

# The Rare Cancer Network Study Group

*Learning more about rare cancers*

The Rare Cancer Network (RCN) is an international network of more than 120 investigators in 24 countries aiming at the study of rare cancers mainly through the gathering of a large number of patients on specific tumour types. RCN is open to new members interested in bringing their input and new ideas.

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Rare Cancers, like many orphan diseases, are poorly studied: interest from academic institutions and pharmaceutical industry is limited to a few rare cancers and prospective trials are quasi-inexistent. From our RCN, information on initial pattern, work-up, treatment, outcome and prognostic factors could be derived and published. These data may serve as a basis for the management of numerous rare cancers.

## Introduction and Definitions

Facing a patient presenting with a rare type of cancer represents most of the times a challenging experience for the medical oncologist, the radiation oncologist and the surgeon, due to the relative paucity of information in medical literature, and the quasi-absence of high-level evidence-based data.

There is at present no uniform definition of what is a rare tumour or a rare cancer, although the European Commission has defined more broadly rare diseases as «life-threatening or debilitating diseases (...) that affect less than 4 per 10'000 persons» (1). A modification of the definition of rare cancers by the Rare Cancer Network (RCN) (2) is presented on the *table*.

- ▲ *In the first category*, rarity is due to the rare histopathological nature of the cancer or tumour.
- ▲ *The second category* encompasses histopathologically frequent cancers, however due to rare or unexpected anatomical primary site, age, sex, biology or geographical distribution, these cancers may present with a completely different behaviour, and therefore management should be different from that of their more common counterparts.

With a few exceptions, rare cancers are usually reported as single case reports or small series from a single institution, with obvious bias such as reporting «good» cases, non-consecutive patients etc. which make interpretation on treatment and outcome ha-

zardous. In a few situations, progress was made thanks to some understanding of underlying molecular, biological or immunological mechanisms. Such examples are the GIST, the Burkitt's lymphoma and Kaposi's sarcoma in AIDS. However these represent a tiny proportion of all rare cancers. At the same time, research and the commitment of the pharmaceutical industry have been quite limited in the vast majority of rare cancers. Obviously, the rare occurrence of rare cancers has also precluded the initiation of prospective controlled trials.

## Objectives

Internet has greatly facilitated the identification and collection of data on rare cancers from multiple institutions, and was used to investigate a rather wide range of rare cancers, as demonstrated by our Rare Cancer Network (RCN) ([www.rarecancer.net](http://www.rarecancer.net)).

A first preliminary study was a multi-institutional series on HCG-producing seminoma (HCG-S) published in 1993 (3). At this time, it was the largest series on HCG-S, and it enabled us to settle a controversy: it demonstrated that HCG-S had the same and excellent prognosis as that of non-secreting seminoma. This study triggered the creation of the RCN by Drs Mirimanoff and Ozsahin at the CHUV in Lausanne.

*The objective of the RCN was, and still is, to initiate large, multicentre, international retrospective studies on rare tumours.* Multicentre databases were created and based on all consecutive patients for each type of tumour from committed member institutions. Enough patients had to be collected to obtain enough statistical power to derive reliable outcome data as well as prognostic and therapeutic factors. Strict methodological and ethical rules were established from the beginning, to ensure the quality of collected data. Minimal set of data for each study comprised basic patient's characteristics, pathology,

Table 1:

**The RCN definition of rare tumours**

Categories	Features	Examples
I) Rare pathologies		Erdheim-Chester Merkel Tumour
II) Common pathologies	Site	Extranodal NHL Non-lung small cell cancer Cerebellar glioblastoma
	Age	Pediatric nasopharyngeal cancer (NPC) Adult medulloblastoma
	Sex	Male breast cancer
	Behaviour	Solitary plasmocytoma
	Biology	HCG+ seminoma
	Geography	NPC in nordic countries

initial work-up, therapy (including surgical, radiotherapy and medical oncology details), follow-up data, patterns of failures, and complications (4).

**Current studies**

Currently, the RCN has 123 local investigators in 24 countries, mainly in Europe (90, of which 13 in Switzerland), North America (17), the Middle East (11) and also in South America (4), Asia (2) and Australia (1). So far, 56 studies were initiated, of which 36 are now published in international peer-reviewed journals, such as Lancet Oncology, International Journal of Radiation Oncology Biology Physics, Annals of Oncology, Radiotherapy Oncology, European Journal of Cancer etc. (see : [www.rarecancer.net](http://www.rarecancer.net) ). Currently, 15 studies are open for patients' inclusion. Many of the RCN studies represent the largest or second-largest series worldwide. All RCN reports con-

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Internet: [www.rarecancer.net](http://www.rarecancer.net)

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tain at least information not only on the initial pattern of the rare cancer, but also on overall and disease-free survival, therapy, pattern of failure and univariate and multivariate analyses on prognostic factors. These can be quite useful in daily practise: For example the optimal use (or abstention!) and timing of surgery, radiotherapy and chemotherapy in non-metastatic stages of various rare cancers could be reasonably clarified in many of our studies.

Thus, the RCN has produced data for example on several rare forms of CNS (11 studies), head and neck (4 studies), breast (5 studies), gastro-intestinal (4 studies) uro-genital (11 studies) and other very rare types of cancers (see : [www.rarecancer.net](http://www.rarecancer.net)).

A book on the management of adult rare cancers was published by three of the main contributors of the RCN and comprises 61 chapters in 9 main sections (5). Many of the chapters are based on RCN studies and review the principal publications on a large variety of rare cancers.

*Our RCN is still active in recruiting patients in current studies, and is open to new members interested in bringing their input and new ideas.* ▲

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