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In coming years, the major challenge will be to harness the power of these discoveries to more accurately diagnose patients and to identify potential therapeutic targets in a more personalized way, so that such an approach can hold, but it will require a fundamental shift in the way that clinical trials are planned and conducted in order to optimize patient care.

This talk will highlight some of the most striking developments in the field, and look at the challenges that remain before these can lead to improved patient outcomes.

Key words: Genomics, Pediatric, Epigenetics

AS1-KL1
DEVELOPMENT OF HIGH-DOSE CHEMOTHERAPY INCLUDING THIOTEPA COMBINED WITH AUTOLOGOUS PERIPHERAL BLOOD STEM CELL RESCUE
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Thiotepa is a classic alkylating agent that was launched in 1958 in Japan. We have consistently developed thiotope-containing HDC since 1992, inspired by the fact that thiotope was used as an alternative to melphalan as a high-dose chemotheraphy (HDC) drug for neuroblastoma in the United States. Thiotope is considered to be a drug suitable for brain tumor treatment because of its good BBB permeability, equal concentration in cerebrospinal fluid and blood, and the characteristics of alkylating agents that enhance the efficacy by high ratio of dose. Melphalan, which is also an alkylating agent as a central agent of HDC, has a strong antitumor effect, so we planned to use both at the maximum tolerated dose for each. Therefore, in order to reduce toxicity, it was decided to divide it into two doses at weekly intervals and to administer thiotope for 24 hours in order to prevent hepatic sinus obstruction syndrome (SOS). Since 1993, a dose determination study was conducted, and the doses of thiotope and melphalan were determined to be 800 mg/m² and 280 mg/m², respectively. Autologous peripheral blood stem cell transplantation using this regimen was performed as a consolidation therapy for metastatic pediatric medulloblastoma in 28 and 15 patients, respectively, in 2 series. Five-year progression-free survival rates of 82.1 ± 7.2% and 92.9 ± 6.9% were obtained. After that, the supply was stopped in 2009. This time, a new indication (pretreatment for autologous hematopoietic stem cell transplantation in childhood malignant solid tumors) was acquired and launched. By this dose reduction, reduced gastro-intestinal toxicity such as mucosal damage is expected. The JCCG clinical trials incorporating HDC will be conducted in medulloblastoma, ATRT, and refractory germ cell tumors.

Key words: thiotope, melphalan, high-dose chemotherapy