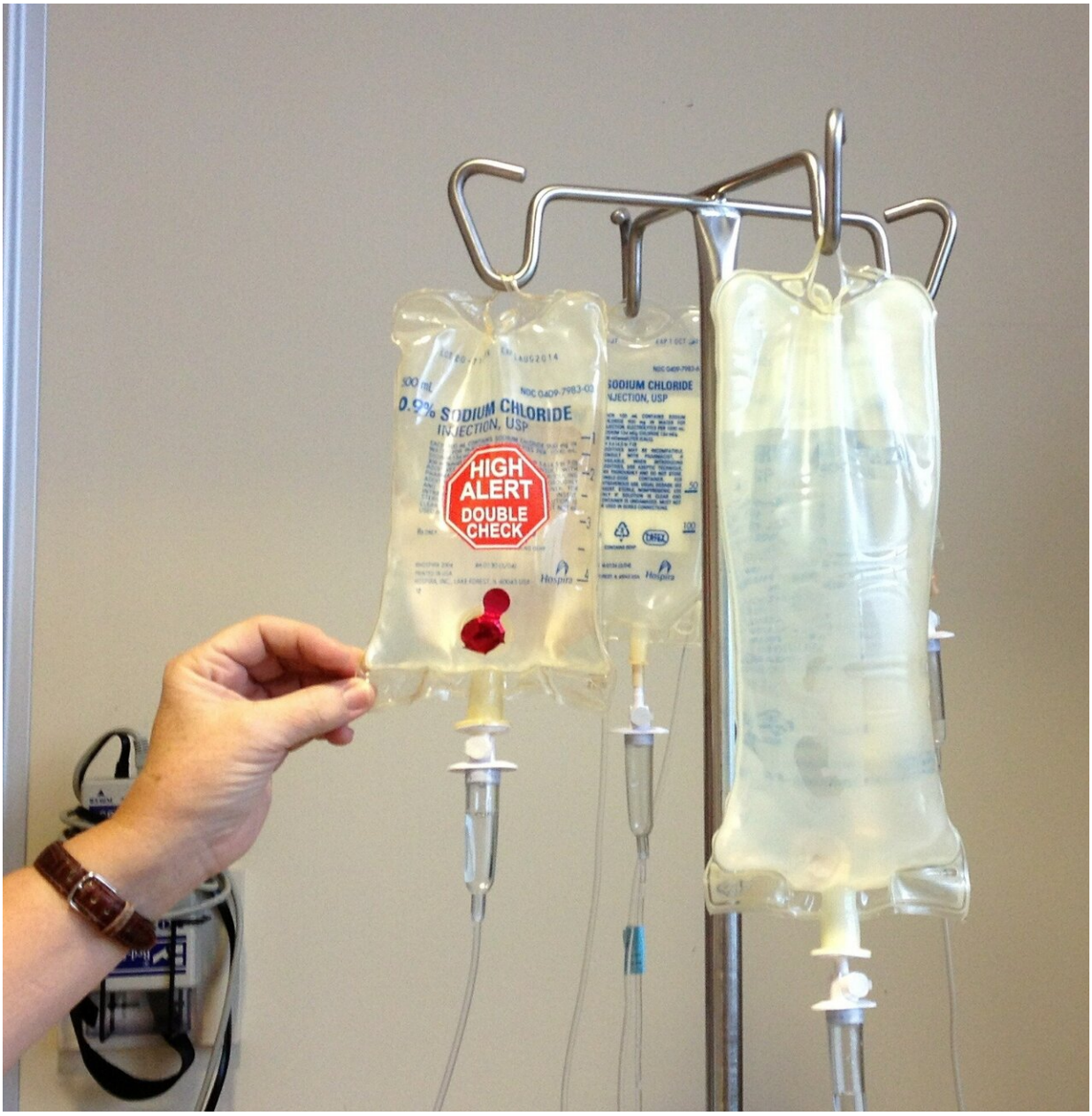
Investigating novel treatment options in systemic sclerosis

June 14 2024



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EULAR, The European Alliance of Associations for Rheumatology, updated its recommendations for systemic sclerosis (SSc) in 2023. Notably, four new therapies were added that had not been included in 2017—highlighting how fast the field is changing. New, strong evidence is now available to help better manage patients with this life-threatening condition, but gaps remain.

Autologous hematopoietic stem cell transplantation (aHSCT) for SSc has been proven the most effective treatment strategy with regard to overall and event free survival in selected patients. But a key limitation is its toxicity, and new treatment options are needed. Two abstracts presented at the 2024 EULAR congress in Vienna focused on novel approaches.

Jörg Henes presented on behalf of the AST MOMA investigators. This prospective, open-label, study evaluated the feasibility of aHSCT in patients with impaired lung or heart function, and also assessed the efficacy of a reduced-toxicity regimen. Patients were stratified according to their manifestations, and mobilization was conducted with reduced (2x 1000 mg) cyclophosphamide plus lenograstim before CD34+ selection.

For patients with active alveolitis, cyclophosphamide was increased to 2 x 1500 mg, and those with functional heart involvement received a conditioning regimen with thiotepa, a half dose of cyclophosphamide, and rATG before reinfusion of the selected stem cells. The primary endpoint was overall survival.

Over 3-year follow-up, 8 of the 35 included patients died. The overall

response rate was 71.4% after 12 months and 60% after 36 months. Progressive disease was reported in 4 patients, and 1 relapsed during the first year—whereas 4 others relapsed at a later time point.

Overall, the primary endpoint was reached, since the overall survival rate after 3 years was comparable to available data. The treatment-related mortality rate of 11.4% was higher than the researchers had expected, but could be attributed to a high-risk population—being predominately male, with functional cardiac involvement, and over 90% having diffuse cutaneous disease.

The authors believe this is the first prospective study using a reduced cyclophosphamide mobilizing and conditioning regimen in patients with cardiac involvement, and it is impressive that this reduced-toxicity regimen showed a comparable outcome regarding the overall survival.

Within the same session, Panagiota Xanthouli presented new data from the EDITA trial, focusing on patients with SSc and mild pulmonary arterial hypertension (PAH) treated with ambrisentan. Previous data show this option delivered a significant decline of pulmonary vascular resistance (PVR) but not of mean pulmonary arterial pressure (mPAP) versus placebo after 6 months.

The current study aimed to assess the long-term effects of continued therapy with ambrisentan versus a control group which received no vasodilative treatment. The primary endpoint was to assess whether continued treatment with ambrisentan prevented the development of PAH according to the new definition.

The results revealed significant improvement of mPAP in the group receiving ambrisentan versus control. Additionally, 4 patients in the control group developed new PAH with mPAP >20 mmHg, compared to none of the patients receiving ambrisentan. This suggests that continued

targeted PAH therapy protects patients with SSc from deteriorating haemodynamics.

Taken together, these new findings could have an important bearing on the current standard of care for patients with SSc.

More information: A. C. Pecher et al, OP0212 Highdose chemotherapy and transplantation of 34+ selected stem cells for progressive systemic sclerosis with or without cardiac involvement or alveolitis - modification according to manifestation (AST MOMA), *Scientific Abstracts* (2024). DOI: 10.1136/annrheumdis-2024-eular.1742

P. Xanthouli et al, OP0241 Effect of treatment with ambrisentan in patients with systemic sclerosis and mild pulmonary arterial hypertension: Long-term follow-up data from EDITA Study, *Scientific Abstracts* (2024). DOI: 10.1136/annrheumdis-2024-eular.1986

Provided by European Alliance of Associations for Rheumatology (EULAR)