

Hematology

Introduction

The Hematology Division is a part of the Division of Oncology and Hematology. Accordingly, all five staff physicians and two residents are involved in the clinical and research activities of chemotherapy for patients with both hematological and non-hematological tumors in this division. The same physicians also perform stem cell harvest by apheresis, cell processing and high dose chemotherapy with autologous stem cell transplantation. The number of patients with hematological malignancies has been increasing annually. In particular, more than 100 patients with malignant lymphoma were consulted in this year. Clinical studies for haematological malignancies in our division consist of the protocol studies prepared in house, the participation in Japan Clinical Oncology Group-Lymphoma Study Group (JCOG-LSG) 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. 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. High-dose chemotherapy with autologous hematopoietic stem cell transplantation is considered the standard treatment for patients with relapsed NHL and/or multiple myeloma that responded to the prior chemotherapy. Therefore, the procedure of peripheral blood stem cell harvest and transplantation is increasing. Our clinical practice consists not only of the treatment of patients but also of 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 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 biweekly etoposide and cytarabine for relapsed diffuse large B-cell and peripheral T-cell lymphoma

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

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

Randomized study of EPOCH (erythropoietin) for anemic patients with NHL

Randomized study of EPOCH (erythropoietin) for anemic patients with NHL

Others

Pharmacological study of cyclophosphamide

PET study in NHL

New Developments in 2004

In Hodgkin's lymphoma, ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) is considered as the standard therapy because of high efficacy and low toxicities. Since Hodgkin's lymphoma is not common in Japan, JCOG-LSG has conducted phase II studies to apply the standard chemotherapy regimens to Japanese patients due to practical limitations. Namely, ABVD in JCOG9305, consist of reduced dose of dacarbazine (DTIC), has been investigated because a full dose of DTIC was

considered intolerable due to severe emesis at that time. Subsequently, to explore a less toxic and equally effective chemotherapy regimen against advanced Hodgkin's lymphoma, JCOG-LSG conducted a multicenter phase II study (JCOG9705) of ABV with increased dose of doxorubicin and deleted DTIC, because of frequent gastrointestinal toxicity and phlebitis associated with DTIC. Patients with newly diagnosed Hodgkin's lymphoma, clinical stage of IB/ IIB/III/IV or any stage with bulky tumor, age less than 70 years, performance status 0-3 (ECOG-PS) were enrolled and received 6 or 8 courses of ABV. Between Jan 1998 and Dec 2000, 72 patients were enrolled, but one was ineligible for non-bulky IIA. Although there was no treatment-related death and no grade 4 non-hematological toxicity, 2-year progression-free survival (%PFS) was 51% (95%CI: 39-63), which was remarkably worse than 2-year %PFS of 83% in JCOG9305 (ABVD). Complete response rate was 68% (95%CI: 56-79) and 2-year overall survival was 92% (95%CI: 85-98). The low %PFS was considered to reflect too many early relapses after ABV-involved-field radiotherapy, and according to the recommendations by the Data and Safety Monitoring Committee of JCOG, patient enrolment into JCOG 9705 was closed. In conclusion,

the early results of JCOG9705 suggested that the efficacy of ABV with increased dose of doxorubicin and deleted DTIC was inferior to ABVD. It is also suggested that DTIC is a key agent in ABVD therapy.

In aggressive non-Hodgkin's lymphoma (NHL), CHOP has been accepted as the gold standard for first-line chemotherapy. However the therapeutic outcome of CHOP remained unsatisfactory and JCOG-LSG has conducted the randomized phase III study of standard CHOP and biweekly CHOP to improve treatment results in aggressive NHL. Unfortunately, a dose-dense strategy by interval shortening of CHOP chemotherapy with the prophylactic use of G-CSF (biweekly CHOP) was unable to prolong progression free survival in patients with aggressive NHL. Furthermore, a phase III study comparing CHOP plus rituximab, a mouse-human chimeric anti-CD20 monoclonal antibody, (R-CHOP) and CHOP for untreated patients with diffuse large B-cell lymphoma has revealed that the efficacy of R-CHOP was superior to CHOP. Based on these findings, JCOG-LSG is currently planning future trials of rituximab-containing chemotherapy for aggressive B-cell NHL.

● K. Itoh ●

Number of patients consulted in this year	
	Number of patients
Non-Hodgkin's lymphoma	106
Hodgkin's lymphoma	8
Acute leukemia	10
Multiple myeloma	18
Chronic leukemia	2

Number of patients enrolled in clinical trials		
	Protocol	Number of patients
Non-Hodgkin's lymphoma	SHL 749	4
	JK 6251	4
	JCOG-0203	5
	CPT-11/CDDP	4
	MEAM	3
	Etoposide/cytarabine	15
	CEP	2
	EPOCH	7
	PK of cyclophosphamide	52
Acute myeloid leukemia	PET study	88
	JALSG AML 201	4
Multiple myeloma	Bortezomib	3