

## Department of Internal Medicine

### Division of Clinical Oncology/Hematology

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### General Summary

The immediate goals of our clinical and basic research are to investigate basic and clinical aspects of malignant diseases and to try to improve outcomes for patients with solid tumors and hematological malignancies, leading to the ultimate goals of improving the natural history of malignant diseases. We have also been performing several clinical trials and basic research studies successfully throughout 2017.

### Research Activities

#### *Leukemias*

Many patients with previously untreated hematological disorders have been referred to our department. The disorders in 2017 included acute myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL), 28 cases and chronic myeloid leukemia (CML), 11 cases. We have performed clinical trials as a member of the Japan Adult Leukemia Study Group (JALSG), which is a distinguished leukemia research group established more than 20 years ago in Japan for clinical research and treatment of AML, ALL, and CML.

#### *Lymphomas*

In 2017 we registered 117 patients with newly diagnosed non-Hodgkin's lymphoma. We have performed clinical trials as a member of the Lymphoma Study Group of the Japan Clinical Oncology Group (JCOG). The study JCOG0601 (newly diagnosed low risk advanced diffuse large B cell lymphoma: phase II/III) was pivotal protocol studies beginning in 2007.

#### *Myeloma*

We registered 15 patients with newly diagnosed multiple myeloma in 2017. A novel agent, the proteasome inhibitor bortezomib, became available in 2007, and we have used it with or without dexamethasone to treat patients who have refractory myeloma. In-house protocols are also under investigation. A phase II study of CVD regimen (cyclo phosphamide+bortezomib+dexamethasone) for patients with newly diagnosed multiple myeloma.

### *Hematopoietic stem cell transplantation*

To investigate and establish safer and more effective hematopoietic stem cell transplantation (HSCT), we have performed serial clinical studies examining umbilical cord blood transplantation, reduced-intensity stem cell transplantation from haploidentical donor, and investigation of mechanisms of graft-versus-host disease in HSCT.

### *Solid tumors*

Many patients with solid cancers have been referred to our department from related divisions or departments from both inside and outside our hospital. Several of our studies seeking improved therapeutic outcomes are in progress throughout our university hospital with related divisions or departments. Since late 2008 we have been investigating a combined-modality therapy of radiation and chemotherapy with docetaxel, cisplatin, and 24 hours' continuous infusion of 5-FU (DCF regimen) for patients with locally advanced esophageal cancer. The study has been completed and the results have published recently. Successively an improved protocol was launched 4 years ago and now has been investigating. We performed a novel drug-development study with an orally decaying formulation of S-1 co-operating with a colleague department had completed in patients with advanced gastric cancer and the new formulation of S-1 became now available in daily practice. Our first-line chemotherapies for patients with advanced colorectal cancer are folinic acid, fluorouracil, and oxaliplatin (FOLFOX) and folinic acid, 5-FU, and irinotecan (FOLFIRI). Since antibodies against vascular endothelial growth factor (VEGF) and against epidermal growth factor receptor (EGFR) became available in 2007 and 2008, respectively, combination therapies of these antibodies and FOLFOX or FOLFIRI have also been performed. Since oral drugs are more convenient and safer, 5-FU is replaced by S-1 or capecitabine in such i.v. combination chemotherapy as FOLFOX or FOLFIRI, leading to develop improved regimens of SOX, ZELOX, IRIS and ZELIRI. Salvage therapies using regorafenib or TAS102 became standard care for resistant and refractory advanced colorectal cancer.

### *Basic research*

One of our important activities is translational research on solid cancers and hematological malignancies. Since clinical requirement is urgent, persistent research is warranted. Cancer fatigue is now an emerging issue for patients with advanced malignant disease. We have been evaluating the correlation between cancer fatigue and HHV-6 reactivation using patient's salivary juice and blood samples, collaborating with the department of Virology. The preliminary result was reported at the annual meeting of MASCC in Miami USA.

Life-threatening disease, such a study seems to be highly of great consequence. Supportive care in cancer is also very important for patients with malignant disease. We have been working on such a field for years. Measuring L-FABP level in patient's urine can predict renal damage caused by cisplatin. Therefore, we have been trying to see if L-FABP is worth enough to measure for early detection of renal damage in patients undergoing cisplatin combination chemotherapy such as DCF and GDP. The studies are vigorously in progress.

## Publications

- Fujisawa S<sup>1</sup>, Mizuta S<sup>2</sup>, Akiyama H<sup>3</sup>, Ueda Y<sup>4</sup>, Aoyama Y<sup>6</sup>, Hatta Y<sup>6</sup>, Kakihana K<sup>7</sup>, Dobashi N, Sugiura I<sup>8</sup>, Onishi Y<sup>9</sup>, Maeda T<sup>10</sup>, Imai K<sup>11</sup>, Ohtake S<sup>12</sup>, Miyazaki Y<sup>13</sup>, Ohnishi K<sup>14</sup>, Matsuo K<sup>15</sup>, Naoe T<sup>16</sup> (Yokohama City Univ, <sup>2</sup>Fujita Health Univ, <sup>3</sup>Tama-Hokubu Med Hosp, <sup>4</sup>Kurashiki Central Hosp, <sup>5</sup>Seichokai Fuchu Hosp, <sup>6</sup>Nihon Univ, <sup>7</sup>Komagome Hosp, <sup>8</sup>Toyohashi Municipal Hosp, <sup>9</sup>Tohoku Univ, <sup>10</sup>Saitama Med Univ, <sup>11</sup>Sapporo Hokuyu Hosp, <sup>12</sup>Kanazawa Univ, <sup>13</sup>Nagasaki Univ, <sup>14</sup>Hama-matsu Univ, <sup>15</sup>Aichi Cancer Center, <sup>16</sup>Nagoya Med Center). Phase II study of imatinib-based chemotherapy for newly diagnosed BCR-ABL-positive acute lymphoblastic leukemia. *Am J Hematol*. 2017; **92**: 367-74.
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- Kondo T, Nagamura-Inoue T<sup>2</sup>, Tojo A<sup>2</sup>, Nagamura F<sup>2</sup>, Uchida N<sup>3</sup>, Nakamae H<sup>4</sup>, Fukuda T<sup>5</sup>, Mori T<sup>6</sup>, Yano S, Kurokawa M<sup>2</sup>, Ueno H<sup>7</sup>, Kanamori H<sup>8</sup>, Hashimoto H<sup>9</sup>, Onizuka M<sup>10</sup>, Takanashi M<sup>11</sup>, Ichinohe T<sup>12</sup>, Atsuta Y<sup>13</sup>, Ohashi K<sup>14</sup> (Hokkaido Univ, <sup>2</sup>Tokyo Univ, <sup>3</sup>Toranomon Hosp, <sup>4</sup>Osaka City Hosp, <sup>5</sup>National Cancer Center, <sup>6</sup>Keio Univ, <sup>7</sup>Tokyo Medical Center, <sup>8</sup>Kanagawa Cancer Center, <sup>9</sup>Kobe General Hosp, <sup>10</sup>Tokai Univ, <sup>11</sup>Japanese Red Cross Society, <sup>12</sup>Hiroshima Univ, <sup>13</sup>Nagoya Hosp, <sup>14</sup>Komagome Hosp). Clinical impact of pretransplant use of multiple tyrosine kinase inhibitors on the outcome of allogeneic hematopoietic stem cell transplantation for chronic myelogenous leukemia. *Am J Hematol*. 2017; **92**: 902-8.
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