Modern Treatment Usage and Outcome of Patients with Advanced and High-risk Non-Melanoma Skin Cancer (NMSC) – a Registry Based Cohort Study

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Background

Among non-melanoma skin cancer (NMSC), basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (cSCC) are the predominant histologic subtypes. Real-world data systematically recorded in registries are limited. Many cancer databases do not register NMSCs at all. For patients with advanced and high-risk NMSC, the EUMelaReg consortium (EMR) introduced a registry for NMSC across Europe. The aim of this registry is to collect real-world data of the available tumor and treatment patterns of advanced and high risk NMSC patients at a European level. Data of the EMR NMSC-Registry can be used for specific analyses regarding drugs, availability, and affordability of various treatments for different patient populations, data on health-related resource utilization, and patient outcomes. It is of importance to have a comprehensive picture on various treatments, or non-treatment strategies across Europe.

The Registry

Participating sites collect data (demographic and clinical characteristics) from medical records. Inclusion criteria specify the minimum requirements for a given case to be eligible for registration in NMSC-Registry forms. Cases that fulfill minimum criteria regarding completeness and plausibility of the standardized core dataset will be evaluated further in the registry's data warehouse. Standard procedures are implemented to ensure quality, integrity and validity of the data and created variables as well as archiving of statistical programs, description of available data, and validation results.

Data transfer into the EMR-NMSC registry can be achieved in various ways. Participating sites can use direct access to the forms to document the patients' relevant data. Alternatively, participating centers from certain countries may already collect the data relevant to the registry regarding demographic, diagnostic and treatment data in a country specific registry. From the national registry, data are then transferred on a regular basis into NMSC-Registry database. Transfer of registry data is performed via XML file which is first checked electronically for structural integrity and quality via XSD based on current version of data validation plan (valid for both ways of data intake). The content of files meeting the prespecified structural requirements is further checked electronically and manually for data quality and plausibility. Inconsistencies are queried. If major deficiencies cannot be ruled out, the registry data will not be transferred into NMSC registry data base. Only non-identifiable data is transferred to maintain patient confidentiality.

Data of the EMR NMSC-Registry can be used for specific pre-defined analyses regarding drugs, availability and affordability of various treatments for different patient populations, data on health-related resource utilization, outcome data, and risk factors.

Table 1: Data Collection

	Cohort 1 – high risk cSCC	Cohort 2 – advanced cSCC	Cohort 3 – advanced BCC
Patient characteristics	• **Demographics and baseline characteristics:** Age, Sex, ECOG status, baseline comorbidities - immunosuppression skin phototype		
Tumor characteristics	• **Initial Tumor status:** Histopathology subtype, histologic risk factors, lesion(s) site, ICD-O codes, primary clinical stage, localization (site)		
	• **Date of first diagnosis of high risk cSCC** • **Previous treatment:** Surgery/ Radiotherapy/ other • **Baseline demographics:** Immunosuppression/ Transplant/ other • **Baseline characteristics at index surgery:** site(s), stage, resection margins, risk factors	• **Date of first diagnosis of cSCC/ BCC, Date of advanced cSCC/ BCC initial diagnosis and description** • **Metastasis site(s):** Locoregional/ Distant (type, number, specificity) • **Treatment of another primary tumor:** type, number, site • **Previous treatments:** Surgery/ Radiotherapy/ Immunosuppression/ Transplant/ Systemic treatment/ others • **Recurrence/relapse:** date and characteristics of relapse - histopathology, stage, risk factors, treatment, locoregional or distant metastasis • **Baseline characteristics for systemic treatment:** local, regional and distal site(s), stage, LDH, metastatic	
Treatment patterns decision pathways	**Treatment for high risk cSCC**: surgery (resection margins, safety margins), post-surgery Radiotherapy (anatomic site of RT, RT technique, total dose, total number of fractions, fractions schedule, treatment interruption, start/end date)	**Systemic medical treatment for acSCC**: type of systemic treatment (CT, Cemiplimab, others), indication (1L, 2L), treatment regiment, dose, frequency, changes (reduction of the dose), duration of the treatment, the percentage of patients treated until response, stable disease (SD) or progressive disease (PD), reasons for discontinuation	**Systemic medical treatment for aBCC**: treatment with HHI or Cemiplimab or other treatments:, indication (adjuvant, neoadjuvant, 1L, 2L), treatment regiment, dose, frequency, changes (reduction of the dose, break- schedule use, stop), duration of the treatment, reasons for discontinuation, Subsequent treatment regimen preferences post-HHI (surgery/RT/CT/others -to be specify)
	Guidelines used in the center for deciding upon or giving guidance on treatment strategy for high risk cSCC	**Guidelines used in the center** for deciding upon or giving guidance on treatment strategy for advanced NMSC • **The method of the center for deciding on patients' treatment strategies** through a Multidisciplinary Tumor Bord (MDT) or by a single treating clinician, for advanced cSCC/BCC	
Treatment outcomes	• **RFS, OS, FFLRR, FFDR** • **Cumulative incidence of further primary cSCC tumors**	• **Best overall response rate, PFS, OS, TTP** • **Resistance** (primary, secondary) • **Mortality** • **How is 'Treatment Outcome' evaluated in the center**, through an MDT or by a treating clinician?	
		• **Safety –** type of ADR (Gr 3-4 toxicity in routine practice) • **Reason for end of treatment** • **Follow-up survival status and date** • **Subsequent treatment schedule (including BSC) and outcome**	

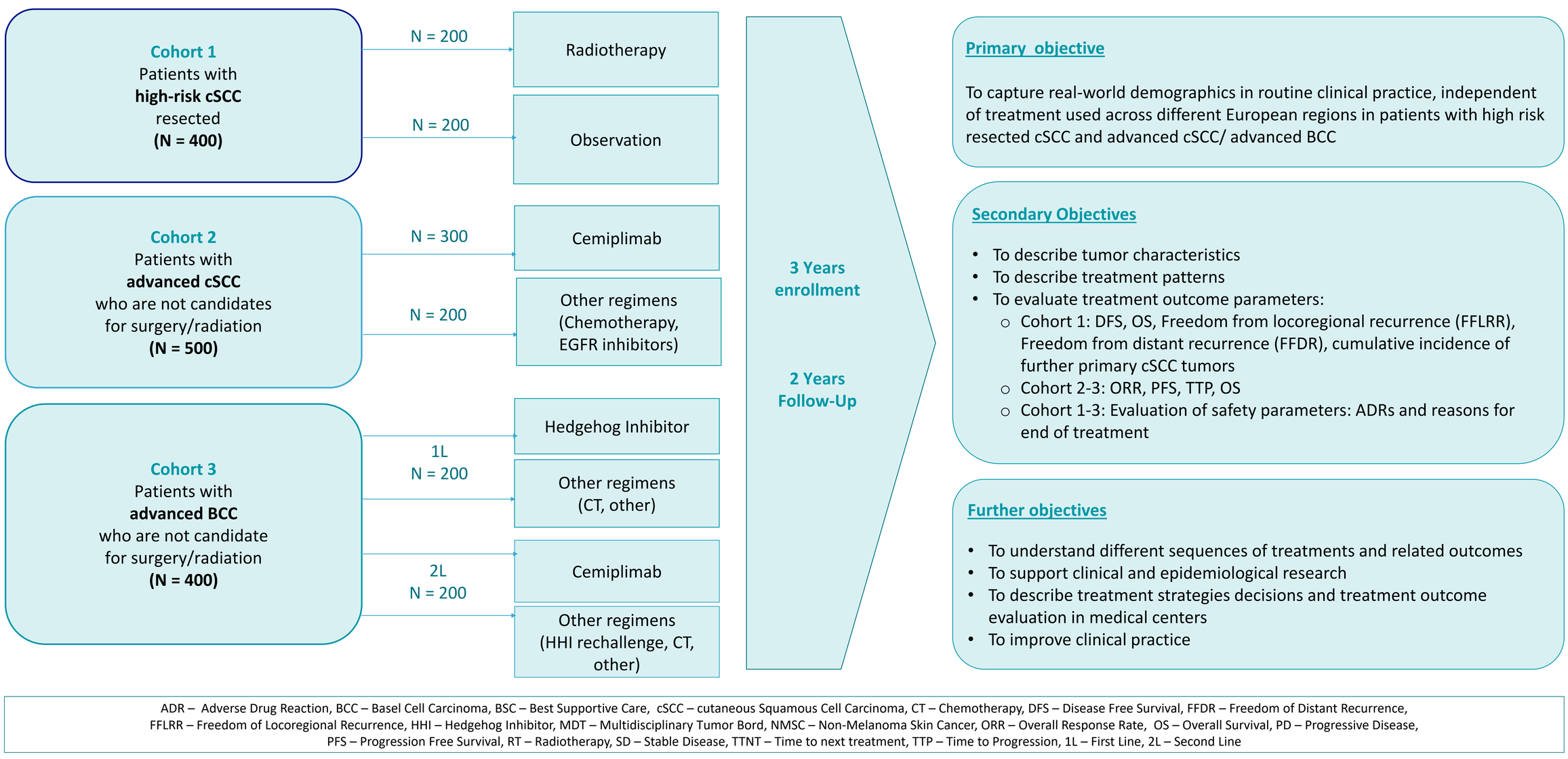
Methods and patients

This is a multi-national ambispective (retrospective and prospective) registry-based cohort study in patients with advanced and high risk NMSC. Data from cases with a documented index date from August 2019 and until December 2026 in the disease-specific EMR NMSC-registry will be used for evaluation. These data include historic data (demographic and clinical characteristics) as well as data collected during visits which will be performed during the registry participation.

All patients will be followed for a maximum of 2 years after last patient included (LPI). It is planned to enroll a total of 1,300 patients according to the following cohorts: Cohort 1 covers patients with resected high-risk cSCC receiving only postoperative radiotherapy or watchful waiting, cohort 2 contains patients with advanced cSCC who are not candidates for curative surgery or radiation in routine clinical practice and cohort 3 contains patients with advanced BCC who are not candidates for curative surgery or radiation in routine clinical practice.

Primary endpoint focusses on real-world demographics in routine clinical practice, independent of treatment used across different European regions in patients with advanced cSCC, advanced BCC, and completely resected high risk cSCC. Depending on the cohort following secondary endpoints will be evaluated: e.g. tumor characteristics, treatment patterns in routine practice, Overall Survival (OS), Time to Progression (TTP), Time to next treatment (TTNT), disease free survival (DFS), Overall response rate (ORR).

Figure 1: Study Design



ADR – Adverse Drug Reaction, BCC – Basel Cell Carcinoma, BSC – Best Supportive Care, cSCC – cutaneous Squamous Cell Carcinoma, CT – Chemotherapy, DFS – Disease Free Survival, FFDR – Freedom of Distant Recurrence, FFLRR – Freedom of Locoregional Recurrence, HHI – Hedgehog Inhibitor, MDT – Multidisciplinary Tumor Bord, NMSC – Non-Melanoma Skin Cancer, ORR – Overall Response Rate, OS – Overall Survival, PD – Progressive Disease, PFS – Progression Free Survival, RT – Radiotherapy, SD – Stable Disease, TTNT – Time to next treatment, TTP – Time to Progression, 1L – First Line, 2L – Second Line

Contact

Interested in participating? Mail to: office@eumelareg.org

This study is registered @ clinicaltrials.gov: NCT05741073

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