RARECARENet country report

Slovenia

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EUROPEAN CANCER PATIENT COALITION

CANCER PATIENTS ASSOCIATION OF SLOVENIA

DRUŠTVO ONKOLOŠKIH BOLNIKOV SLOVENIJE

ONKOLOŠKI INŠTITUT LJUBLJANA

Table of Contents

1. Introduction

In 2011 the RARECARE (surveillance of rare cancers in Europe) project proposed a new definition for rare cancers and quantified the burden of rare cancers in Europe. RARECARE showed that rare cancers pose an important challenge in Europe. They are thought to represent nearly one quarter of all new diagnoses of cancer in Europe (22%) and have lower survival rates than common cancers. Thus obtaining reliable estimates of the number and type of rare cancers, and identifying ways to improve the quality of care for patients should be recognised as a public health priority.[1]

A second project, **Information Network on Rare Cancers (RARECARENet)** was established in 2012 with the aim **to build an information network that may provide comprehensive information on rare cancers to the community at large.**

The RARECARENet project had 3 main components:

- **European and country-specific epidemiological indicators** were estimated on the basis of population-based cancer registries (94 cancer registries from 24 European countries corresponding to 46% of the population of the European Union).
- A '**Pilot Study on hospital volume**' examined at the extent of rare cancer treatment centralisation, and looked at the association between hospital volume and outcomes for two types of rare cancers – sarcomas and head and neck cancers.
- A wide consensus process together with a '**High resolution study on Centres of Expertise for rare cancers'** identified quality criteria for centres of expertise in the management of rare cancers.

*(For a fuller description of the RARECARENet project, see **Appendix 1**).*

In addition, multi-stakeholder meetings were organised in four countries (Belgium, Bulgaria, Slovenia and Ireland) to discuss the emerging public health issue of rare cancers in each country. These meetings allowed the RARECARENet team to present country-specific findings to participating local experts, and discuss how the management of rare cancers may be improved locally for the benefit of patients.

The purpose of this report is to summarise the main discussions and recommendations from the RARECARENet meeting that took place at the Institute of Oncology in Ljubljana, Slovenia on 12th June 2015. The meeting gathered European and local experts on rare cancers (epidemiologists, oncologists, surgeons, and pathologists), cancer registrars, patient organisations and representatives of the Ministry of Health and was co-hosted by the European Cancer Patients Coalition (ECPC), the Cancer Patients Association of Slovenia (Društvo onkoloških bolnikov Slovenije) and the Institute of Oncology Ljubljana. (*The meeting agenda is provided in* **Appendix 2***).*

Discussions focused on four key priorities which correspond to the objectives of the RARECARENet project:

- Describing the epidemiology of rare cancers in Slovenia
- Discussing the most appropriate quality indicators for centres of expertise for specific rare cancers
- Discussing the availability of centres that treat rare cancers in Slovenia
- Identifying existing challenges in the management of rare cancers in Slovenia.

2. The epidemiology of rare cancers in Slovenia

Rare cancers account for 23% of all cancer diagnoses in Slovenia.

The incidence of rare cancers in Slovenia, grouped by different incidence cut-off rates, can be seen in **Appendix 3**.

Slovenia has 2,363 new cases of rare cancers per year, accounting for 23% of all cancer diagnoses. This proportion is comparable to European figures (22%). A large proportion of rare cancers are designated as 'very rare', having an incidence of <0.5 per 100,000 per year. Also, given the small population size of Slovenia, the absolute numbers of rare cancers are low for each cancer type. This will have important implications for the planning and management of these diseases.

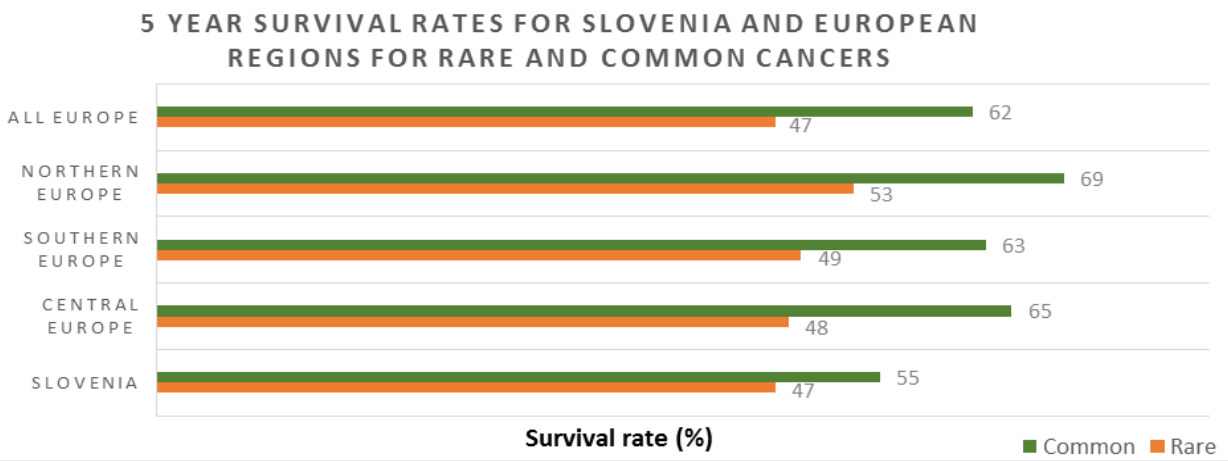
Utilising the RARECARE threshold of <6 per 100,000 incidence per year, all common cancers in Europe are classified as common in Slovenia, and all rare cancers in Europe are also rare in Slovenia.

The survival of people who are diagnosed with a rare cancer is lower than in common cancers.

Using the RARECARENet database, survival analysis for rare cancers was conducted per country. Data from Slovenia follow a similar trend to what is observed in other countries: survival rates for rare cancers are lower than those for common cancers.

Figure 1 shows the 5-year survival rates of cases diagnosed between 2000 and 2007 (and followed up to 31st December 2008) for rare and common cancers in Slovenia and various European regions.

*Figure 1 - 5 year survival rates for Slovenia and European Regions for rare and common cancers**



*Slovenia is presented separately in this figure, however it is also included in the Southern European region. Also, no data were provided for Eastern Europe.

A few trends are apparent with the data available:

- The overall 5-year survival rate for rare cancers in Slovenia is 47%, which is equivalent to the European average, but **lower than survival rates in Northern Europe**.
- Slovenia demonstrates **the lowest difference between common and rare cancer survival rates**, possibly suggesting smaller inequalities in treatment between rare and common cancers.

3. Quality indicators for centres of expertise for rare cancers

Criteria for centres of expertise in the management of rare cancers

As mentioned previously, one of the main outputs of the RARECARENet project was the specification of general quality criteria for centres of expertise in the management of rare cancers. These criteria were then used to develop specific quality indicators for different cancer types (see **Appendix 4**). The general quality indicators were developed at a European level, based on a consensus approach, utilising both evidence from previous experience at the European level (the European Commission committee of experts on rare diseases) and country level.

According to the general quality criteria, centres of expertise should:

1. Ensure appropriate **clinical management** according to evidence-based guidelines and based on **a patient-centered multidisciplinary approach**
2. Develop/support **patient pathways** nationally and across borders
3. Develop **clinical guidelines** and **good service delivery guidelines**
4. Guarantee a learning environment by **promoting training** and continuing education activities
5. Foster clinical, translational and epidemiological **research for rare cancers**
6. **Empower patients** by providing information adapted to their specific needs, culture and ethnic group
7. Possess an **e-health platform** to process and share information, biomedical images or clinical samples supported by enough human and structural resources as well as equipment
8. Have a transparent quality assurance system including **monitoring and evaluation** of the service provided
9. Consistently **report the volume** of patients treated for rare cancers.

These general quality criteria for centres of expertise aided the development of **specific quality criteria for the clinical management of rare cancers**. Key aspects of clinical management relevant to all rare cancers are presented in **Table 1**. These aspects are important to consider in identifying and evaluating centres of expertise. Specific indicators, based on these key aspects, relevant to two particular rare cancers (soft tissue sarcomas and head and neck cancers) are presented in **Appendix 4**.

Table 1: Main areas of the clinical management from which rare cancer specific quality criteria for centres of expertise have been proposed.

Critical areas	Why is this important for rare cancers?
Appropriate and timely diagnosis and staging procedures	Due to the rarity of these cancers, many doctors are unable to make a prompt diagnosis, and pathologists may not have enough experience to identify the cancer. A high level of experience is also necessary for performing all correct staging procedures. The lack of experience due to the rarity of these tumours leads to the use of inadequate diagnostic procedures, incorrect or delayed diagnosis and poor staging procedures. Additionally the referral pathway is not always clear, since centres dedicated to rare cancers may not exist.
Quality of care	Lack of knowledge and clinical expertise among health professionals treating rare cancers may result in suboptimal care.[1] Because of the rarity,

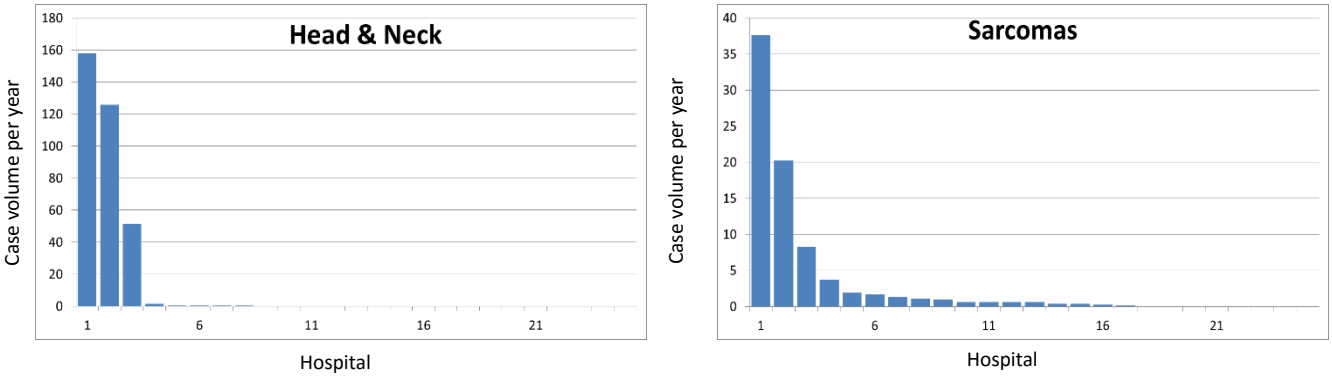
	it is difficult to perform clinical trials and therefore develop evidence-based clinical guidelines. When available, the adherence to clinical guidelines is critical to ensure patients receive the most appropriate, evidence-based care. Independent of clinical guideline availability, it is important to have treatment by a multidisciplinary team, as it provides a higher quality of care for patients.
Quality of pathological report after surgery	Pathological reports are essential for planning appropriate treatment post-surgery. Ideally, pathology reports should contain a full set of the core data defined by the relevant scientific society guidelines, however a complete set of these standardized data are often missing in reports, challenging post-surgical treatment plans.
Quality surgery and radiotherapy	Due to the rarity of these cancers, it is difficult to find experienced surgeons and/or radiotherapists. Poor quality surgery and radiotherapy can lead to re-operation or recurrences, which are avoidable and may have a high impact on the quality of life for patients.
Availability of formalised multidisciplinary decision-making	Multidisciplinary teams are important for the management of rare cancers,[2] as they allow health care professionals from a range of disciplines to work together to provide a comprehensive treatment plan for patients. This is of particular importance for rare cancers due to the limited availability of scientific evidence. Additionally, multidisciplinary teams in high volume centres have been associated with better outcomes, shorter delays between diagnosis and treatment and a greater availability and range of therapeutic options.[2]
Participation in clinical and translational research	Given the small number of rare cancer cases each year, it is often difficult to obtain a strong evidence base on which to build clinical management guidelines and protocols. Therefore centres of expertise should network with other centres across Europe to participate in clinical trials and develop alternative study designs and approaches to with the aim to improve accuracy and standardisation of treatment for rare cancers. [1]

4. Treatment centres for rare cancers in Slovenia

Centralisation of care is viewed as critical for the management of rare cancers as it allows specialists and health professionals to diagnose and treat a larger number of cases. Greater centralisation of the treatment of rare cancers into centres of expertise is one of the explicit priorities stated in the National Cancer Control Plan 2010-2015 for Slovenia.

The degree of centralisation of treatment appears to vary by cancer type in Slovenia. **Figure 2,** from the RARECARENet Pilot Study, shows a much higher level of treatment centralisation for head and neck cancers than for sarcomas. Treatment of head and neck cancers is concentrated in three hospitals, with 99% of surgeries being performed in two hospitals and all radiotherapy occurring in one hospital. These hospitals work as one network, sharing patients and expertise between them. By contrast, treatment of sarcoma appears to be less centralised.

Figure 2 – Hospital volumes for the main treatment of head and neck cancers and sarcomas. Hospitals were ranked by decreasing volume after blind coding.



Preliminary results from the pilot study in Slovenia, which assessed the relationship between hospital volume and outcomes of treatment, found that patients with aggressive sarcomas treated in low-volume hospitals had a two-fold higher risk of death than those treated in high-volume hospitals in Slovenia.

The EU Joint Action "Comprehensive Cancer Control" (CanCon) was established to reduce cancer mortality and improve survival, through identifying quality standards and guidelines for care, improving quality of life for patients and facilitating cooperation between member countries. Following the establishment of CanCon, the European Cancer Patients Coalition (ECPC) conducted a survey of 23 CanCon EU Member-State representatives to further understand the referral for rare cancers in each country represented in CanCon and whether specific treatment centres had been identified.

For Slovenia Mrs. Presečnik, from the Ministry of Health, provided a list of centres which were identified as providing treatment for rare cancers in Slovenia (featured in **Appendix 5).** Due to the small size of Slovenia, some rare cancers are referred to the Institute of Oncology Ljubljana, which is the only comprehensive cancer centre. However, often rare cancer patients are referred to multiple institutions over the course of their treatment. It was beyond the scope of the RARECARENet project to determine specific centres of expertise for rare cancers in Slovenia, therefore it focused on developing quality criteria to support their selection in the future.

5. Challenges in the clinical management of rare cancers in Slovenia

A. General challenges in the management of rare cancers in Slovenia

The management of rare cancers may poses challenges due to their small numbers and lack of available specialists. These challenges are particularly acute in a small country like Slovenia. For example, it is difficult for pathologists to gain experience in diagnosing rare cancers (and particularly very rare cancers) as the number of cases they may see per year is very small.

Some of the most important challenges raised in Slovenia for the management of rare cancers confirm the relevance of the quality criteria chosen. They included:

- **Delays in diagnosis,** due to inadequate referrals to appropriate multidisciplinary teams

- **Primary treatment not always planned at a multidisciplinary meeting,** despite the fact that multidisciplinary care teams were introduced in Slovenia in 1963
- **Pathways for second opinions for very rare cancers not yet formally established**, but are often in place
- **Limited access to new systemic treatments for very rare diseases**
- **Long waiting times for radiotherapy and inadequate adherence to guidelines** for treatment due to poor access to multidisciplinary teams
- **Poor patient understanding of the importance of centralising** treatment and limited patient involvement in clinical decision-making generally.

B. Specific challenges in the management of sarcomas and head and neck cancers

The following challenges were highlighted specifically for the management of sarcoma and head and neck cancers. *(Further details from the High Resolution Study can be found in **Appendix 4.)***

Table 2: Main challenges in the management of sarcomas and head and neck cancers in Slovenia

i) Sarcomas

Area for improvement	Identified challenges
Diagnostic management	The high resolution study found that few hospitals request a second opinion when the primary diagnosis is not carried out by an expert pathologist. Of the hospital with low volume (fewer than 20 surgeries/year), only 30% requested a second opinion. Also in these low volume hospitals, 8% of cases were not biopsied before surgery (even if the tumour size was > 5 cm), which is contrary to ESMO guideline recommendations.
Decentralisation	Treatment is often scattered across many treatment centres, many of which treat less than 5 cases per year (as illustrated in **Figure 2**).

ii) Head and neck cancers

Area for improvement	Identified challenges
Diagnostic management	According to the high resolution study, 41% of laryngeal cancer cases are detected at an advanced stage. Long waiting times for access to diagnosis and treatment are also an issue. 60% of cases of laryngeal cancers started radiotherapy > 1 month from diagnosis. However, the waiting times have improved dramatically in recent years due to new equipment increasing access.
Quality of pathological report after surgery	Only 31% of pathological reports had all information and 39% had partial information.

6. Recommendations for the future

Discussions during the meeting identified a number of key recommendations for the improved management of rare cancers in Slovenia. These are summarised below for rare cancers in general (A), and specifically for sarcomas and head and neck cancers (B).

A. Overall recommendations for rare cancers

1. Improve the standardisation of care for rare cancers to reduce treatment inequalities (across Slovenian treatment centres) and increase the quality of care:

    - **Ensure that primary treatment is planned at a multidisciplinary meeting** to ensure collaboration among different specialists, better quality of pathological reporting and timely start to treatment
    - **Set minimum standards of quality for services**
    - **Implement national and international pathways for rare cancers**
    - **Standardise pathological reporting after surgery**, with a common set of information to be collected for every patient
    - **Define a pathway for second opinion for diagnosis/treatment of extra rare cancers** and ensure that second opinions are properly reimbursed.

2. Empower patients to take a stronger role in their care:

    - **Organise meetings with patients and patient associations to discuss the importance of centralisation for quality of care and better outcomes for rare cancers** to ensure that patients receive care from experienced physicians and pathologists in high volume centres
    - **Improve communication between clinical experts and patient representatives to create a stronger local advocacy base for the better management of rare cancers.**

3. Increase the research base and collaboration in rare cancer care:

    - **Use a population-based cancer registry as the data source to identify and monitor centres of expertise**
    - **Involve scientific societies in the discussion on quality indicators**
    - **Publish scientific papers to support the importance of centralisation** for rare cancer care in Slovenia
    - **Utilise European Reference Networks to enable cross-border collaboration for clinical management, second opinions and clinical research.**

B. Cancer-specific recommendations

Sarcomas:

- **Ensure diagnosis is always performed by an expert pathologist**, if this is not possible, the patient should be referred to an expert pathologist for a second opinion
- **Always conduct a biopsy before surgery** in order to confirm the diagnosis and properly define the treatment plan

- **Treatment centralisation should be increased**, allowing more patients to be seen in high volume hospitals.

Head and neck cancers:

- **Initiate preventive activities (primary and secondary prevention)** to reduce the number of patients getting a preventable cancers such as those of the head and neck, as well as to reduce patients presenting with advanced stage cancer
- **Reduce waiting times for diagnostic procedures**, to ensure a timely start of treatment. Recently the waiting time for treatment initiation was reduced to just 10 days, and waiting times for diagnostic procedures should also be reduced.

Appendices

Appendix 1: About the RARECARENet Project

RARECARE (Surveillance of rare cancers in Europe) data provided a first understanding of the burden posed by rare cancers. RARECARENet project aims at create an information network to provide and disseminate comprehensive information on rare cancers to oncologists, general practitioners, researchers, health authorities, patients and the general public. Additionally, RARECARENet aims to further develop a comprehensive list of patient associations which are dedicated to rare cancers. These objectives are carried out with the eventual aim to improve the timeliness and accuracy of diagnosis, facilitate access to high quality treatment for patients with rare cancers, to identify centres of expertise for rare cancers in Europe and standardise practice across member states. The data facilitating these improvements has been found through the following studies:

RARECARENet EUROCARE-5 is an adult database which was created to update the epidemiological indicators for rare cancers. It covers 94 cancer registries (89 of which were in RARECARE) in 24 countries (19 of which participate in RARECARE). The database covers 48% of the population of the countries participating in RARECARENet, and 46% of the population in the European Union (excluding Norway, Switzerland and Iceland). This database was used to calculate incidence, prevalence and survival of rare cancers.

RARECARENet 'Pilot Study on hospital volume' investigated the extent of centralisation of rare cancer treatment in selected European countries on the basis of population based cancer registries with national coverage. Countries with national coverage were Belgium, Bulgaria, Finland, Navarra (a region of Spain), Ireland, Slovenia and the Netherlands. Objectives of this study were to estimate indicators of the degree of centralisation, map the hospitals where rare cancers are most frequently treated, and analysing the association between hospital volume and outcome for select rare cancers.

RARECARENet 'High resolution study on Centres of Expertise for rare cancers' looked to identify quality criteria for centres of expertise for the management of rare cancers. Through discussion with clinicians, experts, epidemiologists, patient representatives, and cancer registries, general criteria for centres of expertise and specific indicators for selected rare cancers (sarcomas, testicular and head and neck tumours) were identified. The cancer-specific indicators were analysed to test their appropriateness on a retrospective analysis of studying hospital patient files and pathological reports in selected participating cancer registries from Belgium, Bulgaria, Finland, Ireland, Italy, Slovenia and the Netherlands.

RARECARENet 'Information for patients and professionals' was created to provide meaningful information to the community at large. A list of clinical guidelines on rare cancers was developed based on already available information and on new information collected and created in collaboration with State-of-the-Art Oncology in Europe (START), the European Society for Medical Oncology (ESMO) and epidemiological data from the project, Surveillance of Rare Cancers in Europe. The RARECARENet website also provides a list of information materials on rare cancers for patients on the diagnosis, treatment and follow-up of any type of rare cancer. The information has been collected from rare cancer patient organisations participating in the project, more information can be found on the RARECARENet website - http://www.rarecarenet.eu/rarecarenet/index.php/information-on-rare-cancers

Finally, a list of 144 rare cancer patient organisations in Europe was created with the aim to build a network to support patients with rare cancers. The list is available on the RARECARENet website - http://www.rarecarenet.eu/rarecarenet/index.php/patient-organisations

Appendix 2: Agenda for the Ljubljana meeting on Rare Cancers

Meeting Agenda

RARECAREnet meeting on results of the high resolution studies in Slovenia and on quality of care for rare cancers

June 12, 2015, 9:00–16:00

Location: Institute of Oncology Ljubljana

Contact Persons: Kalliopi Christoforidis, +32 48 580 1429

Slovenija: Blaž Bajec, +386 41 835 460

Organisers: RARECARENet, ECPC, Institute of Oncology Ljubljana, Cancer Patients' Association of Slovenia

Time	Topic	Responsibility
9:00-10:00	**Registration**	
10:00–10:30	**Welcome, introduction round, program and aim of the meeting**	Ministry of Health Director general of IOL, President of Cancer Patients' Association of Slovenia, RARECARE team, ECPC team, Lojze Peterle, MAC
10:30–11:00	**RARECARENet project overview**	Gemma Gatta, RARECAREnet
11:00–11:15	**Policy on rare cancers in Republic of Slovenia**	Representative from the Ministry of Health
11:15–12:00	**Presentations on the situation in the country on rare cancers:** - **Clinical situation** - **Rare Cancer Patient story**	Branko Zakotnik Mojca Unk Nataša Elvira Jelenc
12:00-12:30	**Presentation of quality criteria**	Annalisa Trama, RARECAREnet
12:30-13:00	**Discussion on the quality criteria proposed**	Annalisa Trama, Branko Zakotnik
13:00–14:00	**L U N C H**	
14:00-14:30	**Results of the volume analyses of the country**	Riccardo Capocaccia, RARECAREnet
14:30-15:00	**List of centres of treatment for rare cancers identified by ECPC**	Kalliopi Christoforidis, Blaž Bajec
15:00-16:0	**ROUND TABLE:** **Discussion on the level of centralization of rare cancers treatment and on the impact of hospital volume on rare cancers outcome**	Branko Zakotnik and the RARECARENet team
	Conclusions and way forward	
16:00	**Close of the Day**	Branko Zakotnik Marija Vegelj Pirc RARECARENet team

Appendix 3: Rare cancer incidence in Slovenia (estimated new cases, 2013)

Cancer entity	Crude incidence rate x 100,000 per year	Estimated new cases in Slovenia (2013)
Rare epithelial tumours of lung	3<incidence<6 'Rare cancers'	100
Epithelial tumours of oropharynx		78
Epithelial tumours of oral cavity and lip		110
Carcinomas of thyroid gland		110
Tumours of the central nervous system		128
Epithelial tumours of liver and intrahepatic bile tract		106
Testicular and paratesticular cancers		69
Soft tissue sarcoma		104
Epithelial tumours of oesophagus		154
Acute myeloid leukaemia and related precursor neoplasms		85
Rare epithelial tumours of breast		93
Myeloproliferative neoplasms		75
Neuroendocrine tumours		79
Myelodysplastic syndrome and myelodysplastic/myeloproliferative diseases	0.5<incidence<3	56
Epithelial tumours of vulva and vagina		45
Epithelial tumours of pelvis and ureter		36
Malignant mesothelioma		49
Epithelial tumours of major salivary glands and salivary-gland type		31
Rare epithelial tumours of corpus uteri		16
Bone sarcoma		18
Epithelial tumours of anal canal		26
Malignant melanoma of uvea		16
Gastrointestinal stromal sarcoma		7
Epithelial tumours of nasal cavity and sinuses		10
Epithelial tumours of penis		15
Rare epithelial tumours of bladder		15
Epithelial tumours of small intestine		18
Epithelial tumours of nasopharynx	Incidence<0.5 'Very rare cancers'	11
Adenexal carcinoma of skin		7
Malignant melanoma of mucosa (extracutaneous)		3
Extragonodal germ cell tumours		2
Carcinoma of adrenal gland		5
Non epithelial tumours of ovary		5
Embryonal tumours of central nervous system		4
Epithelial tumour of trachea		3
Epithelial tumours of thymus		4
Nephroblastoma		3
Epithelial tumours of urethra		3
Epithelial tumours of eye and adnexa		1
Neuroblastoma and ganglioneuroblastoma		2

Kaposi’s sarcoma		6
Retinoblastoma		1
Hepatoblastoma		0
Olfactory neuroblastoma		1
Odontogenic malignant tumours		0
Trophoblastic tumour of placenta		0
Epithelial tumours of middle ear		1
Carcinomas of pituitary gland		1
Carcinomas of parathyroid gland		1
Histiocytic and dendritic cell neoplasms		1
Pleuropulmonary blastoma		0
Pancreatoblastoma		0

Appendix 4: Quality indicators and outcomes for three chosen rare cancers in Slovenia.

Soft tissue sarcoma:

Criteria	Quality indicator	Findings from the high resolution study in Slovenia
Diagnostic management	Percentage of patients with sarcoma undergoing preoperative scan and biopsy before treatment (MRI and/or CT locally and lung CT)	6% of patients had no imaging at all and 8% of patients had imaging only after treatment. 78% of cases had received at least imaging on the tumour.
		Types of imaging used to study the tumour are at least CT scan (6%), at least magnetic resonance imaging (82%) and CT scan and magnetic resonance imaging (12%).
		100% of patients had a CT scan when looking for metastasis
		81% had biopsy before surgery. Hospitals with a larger volume of cases had a greater rate of biopsy before diagnosis.
	Diagnosis carried out by an expert pathologist (or second opinion carried out in an expert centre if diagnosis is not carried out by an expert pathologist)	22% of diagnoses requested a second opinion, the highest in low volume hospitals. However, all low volume hospitals should request a second opinion
		91% of second opinions were provided by high volume hospitals.
		One case had a second opinion based outside Slovenia.
Adherence to clinical guidelines	Percentage of patients with low grade and R0 resection margin undergoing surgery alone.	In Slovenia, 100% of low grade, R0 sarcomas underwent surgery alone.
	Percentage of patients with high grade and R0 resection undergoing surgical intervention and radiotherapy or radiotherapy and chemotherapy.	52% of high grade, R0 patients underwent surgery with radiotherapy or with radiotherapy and chemotherapy.
	Percentage of patients with R1 or R2 resection margin undergoing surgical re-intervention or, radiotherapy, or chemotherapy and radiotherapy.	68% of patients with R1 or R2 underwent re-intervention or radiotherapy or radiotherapy and chemotherapy. Cases not treated according to guidelines were mainly old, not advanced stage and were treated in high volume (>20 cases/year)
Quality of surgery and radiotherapy	Complete tumour resection of definitive surgery	100% of surgeries were R+ (i.e. incomplete surgical resection) in low volume hospitals. Whereas only 22% were R+ in high volume hospitals.
	Reoperation after primary definitive surgery	Overall the rate of reoperation was 14%. Low volume hospitals had a 60% reoperation rate, whereas high

		volume hospitals had a 9% re-operation rate.
Quality of pathological report after surgery	Percentage of pathology reports with a full set of core data items recorded according to the European Society for Medical Oncology guidelines.	72% of pathology reports provided all required information
Availability of formalised multidisciplinary decision making and care		The only centre where a multidisciplinary approach was used is at the Oncology Centre in Ljubljana – however data was contained medical records, which were not accessible
Participation in clinical and translational research		No indicators collected by high resolution study because the information was not retrievable

Head and neck cancers:

N.B. Only laryngeal cancer were included in the study

Criteria	Quality indicator	Findings from the high resolution study in Slovenia
Timely start of treatment	Time to start treatment (time between definitive pathological diagnosis and beginning of surgery or radiotherapy)	For radiotherapy or surgery, 40% of patients were treated in under a month from histological verification, and 60% were over one month.
		Of patients starting in over a month after diagnosis, 89% of this were for radiotherapy, and 11% was surgery.
		Of those who were begun in less than 1 month, 53% were early, 43% were advanced and 4% were metastatic.
		Of those who were begun in over a month after diagnosis, 60% were early, 40% were advanced and 1% was metastatic.
	Time in starting postoperative radiotherapy of concomitant chemo-radiotherapy (adjuvant treatments)	57% of adjuvant occurred in under 8 weeks, and 43% took over 8 weeks.
Stage at diagnosis	Definition of stage at diagnosis	54% were localised, 41% were advanced, and 1% were metastatic. Stage at diagnosis was missing in 4% of cases.
Adherence to clinical guidelines	Percentage of patients with early stage I and II referred for either surgery or radiotherapy	Guidelines were followed in patients with early stages when 12% had only surgery, 64% had only radiotherapy. However against guideline recommendations, 23% had surgery plus radiotherapy or surgery plus concomitant radio-chemotherapy, and 2% had no treatment.

	percentage of patients with locally advanced stage III and IV referred for surgery plus postoperative radiotherapy or postoperative chemo-radiotherapy	Guidelines were followed in patients with advanced stages, when 44% had surgery plus radiotherapy or surgery plus concomitant radio-chemotherapy. However guidelines were not followed when 46% had only radiotherapy, 3% had only surgery and 4% had no treatment and 2% had only chemotherapy.
Quality of surgery and radiotherapy	Complete tumour resection (histological verification of tumour free margins after surgery)	Among those surgically treated, 76% of cases were R0, the information was missing in 9% of these cases.
	Readmission, reoperation within 30 days from main surgery	Unknown - the indicator was proposed after the data collection (during a meeting discussing the data collected from the high resolution study with experts in the field)
	Grade 3 or more late toxicities (more than 3 months after radiotherapy)	Unknown - the indicator was proposed after the data collection (during a meeting discussing the data collected from the high resolution study with experts in the field)
	Percentage of patients receiving intensity-modulated radiation therapy vs receiving 3D conformal radiation therapy	Unknown - the indicator was proposed after the data collection (during a meeting discussing the data collected from the high resolution study with experts in the field)
	Availability of all types of surgery and reconstructive surgery	Unknown - the indicator was proposed after the data collection (during a meeting discussing the data collected from the high resolution study with experts in the field)
Quality of pathological report after surgery	Percentage of pathology reports with a full set of core data items recorded according to the ESMO guidelines	31% of reports had all information.
Availability of formalised multidisciplinary decision making and care	No indicators	The only centre where a multidisciplinary approach was used is at the Oncology Centre in Ljubljana – however data was contained medical records, which were not accessible
Participation in clinical and translational research	No indicators	No indicators collected by high resolution study because the information was not retrievable

Appendix 5. Treatment centres identified for rare cancers in Slovenia.

Rare cancer	Treatment centre
Head and Neck	• Clinic for Cervicofacial and Oral Surgery, University Clinical Centre Ljubljana • Clinic for Maxillofacial Surgery, University Clinical Centre Maribor • Clinic for Head and Neck surgery, University Clinical Centre Ljubljana • Institute of Oncology Ljubljana
Central Nervous System	• Clinic for Neurosurgery, University Clinical Centre Ljubljana • Clinic for Neurosurgery, University Clinical Centre Maribor • Institute of Oncology Ljubljana
Neuroendocrine Tumours	• University Clinical Centre Ljubljana • University Clinical Centre Maribor • Institute of Oncology Ljubljana
Endocrine Tumours (Thyroid, pituitary and adrenal gland)	• University Clinical Centre Ljubljana • University Clinical Centre Maribor • Institute of Oncology Ljubljana
Sarcomas (including GIST)	• Institute of Oncology Ljubljana
Haematological Tumours (e.g. Multiple Myeloma, CML, Hodgkin's Lymphoma)	• University Clinical Centre Ljubljana • University Clinical Centre Maribor • Institute of Oncology Ljubljana
Male Genital Organs (Penis, testis)	• Urologic Departments, Institute of Oncology Ljubljana
Embryonal Tumours	• Institute of Oncology Ljubljana
Childhood Cancers	• Clinic for Childhood Diseases, Department for Hemato-oncology, University Clinical Centre Ljubljana
Thymus Cancers	• University Thoracic Clinics Ljubljana • University Clinic for Lung Diseases Golnik • University Thoracic Clinic Maribor • Institute of Oncology Ljubljana
Malignant Mesothelioma	• University Clinic for lung Diseases Golnik • Institute of Oncology Ljubljana

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2. Singh S, Law C. Multidisciplinary reference centers: the care of neuroendocrine tumors. Journal of oncology practice / American Society of Clinical Oncology 2010;**6**(6):e11-6.

Other key reading:

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For further information, please see:

- RARECARENet - http://www.rarecarenet.eu/rarecarenet/
- European Cancer Patients Coalition (ECPC) - http://www.ecpc.org/
- Joint action on Cancer Control (CanCon) - http://www.cancercontrol.eu/index.php