The current standard therapy for aGVHD is glucocorticoid methylprednisolone 2mg/kg/d, but it still has drawbacks. Our recently published data found that low dose of methotrexate can be used to treat different types of GVHD including aGVHD, cGVHD and post-DLI GVHD as salvage therapy. The current study was initiated to evaluate the safety and both the efficacy of low dose of methotrexate combined with low dose of methylprednisolone as first line therapy in the treatment of aGVHD after allo-HSCT.

The study was approved by the Institutional Review Board of the Peking University Institute of Hematology. All included patients were informed and signed an informed consent form. Patients who had not received drug treatments for aGVHD and whose peripheral blood white blood cell counts were higher than 1.5×10^9/L were selected. From May 2007 to June 2008, 32 patients received intravenous MTX at a dose of 10 mg or oral MTX at a dose of 15 mg every 3–7 days (repeated at day three after the first dose and then at a weekly interval) combined with low dose of methylprednisolone (started with 0.5mg/kg/d, and dose was reduced by half after 5-7 days) until a complete or partial response was achieved, or until treatment failure or intolerable side effects were found. Patients were observed for 3-5 days and would be switched to second line treatment (Daclizumab) if no response to first line therapy.

The median time from HSCT to the start of MTX was 32 days. The median number of MTX administrations was four (range, 2–6). Median time to achieve maximal response (CR or PR) was 5 days. By day 30 after drug administration, accumulated MP dose was 5.78 mg/kg. The overall response rate was 81% (26/32 patients). The response rate for GVHD involving various organs was 88% (23/26) in skin, 75% (3/4) in liver, 81% (9/11) in gut. Six of 32 (18%) patients required Daclizumab as second-line treatment. Grade 3 toxicities occurred in only 3 patients presenting cytophenias. Eighteen of 32 (56%) patients developed cGVHD. Two-year cumulative incidence of leukemia relapse was 7%. Two-year cumulative incidence of TRM was 11%. Twenty-seven patients (84%) remain alive without leukemia relapse with a median survival of 682 days from onset of aGVHD and 699 days from HSCT. The estimated survival at 2 years was 77 %.

Our study showed that low-dose MTX combined with low dose of methylprednisolone is effective and safe. There are maybe synergistic effect between methotrexate and methylprednisolone. The combination regimen might be eligible for alternative forms of first-line treatment of aGVHD and it is especially preferential for those high risk patients of relapse. However, a randomized, controlled study is needed to compare the results of this new regimen and the standard therapy with methylprednisolone (2mg/kg/d).

The authors reported no potential conflicts of interest.