— 137 —

Efficacy of Imatinib mesylate dose-escalation in CML patients showing suboptimal response to standard dose

Department of Internal Medicine[1], Diagnostic DNA Chip Center ILCHUN Molecular Medicine Institute MRC[2], Seoul National University College of Medicine

*Dae-Young Kim, M.D.[1], Joo Han Lim, M.D.[1], Myoung-Deok Seo, M.D.[1], Hyeon Gyu Yi, M.D.[1], So Yeon Oh, M.D.[1], Cheung Zhe Piao, PhD.[2], Inho Kim, M.D.[1], Sung-Soo Yoon, M.D.[1], Seonyang Park, M.D.[1], Byoung Kook Kim, M.D.[1]

Introduction : We report an analysis of our prospective single arm study performed to evaluate the efficacy of IMT dose-escalation therapy and the influence of BCR/ABL mutational status on the treatment outcome. **Methods :** Patients with chronic phase CML who had not achieved a complete hematologic response (CHR) after 3 months, a major cytogenetic response (MCyR) after 6 months, nor a complete cytogenetic response (CCyR) after 6-12 months of standard IMT therapy (400mg per day) were included. 600mg of IMT had been administered per day for at least 12 months or until the appearance of a progressive disease, intolerable toxicity. For each patient, BCR/ABL gene mutation test was performed. Cytogenetic response (CyR) was evaluated with the percentage of bcr/abl positive cells in bone marrow aspirate by means of FISH per 6 months. Molecular response (MR) was assessed per 3 months with a logarithmic decrease in BCR-ABL/ABL gene rate (BA/A) in peripheral blood or bone marrow aspirate from a standardized median value of BA/A in 56 patients with newly diagnosed CML. **Results :** Seventy-seven patients were enrolled and 61 patients were eligible for evaluation of MR. Median time from the initiation of IMT therapy to dose-up was 20 months (range: 0-62). The BCR/ABL gene mutational status could be obtained in 24 patients (wild:mutant=20:4). Median follow-up period was 19.9 months (range: 6.5-24.3). For 34 patients whose 6th-month CyR is available, MCyR rate (MCyRR) was 26.5% and CCyR rate (CCyRR) was 23.5%. The 12th-month MCyRR was 61.1% and CCyRR was 50.0%. Patients with wild type showed a MCyRR of 20% and a CCyRR of 15% on the 12th month after dose-up, whereas no patient with mutant type showed CCyR or MCyR. Complete MR (CMR) and major MR (MMR) on the 12th-month were 16.7% and 26.7%. Among 24 patients whose mutational status was known, one patient achieved a 6th-month CMR, 2 patients MMR's, whereas no patient with mutant type could achieve a MMR during the entire treatment period. Toxicities during treatment were tolerable. **Conclusion :** IMT dose-escalation therapy could induce quite a number of durable CyR's and MR's without any serious toxicity in patients who had failed to achieve a CHR or a CyR with a standard IMT therapy.

— 138 —

Experiences of azacitidine treatment for myelodysplastic syndrome (MDS)

Departments of Internal Medicine, Seoul National University College of Medicine[1], Department of Internal Medicine, Seoul National University Bundang Hospital[2]

*So Yeon Oh[1], Soo-Mee Bang[2], Inho Kim[1], Sung-Soo Yoon[1], Jong Seok Lee[2], Seonyang Park[1], Byoung Kook Kim[1]

Background : Azacitidine was approved for treatment of MDS by Korean FDA in January 2006, and became reimbursable from health insurance since August 2006. Until now, few materials are available about azacitidine in Korea. We experienced 26 MDS patients treated with azacitidine, and we report here to share our experiences of azacitidine treatment for MDS patients. **Materials and Methods :** All MDS patients treated with azacitidine were included in analysis. Azacitidine was administered 75mg/m2 SQ D1-7 every 4weeks, in all patients. Retrospective review of medical records was done in Seoul National University Hospital and Seoul National University Bundang Hospital, from August 2006 to April 2007. Results 26 patients treated with azacitidine were collected. Median age was 59.5 years, ranging from 20 to 79. M:F was 1:0.63 (16:10). MDS subtypes were 6 RA(236%), 5 RAEB-1(19%), 11 RAEB-2(42%), 2 RCMD(8%) and 2 other(8%). Median IPSS score was 1.5. Azacitidine was administered median 4 cycles (1-12 cycles). Response determination was done according to modified IWG criteria. Evaluation of response was able in 17 patients. Response was CR in 3, marrow CR in 3, HI in 3 patients. 8 patients are SD. Overall response rate was 53% (including HI). Regarding toxicity, aggravation of cytopenias were present in considerable patients ?leukopenia 62%(n=16), neutropenia 50%(n=13), anemia 31% (n=8), thrombocytopenia 46%(n=12). One death was observed due to ICH that seemed to be related to thrombocytopenia. Leukemic transformation was observed in one patient. Non-hematologic toxicities were generally acceptable. **Conclusion :** Despite its considerable hematologic toxicity, azacitidine is well tolerated in majority of patients, with response rate of 53%. Because short duration and small number, further large scale trial is warranted.