INTERNATIONAL T-CELL NON-HODGKIN'S LYMPHOMA STUDY GROUP

T-cell Project 2.0

Version 1.0 – June 18, 2018

PROSPECTIVE OBSERVATIONAL INTERNATIONAL REGISTRY OF PATIENTS WITH NEWLY DIAGNOSED PERIPHERAL T CELL LYMPHOMA

The T-cell Project 2.0 registry: the more you collect, the more you learn, the more your patients will benefit

Title	Prospective observational international registry of patients with newly diagnosed peripheral t cell lymphoma
Primary Objective	To verify whether a prospective collection of data would allow more accurate information on T-cell lymphomas to be achieved. To better define the clinical relevance of the new WHO Classification, the role of FDG-PET in staging and response assessment, the prognosis of different entities, the genomic landscape of different subtypes, and to investigate the most optimal treatment strategies for these neoplasms in the real-world population.
Secondary Objectives	Moreover, from a molecular point of view, the objective of the study is to estimate prospectively the frequency of pEBVd detection in our cohort of PTCL patients at baseline and at the end of initial therapy, to characterize agreement between pEBVd and EBER in tumor tissue, and to explore the prognostic or predictive implications of detectable pEBVd in PTCL. Finally, to investigate the genetics and pathogenic mechanisms of aggressive PTCLs on an international scale.
Design	A prospective, longitudinal, international, observational study.
Countries/Regions	Europe, United States, South America, Australia, Asia

Number of sites	It is expected that approximately 100 sites will participate in the Registry although no limit on site participation has been set. Both academic and community practices are expected to contribute patients to the Registry.
Number of patients	To estimate the number of observed events we hypothesized that OS has a risk function which follows Weibull distribution with time parameter (in year) λ of 0.369 and form parameter p of 0.773, and a censored distribution with lambda parameter of 0.104 and form parameter of 1.393. The Weibull parameters were estimated from the OS of PTCL-NOS observed from T-Cell project 1.0. After 10,000 Monte Carlo simulations, we calculated that with 1000 cases enrolled in 2 years and followed up for at least 2 years, we would observe 570 events at the end of the study.
Registry duration	Based on the final accrual of the former retrospective International PTCL study and the interest in the project expressed by participants to the previous study, it is planned to complete accrual in 2 years and a half; furthermore, a minimum follow-up of 2 years is required for the final analysis of primary and secondary endpoints.
Inclusion Criteria	• Previously-untreated patients with *de novo* diagnosis of peripheral T-cell or NK/T-cell lymphoma: - T-cell large granular lymphocytic leukaemia; - Chronic lymphoproliferative disorder of NK cells; - Aggressive NK-cell leukaemia; - Adult T-cell leukaemia/lymphoma; - Extranodal NK/T-cell lymphoma, nasal type; - Intestinal T-cell lymphoma; - Hepatosplenic T-cell lymphoma; - Subcutaneous panniculitis-like T-cell lymphoma; - Peripheral T-cell lymphoma, not otherwise specified; - Angioimmunoblastic T-cell lymphoma and other nodal lymphomas of T follicular helper cell origin; - Anaplastic large cell lymphoma, ALK-positive; - Anaplastic large cell lymphoma, ALK-negative; - Breast implant-associated anaplastic large cell lymphoma. • Age 18 and over; • Tissue biopsy adequate for diagnosis and classification and available for centralized review; • Clinical data including baseline information on disease localization and laboratory parameters at staging, features of treatment adopted and assurance of follow-up updating for at least 2 years are requested;

	• Written informed consent.
Exclusion criteria	• Diagnosis of: - EBV-positive T-cell and NK-cell lymphoproliferative diseases of childhood - Mycosis fungoides; - Sézary syndrome; - Primary cutaneous CD30-positive T-cell lymphoproliferative disorders; - Primary cutaneous peripheral T-cell lymphomas, rare subtypes; - T-cell lymphoblastic lymphoma/leukemia - T-cell prolymphocitic leukemia • Age < 18.
Data collection	Patients are evaluated according to the treating physician's standard practice. There are no specific evaluations or visits required for the Registry. Data captured in the Registry reflects what is routinely collected for patients with PTCL.
Statistical Considerations	- Descriptive analysis. Continuous variables will be summarized as median, interquartile distance, or mean and standard deviation (SD). Categorical variables will be expressed as absolute and percentage frequencies. - Comparison of continuous between two or more groups. Continuous covariates will be compared by means of Mann-Whitney test (between two groups) or Kruskal-Wallis test (between more than two groups). - Comparison of categorical covariates between groups. Categorical covariates will be compared using the Fisher's exact test or Chi2 test, if appropriate. - Survival analysis. The survival functions will be calculated and plotted using the Kaplan-Meier method, and the survival rate at 3 and 5 years of follow-up will be reported with the estimated 95% confidence interval (95%CI, standard error from Greenwood's formula). - Covariate effect: The prognostic effect of covariate will be estimated using the Cox proportional hazard (PH) regression model, reported as hazard ratio (HR) with 95%CI. Will be check the proportionality of the hazard by means of the analysis of Schoenfeld residuals.