S26-5 Speciation of arsenic trioxide metabolites in a patioent with acute promyelocytic leukemia (APL)

◯Toshikazu KAISE[1], Bo YUAN[2], Toshihiko HIRANO[2], Hiroo TOYODA[2]

[1]Tokyo Univ. Pharm. & Life Sci. Sch. of Life Sci., [2]Tokyo Univ. Pharm. & Life Sci. Sch. of Pharm.

Arsenic trioxide has been approved as a drug of choice for the treatment of patients with relapsed or refractory acute promyelocytic leukemia (APL) by the Ministry of Health, Labour and Welfare of Japan. We investigated pharmacodynamics of arsenic species in the plasma and blood cells from a relapsed APL patient undergoing arsenic trioxide treatment. The blood samples were collected at various time points over time from the patient after remission induction therapy and during consolidation therapy. The total amounts of arsenic in the plasma and blood cells were measured by inductively coupled plasma – mass spectrometry (ICP-MS). For total arsenic determination, samples were digested with HNO_3 and H_2O_2, following by being filtrated with 0.45 μM filter. The plasma concentrations of inorganic arsenic and methylated metabolites were determined with high performance liquid chromatography / inductively coupled plasma – mass spectrometry (HPLC / ICP-MS). For arsenic speciation, the plasma was ultrafiltered with a 10 kDa molecular weight cut off. In all blood samples collected either after the remission induction therapy or during consolidation therapy, approximately 80-90% of total arsenic in the blood samples was observed in the blood cells. Not only inorganic arsenic, but also methylated metabolites (MA and DMA) were observed in the plasma, and the methylated metabolites were the main arsenic species. These results suggested that arsenic trioxide in the plasma was metabolized by biomethylation pathway. In conclusion, these results may support an idea that methylated metabolites of As_2O_3 contribute to the efficacy of arsenic against APL patients.