European Journal of Haematology 86 (16–22)

ORIGINAL ARTICLE

Addition of thalidomide to oral melphalan/prednisone in patients with multiple myeloma not eligible for transplantation: results of a randomized trial from the Turkish Myeloma Study Group

Meral Beksac[1], Rauf Haznedar[2], Tulin Firatli-Tuglular[3], Hakan Ozdogu[4], Ismet Aydogdu[5], Nahide Konuk[1], Gulsan Sucak[2], Işık Kaygusuz[3], Sema Karakus[4], Emin Kaya[6], Ridvan Ali[7], Zafer Gulbas[8], Gulsum Ozet[9], Hakan Goker[10], Levent Undar[11]

[1]Department of Hematology, Faculty of Medicine, Ankara University, Ankara; [2]Department of Hematology, Faculty of Medicine, Gazi University, Ankara; [3]Department of Hematology, Faculty of Medicine, Marmara University, Istanbul; [4]Başkent University, Adana Practice and Research Center, Adana; [5]Department of Hematology, Faculty of Medicine, Selçuk University, Konya; [6]Department of Hematology, Faculty of Medicine, İnönü University, Malatya; [7]Department of Hematology, Faculty of Medicine, Uludağ University, Bursa; [8]Department of Hematology, Faculty of Medicine, Osmangazi University, Eskişehir; [9]Department of Hematology, Ankara Numune Hospital, Ankara; [10]Department of Hematology, Faculty of Medicine, Hacettepe University, Ankara; [11]Department of Hematology, Faculty of Medicine, Akdeniz University, Antalya, Turkey

Abstract

The combination of melphalan–prednisone–thalidomide (MPT) has been investigated in several clinical studies that differed significantly with regard to patient characteristics and treatment schedules. This prospective trial differs from previous melphalan–prednisone (MP) vs. MPT trials by treatment dosing, duration, routine anticoagulation, and permission for a crossover. Newly diagnosed patients with multiple myeloma (MM) (n = 122) aged greater than 55 yr, not eligible for transplantation were randomized to receive 8 cycles of M (9 mg/m^2/d) and P (60 mg/m^2/d) for 4 d every 6 wk (n = 62) or MP and thalidomide (100 mg/d) continuously (n = 60). Primary endpoint was treatment response and toxicities following 4 and 8 cycles of therapy. Secondary endpoints were disease-free (DFS) and overall survival (OS). Overall, MPT-treated patients were younger (median 69 yr vs. 72 yr; P = 0.016) and had a higher incidence of renal impairment (RI, 19% vs. 7%, respectively; P = 0.057). After 4 cycles of treatment (n = 115), there were more partial responses or better in the MPT arm than in the MP arm (57.9% vs. 37.5%; P = 0.030). However, DFS and OS were not significantly different between the arms after a median of 23 months follow-up (median OS 26.0 vs. 28.0 months, P = 0.655; DFS 21.0 vs. 14.0 months, P = 0.342, respectively). Crossover to MPT was required in 11 patients, 57% of whom responded to treatment. A higher rate of grade 3–4 infections was observed in the MPT arm compared with the MP arm (22.4% vs. 7.0%; P = 0.033). However, none of these infections were associated with febrile neutropenia. Death within the first 3 months was observed more frequently in the MP arm (n = 8, 14.0%) than in the MPT arm (n = 2, 3.4%; P = 0.053). Long-term discontinuation and dose reduction rates were also analyzed (MPT: 15.5% vs. MP: 5.3%; P = 0.072). Although patients treated with MPT were relatively younger and had more frequent RI, better responses and less early mortality were observed in all age groups despite more frequent discontinuation. This study is registered at http://www.clinicaltrials.gov as #NCT00934154.

Key words multiple myeloma; treatment; melphalan; prednisone; thalidomide