aGvHD

Etanercept for the treatment of pediatric patients with steroid refractory graft-versus-host disease

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Researchers from the Istituto Giannina Gaslini, Genova, Italy, conducted a prospective, single-center, non-randomized phase II study in order to assess the safety and efficacy of etanercept as a second-line of therapy for children with steroid-refractory (SR) acute graft-versus-host disease (aGvHD) after allogeneic hematopoietic stem cell transplantation. Etanercept is a soluble recombinant human tumour necrosis factor alpha (TNF-α) receptor fusion protein that binds to soluble TNF-α, which is a key mediator in the pathogenesis of GvHD, and neutralizes its activity. The results were published ahead of print in *Biology of Blood and Marrow Transplantation*.

Patients and methods:

- N = 25 patients
- Median age at transplantation: 7.8 years (range, 0.4–7)
- Patients had grade II-IV SR aGvHD
- Skin involvement: 18 patients (72%)
- Gastrointestinal involvement: 18 patients (72%)
- Liver involvement: 7 patients (28%)
- Patients received etanercept after a median of 14 days (range, 5–135) from aGvHD onset

Key findings:

- Overall response rate (ORR): 68% of patients
  - Fourteen patients achieved complete response (56%)
  - Three patients had partial response (12%)
- ORR was 78% in patients with cutaneous or gastrointestinal SR aGvHD
- ORR was 57% in patients with hepatic aGvHD
- Eight patients, who did not respond to etanercept therapy, received other treatment: MSC infusion (n = 3 patients), increased steroid dosage (n = 2 patients), monoclonal antibody against IL 6 followed by ruxolitinib (n = 1 patient), monoclonal antibody against CD25 (n = 1 patient), and imatinib (n = 1 patient)
- Overall survival (OS) in responders and non-responders: 76.5% *vs*7%, $P = 0.004$
- 5-year transplant-related mortality (TRM): 34.1% (95% CI, 18.6–1)
- Chronic GvHD occurred in 14 patients (63.6%)

- Infectious complications requiring systemic therapy were observed in 17 patients (68%): bacteremia (36%), viral reactivations (76%), and invasive mycoses (20%)
- One child died due to resistant adenovirus infection

This study demonstrates that etanercept is tolerable and effective in children with SR aGvHD. Etanercept therapy resulted in superior response rates and overall survival in this pediatric population. Moreover, the high response rate observed in children with gastrointestinal aGvHD is also encouraging. The authors added that "time to response to etanercept represents a useful tool to evaluate response to this drug to predict the prognosis of these patients. The discovery of new drugs and their use also in children open up new horizons for the treatment of SR aGvHD but, until now, in our transplant centre etanercept represented the best therapy for SR aGvHD."

Reference

1. Faraci M. *et al.* Etanercept as treatment of steroid-refractory acute graft-versus-host disease in pediatric patients. Biol Blood Marrow Transplant. 2018 Nov 21. DOI: 10.1016/j.bbmt.2018.11.017. [Epub ahead of print]