ELSEVIER

Blood 142 (2023) 3541–3542

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

721.ALLOGENEIC TRANSPLANTATION: CONDITIONING REGIMENS, ENGRAFTMENT AND ACUTE TOXICITIES

Recurrence of HBV Reactivation after Allogeneic Hematopoietic Transplantation in Recipients with Resolved HBV Infection: A Nation-Wide Multicenter Retrospective Study

Masahiro Onozawa, MD[1], Shigeru Kusumoto, MD PhD[2], Yuho Najima, MDPhD[3], Hiroya Hashimoto[4], Kohei Okada, MD PhD[5], Masaharu Tamaki[6], Masatsugu Tanaka, MD, PhD[7], Takayuki Sato, MD PhD[8], Tsutomu Takahashi, MD PhD[9], Kaoru Hatano[10], Koichi Onodera[11], Yukiyoshi Moriuchi[12], Kimikazu Yakushijin, MDPhD[13], Junya Kanda[14], Koji Nagafuji, MD PhD[15], Masao Ogata, MD PhD[16], Nobuaki Nakano, MD[17], Akihiro Tamori[18], Masashi Mizokami[19]

[1] Hokkaido University Hospital, Sapporo, Japan
[2] Department of Hematology and Oncology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan
[3] Tokyo Metropolitan Cancer and Infectious Diseases Center, Komagome Hospital, Tokyo, JPN
[4] Core Laboratory, Nagoya City University, Nagoya, Japan
[5] Sapporo Hokuyu Hospital, Sapporo, JPN
[6] Division of Hematology, Jichi Medical University Saitama Medical Center, Saitama, Japan
[7] Department of Hematology, Kanagawa Cancer Center, Kanagawa, Japan
[8] Department of Haematology/Oncology, Kurashiki Central Hospital, Kurashiki, Japan
[9] Shimane University Hospital, Izumo-Shi, Shimane, JPN
[10] Jichi Medical University Hospital, Shimotsukeshi, JPN
[11] Tohoku University Hospital, N/A, JPN
[12] Sasebo City General Hospital, Sasebo, JPN
[13] Kobe University Hospital, Kobe, JPN
[14] Department of Hematology and Oncology, Graduate School of Medicine, Kyoto University, Kyoto, Japan
[15] Department of Medicine Kurume University School of Medicine, Kurume, JPN
[16] Department of Hematology, Oita University Hospital, Yufu-City, JPN
[17] Department of Hematology, Imamura General Hospital, Kagoshima, Japan
[18] Osaka Metropolitan University, Osaka, Japan
[19] National Center for Global Health and Medicine, Ichikawa, Japan

Introduction

Reactivation of hepatitis B virus (HBV) is known to cause fulminant hepatitis after allogeneic hematopoietic stem cell transplantation (allo-HSCT) in recipients with resolved HBV infection. Monitoring of HBV-DNA and HBV-DNA-guided preemptive therapy using nucleotide analogue (NA) is recommended to prevent developing hepatitis due to HBV reactivation after allo-HSCT. However, little is known about the adequate duration of NA treatment and the frequency of the recurrence of HBV reactivation (2nd HBV reactivation) after discontinuation of NA. We conducted a nationwide retrospective study of HBV reactivation after allo- HSCT.

Patients and Methods

We retrospectively reviewed the clinical information of recipients with resolved HBV infection (HBsAg-negative, anti-HBc-positive) before allo-HSCT and were diagnosed as HBV reactivation (HBsAg and/or HBV-DNA positive) after allo-HSCT from January 2010 to December 2020. Patients who received prophylactic NA before HBV reactivation were excluded. This study was approved by the Hokkaido University Hospital institutional review boards and registered as UMIN 000046803.

Results

A total of 72 patients were enrolled (median age of 60 years, range, 27-73 years; 42 males and 30 females) from 16 institutions. Initial hematological diseases were acute myeloid leukemia 21, myelodysplastic syndrome 14, chronic myeloid leukemia 4, acute lymphoblastic leukemia 12, non-Hodgkin lymphoma 8, adult T cell leukemia-lymphoma 6, mixed phenotype acute leukemia 4, and others 3. HSCT details were as follows: donor source, unrelated bone marrow 33, cord blood 24, related peripheral blood 11, unrelated peripheral blood 4; acute graft versus host disease (GVHD) 48 (66.7%); chronic GVHD 44 (61.1%); systemic steroid usage 41 (56.9%). Initial HBV reactivation after allo-HSCT was observed on day 10-3034 (median

512.5). Immunosuppressants and systemic steroids were administered in 35 (48.6%) and 28 (38.9%) patients respectively at the time of HBV reactivation. The patients who showed anti-HBs below protection levels (<10mIL/mL) were 18 (25%) of 72 patients at pre-HSCT, however, the number increased to 35 (81.4%) of 43 patients who were analyzed at the point of HBV reactivation after allo-HSCT. All patients received preemptive NA (entecavir 65, tenofovir alafenamide 6, tenofovir 1). Elevated aspartate transaminase of more than 200 U/L was observed in 7 cases at HBV reactivation, and all of them showed HBV-DNA more than 4 Log IU/mL. No one developed fulminant hepatitis but 5 patients resulted in continuous HBV carriers. Twenty-four of 72 patients were discontinued NA by each physician's decision. Of 24 patients who discontinued NA, 11 (45.8%) patients developed 2 nd HBV reactivation. The median duration from discontinuation of NA to 2 nd HBV reactivation was 113 days (range, 15 to 434). Duration of initial NA administration was not significantly different between patients with 2 ndHBV reactivation and those without 2 nd HBV reactivation (90-1968 days, median 553 vs 145-3734 days, median 861; p=0.11). In those who analyzed anti-HBs at discontinuation of NA, 4 of 8 cases (50.0%) with anti-HBs <10 mIU/mL developed 2 nd HBV reactivation, whereas only 1 of 6 cases (16.7%) with anti-HBs >10 mIU/mL developed 2 nd HBV reactivation. Four of the 11 cases with 2 nd HBV reactivation were attempted rechallenge of NA discontinuation, however, all 4 cases developed 3 rd HBV reactivation on day 28-127 after discontinuation of NA. These 4 cases further developed 4 th HBV reactivation after the rechallenge of discontinuation of NA. One patient developed protective anti-HBs titer after 2 courses of HB vaccination, and finally successfully discontinue the NA after 4 th HBV reactivation. The patient did not develop further reactivation for more than 3 years.

Conclusion

2 nd reactivation of HBV after NA discontinuation was common in patients with HBV reactivation who received allo-HSCT despite the long duration of NA. Acquisition of anti-HBs by HBV reactivation itself or HB vaccine would be necessary to suppress further HBV reactivation. Careful monitoring of HBV-DNA is important even after the discontinuation of NA in the case with HBV reactivation after allo-HSCT because multiple reactivations could occur. A prospective randomized trial of the HB vaccine after allo-HSCT for preventing HBV reactivation is now ongoing (UMIN000034113).

Disclosures Onozawa: *Astellas:* Speakers Bureau; *Otsuka Pharmaceutical:* Speakers Bureau; *Daiichi Sankyo:* Speakers Bureau. **Kusumoto:** *AstraZeneca:* Honoraria; *Bristol Myers Squibb:* Research Funding; *Shionogi:* Research Funding; *Ono:* Honoraria; *Eil Lilly:* Honoraria; *Takeda:* Honoraria; *Kyowa-Kirin:* Honoraria; *Astellas:* Honoraria; *SymBio:* Honoraria; *Eisai:* Honoraria; *Janssen:* Honoraria, Research Funding; *Chugai:* Honoraria, Research Funding; *Daiichi-Sankyo:* Honoraria, Research Funding; *Meiji-Seika:* Honoraria; *AbbVie:* Honoraria; *Nippon-Shinyaku:* Honoraria; *Mundipharma:* Honoraria. **Najima:** *Takeda Pharmaceutical Company Limited.:* Speakers Bureau; *CSL Behring K.K.:* Speakers Bureau; *Janssen Pharmaceutical K.K.:* Speakers Bureau; *Daiichi Sankyo Co. Ltd.:* Consultancy, Speakers Bureau; *AbbVie GK:* Speakers Bureau; *Amgen Inc.:* Speakers Bureau; *Bristol-Myers Squibb K.K.:* Speakers Bureau; *Chugai Pharmaceutical Co., Ltd.:* Speakers Bureau; *Astellas Pharma Inc.:* Consultancy, Speakers Bureau; *Nippon Shinyaku Co., Ltd.:* Speakers Bureau; *Novartis Pharma K.K.:* Speakers Bureau; *Sumitomo Pharma Co., Ltd.:* Speakers Bureau; *Otsuka Pharmaceutical Co., Ltd.:* Speakers Bureau; *Kyowa Kirin Co., Ltd.:* Speakers Bureau. **Hashimoto:** *Chugai Pharmaceutical:* Honoraria. **Tamaki:** *Chugai Pharmaceutical:* Honoraria. **Tanaka:** *Otsuka Pharmaceutical:* Speakers Bureau; *MSD:* Speakers Bureau; *Kyowa-Kirin:* Speakers Bureau; *Daiichi Sankyo:* Speakers Bureau; *Chugai Pharmaceutical:* Speakers Bureau; *Astellas Phrama:* Speakers Bureau; *Asahi Kasei Pharma:* Speakers Bureau; *Abbvie:* Speakers Bureau; *Pfizer:* Speakers Bureau; *Sumitomo Pharma:* Speakers Bureau. **Onodera:** *Otsuka:* Honoraria; *Novartis:* Honoraria; *Nippon Shinyaku:* Honoraria; *Celgene:* Research Funding; *BMS:* Research Funding; *Astellas:* Honoraria; *Agios:* Research Funding; *Abbie:* Research Funding. **Yakushijin:** *Nippon Shinyaku:* Honoraria; *Astrazeneca:* Honoraria; *Janssen Pharmaceutical:* Honoraria; *Novartis:* Honoraria; *Asahi Kasei Pharma:* Honoraria; *Otsuka Pharmaceutical:* Honoraria; *Pfizer:* Honoraria; *Jazz Pharmaceuticals:* Honoraria; *Chugai Pharmaceutical:* Research Funding. **Kanda:** *Megakaryon Co:* Consultancy; *AbbVie Inc.:* Honoraria; *asclepia:* Honoraria; *MSD K.K.:* Honoraria; *NIPPON KAYAKU CO. LTD.:* Honoraria; *CSL Behring K.K.:* Honoraria; *Otsuka Pharmaceutical Co., Ltd.:* Honoraria; *Nippon Shinyaku Co., Ltd.:* Honoraria; *Amgen Pharma Inc.:* Honoraria; *Takeda Pharmaceutical Company Limited:* Honoraria; *ASAHI KASEI PHARMA CORPORATION:* Honoraria; *Novartis Pharma K.K.:* Honoraria; *Bristol-Myers Squibb Co:* Honoraria; *Wakunaga Pharmaceutical Co., Ltd.:* Honoraria; *Kyowa Kirin Co., Ltd.:* Honoraria; *Astellas Pharma Inc.:* Honoraria; *DAIICHI SANKYO Co., Ltd.:* Honoraria; *TERUMO CORPORATION:* Honoraria; *CHUGAIIGAKU CO., LTD.:* Honoraria; *Fujimoto Pharmaceutical Corporation.:* Honoraria; *Eisai:* Research Funding; *Sanofi K.K.:* Honoraria; *CHUGAI PHARMACEUTICAL Co., Ltd.:* Honoraria; *Janssen Pharmaceutical K.K.:* Honoraria. **Mizokami:** *Gilead Sciences:* Honoraria; *Sysmex:* Honoraria.

https://doi.org/10.1182/blood-2023-173461