Lima M, Caimi PF.
Bone Marrow Transplant. 2017 Mar 27. doi: 10.1038/bmt.2017.44.
PMID: 28346414

Splenic marginal zone lymphoma: excellent outcomes in 64 patients treated in the rituximab era.
Starr AG, Caimi PF, Fu P, Massoud MR, Meyerson H, Hsi ED, Mansur DB, Cherian S, Cooper BW, De Lima MJ, Lazarus HM, Gerson SL, Jagadeesh D, Smith MR, Dean RM, Pohlman BL, Hill BT, William BM.
Hematology. 2017 Jan 20:1-7. doi: 10.1080/10245332.2017.1279842.
PMID: 28105889

Outcomes of allogeneic hematopoietic stem cell transplantation for lymphomas: a single-institution experience.
Massoud MR, Caimi PF, Ferrari N, Fu P, Creger R, Fox R, Carlson-Barko J, Kolk M, Brister L, Cooper BW, Gerson S, Lazarus HM, de Lima M, William BM.
Rev Bras Hematol Hemoter. 2016 Oct-Dec;38(4):314-319. doi: 10.1016/j.bjhh.2016.07.003.
PMID: 27863759

Clinical approach to diffuse large B cell lymphoma.
Caimi PF, Hill BT, Hsi ED, Smith MR.
Blood Rev. 2016 Nov;30(6):477-491. doi: 10.1016/j.blre.2016.06.003. Epub 2016 Jun 30.
PMID: 27596109

Bortezomib for the treatment of mantle cell lymphoma: an update.
Hambley B, Caimi PF, William BM.
Ther Adv Hematol. 2016 Aug;7(4):196-208. doi: 10.1177/2040620716648566. Epub 2016 May 21.
PMID: 27493710

Dual institution experience of nodal marginal zone lymphoma reveals excellent long-term outcomes in the rituximab era.
Starr AG, Caimi PF, Fu P, Massoud MR, Meyerson H, Hsi ED, Mansur DB, Cherian S, Cooper BW, De Lima MJ, Lazarus HM, Gerson SL, Jagadeesh D, Smith MR, Dean RM, Pohlman BL, Hill BT, William BM.
Br J Haematol. 2016 Oct;175(2):275-280. doi: 10.1111/bjh.14228.
PMID: 27443247

Low immunosuppressive burden after HLA-matched related or unrelated BMT using posttransplantation cyclophosphamide.
Kanakry CG, Bolaños-Meade J, Kasamon YL, Zahurak M, Durakovic N, Furlong T, Mielcarek M, Medeot M, Gojo I, Smith BD, Kanakry JA, Borrello IM, Brodsky RA, Gladstone DE, Huff CA, Matsui WH, Swinnen LJ, Cooke KR, Ambinder RF, Fuchs EJ, de Lima MJ, Andersson BS, Varadhan R, O'Donnell PV, Jones RJ, Luznik L.
Blood. 2017 Mar 9;129(10):1389-1393. doi: 10.1182/blood-2016-09-737825.
PMID: 28049637

Impact of pre-transplant depression on outcomes of allogeneic and autologous hematopoietic stem cell transplantation.
El-Jawahri A, Chen YB, Brazauskas R, He N, Lee SJ, Knight JM, Majhail N, Buchbinder D, Schears RM, Wirk BM, Wood WA, Ahmed I, Aljurf M, Szer J, Beattie SM, Battiwalla M, Dandoy C, Diaz MA, D'Souza A, Freytes CO, Gajewski J, Gergis U, Hashmi SK, Jakubowski A, Kamble RT, Kindwall-Keller T, Lazarus HM, Malone AK, Marks DI, Meehan K, Savani BN, Olsson RF, Rizzieri D, Steinberg A, Speckhart D, Szwajcer D, Schoemans H, Seo S, Ustun C, Atsuta Y, Dalal J, Sales-Bonfim C, Khera N, Hahn T, Saber W.
Cancer. 2017 Jan 19. doi: 10.1002/cncr.30546.
PMID: 28102896.

Pre-existing invasive fungal infection is not a contraindication for allogeneic HSCT for patients with hematologic malignancies: a CIBMTR study.
Maziarz RT, Brazauskas R, Chen M, McLeod AA, Martino R, Wingard JR, Aljurf M, Battiwalla M, Dvorak CC, Geroge B, Guinan EC, Hale GA, Lazarus HM, Lee JW, Liesveld JL, Ramanathan M, Reddy V, Savani BN, Smith FO, Strasfeld L, Taplitz RA, Ustun C, Boeckh MJ, Gea-Banacloche J, Lindemans CA, Auletta JJ, Riches ML.
Bone Marrow Transplant. 2017 Feb;52(2):270-278. doi: 10.1038/bmt.2016.259
PMID: 27991895.

Allogeneic Transplantation for Relapsed Waldenström Macroglobulinemia and Lymphoplasmacytic Lymphoma.
Cornell RF, Bachanova V, D'Souza A, Woo-Ahn K, Martens M, Huang J, Al-Homsi AS, Chhabra S, Copelan E, Diaz MA, Freytes CO, Gale RP, Ganguly S, Hamadani M, Hildebrandt G, Kamble RT, Kharfan-Dabaja M, Kindwall-Keller T, Lazarus HM, Marks DI, Nishihori T, Olsson RF, Saad A, Usmani S, Vesole DH, Yared J, Mark T, Nieto Y, Hari P.
Biol Blood Marrow Transplant. 2017 Jan;23(1):60-66. doi: 10.1016/j.bbmt.2016.10.010.
PMID: 27789362.

Prevention and Treatment of Cancer-Related Infections, Version 2.2016, NCCN Clinical Practice Guidelines in Oncology.
Baden LR, Swaminathan S, Angarone M, Blouin G, Camins BC, Casper C, Cooper B, Dubberke ER, Engemann AM, Freifeld AG, Greene JN, Ito JI, Kaul DR, Lustberg ME, Montoya JG, Rolston K, Satyanarayana G, Segal B, Seo SK, Shoham S, Taplitz R, Topal J, Wilson JW, Hoffmann KG, Smith C.
J Natl Compr Canc Netw. 2016 Jul;14(7):882-913.
PMID: 27407129.

THE UH SEIDMAN CANCER CENTER DIFFERENCE

- The UH Seidman Cancer Center Bone Marrow Transplant program is celebrating 40 years and over 3,000 transplants.
- UH Seidman Cancer Center has over 300 clinical trials. Currently, our hematology program has three studies open for diffuse large-cell lymphoma salvage.
- FACT accreditation. Our stem cell transplant program is one of the few in the U.S. accredited to perform more than minimal manipulation.
- UH Seidman Cancer Center is a freestanding, 120-bed hospital dedicated to caring for patients with cancer. With 17 satellite locations at UH facilities across Northeast Ohio, we are able to provide our patients with the most comprehensive, integrated care available in the region.
- We were the first in Ohio to offer proton therapy and remain the only center in the region to offer this innovative therapy to patients.
- UH Seidman Cancer Center is consistently ranked by U.S. News & World Report as one of the nation's best hospitals for the treatment of cancer. We are also a founding member of the National Cancer Institute (NCI)-designated Case Comprehensive Cancer Center at Case Western Reserve University School of Medicine, making us one of only 47 centers in the nation to hold this designation.

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