The present and future opportunities of the Rare Cancer Network: an international consortium for advancement of oncologic care

The Rare Cancer Network

Abstract

To date, the Rare Cancer Network (RCN) has initiated more than 90 studies and 54 peer-reviewed publications were produced as a result. The *Second International Symposium of the Rare Cancer Network* recently took place in Istanbul, Turkey on April 17-18, 2015, and update was given on multiple currently ongoing projects, while also giving room for new proposals which will shape the direction of future studies for the group. This companion issue of the RCN *Proceedings* summarized the findings of this meeting, while also serving as a call for fresh projects and papers which will continue to energize the group and advance the oncologic science. A brief introduction to the principles, history, and vision of the RCN was also included. To review, the academic year of 2014-15 marked an enormous success for the international members of the RCN, with the generation of 8 fully published papers and more than 12 newly proposed topics. By the collective efforts of all RCN members, in the future, we look forward to the upcoming opportunities in continuing to advance the standard of chemo- and radiotherapeutic oncologic care for selected rare tumor topics. The studies of these rare cancers often do not allow the design and execution of prospectively enrolled trials; however, these uncommon malignancies do impact the humankind and add to its suffering globally in significant ways.

Contributors (on behalf of the Rare Cancer Network investigators)

Terence T. Sio (*Department of Radiation Oncology, Mayo Clinic, Rochester, MN, USA; Department of Radiation Oncology, Mayo Clinic, Scottsdale, AZ, USA*); René-Olivier Mirimanoff (*Department of Radiation Oncology, University of Lausanne Medical Center, Lausanne, Switzerland*); Enis Özyar (*Department of Radiation Oncology, Acibadem University, Acibadem Maslak Hospital, stanbul, Turkey*); Yazid Belkacemi (*AP-HP, GH Henri Mondor. Service d'Oncologie-Radiothérapie et Centre Sein Henri Mondor. Université Paris-Est Créteil, Créteil, France*); Robert C. Miller (*Department of Radiation Oncology, Mayo Clinic, Jacksonville, FL, USA*); Salvador Villà (*Radiation Oncology, Germans Trias i Pujol Hospital, Catalan Institute of Oncology Badalona, Barcelona, Catalonia, Spain*); Juliette Thariat (*Department of Radiation Oncology, Centre Lacassagne, Nice, France*); Marco Krengli (*Division of Radiotherapy, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy*); Luciano Scandolaro (*Department of Radiotherapy, Ospedale S. Anna, Como, Italy*); Banu Atalar (*Department of Radiation Oncology, Acibadem University, Acibadem Maslak Hospital, stanbul, Turkey*); Gamze Uğurluer (*Department of Radiation Oncology, Acibadem University, Acibadem Adana Hospital, Adana, Turkey*); Beatriz Gutiérrez García (*Radiation Oncology, Germans Trias i Pujol Hospital, Catalan Institute of Oncology Badalona, Barcelona, Catalonia, Spain*); Jonathan B. Ashman (*Department of Radiation Oncology, Mayo Clinic, Scottsdale, AZ, USA*); Yavuz Anacak *(Department of Radiation Oncology, Ege University, School of Medicine, Izmir, Turkey*); Cem Önal (*Department of Radiation Oncology, Baskent University Faculty of Medicine, Ankara, Turkey*); Mutlu Arat (*Group Florence Nightingale Hospitals, Istanbul Bilim University, Istanbul, Turkey*); Xu Shan Sun (*Department of Radiation Oncology, CHRU, Besancon, France*); Dusanka Tesanovic (*Department of Radiation Oncology, Institute of Oncology Vojvodine, Serbia*); Yasmin Lassen-Ramshad (*Department of Oncology, Aarhus University Hospital, Aarhus, Denmark*); Didem Öksüz (*Department of Radiation Oncology, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey*); Fazilet Dinçbaş (*Department of Radiation Oncology, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey*); Duygu Sezen (*Department of Radiation Oncology, Koç University, stanbul, Turkey*); Serap Akyürek (*Department of Radiation Oncology, Ankara University, Ankara, Turkey*); Tuğçe Kütük (*Department of Radiation Oncology, Ankara University, Ankara, Turkey*); Yasemin Bölükbaşı (*American Hospital, M.D. Anderson Radiation Treatment Department, Istanbul, Turkey*); Gülnihan Eren (*Diyarbakır Gazi Yasargil Education and Research Hospital, Diyarbakir, Turkey*); Nitesh N. Paryani (*Department of Radiation Oncology, Mayo Clinic, Jacksonville, FL, USA*); Safia K. Ahmed (*Department of Radiation Oncology, Mayo Clinic, Rochester, MN, USA*); Luigi Moretti (*Department of Radiation Oncology, Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium*); Kenneth W. Merrell (*Department of Radiation Oncology, Mayo Clinic, Rochester, MN, USA*); Kenneth Chang (*Department of Radiation Oncology, Mayo Clinic, Rochester, MN, USA*); Mark Mayeda (*Department of Radiation Oncology, Mayo Clinic, Jacksonville, FL, USA*); Andrea L. Arnett (*Department of Radiation Oncology, Mayo Clinic, Rochester, MN, USA*); Jacob Y. Habboush *(Department of Radiation Oncology, Mayo Clinic, Jacksonville, FL, USA*); Mahmut Ozsahin (*Department of Radiation Oncology, University of Lausanne Medical Center, Lausanne, Switzerland*)

Correspondence: (on behalf of the Rare Cancer Network) Terence Tai-Weng Sio, Department of Radiation Oncology, Mayo Clinic, 200 First St, SW, Rochester, MN 55905, USA.
E-mail: Sio.Terence@mayo.edu

Key words: Rare Cancer Network; radiation oncology; radiotherapy; rare tumor; carcinoma.

Acknowledgements: Congress reports of the Second International Symposium of the Rare Cancer Network, Istanbul, Turkey, April 17-18, 2015.

Contributions: all authors contributed to the writing of this report and are responsible for the intellectual content of this work; they approved the final version of this manuscript.

Conflict of interest: the authors declare no potential conflict of interests.

Received for publication: 8 May 2015.
Accepted for publication: 8 May 2015.

This work is licensed under a Creative Commons Attribution NonCommercial 3.0 License (CC BY-NC 3.0).

©Copyright The Rare Cancer Network, 2015
Licensee PAGEPress, Italy

Rare Tumors 2015; 7:5998
doi:10.4081/rt.2015.5998

Introduction

Following the successful completion of the *First International Symposium of the Rare Cancer Network* (RCN),[1] the RCN members organized *the Second International Symposium of the RCN*, generously hosted by Drs. Özyar and Atalar at the Department of Radiation Oncology, Acibadem Maslak Hospital in stanbul, Turkey on April 17-18, 2015 (Figure 1). The location was particularly fitting, as 33 scientists from over 20 Turkish centers have participated in 20 of the 54 published RCN studies, and 5 of them were mentors of prior

studies which had been published (prostatic ductal carcinoma, salivary gland indolent mucosal associated lymphoma, thyroid non-Hodgkin's lymphoma, pediatric nasopharyngeal carcinoma, and adult Langerhans cell histiocytosis of bones). The continued activities have fostered and strengthened the collaborations mainly among European and American oncologists and investigators within the RCN (Figure 2); more Asian and Australian alliances are possible in the future.

For the proceedings and academic findings of the *Second International Symposium*, they will be reported in this article as a companion and special report in the current issue of *Rare Tumors*. Previously, the historical highlights of the group have been described in detail,[2] emphasizing the collegial nature of this global network for oncologic advancement. This report will update the findings of the *First International Symposium of the RCN* to date,[1] while reviewing some of the ongoing and all newly proposed studies which were presented in the meeting; the first 20-years' achievement of the RCN has been previously reported.[3] For more information regarding the RCN and our ongoing studies, please also visit our home webpage at www.rarecancer.net. On April 17, 2015, sessions have also been dedicated to report and update the attending RCN members regarding the current knowledge, recommendations, and guidelines of extranodal non-Hodgkin's lymphoma (NHL). The RCN contributions for the selected rare NHL topics were emphasized. These lectures included an overview of extranodal NHL (M. Arat), primary breast lymphoma (Y. Belkacemi), primary bone lymphomas (J. Ashman/R.C. Miller), orbital lymphoma (M. Ozsahin), mycosis fungoides focusing on the total skin electron-beam irradiation experience at a single institution (B. Gutiérrez García), NHL of salivary glands (Y. Anacak), testicular NHL (S. Villà), primary spinal epidural lymphoma (R-O. Mirimanoff), and thyroidal lymphoma (C. Onal). The updated knowledge and RCN recommendations of the diagnosis and management of extranodal NHL sites are the subject of a comprehensive review paper, currently under preparation (Y. Belkacemi).



Figure 2. The global geographic distribution of the Rare Cancer Network members in 2015; the countries (and cities) represented include Canada, United States of America (Rochester, Minnesota; Scottsdale, Arizona; Jacksonville, Florida), Brazil, Chile, Sweden, Denmark, Netherlands, United Kingdom, Belgium, Switzerland, France, Portugal, Spain, Morocco, Greece, Israel, Turkey, Italy, Austria, Germany, China, and Australia.



Figure 1. The Second International Symposium of the Rare Cancer Network, Istanbul, Turkey, April 17-18, 2015.

A brief history of the Rare Cancer Network

The Rare Cancer Network was first founded by Professors Mirimanoff and Ozsahin in the early 1990's, radiation oncologists and scholars practicing at the Department of Radiation Oncology, Centre Hospitalier Universitaire Vaudois in Lausanne, Switzerland. The administrator for the RCN is Ms. Brigitte Pointet. The founding principle of the RCN is to provide a platform and international resource for the study of radiation and also other modality treatments in rare tumors.[2] We aim to collect, analyze, and ultimately publish quality clinical data on either a rare type of cancers in which radiotherapy and/or chemoradiation play an important role, or rare presentations of common cancers which are of interest to the globally practicing radiation oncologists, including management of unusual paraneoplastic syndromes.[3,4] The most common tool for clinical investigation is typically retrospective methods, however, prospectively followed protocols and registries (J. Thariat) and case control studies (other investigators) have been previously proposed. The announcement of new studies must first be coordinated with the secretariat office (B. Pointet) so that RCN research activities can be tracked. To date, more than 50 original research articles have been published by the group, indicating the strength of our collaborators as a result of the ongoing research activities that have been generated. We praise ourselves that the characteristics of the RCN include rapid collection, analysis, and dissemination of accurate scientific and clinical data, informality, and also the low cost needed for the start-up of meaningful scientific projects and forming collaborative groups. We are friendly in spirit, mutually confident, trustworthy, and loyal to each other. For consideration of RCN membership, please visit www.rarecancer.net and contact Ms. Brigitte Pointet and Professor Mahmut Ozsahin.

Published studies and other active investigations

Overview and summary (T.T. Sio)

Since the last RCN meeting, 8 manuscripts including 5 retrospective studies,[5-9] 2 proceedings papers,[1,2] and 1 editorial article have been published.[10] The collective work of these 8 publications represented 85 authors with 108 authorships total. Nine (9) authors were with 2 inclusions, and 5 authors had 3 or more inclusions. U. Schick and colleagues reported a series of 20 patients with adenosquamous carcinoma of the head and neck,[9] and showed that the overall prognosis of locoregionally advanced cases still remained poor. In the extraskeletal osteosarcoma study,[6] Sio TT *et al.* confirmed the importance of trimodality therapies in the management of rare extraosseous sarcomas, and elucidated important prognostic factors for worse overall (stage IV, and primary size >10 cm) and disease-free (older age, and also primary size >10 cm) survivals. A large series of 107 patients with small cell carcinoma of the urinary bladder has recently been reported by Pasquier D *et al.*,[8] which represented the effort of 15 RCN-affiliated medical centers across the globe. The study investigators concluded that, in the majority of the patients who presented with T2-4N0M0 and T2-4N1-3M0 stages, the use of radical cystectomy (with or without chemotherapy) and conservative, non-surgical approach resulted in comparable overall and disease-free survivals; organ preserving strategies should be encouraged for patients afflicted with locally advanced small cell bladder carcinoma. Weber DC *et al.*[7] reported a series of 194 patients with spinal myxopapillary ependymoma who were treated at both MD Anderson Cancer Center and also institutions from the Rare Cancer network. In this cohort of patients, about one third of patients experienced disease relapse after primary treatment, and not having adjuvant RT nor gross total resection were identified as risk factors in young patients. Along with GSF-GETO, GETTEC/REFCOR and SFCE, Thariat J *et al.*[5] reported a large series of multi-institutional, multidisciplinary management of mainly young adult patients with osteosarcomas of the mandible (MOS). Having clear margins at the time of surgery and also involving multidisciplinary management were essential and impactful for successful outcome; neoadjuvant chemotherapy should be considered for patients presenting with intermediate or high-grade MOS. For other RCN projects, a manuscript for glomus tumors (Y. Lassen-Ramshad) is currently under preparation. The extracranial hemangiopericytoma/solitary fibrous tumor project (M. Krengli) is also actively accruing for more patient data: 4 centers have already sent 22 cases, and at least other 6 centers are expected to collaborate in this study. Dr. Tesanovic discussed the epidemiology and specific issues regarding Mediterranean rare cancers. We also extended the accrual period for the adult medulloblastoma project (B. Atalar) for six more months, with the hope that more patients' data can be accrued from additional institutions; currently, data from 115 patients from European hospitals and 66 patients from Mayo (United States) have been successfully collected.

Other ongoing studies (J. Thariat, X.S. Sun)

Differentiated non-anaplastic thyroid cancers (follicular, papillary, medullary, insular types) are relatively common tumors but are irradiated in exceptional situations only. While irradiation of cases with radioiodine-negative massive extrathyroidal extension is consensual, other indications are highly controversial. The sole randomized study conducted to date on that topic was terminated early because of slow accrual. Several retrospective studies raise the question of irradiation for poor prognostic histological variants (such as Hurtle-oncocytic and tall cell variants), for incomplete resection and extensive extracapsular nodal disease. Because a randomized trial is unlikely to be feasible, we proposed a retrospective study, with the aim of collecting ≥400 cases irradiated between 2000 and 2010 to assess the role of radiation therapy in non-anaplastic thyroid cancers, including irradiated cases and also non-irradiated cases (T3/T4 and/or R1/R2 and/or N+ and/or and radioiodine negative and/or recurrent). One hundred and sixty-seven (167) patients are currently collected; however, the publication will be launched at 200 or above to obtain adequate statistical power which will represent one of the largest studies to date.

Anaplastic thyroid carcinoma (ATC) is a rare very aggressive tumor. To date, most findings about ATC have been derived from single institution studies with limited numbers of cohorts, with no randomized therapeutic clinical trials and consequently no standard of care. The management of ATC involves a combination of surgery (often debulking surgery), radiotherapy, and chemotherapy. Accelerated twice daily irradiation appears to be more efficacious although it is not convenient in routine practice. Neoadjuvant chemotherapy followed by chemoradiation may be of interest in rapidly-growing tumors. We aim at inquiring the current practices within the RCN network and also determining the best combination of multimodality strategy for ATC with regard to extent of surgery, addition of chemotherapy, and also radiotherapy fractionation. Currently, 152 patients have been included. We are hoping to add about 50 more cases prior to the closing of this study.

The mainstay of treatment for *salivary gland carcinomas* (SGT) is surgery. Radiotherapy is recommended in the postoperative setting following incomplete surgery and/or for high grade stage II- IV tumors, however, typically low grade stage III-IV and also intermediate grade stage I-II tumors are considered only on a case-by-case basis. It is also advocated for unresectable disease, recurrent disease, and patients with inoperable tumors.[11,12] Despite the absence of level I-II evidence, chemotherapy is added to radiation therapy in a number of cases with inadequate resection margins, extra-nodal spread, or multiple involved lymph nodes.[13] Several studies have demonstrated

that concurrent treatment with radiotherapy and chemotherapy is a validated approach for certain postoperative cases of locally advanced squamous-cell carcinoma;[14,15] this strategy for SGT has indeed been largely extrapolated from those head and neck cancer-based data. We assess whether the addition of chemo or targeted therapies to radiation therapy either in the postoperative or definitive setting may improve outcomes in the management of patients with SGT. To date, 657 patients have been included, and 103 of those had chemotherapy. Intermediate analyses have trends for several histological types; however, the statistical power remained low, especially for the role of concomitant chemotherapy in addition to irradiation. As a result, we will continue to open the study and call for cases in which patients undergo chemo or targeted therapies in addition to radiation therapy.

New proposed studies

On April 18, 2015, twelve (12) new RCN studies were introduced to the participating oncologists and clinicians in the meeting. They are reported as follows: Table 1 represents a summary of these studies and their intended number for patient/case accruals among the RCN-affiliated institutions. After a Questions and Answers session, the level of interest for each study was immediately sampled among the audiences (from their institutional representatives) and recorded accordingly. Instant feedback was given to the mentors/principle investigators for each of their individual studies. Drs. Jonathan B. Ashman and Mahmut Ozsahin chaired this session for the new RCN investigators.

Metaplastic breast cancer (A. Arnett)

Rare breast malignancies with mixed epithelial and mesenchymal differentiation are termed metaplastic breast cancer (MBC, <1% of all diagnoses). Early studies and other case reports suggested that patients with MBC may have worse outcomes.[16,17] The tumors are often more poorly or entirely undifferentiated at presentation, and with a higher percentage of triple-negative molecular phenotypes; they tend to present with an advanced primary tumor. The proposed study will place emphasis on correlating the treatment modalities and also histologic variants of MBC with patient's outcome, and aim to provide strategies for risk stratification; the number of patients desired for enrollment is higher as a result, and a large number of institutions expressed interest in the meeting (Table 1).

Langerhans cell sarcoma (N. Paryani)

The World Health Organization (WHO) classifies Langerhans Cell Sarcoma (LCS) under histiocytic and dendritic cell neoplasm, which was an exceedingly rare tumor first recognized in 1984 as malignant histiocytosis X.[18] Now, there are still fewer than 40 cases reported in the English medical literature. LCS often presents as a high grade neoplasm and harbors an aggressive clinical course; the survival was very poor, with a rate of 50% at 2 years. As the optimal treatment regimen has yet to be defined for this rare cancer, the RCN proposes this topic as a new study which will represents an excellent focus for the group.

Primary central nervous system rhabdomyosarcoma (S. Ahmed)

Primary rhabdomyosarcoma arising from the brain or spinal cord carries very poor outcomes, in both pediatric and also adult populations. In the modern era, immunohistopathologic confirmation such as detection of *PAX3/FOXO1* fusion transcript is desired. For primary CNS rhabdomyosarcoma, there have only been 42 reported cases in between 1958 and 2014, with patients' age ranging 1 to 68 years; spinal seeding happened in 4 (9.5%) cases. The mean survival was only 9.1 months, with only 5 (12%) patients surviving for more than 2 years. Although there is no standard therapy, the typical patient received surgery, radiation therapy, or tri-modality therapy including chemotherapy. An international RCN study will help characterize this particularly rare cancer and provides insight regarding the optimal therapy plan for future patients.

Adenoid cystic and squamous cell carcinomas of the trachea (L. Moretti and K. Merrell)

Primary tumors of the trachea are very rare in general (both types at incidence rates of 0.1 per 100,000 capita or lower). Two particular histologies, adenoid cystic,[19] and also squamous cell carcinoma, warrant further investigations. Led by two international oncologists, we aim to study these variants of tracheal cancers and report an updated multi-institutional experience, as improved staging procedures, radiotherapy techniques and chemoradiation

Table 1. A summary of the newly proposed studies and the expected patient accrual numbers.

Leading author(s)/mentor(s)	Rare cancer topics	Pts desired	Level of interest among institutions
A. Arnett	*Metaplastic breast cancer*	*150-200*	*Very High*
N. Paryani	Langerhans cell sarcoma	5-10	High
S. Ahmed	Primary CNS rhabdomyosarcoma	5-10	Average
L. Moretti/P. Van Houtte	Tracheal adenoid cystic carcinoma	5-20	High
K. Merrell	Tracheal squamous cell carcinoma	5-20	High
G. Eren	Clival chordoma	5-10	Average
S. Akyürek/T. Kütük	*Gliomatosis cerebri*	*25-100*	*Very High*
Y. Bölükbaşı	Extraosseous Ewing's sarcoma	15-50	High
D. Ç. Öksüz	Extranodal NK/T-cell NHL, nasal-type	15-50	High
F. Dincbas	*Dermatofibrosarcoma protuberans*	*25-100*	*Very High*
D. Sezen	Central neurocytoma	5-20	High
Y. Belkacemi	Primary breast NHL	5-20	High

CNS, central nervous system; Pts, patients; NK, Natural Killer; NHL, Non-Hodgkin's Lymphoma. Level of interest among institutions: Average, 1-3 institutions interested in contributing patient cases to the proposal; High, 3-8 institutions; Very high, more than 8 institutions (priority studies, in italics).

approaches have increased the chance of organ preservation, with potentials to improve quality of life in an otherwise surgically potentially morbid treatment paradigm.[20,21] Currently, there are no formal guidelines across multiple American and European-based oncologic societies and organizations. This RCN study will assess treatment outcome and pattern of failure, and provide insights on the most favorable radiation dose fractionation schedule for tracheal carcinomas.

Clival chordoma (G. Eren)

Thirty-five (35) percents of chordoma are skull based including the clivus; nevertheless, they are so rare that it represents only less than 1% of all intracranial tumors. Originated from the remnants of the notochord, clival chordoma is locally expansive and characterized by high recurrence rates. Clival chordoma is resistant to systemic therapies, and surgical gross total resection is often not possible due to the centrally skull-based location. A study is proposed to evaluate the effectiveness and safety of dose-escalated radiotherapy modalities including particle-based treatments such as proton; the data collected will also focus on treatment side effects including temporal lobe injuries and brainstem necroses.

Gliomatosis cerebri (S. Akyürek and T. Kütük)

Gliomatosis cerebri (GC) refers to a clinical diagnosis of diffuse neoplastic glial process which involves more than 2 anatomic lobes of the brain parenchyma, typically with bilateral involvement of the supratentorial structures along with deep gray matter. Histopathologically, GC is typically found to be as World Health Organization (WHO) grade II, III, or IV glial tumors. The epidemiology of this rare disease called GC is poorly understood, and survival is poor (median, 11-38 months). The potential difference in therapeutic response and prognostic impact of molecular makers (MGMT methylation, 1p/19q co-deletion, and IDH mutation, etc.) may be different in this subgroup of clinically aggressive yet diffuse gliomas; however, evidence is very limited especially for patients who were treated in the modern era, after the widely global adoption of temozolomide.[22,23] Due to its often fairly extensive and diffuse involvement of GC, specifically, what extent of maximally safe surgery should be performed? What are the indications and roles of chemotherapy and also radiotherapy (sequential *vs*. concurrent) in this setting? Is there a role of whole brain radiotherapy? How should patient factors such as performance status and age be integrated in treatment decision making? The effective and optimal treatment schema and choice and sequence of modalities are clearly not well defined as of currently, as a result, a multi-institutional study within the context of RCN is urgently required. This has been voted as one of the top 3 priority projects for the year, as a large number of RCN members expressed interest in joining the current study (Table 1).

Extraosseous Ewing's sarcoma (Y. Bölükbaşı)

Although Ewing's sarcoma may be relatively common especially in pediatric population, extraosseous, peripherally primitive (*i.e.,* with PNET differentiation) and non-central nervous system involved cases are rare. These tumors are aggressive in nature, with high local recurrent rates and often accompanied by distant metastases.[24,25] The proposed study will focus on collecting Ewing's sarcoma cases which are extraskeletal in nature, and information regarding patient and tumor characteristics including chemotherapy responses will be included. A careful mapping of locoregional recurrence patterns will also be evaluated.

Extranodal nasal-type Natural Killer/T-Cell non-Hodgkin's lymphoma (D.Ç. Öksüz)

Extranodal nasal-type Natural Killer/T-Cell lymphoma (ENKTL) is a rare yet very aggressive subtype of non-Hodgkin's lymphoma (NHL). It typically involves the upper aerodigestive tracts including the nasal cavity and nasopharynx, and is Epstein Barr Virus (EBV)-related. Eighty (80) percents of the patients presented with localized disease, *i.e.,* extranodal stages I and II. Although this particular lymphoma is relatively more common in Asia and South America, the incidences are much lower in Europe and also United States (<1% of all NHL's); the epidemiology, pattern of care and outcome may be different.[26-28] Consequently, a study was proposed to gather patient cases with stages IE to IIE ENKTL, focusing on a non-Asian population which may be more prevalent amongst the RCN members' institutions.

Dermatofibrosarcoma protuberans (F. Dinçbaş)

Dermatofibrosarcoma Protuberans, or DFSP, is an uncommon cutaneous sarcoma (<1%) which is exceedingly locally aggressive and infiltrative. It tends to recur locoregionally but rarely distantly; it is characterized by a t(17:22) chromosomal translation. Its irregular, tentacle-like microscopic projections give its name, *Protuberans*. Although the majority of these tumors are low grade, the adjuvant radiotherapy indications are less clear, especially in cases where close or positive margins are obtained surgically.[29] As a result, a RCN study was proposed to study the role of neoadjuvant and also adjuvant radiotherapy, international patterns of care, and also elucidation of prognostic factors such as tumor size and age. This is a high priority study as members from multiple institutions indicated that they have a strong number of cases to supply (Table 1).

Central neurocytoma (D. Sezen)

Central neurocytoma (CN) is a World Class Organization (WHO) grade II neuroepithelial-based tumor most commonly located intraventricularly.[30,31] They compromise of 0.1-0.5% of all intracranial tumors, and typically occur in patients of younger age (mean, 29 years). Surgery remains the mainstay of treatment, however, the role of adjuvant radiation therapy is less clear.[32] Thus, the RCN investigators proposed a study to assess the clinical characteristics, treatment outcome, and patterns of failure for patients with central neurocytoma, focusing on the evaluation of optimal dose and fractionation of radiotherapy (including use of stereotactic radiosurgery) and chemotherapy use in the modern era; prognostic factors will also be evaluated.

Implant-associated primary breast Non-Hodgkin's lymphoma (Y. Belkacemi)

The Rare Cancer Network, led by Jeanneret-Sozzi *et al.*,[33] has previously published a large series of 84 consecutive patients with primary breast lymphoma (PBL) in 20 institutions. They noticed that while local control and overall survival were fair to excellent with RT or combined modality treatments, systemic relapses including intracranial seeding could still happen. Others have reported their experiences with primary follicular and marginal-zone lymphoma of the breast,[34] which tended to behave more indolently. In this proposed study, the RCN investigators will gather PBL cases associated with breast implants; this tumor will typically harbor an *ALK*- or *ALK1*-genetic mutation, and is usually histopathologically anaplastic with large cell features. The additional series from RCN will help further characterize the natural history of this rare disease and also summarize the treatment experiences (which often involve chemotherapy and radiation) across different institutions.

Future research directions and closing remarks

The future research directions include involving more resident physicians and junior faculty members globally in the participation of RCN projects and also its leadership roles. More promotions will be performed using social network tools such as Facebook (B.

Gutiérrez García). We will also expand our presence by presenting more RCN abstracts to ESTRO, ASTRO, and other oncologic conferences globally, while also generating quality papers in highly impactful oncologic journals. We are also looking for opportunities to expand our professional network and collaborate with other corporate groups and institutions,[5,7] comprising increased efforts from other continents such as Asia (including Taiwan) and also Australia. Within the context of RCN, the evolving challenges and issues related to multi-institutional research have been previously discussed.[1] The future of the RCN group remains bright and prosperous, as we continue to refine and improve the roles of radiation and also chemoradiation therapies in the management of rare cancers throughout the world.

The *Third International Symposium of the Rare Cancer Network* will be held in Paris, France in the spring of 2016.

References

1. Ozsahin M, Mirimanoff RO, Thariat J, et al. The rare cancer network: ongoing studies and future strategy. Rare Tumors 2014;6:5465.
2. Mirimanoff RO, Ozsahin M, Thariat J, et al. History of the rare cancer network and past research. Rare Tumors 2014;6:5462.
3. Patel A, Ozsahin M, Mirimanoff RO, et al. The Rare Cancer Network: achievements from 1993 to 2012. Rare Tumors 2012 ;4:e35.
4. Sio TT, Paredes M, Uzair C. Neurological manifestation of colonic adenocarcinoma. Rare Tumors 2012;4:e32.
5. Thariat J, Schouman T, Brouchet A, et al. Osteosarcomas of the mandible: multidisciplinary management of a rare tumor of the young adult a cooperative study of the GSF-GETO, Rare Cancer Network, GETTEC/REFCOR and SFCE. Ann Oncol 2013;24:824-31.
6. Sio TT, Vu CC, Sohawon S, et al. Extraskeletal osteosarcoma: an international Rare Cancer Network Study. Am J Clin Oncol 2014;7:7.
7. Weber DC, Wang Y, Miller R, et al. Long-term outcome of patients with spinal myxopapillary ependymoma: treatment results from the MD Anderson Cancer Center and institutions from the Rare Cancer Network. Neuro Oncol 2015;17:588-95.
8. Pasquier D, Barney B, Sundar S, et al. Small-cell carcinoma of the urinary bladder: a retrospective, multicenter Rare Cancer Network study of 107 patients. Int J Radiat Oncol Biol Phys 2015;92:904-10.
9. Schick U, Pusztaszeri M, Betz M, et al. Adenosquamous carcinoma of the head and neck: report of 20 cases and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol 2013;116:313-20.
10. Mirimanoff RO, Thariat J, Belkacemi Y, et al. RCN, Rare Cancer Network. Bull Cancer 2014;101:778-9.
11. Cerda T, Sun XS, Vignot S, et al. A rationale for chemoradiation (vs radiotherapy) in salivary gland cancers? On behalf of the REFCOR (French rare head and neck cancer network). Crit Rev Oncol Hematol 2014;91:142-58.
12. Chen AM, Grekin RC, Garcia J, et al. Radiation therapy for cutaneous squamous cell carcinoma involving the parotid area lymph nodes: dose and volume considerations. Int J Radiat Oncol Biol Phys 2007;69:1377-80.
13. Tanvetyanon T, Qin D, Padhya T, et al. Outcomes of postoperative concurrent chemoradiotherapy for locally advanced major salivary gland carcinoma. Arch Otolaryngol Head Neck Surg 2009;135:687-92.
14. Cooper JS, Pajak TF, Forastiere AA, et al. Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. N Engl J Med 2004;350:1937-44.
15. Bernier J, Domenge C, Ozsahin M, et al. Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. N Engl J Med 2004;350:1945-52.
16. Nelson RA, Guye ML, Luu T, Lai LL. Survival outcomes of metaplastic breast cancer patients: results from a US population-based analysis. Ann Surg Oncol 2015;22:24-31.
17. Yu JI, Choi DH, Huh SJ, et al. Unique characteristics and failure patterns of metaplastic breast cancer in contrast to invasive ductal carcinoma: a retrospective multicenter case-control study (KROG 13-07). Clin Breast Cancer 2015;15:12.
18. Howard JE, Dwivedi RC, Masterson L, Jani P, Langerhans cell sarcoma: a systematic review. Cancer Treat Rev 2015;41:320-331.
19. Chen F, Huang M, Xu Y, et al. Primary tracheal adenoid cystic carcinoma: adjuvant treatment outcome. Int J Clin Oncol 2014;21:21.
20. Nouraei SM, Middleton SE, Nouraei SA, et al. Management and prognosis of primary tracheal cancer: a national analysis. Laryngoscope 2014;124:145-50.
21. Gaissert HA, Grillo HC, Shadmehr MB, et al. Long-term survival after resection of primary adenoid cystic and squamous cell carcinoma of the trachea and carina. Ann Thorac Surg 2004;78:1889-96.
22. Jung TY, Yoon MS, Kim YH, et al. Gliomatosis cerebri having a poor performance status without recurrence after radiotherapy: a single institutional experience. Clin Neurol Neurosurg 2015;130:1-5.
23. Perkins GH, Schomer DF, Fuller GN, et al. Gliomatosis cerebri: improved outcome with radiotherapy. Int J Radiat Oncol Biol Phys 2003;56:1137-46.
24. Applebaum MA, Worch J, Matthay KK, et al. Clinical features and outcomes in patients with extraskeletal Ewing sarcoma. Cancer 2011;117:3027-32.
25. Tao HT, Hu Y, Wang JL, et al. Extraskeletal Ewing sarcomas in late adolescence and adults: a study of 37 patients. Asian Pac J Cancer Prev 2013;14:2967-71.
26. Zang J, Li C, Luo SQ, et al. Early radiotherapy has an essential role for improving survival in patients with stage I-II nasal-type of NK/T cell lymphoma treated with L-asparaginase-containing chemotherapy-a single institution experience. Ann Hematol 2015;94:583-91.
27. Yamaguchi M, Tobinai K, Oguchi M, et al. Phase I/II study of concurrent chemoradiotherapy for localized nasal natural killer/T-cell lymphoma: Japan Clinical Oncology Group Study JCOG0211. J Clin Oncol 2009;27:5594-600.
28. Deng T, Zhang C, Zhang X, et al. Treatment outcome of radiotherapy alone versus radiochemotherapy in IE/IIE extranodal nasal-type natural killer/T cell lymphoma: a meta-analysis. PLoS One 2014;9: e106577.
29. Castle KO, Guadagnolo BA, Tsai CJ, et al. Dermatofibrosarcoma protuberans: long-term outcomes of 53 patients treated with conservative surgery and radiation therapy. Int J Radiat Oncol Biol Phys 2013;86: 585-90.
30. Barani IJ, Raleigh DR, Larson D. The management of central neurocytoma: radiotherapy. Neurosurg Clin N Am 2015;26:45-56.
31. Hassoun J, Gambarelli D, Grisoli F, et al. Central neurocytoma. An electron-microscopic study of two cases. Acta Neuropathol 1982;56:151-6.
32. Leenstra JL, Rodriguez FJ, Frechette CM, et al. Central neurocytoma: management recommendations based on a 35-year experience. Int J Radiat Oncol Biol Phys 2007;67:1145-54.
33. Jeanneret-Sozzi W, Taghian A, Epelbaum R, et al. Primary breast lymphoma: patient profile, outcome and prognostic factors. A multicentre Rare Cancer Network study. BMC Cancer 2008;8:1471-2407.
34. Martinelli G, Ryan G, Seymour JF, et al. Primary follicular and marginal-zone lymphoma of the breast: clinical features, prognostic factors and outcome: a study by the International Extranodal Lymphoma Study Group. Ann Oncol 2009;20:1993-9.