

Short communication

Prednisolone versus high-dose dexamethasone in newly diagnosed primary immune thrombocytopenia: which is more effective?

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Dear Editor,

Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by the immune-mediated destruction of platelets. Primary immune thrombocytopenia (pITP), a subtype of this condition, is defined by thrombocytopenia that arises without other underlying causes. The incidence of pITP exhibits a bimodal distribution, primarily affecting young adults and the elderly.¹ The pathogenesis of pITP is not completely understood. However, it is hypothesized that the generation of autoreactive antibodies targeting platelet antigens significantly contributes to both the destruction of platelets and a reduction in their production.

Corticosteroids remain the cornerstone of initial treatment for pITP. According to the 2019 American Society of Hematology (ASH) guidelines for managing adult pITP patients, either prednisolone or high-dose dexamethasone is recommended as first-line therapy.² Prednisolone is typically administered at a starting dose of 0.5 to 2 mg/kg per day for 2 to 4 weeks. This regimen achieves an initial response rate of 50% to 80% or more, according to various studies³⁻⁵, with a long-term response rate of approximately 30% after treatment discontinuation.⁶ High-dose dexamethasone (40 mg per day) is given every 28 days for a 4-day course, resulting in impressive outcomes: a high initial response rate of 85%, a sustained response rate of 50%, and a relapse rate of 50%.⁷ Prospective pilot studies conducted by the A Gruppo Italiano Malattie EMatologiche dell'Adulto (GIMEMA) group found that repeated pulses of high-dose dexamethasone could be an effective first-line treatment for ITP, offering substantial response rates and relapse-free survival.⁸ A systematic review and meta-analysis of randomized controlled trials (RCTs)

comparing the efficacy of dexamethasone to prednisolone in treating acute pITP suggest that high-dose dexamethasone does not improve long-term platelet responses compared to prednisolone but may be preferred for rapidly increasing platelet counts in severe pITP cases.⁵ Another recent randomized trial reported that three-pulse of high-dose dexamethasone led to significantly better initial and sustained response (SR) rates than standard-dose prednisolone.⁹ These findings demonstrated the high effectiveness of high-dose dexamethasone, raising several questions about its effectiveness compared to prednisolone in adults newly diagnosed with pITP. To address this, a recent prospective randomized controlled trial by the GIMEMA group¹⁰ explored the efficacy of standard-dose prednisolone versus high-dose dexamethasone in treating newly diagnosed, untreated pITP adult patients (aged 18 to 80 years) with platelet counts ≤ 20 or > 20 but $< 50 \times 10^9/L$ and a bleeding score ≥ 8 . Patients were randomly assigned to receive either prednisolone (Arm A: 1 mg/kg per day from days 0 to 28) or high-dose dexamethasone (Arm B: 40 mg per day for 4 days every 14 days over three consecutive courses). Of the 113 patients, 59 (52.2%) were assigned to Arm A and 54 (47.8%) to Arm B. The treatment scheme is depicted in Figure 1. In Arm A, prednisolone was administered orally at a dose of 1 mg/kg per day for four consecutive weeks (from day 0 to day 28). After day 28, prednisolone was tapered over 14 days as follows: 0.8 mg/kg per day from days 1 to 3, 0.6 mg/kg per day from days 4 to 6, 0.4 mg/kg per day from days 7 to 9, 0.2 mg per day on days 10 and 11, 0.1 mg per day on days 12 and 13, and cessation on day 14. Patients who were unresponsive by day 42 or who lost their response before the final assessment were

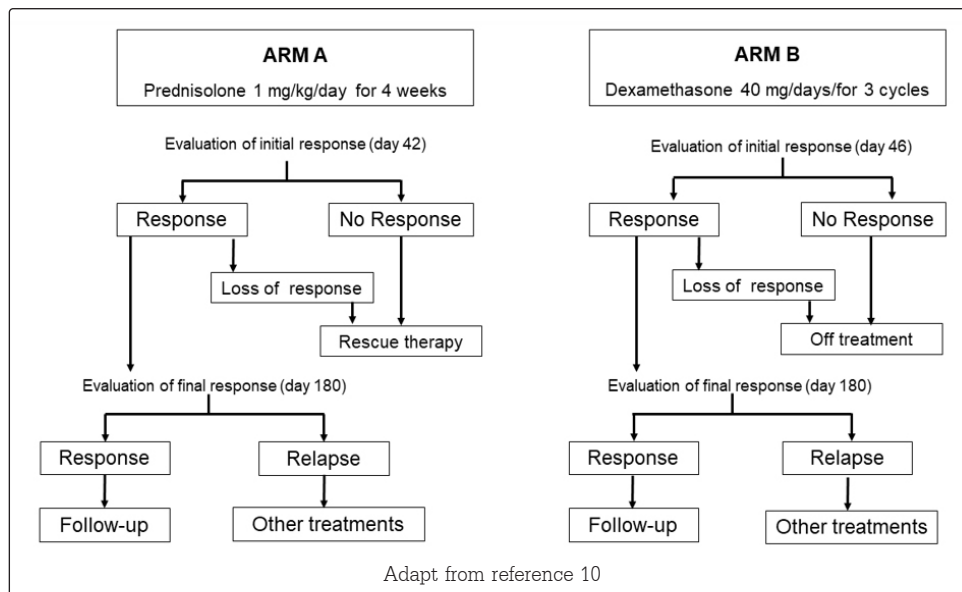


Figure 1 Treatment scheme

Table 1 Response to therapy

Response to therapy		ARM A Prednisolone 1 MKD for 4 weeks	ARM B Dexamethasone 40 mg/day for 3 cycles
Initial response			
ARM A, n = 56	Response	44 (78.57%)	46 (93.88%)
ARM B, n = 46	No response	12 (21.43%)	3 (6.12%)
Final response			
ARM A, n = 43	Response	26 (60.47%)	23 (58.97%)
ARM B, n = 39	No response	17 (39.53%)	16 (41.03%)
Persistent response			
ARM A, n = 31	Response	25 (80.65%)	20 (55.56%)
ARM B, n = 36	No response	6 (19.35%)	16 (44.44%)

Adapt from reference 10

eligible for optional rescue treatment with high-dose dexamethasone. Responses to therapy are summarized in Table 1. In the evaluable patients, the initial total response rates [complete response (CR), partial response (PR), minimal response (MR)] were 78.57% (44 of 56) in Arm A and 93.88% (46 of 49) in Arm B at days 42 and 46, respectively ($p = 0.0284$). The final total response rates at day 180 from the initial response were 60.47% (26 of 43) in Arm A and 58.97% (23 of 39) in Arm B ($p = 0.8907$). The total persistent response rates at 12 months from the initial response were 80.65% (25 of 31) in Arm A and 55.56% (20 of 36) in Arm B ($p = 0.0292$). There were seven relapses during the study. The me-

dian follow-up period was 44.4 months, with overall survival at 100% and disease-free survival at 81.11% at 48 months from day 180. Both prednisolone and pulsed high-dose dexamethasone were well-tolerated, with high-dose dexamethasone providing effective initial responses but less durable results compared to prednisolone.

The results from this study suggest that while high-dose dexamethasone facilitates an effective initial response, its long-term sustainability may not be as enduring as that achieved with prednisolone. It is important to note that several patients were not evaluable for initial and final response assessments.

In conclusion, corticosteroids remain a proven effective and safe first-line treatment for adults with newly diagnosed pITP. High-dose dexamethasone tends to provide a superior initial response, while prednisolone is more effective in sustaining long-term responses. However, the choice between high-dose dexamethasone and prednisolone should be tailored to individual patient profiles, considering factors such as age, existing comorbidities, and treatment preferences, to optimize both efficacy and quality of life. Ongoing research continues to refine these therapeutic strategies, emphasizing the need for personalized treatment plans in managing ITP.

Conflict of Interest Disclosures: The author reports no conflicts of interest.

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