Protocol synopsis

Multicenter retrospective study for primary cutaneous B-cell lymphoma: DLBCL-leg type

Registration number	
Protocol version	v.1 (April 2024)
Coordinator/Sponsor	DEGRO (AG Dermatoonkologie)
Methodology	Multicenter, retrospective study
Number of centers	10-15
Principal Investigator (PI)	PD Dr.med. Khaled Elsayad/Univ.-Prof. Dr. med. Hans T. Eich University Hospital Münster Albert-Schweitzer-Campus 1, Gebäude A1 48149 Münster +49 251 / 83 - 47384 Khaled.Elsayad@ukmuenster.de Hans.Eich@ukmuenster.de
Project title	Multicenter retrospective study for primary cutaneous B-cell lymphoma: DLBCL-leg type
Background and Rational	Primary cutaneous aggressive B-cell lymphoma, such as diffuse large B-cell lymphoma (DLBCL)-leg type, is an ultra-rare disease with a worse prognosis. The treatment algorithm is adopted from the nodal type due to a lack of studies in this type. Patients usually require combined modality (rituximab-based) and local RT with 36-40 Gy. RT doses of nodal DLBCL may be reduced to 30 Gy with similar efficacy [3]. Recently, DLBCL patients with complete response to systemic agents were treated with 20 Gy successfully (with a 2% local relapse rate and a 5-year freedom from local recurrence rate reaching 98%) with relatively low toxicities [4]. However, most elderly patients with comorbidities and palliative cases can be treated with local radiation alone with comparable results [2]. In addition, the role of chemotherapy in localized DLBCL-leg type needs to be clearly defined. Zehnder et al. [2] show similar efficacy of RT when compared to immunochemotherapy alone, while Kraft et al. [1] proved an additional benefit of local radiotherapy following systemic treatments. In selected cases, hypofractionation with a weekly dose of 4 Gy until response or up to 24 Gy (biologically effective dose of 40 Gy) might yield comparable efficacy and can be recommended to reduce hospital visits [2].
Objectives	Determine objective response rate, progression-free survival rate, and duration of response following different radiation doses (<30Gy vs. ≥ 30Gy).
Study endpoints	**Primary endpoints:** - Overall Response Rate (ORR) - Acute and chronic toxicities (evaluated with CTCAE 5.0)

	Secondary endpoints: - Local control (LC) - Time to next treatment (TTNT) - Progression Free Survival (PFS) - Overall Survival (OS)
Sample size	Approximately 50 patients
Study duration	2 years
Participating centers	Department of Radiation Oncology, University Hospital Muenster, Germany
Inclusion criteria	- Histologically-confirmed diagnosis cutaneous B-cell lymphoma (DLBCL-leg type). - Age ≥ 18 years
Exclusion criteria	- Prior or active skin malignancy (except for completely excised, non-invasive basal cell or squamous cell carcinoma diagnosed > 2 years prior to enrollment) - Pregnancy or lactation - Age < 18 years
Data management and data protection	The data to be collected is already available in all participating centers and will be anonymized for evaluation
Authorship	All participating centers contributing a complete dataset for ≥1 patient can name co-authors (radiation oncologist and dermatologist) on each publication and will be listed according to the number of recruited patients.
Statistical considerations	Overall Response Rate (ORR) will be evaluated 8-12 weeks after the end of RT. Time-to-event endpoints will be estimated using the Kaplan-Meier method and compared among subgroups using the log-rank test. Categorical variables will be evaluated using the $\chi 2$ test, and the T-test will analyze continuous variables. Univariate and multivariate Cox proportional hazard models will be calculated to identify the prognostic factors in patients' outcomes.
References	1) *Kraft RM et al. Outcomes in primary cutaneous diffuse large B-cell lymphoma, leg type. Hematol Oncol 2021* 2) *Zehnder M et al. Radiotherapy as a Treatment Option for Local Disease Control in Primary Cutaneous Diffuse Large B-Cell Lymphoma, Leg Type. Dermatology (Basel, Switzerland) 2022* 3) *Lowry L et al. Reduced dose radiotherapy for local control in non-Hodgkin lymphoma: a randomised phase III trial. Radiotherapy and oncology journal of the European Society for Therapeutic Radiology and Oncology 2011* 4) *Kelsey CR et al. Phase 2 Study of Dose-Reduced Consolidation Radiation Therapy in Diffuse Large B-Cell Lymphoma. International journal of radiation oncology, biology, physics 2019*