Background: Autoimmune haematoopoietic stem cell transplantation (HSCT) ameliorates event-free survival, skin thickening and lung function in patients with progressive diffuse cutaneous systemic sclerosis (dcSSc). Anti-thymocyte globulin (ATG) is a key lymphoablative constituent of conditioning protocols and is administered in a body weight-based dose. Response to HSCT and occurrence of infections is still highly variable across dcSSc patients. Studies in haemato-oncological patients suggest that ATG exposure varies across subjects and impacts outcomes [1].

Objective: To explore the relation between rabbit derived ATG exposure, lymphocyte reconstitution and clinical outcomes in patients with dcSSc undergoing autologous HSCT.

Methods: We retrospectively analysed patients with dcSSc undergoing autologous HSCT between 2014 and 2020. ATG levels were measured in cryopreserved serum samples at four time points (day 1 and week 1, 2 and 4) after stem cell reinfection. ATG exposure was estimated using population pharmacokinetics models [1]. Treatment response was defined as pulmonary stabilisation (with no decline more than 10% in forced vital capacity and 15% in diffusing capacity for carbon monoxide) and/or skin improvement (modified Rodnan skin score reduction of more than 30%). Differences between groups were examined with Wilcoxon rank-sum test for contentious variables and Fisher exact test for categorical variables.

Results: Fifteen patients were included in this study with median age 43 years-old (IQR 37–50). During a median follow-up of 45 months (IQR 19–66), 73% (n=11) of patients had a treatment response, and 27% (n=4) were non-responders. Eight (73%) responders achieved long-term remission and three (27%) responders had progressive disease in the follow-up, at a median time of eight months (IQR 5–17) post-HSCT. Although all patients received the same weight-based ATG dosage (7.5 mg/kg), ATG exposure varied across patients. ATG exposure was higher in responders than non-responders (p = 0.026, Table 1) but was not correlated with lymphocyte reconstitution or infection rate.

Conclusion: In our study, ATG exposure highly varied across dcSSc patients undergoing HSCT despite the same weight-based dosage. Responders had a higher ATG exposure than non-responders. More research into optimal ATG dosing is needed to improve HSCT outcomes.

REFERENCES:

Table 1. ATG-exposure comparison on outcomes

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Yes</th>
<th>No</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response to aHSCT</td>
<td>163 (153–183)</td>
<td>137 (101–149)</td>
<td>0.026*</td>
</tr>
<tr>
<td>Exposure before stem cell reinfection</td>
<td>30 (30–33)</td>
<td>27 (23–30)</td>
<td>0.226</td>
</tr>
<tr>
<td>Exposure after stem cell reinfection</td>
<td>130 (120–153)</td>
<td>108 (78–117)</td>
<td>0.026*</td>
</tr>
</tbody>
</table>

The median (interquartile range) anti-thymocyte globulin (ATG) exposure was presented in the cumulative area under the concentration–time curves (AU/day/mL).

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Objectives: longitudinal data for follow-up among SSc patients. Systemic sclerosis (SSc). Currently, no predictor of LVSD has been defined by mean, resulting in its being the leading cause of death among patients with systemic sclerosis (SSc). Currently, no predictor of LVSD has been defined by mean, resulting in its being the leading cause of death among patients with systemic sclerosis (SSc).

Methods: We conducted a cohort study among adult SSc patients who were followed up at the Scleroderma Clinic, Khon Kaen University, between 2013 and 2020. Semi-parametric Cox regression analysis with robustness clustering by cohort identification number was used for evaluating the predictors of LVSD.

Results: Among the 55,056 person-years, LVSD was defined in 35 of 419 SSc patients for an incidence of 0.25 per 100 person-years. The majority were female (23 cases) with diffuse cutaneous SSc (dcSSc) (26 cases). The median duration of the disease was 8.5 (IQR 4.9-12.9) years. Every 1-point increase in the modified Rodnan skin score (mRSS) and salt and pepper skin were strong predictors of LVSD, with a respective adjusted hazard ratio (HR) of 1.05 and 3.17. During follow-up, 26 cases (74.3%) had worsening LVSD. The strong predictors of the worsening of LVSD were every 1-point increase in mRSS (HR 1.05), every 1 mg increase in prednisone treatment (HR 1.05), and every 1 U/L increase in creatine kinase (CK) (HR 1.01). Meanwhile, mycophenolate treatment was a protective factor against the worsening of LVSD in SSc (HR 0.15).

Conclusion: LVSD was frequently found in dcSSc, and most cases worsened during follow-up. The severity of skin thickening increases the risk of LVSD. High mRSS, steroid use, and high CK were predictors of worsening LVSD, while mycophenolate treatment might prevent the progression of LVSD. Steroids should be prescribed with caution to patients with longer disease duration.

References:


