ELSEVIER

Blood 142 (2023) 4007–4008

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

331.THROMBOTIC MICROANGIOPATHIES/THROMBOCYTOPENIAS AND COVID-19-RELATED THROMBOTIC/VASCULAR DISORDERS: CLINICAL AND EPIDEMIOLOGICAL

Phase II Study of Danazol with Plasma Exchange and Corticosteroids for the Treatment of Thrombotic Thrombocytopenic Purpura

Vamsee Torri, MD[1,2], *Mark Friedman, DO*[3,4], *Ilan Shapira, MD*[5], *Amit A. Patel, MD*[1,6,7,8], *Joseph Yoe, MD*[1], *Vijay P. Shah, MD*[9], *Tahir Mirzoyev, MD*[1], *Maria Machuca, RN*[5], *Mala Varma, MD*[1]

[1] Hematology-Oncology, Mount Sinai West and Mount Sinai Morningside, New York, NY
[2] St. Joseph's Hospital and Medical Center, Phoenix, AZ
[3] Pathology/Blood Bank, Mount Sinai West and Mount Sinai Morningside, New York, NY
[4] NYU Langone Hospital-Long Island, Mineola, NY
[5] Hematology-Oncology, Mount Sinai Beth Israel, New York, NY
[6] RWJ Barnabas Health - Jersey City Medical Center, Jersey City, NJ
[7] St. George's University School of Medicine, St. George's, Grenada
[8] New York Institute of Technology, New York, NY
[9] Pathology/Blood Bank, Mount Sinai Beth Israel, New York, NY

Background: Ahn and colleagues reported a decrease in plasma exchange (PE)/plasma infusion requirement with danazol in seven cases of thrombotic thrombocytopenic purpura (TTP) (Ahn Blood 2006;108(11):1057a). We reported an increase in platelet count (PLT) within 24 hours with danazol in two of three cases of human immunodeficiency virus-associated TTP resistant to PE (Torri Transfusion 2010;50:86a). In 2009, we initiated a phase II study of danazol with PE and corticosteroids (CS) for the treatment of TTP. This trial was approved by the institutional review board and was registered at ClinicalTrials.gov (ID# NCT00953771). We report the final results.
Aims: To determine if danazol reduces number of PE's, time to remission (TR), and length of stay (LOS) when administered with standard therapy for the initial treatment of TTP.
Methods: Experimental Group (EG): Patients with TTP (PLT < 100,000/μL and microangiopathy) receive daily PE, prednisone 1 mg/kg, and danazol 600 mg. Following remission (PLT > 150,000/μL for three consecutive days), PE is tapered to every other day for one week then stopped. Then prednisone is tapered weekly over four weeks then stopped. After one week danazol is tapered by 200 mg weekly then stopped. Historical controls (HC): Patients treated for TTP at St. Luke's-Roosevelt Hospital Center with PE with or without CS from 2000 to 2007 (n=20). Relapse definition: PLT < 100,000/μL with microangiopathy > 30 days after remission. Total number of PE's, TR, LOS, and continuous response rates are compared between the 2 groups. Accrual target: 16 patients to detect a 40% decrease in the number of PE's with 80% power and a level of significance of 0.05.The study was terminated in 2018 due to low accrual.
Results: Nine patients were enrolled. Mean number of PE's (days) was 14.8 (EG) and 16.1 (HC), mean TR (days) was 11.4 (EG) and 11 (HC), and mean LOS (days) was 27.3 (EG) and 24.9 (HC), p > 0.05. Four patients in HC had a total of 6 relapses at our institution at a median of 28.25 months, range 2.75 to 97 months after the initial event. One patient in EG relapsed 43 months after study enrollment. One patient in EG died from an unrelated cause. None of the additional seven patients in EG have relapsed during a median follow-up of 49 months, range 12 to 125 months. One episode of pulmonary edema and one episode of hypotension occurred in EG, for which treatment was not discontinued.
Discussion: Our study shows that danazol does not reduce PE requirement, TR, or LOS during treatment of TTP, but may prevent relapse. This pattern of response is similar to that which has been observed with rituximab. In a phase 2 study of rituximab in conjunction with PE and CS for the treatment of TTP (Scully Blood 2011), in which results were compared with historical controls who did not receive rituximab, median number of PE's (days) and median LOS (days) were 16.5 and 16.5 in the rituximab group versus 18.0 and 20 in the historical control group, p=ns. Ten percent of patients relapsed at a median of 27 months in the rituximab group whereas 57% of patients relapsed at a median of 18 months in the historical control group. Of interest, the cost of rituximab 375 mg/m ^{2} weekly for 4 weeks as given would have been approximately $ 25,366.50. The cost of danazol in our protocol would have been approximately $ 2196.00. Caplacizumab is a humanized monoclonal antibody

fragment that inhibits von Willebrand factor binding to platelet glycoprotein Ib-IX-V. In a phase 3 study (Scully N Engl J Med 2019), caplacizumab in conjunction with PE and CS for the treatment of TTP led to reduced PE's, time to normalization of platelet counts, and LOS, but increased relapses in comparison with placebo. In 2020, the International Society on Thrombosis and Haemostasis strongly recommended adding CS to PE for the treatment of TTP and conditionally recommended adding rituximab and caplacizumab to PE and CS (Zheng J Thromb Haemost 2020).
Conclusion: Danazol in conjunction with PE and CS may be a low-cost option to prevent relapses of TTP.

Disclosures Shapira: *Janssen Pharmaceuticals:* Speakers Bureau; *Pharmacyclics:* Speakers Bureau; *Bristol Myers Squibb:* Speakers Bureau; *Genentech:* Speakers Bureau. **Patel:** *Daiichi Sankyo:* Consultancy, Speakers Bureau; *Incyte:* Speakers Bureau; *Astra Zeneca:* Consultancy, Speakers Bureau; *Jazz:* Speakers Bureau; *Bristol Myers Squibb:* Speakers Bureau.

OffLabel Disclosure: The use of danazol, which is FDA-approved for the treatment of endometriosis and fibrocystic breast disease and for the prevention hereditary angioedema, is being discussed off-label for the treatment of thrombotic thrombocytopenic purpura. In addition, published off-label use of rituximab in thrombotic thrombocytopenic purpura is discussed.

https://doi.org/10.1182/blood-2023-178552