

[1805] Pentostatin in Steroid-Refractory Chronic Graft-Versus-Host Disease. Session Type: Poster Session 9-II

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Pentostatin, one of the purine nucleoside analogues, is known to decrease lymphocyte number and function. It has been successfully used to treat steroid refractory acute graft-versus-host disease (GVHD). We are currently investigating pentostatin for refractory chronic GVHD (cGVHD). Fifty-two patients were enrolled and 42 are assessable for response. All patients presented here failed at least two immunosuppressive regimens including steroids at a dose equivalent to at least 1 mg/kg/day prednisone for one month. The treatment protocol consists of giving pentostatin 4 mg/m²/dose IV every 2 weeks for 6 months. Patients with improving disease were permitted to continue pentostatin therapy at a 3 to 4 week interval. To reduce the risk of infection, steroids are tapered early in all patients and they received prophylactic antibiotics (antibiotics, fluconazole, sulfamethoxazole/trimethoprim and valacyclovir). At the end of 3 months, patients with stable or improving cGVHD are weaned off their other medications but maintained on a calcineurin inhibitor. Pentostatin is stopped at 6 months if complete response (CR) is achieved or continued if partial response (PR). Patients are followed for improvement in the skin/fascia, mouth, and liver. The severity of GVHD is scored for each system on a scale from 0 to 4. Complete response is resolution of symptoms (irreversible changes [such as long standing contractures] due to cGVHD were not required to improve to score a CR if all other changes improved); partial response is at least a 1 point improvement in this score system. Mixed response is improvement in 1 system but worsening in another. Fifty-two patients have received a median of 8.5 doses (range 1-34). Median age of the cohort is 40.5 years (range 5 to 67). Diagnoses include AML/MDS (6), ALL (7), hemoglobinopathy (2), aplastic anemia (3), CML (16), myelofibrosis (1), NHL (8), myeloma (4), paroxysmal nocturnal hemoglobinuria (3), CLL (1), and lymphohistiocytosis (1). Graft source included 20 patients: 6/6 sibling BMT; 10 patients: 6/6 sibling PBSCT; 10 patients: MUD BMT; 6 patients 5/6 MUD BMT; 2 patients: 6/6 MUD PBSCT; 1 patient 5/6 sibling BMT; 1 patient: 6/6 sibling BMT followed by DLI; 1 patient 5/6 BMT from a child; and 1 patient, unknown. Most patients were on calcineurin inhibitor, eleven on prednisone, seven on MMF, one on rapamycin, and one was receiving ECP at entry on the study. In the 42 assessable patients, 5 patients attained a CR, 16 a PR, 5 a mixed response (improvement in one organ with deterioration in another one), and 16 patients have progressed. The overall response rate is 50%. Therapy has been well-tolerated with infections being the main concern. Mucormycosis, pneumonia, disseminated fungal infection, fungal pneumonia, progressive disease were the causes of death of the 15 patients who have died and only infections could be related to the study drug. The results suggest that pentostatin has activity in the treatment of cGVHD and may be especially beneficial in children and adolescents as the 5 CR were in this group.

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