

S-5-3

REDUCED-INTENSITY STEM CELL TRANSPLANTATION (RIST): A JAPANESE EXPERIENCE

Yoichi Takaue

Pharmaco-Therapeutic Division/Developmental Therapeutics,
National Cancer Center Hospital

RIST is based on the concept of intensifying immunosuppression to primarily enhance the engraftment of donor cells, rather than cytoreduction. Thereafter, established donor-derived lymphohematopoiesis provides a basis to exert antitumor effects. In our phase I RIST study with fludarabine (180 mg/m²) or cladribine (0.66 mg/kg) plus busulfan (8 mg/kg), with or without anti-thymocyte globulin (ATG), which was performed between April 2000 and December 2003, a total of 231 patients who had a variety of hematological (n=188) or metastatic solid tumors (RCC, 14; non-RCC, 29) were treated. We observed that the underlying immune mechanism involved in chimerism induction, GVHD and graft-versus-tumor effect (GVT) is unclear, complex and disease-specific. Attempts have been made

to intentionally induce the early occurrence of GVHD, which has been considered to be a marker of a GVT effect, through the omission or early withdrawal of prophylaxis for GVHD. However, it has become clear that the maximum induction of GVT does not necessarily rely on the clinical manifestation of GVHD. In contrast to the historically used cutoff of day 100 in conventional transplantation, a significant number of RIST cases develop acute GVHD beyond day 200. Hence, prolongation of the evaluation period should be seriously considered in future cases. Establishment of a suitable treatment strategy that effectively balances GVHD and an anticancer immune effect is urgently required. This presentation will overview our RIST program and highlight several burning issues in this field for interactive discussion.