Proposal for a FungiScope® analysis

Title of Study	Invasive fungal diseases after treatment of hairy cell leukemia – a retrospective cohort study from the FungiScope® registry
Principle Investigator	Department I for Internal Medicine, University Hospital of Cologne
Study centres planned	Multicenter cohort study based on the FungiScope® registry
Target Population	Patients with hairy cell leukemia (HCL) and documented invasive fungal diseases (IFD) following HCL treatment
Rationale / Background	Hairy cell leukemia (HCL) is a rare indolent B-cell neoplasm associated with cytopenias and increased susceptibility to infections. Standard first-line therapies, particularly purine analogues, achieve high remission rates but induce prolonged immunosuppression, including neutropenia and T-cell lymphopenia. Invasive fungal diseases (IFD) represent a major cause of morbidity and mortality in immunocompromised patients, especially in the presence of prolonged neutropenia. Despite this, data on the incidence, timing, risk factors, and clinical outcomes of IFD in HCL patients remain limited and are largely restricted to case reports and small series. Currently, there are no evidence-based recommendations regarding antifungal prophylaxis in HCL. Therefore, a systematic analysis is needed to better understand the burden of IFD and to inform future preventive and therapeutic strategies in this vulnerable patient population.

Objectives	To systematically evaluate the incidence, timing, risk factors, and clinical outcomes of invasive fungal diseases (IFD) in patients with hairy cell leukemia (HCL) following HCL-directed therapy.
	
	- Secondary objectives
	  o To describe the incidence of proven, probable, and possible IFD in patients with HCL (e.g., EORTC/MSG)
	  o To describe clinical outcome, particularly mortality associated with IFD in patients with HCL
	  o To characterize the timing of IFD occurrence in relation to HCL diagnosis and treatment
	  o To describe antifungal treatment strategies and their outcomes in this population
	
	- Exploratory objectives
	  o To describe the burden of IFD in patients with HCL, including treatment delay, treatment interruption, and need for intensive care unit admission
	  o To identify disease- and treatment-related risk factors for the development of IFD in patients with HCL
	  o To explore the impact of immunosuppression (e.g., neutropenia, lymphopenia) on the risk of IFD

	○ To evaluate differences in IFD occurrence depending on HCL treatment regimens (e.g., purine analogues)
Primary Endpoint	Incidence of invasive fungal diseases (IFD) in patients with hairy cell leukemia (HCL)
Secondary Endpoint	- Incidence of invasive fungal disease (IFD) in patients with and without antifungal prophylaxis. Antifungal prophylaxis is defined as continuous systemic antifungal administration for at least 7 consecutive days within the 14 days prior to the diagnosis of IFD. - Outcome of IFD in HCL patients - Onset of IFD in relation to HCL treatment - Effectiveness of antifungal treatment strategies
Study Design	Multicenter retrospective observational cohort study
Sample Size / Population size	All eligible cases available in the FungiScope® registry, supplemented by additional retrospectively reported cases following active solicitation of participating physicians Observational descriptive study without prior sample size calculation
Study Drug	Not applicable (observational study)
Inclusion criteria	- Diagnosis of hairy cell leukemia - Documented invasive fungal disease - Prior or ongoing treatment for HCL - Availability of sufficient clinical data
Exclusion criteria	- Incomplete or missing key data - Uncertain diagnosis of fungal disease - Patients without HCL diagnosis
Study Procedures / Frequency	- retrospective data extraction - no direct patient intervention - Data collected at predefined timepoints (e.g., diagnosis, treatment, outcome)
Outcomes	- Incidence of invasive fungal diseases in HCL patients - Clinical outcomes (e.g., survival, response to antifungal therapy)
Data collection	- General information - Hairy cell leukemia specific risk factors - Sites of infection - Microbiological and radiological findings - Antifungal treatment - Outcome
Statistical Analyses	- Descriptive statistics - Risk factor analysis - Incidence modelling according to epidemiological data from healthcare system registries (German Research Data Centre (FDZ) and Surveillance, Epidemiology, and End Results (SEER) Program of the U.S. National Cancer Institute etc.) and deduction of clinical need for antifungal prophylaxis