

IMSUT Hospital

Department of Infectious Diseases and Applied Immunology 感染免疫内科

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Founded in 1981, IMSUT Hospital started its HIV clinic in 1986, and as of 2023, 1328 HIV-infected patients have visited us. Currently, a total of 572 patients are actively under our clinical management. In addition to HIV infection, we also provide treatment for other infections such as hepatitis and malaria. Furthermore, we have addressed cases of mpox, an emerging and re-emerging infection prevalent among HIV-MSM.

1. Treatment of HIV/AIDS and sexually-transmitted diseases in IMSUT hospital

Statistical characteristics of HIV/AIDS at IMSUT Hospital show that fourteen new patients with HIV infection visited to our hospital this year (from January 1 to December 31, 2022), and 572 patients in total are under medical management in our outpatient clinic. Five hundred fifty-seven people living with HIV (PLWH) are receiving antiretroviral therapy [1] at the hospital, and most of their plasma HIV viral loads have been well controlled. This is due to the fact that the medication adherence of PLWH visiting our clinic is at an adequate level for HIV suppression. Figure 1 shows the number of PLWH attending IMSUT hospital since 1995.

This year, the results of the SOLAR study, Study to Evaluate Efficacy and Safety of Cabotegravir (CAB) Long Acting [1] Plus (+) Rilpivirine (RPV) LA Versus BIKTARVY® (BIK) in Participants With Human Immunodeficiency Virus (HIV)-1 Who Are Virologically Suppressed were presented at national and interna-

tional conferences, and real-world data from our hospital on CAB plus RPV were presented at conferences and in papers. We also published a paper on the treatment and clinical findings of mpox, an emerging infectious disease of HIV-MSM.

2. Changes in inflammatory biomarkers and lipid profiles after switching to long-acting cabotegravir plus rilpivirine

Eisuke Adachi, Makoto Saito, Amato Otani, Michiko Koga, Hiroshi Yotsuyanagi

We assessed whether the impact of cabotegravir plus rilpivirine on inflammation reduction differs from that of oral antiretrovirals, using real-world data. Inflammatory biomarkers and lipid profiles were followed from baseline to 8 months after switching. Seventy-eight participants were analyzed. The CD4/CD8 ratio and C-reactive protein did not change. There were transient decreases in CD8 and CD4 counts in the group that switched from the dolutegra-

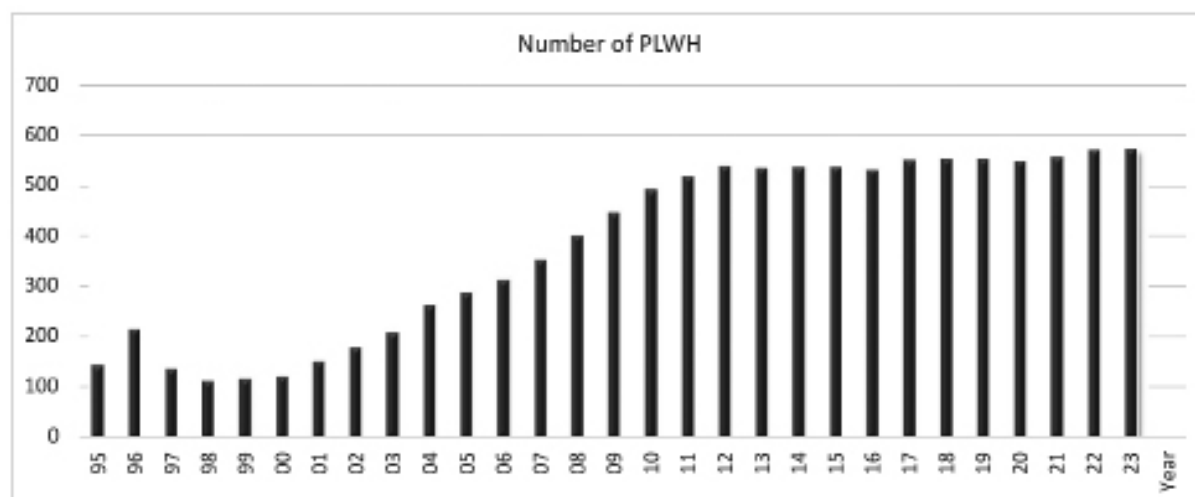


Figure 1. Number of PLWH attending IMSUT Hospital

vir-based regimen, but not in the tenofovir alafenamide-based regimen group. High-density lipoprotein (HDL) cholesterol increased, resulting in a decrease in the total-cholesterol to HDL cholesterol ratio, whereas there was no significant change in low-density lipoprotein cholesterol.

3. Mpox associated with Panton-Valentin leucocidin-producing methicillin-resistant *Staphylococcus aureus* among people with HIV

Eisuke Adachi, Kazuhiko Ikeuchi, Amato Otani, Makoto Saito, Michiko Koga, Hiroshi Yotsuyanagi

We report three cases of mpox (disease caused by the monkeypox virus) that developed in people with HIV co-infected with Panton-Valentin leucocidin-producing methicillin-resistant *Staphylococcus aureus* (PVL-MRSA), diagnosed in mid-February 2023. All three cases had preserved HIV immune status, and their mpox was mild and resolved without antiviral medications, but the trigger for their visit was the presence and history of skin and soft tissue infections. Our cases suggest that mpox is already prevalent among sexually active MSM in Tokyo, Japan. PVL-MRSA has been extremely rare in the general population of Japan, but several literatures reported widespread prevalence of PVL-MRSA among sexually active MSM-HIV. Mpox will become prevalent in the future in a population of sexually active MSM at high risk for PVL-MRSA infection, requiring an understanding of the interaction and pathogenesis of the two diseases.

4. Treatment of COVID-19 in IMSUT hospital

We started to treat COVID-19 patients at the IMSUT Hospital in February, 2020. To date, the number of patients hospitalized at the request of public health centers, etc., is the second largest among all public

university hospitals in Japan. We participated in several international clinical trials. (e.g., S-217622) and conducted a phase I trial to evaluate the safety, tolerability, and immunogenicity of KM-414 (KM Biologics, Kumamoto, Japan), an inactivated vaccine against SARS-CoV-2 developed by KM biologics and IMSUT (The investigator-initiated clinical trial, phase I trial, investigating the safety and immunogenicity of booster vaccination against COVID-19, jRCT2031210503).

5. Bioterrorism-related information website management and crisis management

“バイオテロ対応ホームページ” (a website providing information on bio-terrorism in Japanese), which was developed in 2008 to provide information on clinical diagnosis and testing procedures for bioterrorism-related diseases for medical institutions, and was opened to the public in 2016 in anticipation of international situations and mass gathering events in Japan.

6. Crisis management for the future: Building a platform to provide information on emerging and re-emerging infectious diseases from normal times in Japan

Eisuke Adachi, Amato Otani, Hiroshi Yotsuyanagi, Masayuki Saijo¹, Tomoya Saito²

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At the beginning of the mpox (disease caused by monkey pox) epidemic, there was no platform in Japan to provide appropriate information on emerging and reemerging infectious diseases, and the number of accesses to bioterrorism-related information sites increased rapidly. Even though the interest in mpox

was much smaller than in coronavirus infectious disease, emerged in late 2019 (COVID-19), the increase in the number of views were much greater than during the COVID-19 epidemic. This may not be because mpox is bioterrorism-related as an analog of smallpox, but rather because there were no other websites providing information on mpox. For future crisis management, there should be a platform for providing information on emerging and reemerging infectious diseases from normal times.

7. Pre- and post-travel treatment of imported infectious diseases and tropical diseases at IM-SUT Hospital

The pandemic of COVID-19 had unprecedented impact of our life; global transport and travelling was one of the most affected areas. In mid 2022, the number of returnees and travelers consulted gradually increased, and two cases of malaria patients visited the hospital. For the tropical and parasitic diseases, dozens of important medicines essential for treatment of them are not licensed in Japan. Research Group on Chemotherapy of Tropical Diseases, Research on Publicly Essential Drugs and Medical Devices, Grant from Japan Agency for Medical Research and Development had been established to cope with this situation. We are the medical institution of the research group using these orphan drugs if needed, and collecting clinical data.

8. Treatment of hepatitis in IMSUT hospital:

About 300 HIV-non-infected patients with liver diseases such as viral hepatitis and NAFLD are under medical management in our outpatient clinic. Several patients were introduced from outside for the treatment of chronic hepatitis C with direct acting anti-vi-

ral (DAA) and successfully achieved the sustained viral response (SVR). In addition, we treated HIV-infected patients who developed acute hepatitis C with DAAs, who achieved SVR.

9. Incidence of sexually transmitted hepatitis C virus infection among men who have sex with men in Japan from 2009 to 2023

Eisuke Adachi, Makoto Saito, Tadashi Kikuchi, Kazuhiko Ikeuchi, Michiko Koga, Takeya Tsutsumi, Hiroshi Yotsuyanagi

Although the prevalence of hepatitis C virus (HCV) infection has decreased significantly with the advent of direct-acting antiviral agents, HCV is known to spread as a sexually transmitted disease among men who have sex with men (MSM), and this study aims to provide a perspective on the future prevalence of HCV in Japan. We examined incidence in two groups of MSM with HIV attending our institution in this retrospective cohort study, from 2009 to 2019 and from 2020 to May 2023 and investigated their background factors. Twenty-two cases were newly confirmed to be HCV infection in 2009-2019 and a total of 9 cases in 2020-2023, with an incidence rate of 5.04 per 1000 person-years in 2009-2019 and 5.55 per 1000 person-years in 2020-2023. All of them were diagnosed at routine outpatient visits for HIV, and few cases were considered to have symptoms of suspected hepatitis that led to a visit to the hospital and a diagnosis of HCV. Although HCV is still prevalent among MSM in Japan, it is possible that it would not have been diagnosed without testing at regular visits as in the case of people with HIV, and that the true prevalence rate among MSM, including non-HIV-infected persons, may be much higher.

Publications

1. Adachi E, Saito M, , Otani A, Koga M and Yotsuyanagi H Changes in inflammatory biomarkers and lipid profiles after switching to long-acting cabotegravir plus rilpivirine. *AIDS Res Treat* 2023 in press.
2. Adachi E, Otani A, Yotsuyanagi H, Saijo M and Saito T. Crisis management for the future: Building a platform to provide information on emerging and re-emerging infectious diseases from normal times in Japan, *Global Health & Medicine* 2023, DOI: 10.35772/ghm.2023.01089
3. Adachi E, Ikeuchi K, Otani A, Saito M, Koga M and Yotsuyanagi H. Mpox associated with panton-valentin leucocidin-producing methicillin-resistant staphylococcus aureus among people with HIV. *J Infect Chemother.*29:710-12.2023
4. Adachi E, Owada R, Sato S, Kono M and Yotsuyanagi H. Febrile gluteal inflammation evident on imaging findings after long-acting cabotegravir administration. *Clin Infect Dis*, doi 10.1093/cid/ciad705.2023
5. Adachi E, Saito M, Kikuchi T, Ikeuchi K, Koga M, Tsutsumi T and Yotsuyanagi H. Incidence of sexually transmitted hepatitis c virus infection among men who have sex with men in japan from 2009 to 2023. *J Med Virol.*95:e29039.2023
6. Adachi E, Saito M, Otani A, Koga M and Yotsuyanagi H. Transient decrease in t cells and atypical lymphocyte proliferation after the onset of mpox. *J Med Virol.*95:e29021.2023
7. Ikeuchi K, Saito M, Adachi E, Koga M, Okushin K, Tsutsumi T and Yotsuyanagi H. Injection drug use and sexually transmitted infections among men who have sex with men: A retrospective cohort

- study at an hiv/aids referral hospital in tokyo, 2013-2022. *Epidemiol Infect.*151:e195.2023
8. Mori N, Mikamo H, Mukae H, Yanagihara K, Kunishima H, Sasaki J and Yotsuyanagi H. Influence of the coronavirus infectious disease 2019 pandemic on infectious disease practice and infection control in japan: A web questionnaire survey. *J Infect Chemother.*30:1-6.2024
 9. Mukae H, Yotsuyanagi H, Ohmagari N, Doi Y, Sakaguchi H, Sonoyama T, Ichihashi G, Sanaki T, Baba K, Tsuge Y and Uehara T. Efficacy and safety of ensitrelvir in patients with mild-to-moderate coronavirus disease 2019: The phase 2b part of a randomized, placebo-controlled, phase 2/3 study. *Clin Infect Dis.*76:1403-11.2023
 10. Soga T, Duong C, Pattinson D, Sakai-Tagawa Y, Tokita A, Izumida N, Nishino T, Hagiwara H, Wada N, Miyamoto Y, Kuroki H, Hayashi Y, Seki M, Kasuya N, Koga M, Adachi E, Iwatsuki-Horimoto K, Yotsuyanagi H, Yamayoshi S and Kawaoka Y. Characterization of influenza a(h1n1)pdm09 viruses isolated in the 2018-2019 and 2019-2020 influenza seasons in japan. *Viruses.*15.2023
 11. Takahashi R, Matsubara Y, Takahashi S, Yokoyama K, Ahyoung LL, Koga M, Sakamoto H, Boku N, Shida D and Yotsuyanagi H. Refractory intestinal behçet-like disease associated with trisomy 8 myelodysplastic syndrome resolved by parenteral nutrition. *Case Rep Gastroenterol.*17:287-93.2023
 12. Uraki R, Ito M, Furusawa Y, Yamayoshi S, Iwatsuki-Horimoto K, Adachi E, Saito M, Koga M, Tsutsumi T, Yamamoto S, Otani A, Kiso M, Sakai-Tagawa Y, Ueki H, Yotsuyanagi H, Imai M and Kawaoka Y. Humoral immune evasion of the omicron subvariants bq.1.1 and xbb. *Lancet Infect Dis.*23:30-32.2023
 13. Uraki R, Ito M, Kiso M, Yamayoshi S, Iwatsuki-Horimoto K, Furusawa Y, Sakai-Tagawa Y, Imai M, Koga M, Yamamoto S, Adachi E, Saito M, Tsutsumi T, Otani A, Kikuchi T, Yotsuyanagi H, Halfmann PJ, Pekosz A and Kawaoka Y. Antiviral and bivalent vaccine efficacy against an omicron xbb.1.5 isolate. *Lancet Infect Dis.*23:402-03.2023
 14. Uraki R, Ito M, Kiso M, Yamayoshi S, Iwatsuki-Horimoto K, Sakai-Tagawa Y, Furusawa Y, Imai M, Koga M, Yamamoto S, Adachi E, Saito M, Tsutsumi T, Otani A, Kashima Y, Kikuchi T, Yotsuyanagi H, Suzuki Y and Kawaoka Y. Efficacy of antivirals and bivalent mrna vaccines against sars-cov-2 isolate ch.1.1. *Lancet Infect Dis.*23:525-26.2023
 15. Uraki R, Ito M, Kiso M, Yamayoshi S, Iwatsuki-Horimoto K, Sakai-Tagawa Y, Imai M, Koga M, Yamamoto S, Adachi E, Saito M, Tsutsumi T, Otani A, Kashima Y, Kikuchi T, Yotsuyanagi H, Suzuki Y, Korber B and Kawaoka Y. Antiviral efficacy against and replicative fitness of an xbb.1.9.1 clinical isolate. *iScience.*26:108147.2023
 16. Uraki R, Ito M, Kiso M, Yamayoshi S, Iwatsuki-Horimoto K, Sakai-Tagawa Y, Imai M, Koga M, Yamamoto S, Adachi E, Saito M, Tsutsumi T, Otani A, Kashima Y, Kikuchi T, Theiler J, Yotsuyanagi H, Suzuki Y, Korber B and Kawaoka Y. Efficacy of antivirals and mrna vaccination against an xbf clinical isolate. *Lancet Reg Health West Pac.*34:100777.2023
 17. Yamamoto S, Yamayoshi S, Ito M, Sakai-Tagawa Y, Nakachi I, Baba R, Kamimoto S, Ogura T, Hagiwara S, Kato H, Nakajima H, Uwamino Y, Yagi K, Sugaya N, Nagai H, Saito M, Adachi E, Koga M, Tsutsumi T, Duong C, Okuda M, Murakami J, Furusawa Y, Ujie M, Iwatsuki-Horimoto K, Yotsuyanagi H and Kawaoka Y. Differences among epitopes recognized by neutralizing antibodies induced by sars-cov-2 infection or covid-19 vaccination. *iScience.*26:107208.2023
 18. Yotsuyanagi H, Ohmagari N, Doi Y, Imamura T, Sonoyama T, Ichihashi G, Sanaki T, Tsuge Y, Uehara T and Mukae H. A phase 2/3 study of s-217622 in participants with sars-cov-2 infection (phase 3 part). *Medicine (Baltimore).*102:e33024.2023
 19. Karver TS, Pascual-Bernaldez M, Berni A, Hnoosh A, Castagna A, Messiaen P, Puerto MJG, Bloch M, Adachi E, Sinclair G, Felizarta F, Angel JB, Sutton K, Sutherland-Phillips D, D'Amico R and Kerrigan D. Factors associated with health care providers' preference for forgoing an oral lead-in phase when initiating long-acting injectable cabotegravir and rilpivirine in the solar clinical trial. *AIDS Patient Care STDS.*37:53-59.2023
 20. Nakagama Y, Candray K, Kaku N, Komase Y, Rodriguez-Funes MV, Dominguez R, Tsuchida T, Kunishima H, Nagai E, Adachi E, Ngoyi DM, Yamasue M, Komiya K, Hiramatsu K, Uemura N, Sugiura Y, Yasugi M, Yamagishi Y, Mikamo H, Shiraishi S, Izumo T, Nakagama S, Watanabe C, Nitahara Y, Tshibangu-Kabamba E, Kakeya H and Kido Y. Antibody avidity maturation following recovery from infection or the booster vaccination grants breadth of sars-cov-2 neutralizing capacity. *J Infect Dis.*227:780-787.2023
 21. Adachi E, Ikeuchi K, Koga M and Yotsuyanagi H. Background factors in people living with hiv in japan who switch to cabotegravir plus rilpivirine: A pilot study. *J Infect Chemother.*29:109-111.2023