Allogeneic Hematopoietic Stem Cell Transplantation Outcomes After Nivolumab Monotherapy for Relapsed/Refractory Hodgkin Lymphoma (CheckMate 039 and CheckMate 205)

Carlo-Stella, Carmelo 1; Collins, Graham 2; Armand, Philippe 3; Zinzani, Pier Luigi 4; Cohen, Jonathon B 5; Halwani, Ahmad 6; Millenson, Michael 7; Provencio, Mariano 8; Domingo Domenech, Eva 9; Giulino-Roth, Lisa 10; Castagna, Luca 11; Kato, Kazunobu 12; Popa Mckiver, Mihaela 13; Sumbul, Anne 12; Zhu, Lili 12; Trneny, Marek 14; Minnema, Monique C. 15; Rueda, Antonio 16; Cunningham, David 17; Reddy, Nishitha 18; Younes, Anas 19; Santoro, Armando 20

1Humanitas Cancer Center, Humanitas Research Hospital, Rozzano, Milan, Italy; 2Churchill Hospital; 3Dana-Farber Cancer Institute; 4Institute of Hematology Seràgnoli University of Bologna, Bologna, Italy; 5Winship Cancer Institute, Emory University; 6Huntsman Cancer Institute, University of Utah; 7Fox Chase Cancer Center; 8Hospital Universitario Puerta de Hierro; 9Institut Català d’Oncologia (ICO); 10Weill Cornell Medical College; 11Humanitas Cancer Center, Humanitas Research Hospital; 12Bristol-Myers Squibb; 13Bristol-Myers Squibb, Princeton, NJ, US; 14Charles University in Prague and General University in Prague; 15University Medical Center Utrecht Cancer Center; 16Hospital Costa Del Sol; 17Royal Marsden Hospital; 18Vanderbilt University; 19Memorial Sloan Kettering Cancer Center; 20Humanitas Cancer Center, Humanitas University

Abstract

Introduction: Hodgkin lymphoma (HL) patients (pts) who have relapsed after autologous hematopoietic stem cell transplantation (HSCT) and received nivolumab (nivo), a PD-1 checkpoint inhibitor, may achieve adequate disease control with nivo (Ansell et al, N Engl J Med 2015; Younes et al, Lancet Oncol 2016) or subsequent therapy and, in some cases, can be considered for potentially curative treatment with allogeneic (allo)-HSCT. However, US Prescribing Information recommends monitoring for allo-HSCT complications after nivo, eg, hyperacute graft-versus-host disease (GVHD), grade (G) 3–4 GVHD, steroid-requiring febrile syndrome (SRFS), and other immune-mediated reactions. Methods: This post-hoc analysis evaluated allo-HSCT safety outcomes in HL pts who received prior nivo therapy in clinical studies: CheckMate 039 (n=23) and CheckMate 205 (n=243). Outcomes data (eg, transplantation date, GVHD, and tumor assessment) were collected prospectively in CheckMate 205 and retrospectively in CheckMate 039. Transplant characteristics (eg, stem cell source, preparative regimen, and post-allo-HSCT safety data) were collected retrospectively. Transplant-related mortality (TRM) was defined as death by any reason other than disease progression. SRFS was defined as steroid-responsive, noninfectious fever that could be accompanied by skin, joint, or liver symptoms. Cumulative incidence of TRM and acute GVHD was assessed by the Kaplan-Meier method. Results: Forty pts (n=5, CheckMate 039; n=35, CheckMate 205) who received allo-HSCT after nivo were included. Median (range) age was 34 (18–62) years, pts received 4 (2–9) therapies prior to nivo, and time from last nivo dose to allo-HSCT was 42 (11–411) days. Additional therapy between nivo and allo-HSCT was received by 25%. Stem cell source was peripheral blood in 33 pts and bone marrow in 7. Fifteen percent received stem cells from a matched HLA-identical sibling, 3% 1 HLA-mismatched relation, 30% a haploidentical relation, and 43% an unrelated donor (10%, donor not reported). Myeloablative conditioning was used in 10% and reduced-intensity conditioning in 68%; conditioning regimen was unreported in 23%. In-vivo T-cell depletion was performed in 10 pts, 3 with anti-thymocyte globulin, 7 with alemtuzumab. After allo-HSCT, 6 deaths, all from TRM, occurred; median (range) time from allo-HSCT to death was 120 (40–441) days. No deaths due to disease progression occurred. Any-grade GVHD occurred in 18 pts (45%), G2-4 GVHD in 13 (33%), and G4 GVHD in 7 (18%; including 2 cases of unknown grade, imputed to G4). The organ most commonly affected by any grade GVHD was skin. The 6-mo Kaplan-Meier estimates (95% CI) of TRM (Figure), G2-4 and G3–4 acute GVHD, were 16.8% (6.5–39.4), 41.5% (24.7–63.7), and 25.7% (12.4–48.7), respectively. There were 6 cases of SRFS, 2 of chronic GVHD, 2 of encephalitis (G3 lymphocytic encephalitis and G3 suspected viral encephalitis; both resolved with treatment), and 1 of hepatic veno-occlusive disease (died of multi-organ GVHD). Conclusions: Our results suggest that nivo treatment does not preclude subsequent allo-HSCT. Monitoring of pts undergoing allo-HSCT post-PD-1 blockade is recommended for detection and management of early/severe GVHD. Follow-up in a
larger number of pts is ongoing to help establish pt characteristics, clinical factors, and treatment timings that may influence outcomes. Study funding: Bristol-Myers Squibb.

Data up to 200 days only are presented; patient numbers post 100 days were small.

Disclosure of conflict of interest