Autologous stem cell transplantation for progressive systemic sclerosis: a prospective non-interventional study from the European Society for Blood and Marrow Transplantation Autoimmune Disease Working Party

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Supplementary appendix

Table S1: Inclusion / exclusion criteria and endpoints

Inclusion/ exclusion criteria

Inclusion criteria:
- a. Autologous HSCT
- b. Age between 18 and 65 years at time of transplant.
- c. Established diagnosis of progressive SSc according to ACR/EULAR-criteria

Exclusion criteria:
- Age <18 years at transplant
- Pregnancy or inadequate contraception
- Severe concomitant disease
  - Severe heart failure with Ejection Fraction < 40% by cardiac echo
  - Pulmonary arterial hypertension with systolic PAP > 50mm Hg
  - Kidney insufficiency: creatinine clearance <30ml/min (recommended: Cockcroft-Gault formula)
  - concurrent neoplasms or myelodysplasia
- Reduced lung function
  - FVC < 50% of normal
  - DLCO < 30%
- Previously damaged bone marrow
  - Leukopenia < 2,000/mmm3
  - Thrombopenia < 100,000/ mmm3
- Uncontrolled severe infection (Hepatitis B/C, HIV, Salmonella carrier, syphilis, tuberculosis)
- Severe concomitant psychiatric illness (depression, psychosis)

Study endpoints

Primary end point:
Progression free survival (PFS), defined as survival since Baseline (the 1st day of mobilisation) without evidence of progression of SSc.

Progression is defined as any of the following changes from baseline:
- Death from SSc
- 10% drop in FVC and/or 15% drop in DLCO (of predicted values)
- 15% drop in LVEF by echo or MUGA
- 15% drop in body weight
- 30% drop in creatinine clearance
- 25% increase in modified Rodnan skin score (mRSS)
- 0.5 increase in SHAQ

Secondary end points:

Safety
Treatment related toxicity throughout the study period
Incidence of Adverse Events (AE) and Serious Adverse Events (SAE)
Neutrophil and platelet engraftment, defined as first day after transplantation with absolute neutrophil count > 500 cells/μL and >20,000 platelets/μL without platelet transfusion, respectively

Overall Survival
Response to treatment
Response to treatment within 1 year following autologous HSCT, defined as
- 25% improvement in mRSS and/or
- ≥10% improvement in DLCO or FVC
as compared to baseline without need of further immunosuppression

Improvement in Quality of life assessed by SHAQ evolution (Scleroderma Health Assessment Questionnaire)

100-day Treatment related mortality (TRM) defined as any death during 100 day following transplant that cannot be attributed to progression or relapse of the disease.
Table S2: Representatives from participating center, in alphabetic order according to city

| Representaive                     | Specialty       | City              | Country     |
|----------------------------------|-----------------|-------------------|-------------|
| Montserrat Rovira                | Hematology      | Barcelona         | Spain       |
| Gerard Espinosa                  | Rheumatology    | Barcelona         | Spain       |
| Jakob Passweg                    | Hematology      | Basel             | Switzerland |
| Thomas Daikeler                  | Rheumatology    | Basel             | Switzerland |
| Roland Schroers                  | Hematology      | Bochum            | Germany     |
| Lars Petersen                    | Rheumatologist  | Bochum            | Germany     |
| Jacques Olivier Bay              | Hematology      | Clermont Ferrand  | France      |
| W.A. Marijt                      | Hematology      | Leiden            | The Netherlands |
| Hans Ulrich Scherer              | Rheumatology    | Leiden            | The Netherlands |
| Francesco Onida                  | Hematology      | Milan             | Italy       |
| Nicoletta Del Papa               | Rheumatology    | Milan             | Italy       |
| Zora Marjanovic                  | Hematology      | Paris (Saint Antoine) | France      |
| Dominique Farge                  | Internal medicine| Paris (Saint Louis)| France      |
| David Michaunneau                | Hematology      | Paris (Saint Louis)| France      |
| Belinda Simoes                   | Hematology      | Ribeirao ¨Preto   | Brazil      |
| Maria Carolina Oliveira          | Rheumatology    | Ribeirao ¨Preto   | Brazil      |
| Bruno Lioure                     | Hematology      | Strasbourg        | France      |
| Thierry Martin                   | Rheumatology    | Strasbourg        | France      |
| Anne Huynh                       | Hematology      | Toulouse          | France      |
| Gregory Pugnet                   | Rheumatology    | Toulouse          | France      |
| Lothar Kanz                      | Hematology      | Tuebingen         | Germany     |
| Joerg Henes                      | Rheumatology    | Tuebingen         | Germany     |
| Marc Schmalzing                  | Rheumatology    | Würzburg          | Germany     |
Table S3: Comparison of infections within the first 100d following aHSCT and CD34+-selection, CYC dose at time of mobilization and use of post-transplant G-CSF

| Infection within the first 100 days | No     | Yes    | p. value |
|------------------------------------|--------|--------|----------|
| **CD34+ selection**                |        |        |          |
| No                                 | 10 (22.2%) | 35 (77.8%) | p = 0.44 |
| Yes                                | 11 (31.4%) | 24 (68.6%) |          |
| **CYC dose at mobilisation**       |        |        |          |
| 2 g/m²                              | 16 (35.6%) | 29 (64.4%) | p = 0.16 |
| 4 g/m²                              | 4 (16.7%)  | 20 (83.3%) |          |
| **G-CSF post transplant**          |        |        |          |
| No                                 | 14 (31.1%) | 31 (68.9%) | p = 0.32 |
| Yes                                | 7 (20.6%)  | 27 (79.4%) |          |