DeSScipher - To decipher the optimal management of systemic sclerosis
Contract number: FP7- HEALTH n°305495
Start Date: 01/12/2012 - Duration: 36 months
Project Coordinator: JLU GIESSEN

I. PUBLISHABLE SUMMARY – PROJECT PERIOD 2

I.1. Project context and objectives

In rare diseases, up to 90% of drug treatment is off-label due to lack of adequate clinical research data. This is particularly true for the rare autoimmune rheumatic disease systemic sclerosis (SSc). Due to the severity of SSc, several immunomodulating drugs such as cyclophosphamide, methotrexate, azathioprine etc. are used off-label in this disease but their use is mostly based on case reports or small trials, which do not meet the usual standards of controlled clinical trials, as is frequently the problem in rare diseases. Thus, it has only been possible to establish preliminary guidelines for the management of SSc so far. The DeSScipher projects aims at improving clinical practice in the management of SSc. The primary objective is to compare the outcomes of different preventive measures and treatments with respect to efficacy and safety of currently used off-label drugs from the early to the advanced phases of the SSc-associated organ system involvements. This approach is based on five observational trials (OTs), which are designed to cover evolution phases of the disease and its related organ involvement from early functionally relevant manifestations such as digital ulcers (OT1) and hand arthritis (OT2) to the morbidity and mortality-driving manifestations such as interstitial lung disease (OT3), pulmonary hypertension (OT4) and severe heart disease (OT5). Based on the data of more than 4000 prospectively enrolled and well-characterised SSc patients, the DeSScipher project aims to evaluate currently used off-label treatment in real-life care and to compare the course of the disease under different therapeutic regimens with respect to their efficacy and safety in the prevention or treatment of the organ manifestations under investigation. In addition, DeSScipher will define and validate appropriate outcome measures.
Achievement of these objectives will be possible through utilization of the unique pan-European EUSTAR group (EULAR Scleroderma Trials And Research group, established and operating under the auspices of the European League Against Rheumatism (EULAR)), which in total includes more than 190 expert centres from all European countries.

I.2. Work performed and main results

To enhance patient recruitment rates, the Project Coordinator team and DeSScipher Consortium continued their efforts to invite all EUSTAR SSc patient care centres world-wide to contribute to the DeSScipher project. In addition to the 10 initial DeSScipher partner centres and 11 additional EUSTAR centres from Croatia, France, Germany, Hungary, Italy, Romania, Russia, Switzerland and United Kingdom of the first project period, further 19 centres from Belgium, Egypt, Serbia, Spain and Turkey have joined the DeSScipher project. Out of these in total 40 contributing study sites, 33 centres actively screened patients and 31 centres have been able to enrol at least one SSc patient into the five OTs.

In the first project period, 1258 people with SSc have been screened for the DeSScipher project between April 2013 and May 2014, and 1061 have been enrolled into at least one of the five OTs. In the second project period between June 2014 and November 2015, additional 1175 people with SSc have been screened and 1101 have been enrolled. Thus, by end of November 2015 in total 2433 people with SSc have been screened and 2162 have been enrolled into at least one of the five OTs. As one patient can be simultaneously included in multiple observational trials, overall 4686 datasets of people with SSc were followed prospectively in OT1-5 until the end of project month M36. An interim report of the DeSScipher project as well as preliminary results of different subprojects, (e.g. with regard to the quality of life, prevention and treatment of digital ulcers, and current vasodilative, vasoactive and immunosuppressive treatment patterns in routine clinical care) have been presented by four abstracts / presentations at the EULAR Congress 2015 in Rome, and recently by five abstracts / presentations at the World Scleroderma Congress 2016 in Lisbon.

While the observational trial number 2 on hand arthritis will not be continued as planned, all DeSScipher partner and contributing EUSTAR centres have been prepared to continue the follow-up of the remaining four observational trials beyond the DeSScipher project period under the auspices of the EUSTAR consortium and the World Scleroderma Foundation up to November 2017 to facilitate the successful outcome of the observational trials. After the completion of the OTs, the prospectively acquired data of the OTs of DeSScipher will be merged with and reintegrated into the database of the EUSTAR cohort to continue successfully the currently largest available long-term clinical database of SSc worldwide.

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I.3. Expected final results and potential impacts

After finalization of the follow-up period and data analysis of the four ongoing OTs, the DeSScipher project will not only be the largest multinational prospective observational research project ever performed in systemic sclerosis but also become a template for how to manage such an approach including all predictable and unpredictable pitfalls prior to and during trials in rare diseases such as systemic sclerosis. Its main achievement will be to provide scientific evidence for key clinical questions and problems and will facilitate to advance from off-label use of treatments to their official approval for everyday clinical use. Moreover, the findings of DeSScipher observational studies will contribute to the development of novel treatment recommendations to improve the management of SSc and its related morbidity and mortality.

The table below summarizes the expected main publications once the follow-up period of the four ongoing observational trials will be completed.

DeSScipher partner	Working titel	Target journal
JLU GIESSEN & **all partners**	Conducting observational studies in rare diseases: a report of the DeSScipher project of the EUSTAR group	The Journal of Scleroderma and Related Disorders (JSRD) (The official journal of the WSF)
UNIBAS	Predictors of disability in systemic sclerosis: an analysis of the DeSScipher cohort of the EUSTAR group	Annals of the Rheumatic Diseases (The official journal of the EULAR)
UNIFI & LEEDS	Best treatment for prevention of digital ulcers in SSc: a report of the prospective observational trial of the DeSScipher project of the EUSTAR group	The Journal of Investigative Dermatology (The official journal of the Society for Investigative Dermatology and The European Society for Dermatological Research)
UNIFI & LEEDS	Best treatment for healing of digital ulcers in SSc: a report of the prospective observational trial of the DeSScipher project of the EUSTAR group	
PECS	Validation of Disease Activity Indices using the 28 Joint Counts in SSc	Rheumatology (Oxford), submitted
PECS	Joint involvement and hand dysfunction in systemic sclerosis: a cross-sectional descriptive analysis of the multicentric prospective observational trial of the DeSScipher project of the EUSTAR group	Annals of the Rheumatic Diseases (The official journal of the EULAR)
JLU GIESSEN & PECS	Real life treatment patterns of arthritis in in systemic sclerosis: an analysis of the DeSScipher cohort of the EUSTAR group	The Journal of Scleroderma and Related Disorders (JSRD) (The official journal of the WSF)
CHARITE	Current state of the art of immunosupressive treatment of SSc-related ILD: a merged analysis of the EUSTAR and DeSScipher cohort	Rheumatology (Oxford), under revision
CHARITE	Immunosupressive teatment of SSc related interstitial lung disease: a report of the prospective observational trial of the DeSScipher project of the EUSTAR group	The European Respiratory Journal (The official journal of the European Respiratory Society)
UPD	Development and prevention of pulmonary hypertension in SSc: a report of the prospective observational trial of the DeSScipher project of the EUSTAR group	
UNINA 2	Development and prevention of severe heart disease in SSc: a report of the prospective oobservational trial of the DeSScipher project of the EUSTAR group	The European Heart Journal (The official journal of the European Society of Cardiology)
JLU GIESSEN & CHARITE	Immunosupressive and vasodilative treatment patterns in systemic sclerosis: a report of the DeSScipher cohort of the EUSTAR group	Annals of the Rheumatic Diseases (The official journal of the EULAR)

Several further publications based on the prospectively collected data of the DeSScipher project are anticipated beyond the DeSScipher funding period and will be facilitated as EUSTAR clinical projects under the umbrella of the World Scleroderma Foundation. Beyond the author citation of the whole DeSScipher consortium and EUSTAR contributing centers in accordance with the EUSTAR publication rules, the FP7 funding by the European Commission will be adequately acknowledged in all upcoming publications usually as follows:

"The DeSScipher project was funded by the European Community's Framework Programme 7 (FP7-HEALTH-2012.2.4.4-2 - Observational trials in rare diseases) under grant agreement N° 305495.