

# Hematology

## Introduction

The Hematology Division is a part of the Division of Oncology and Hematology. Although all staff physicians and residents are involved in the clinical and research activities of chemotherapy for patients with both hematological and non-hematological tumors in this division, three staff physicians are taking a leading part in the treatment for haematological malignancies. Because high-dose chemotherapy with autologous hematopoietic stem cell transplantation is considered the standard treatment for patients with relapsed malignant lymphoma that responded to the prior chemotherapy, these physicians also perform stem cell harvest by apheresis and high dose chemotherapy with autologous stem cell transplantation. More than 100 patients with hematological malignancies were consulted in this division annually. Clinical studies for haematological malignancies in our division consist of the protocols prepared in National Cancer Center Hospital East, the participation in Japan Clinical Oncology Group-Lymphoma Study Group (JCOG-LSG) and in Japan Adult Leukemia Study Group, and the industry-supported trials for new agent.

## Routine Activity

We manage various kinds of hematological malignancies including non-Hodgkin's lymphoma (NHL), Hodgkin's lymphoma, multiple myeloma, acute leukemia, chronic leukaemia and others. Recently, many patients with both hematological and non-hematological tumors in this division tend to receive the routine chemotherapy at the outpatient service. We also manage all patients treated with aggressive chemotherapy in the 8 floor ward in which we have 8 laminar air flow rooms. Case conference on these patients is practiced everyday with nurses. Our clinical practice consists of not only the management of patients but also consultation concerning hematological abnormalities.

There are weekly case conferences on Tuesday afternoon, Wednesday evening and Thursday evening in the Division of Oncology/Hematology and a monthly joint conference on malignant lymphoma with pathologists. There are also morning journal clubs

on Monday, Thursday and Friday in the Division of Oncology/Hematology.

## Research Activities

The following clinical trials for hematologic malignancy were conducted in this year.

### Phase I/II trials

Phase I/II study of SHL 749 (Zevalin) for relapsed or refractory low grade NHL

Phase I/II study of JK 6251 (Cladribine) for relapsed or refractory low grade NHL

Phase I/II study of biweekly etoposide and cytarabine for relapsed diffuse large B-cell and peripheral T-cell lymphoma

Phase I/II and pharmacological study of high dose chemotherapy (MEAM) with autologous stem cell rescue for relapsed aggressive NHL

Phase I/II study of CEP for relapsed NHL in the elderly

Phase I/II study of CPT-11 and CDDP for relapsed NHL

Phase I/II study of Bortezomib (Velcade) for relapsed or refractory multiple myeloma

JCOG0211-DI, phase I/II study of concurrent chemoradiotherapy for newly-diagnosed, localized nasal NK/T-cell lymphoma

### Phase III trials

JALSG (Japan Adult Leukemia Study Group) AML-201 for acute myeloid leukemia

JCOG-0203-MF, randomized study of rituximab-CHOP and rituximab-biweekly CHOP, for low grade NHL

### Others

Pharmacological study of cyclophosphamide  
PET study in NHL

## New Developments in 2005

Because the initial treatment strategy including single alkylating agent, radiation therapy and combination chemotherapy did not affect the overall survival in patients with advanced stage indolent lymphoma, watch-and-wait is also considered an appropriate option. Recently, a mouse-human chimeric anti-CD20 monoclonal antibody, rituximab, seems to be a new promising therapeutic option in indolent lymphoma. Hereby, the randomized study

of rituximab-standard CHOP versus rituximab-biweekly CHOP for newly diagnosed indolent lymphoma in advanced stage is ongoing by JCOG-LSG. On the other hand, radioimmunotherapy is another strategy to optimize the efficacy of anti-CD20 monoclonal antibody therapy by combining the antibody with a radioconjugate, yttrium-90 ibritumomab tiuxetan (Zevalin). A phase I study was completed to evaluate the safety and efficacy of radioimmunotherapy with Zevalin in Japanese patients with relapsed or refractory indolent B-cell lymphoma. After serial gamma-camera imaging to investigate the distribution of Indium-111-labeled ibritumomab tiuxetan (In2B8) in the whole body of patients, Zevalin with a dose of 0.3 mCi/kg or 0.4 mCi/kg was administered. Critical toxicities (prolonged thrombocytopenia or severe non-hematologic toxicities) were observed in 2 of 6 patients in the 0.4-mCi/kg dose group but not seen in any of the three patients in the 0.3-mCi/kg dose group. Although the pharmacokinetic profiles were similar to those in the US study, one of the two patients was clarified retrospectively as showing abnormal biodistribution of In2B8 in the bone marrow, as judged by the independent panel of radiologists. The recommended

dose of Zevalin for the subsequent phase II study for Japanese patients is concluded to be 0.4 mCi/kg. Five of the 10 participants achieved complete responses or unconfirmed complete responses and 2 partial responses.

Nasal NK/T-cell lymphoma is a rare, regional lymphoid neoplasm, and its standard therapy has not been established. To explore a more effective treatment for newly-diagnosed localized nasal NK/T-cell lymphoma, JCOG-LSG completed the phase I portion of a multicenter phase I/II study of concurrent chemoradiotherapy consisted of 50 Gy of radiotherapy and 3 courses of DeVIC chemotherapy (carboplatin, ifosfamide, etoposide, dexamethasone). Two dose levels of DeVIC (Level 1; 2/3-dose, Level 2; 100%-dose) were evaluated. Grade 4 neutropenia and grade 3 mucositis due to radiotherapy were common. Four out of 6 patients at Level 2 developed dose-limiting toxicities. The Level 1 was recommended for the subsequent phase II portion. Seven of all 10 patients enrolled in the study achieved complete response. Feasibility and efficacy of Level 1 will be evaluated in the phase II portion.

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Number of patients consulted in this year

	Number of patients
Malignant lymphoma	143
Leukemia	15
Multiple myeloma	13

Number of patients enrolled in clinical trials

	Protocol	Number of patients
Non-Hodgkin's lymphoma	SHL 749	5
	JK 6251	5
	JCOG-0203	5
	JCOG-0211 DI	1
	CPT-11/CDDP	5
	MEAM	5
	Etoposide/cytarabine	16
	CEP	3
	PK of cyclophosphamide	124
	PET study	102
Acute myeloid leukemia	JALSG AML 201	5
Multiple myeloma	Bortezomib	5