

How is the international Sarcoma/GIST Expert community organized?

Initiatives – Networks/Working Groups – Conferences – EU Activities

Peter Hohenberger

**Div. of Surgical Oncology & Thoracic Surgery
Mannheim University Medical Center
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**WORLD
SARCOMA
NETWORK**

The World Sarcoma Network gathers top level opinion leaders institutions and high added valued funders.

Beside this core partnership, key stakeholders partners like Patient Advocacy Groups and Industry are regularly contacted as advisor or collaborator.

World Sarcoma Network opportunities

- An **unprecedented network** among academics, industry and patient advocacy groups. WSN members are among the most experienced and active clinical investigators in the sarcoma field.
- A global collaboration of outstanding cancer centers and industry partners from all parts of the world **to address the challenge of rarity** in very rare sarcoma subtypes
- The opportunity to **impact the strategies of pharmaceutical and biotechnology companies** to achieve faster and better clinical trials in rare cancer types
- A clear and demonstrated will to overcome barriers in communication between the pharmaceutical industry and academia
- A combination of experienced clinical trial centers, an appropriate panel of technologies and the access to platforms and qualified staff worldwide
- **Innovative clinical trials** involving different pharmaceutical companies
- Standardization of best practices in the area of **international clinical trial development**

CTOS 2018 ANNUAL MEETING

14–17 November 2018 | Rome, Italy



Supported by Eli Lilly and Company.

Eli Lilly and Company has not influenced the content of this publication



Letter from Prof Jean Yves-Blay



Dear Colleagues

It is my pleasure to present this WSN slide set which has been designed to highlight and summarise key findings in sarcoma from the major congresses in 2018. This slide set specifically focuses on the **CTOS 2018 Annual Meeting**.

The area of clinical research in oncology is a challenging and ever changing environment. Within this environment, we all value access to scientific data and research that helps to educate and inspire further advancements in our roles as scientists, clinicians and educators. I hope you find this review of the latest developments in sarcoma of benefit to you in your practice.

I would like to thank our WSN members Drs Piotr Rutkowski, Claudia Valverde, Eva Wardelmann and Axel Le Cesne for their roles as Editors – for prioritising abstracts and reviewing slide content. The slide set you see before you would not be possible without their commitment and hard work.

Finally, we are also very grateful to Lilly Oncology for their financial, administrative and logistical support in the realisation of this activity.

Yours sincerely,
Jean Yves-Blay
WSN Chairman of the Board

WSN Medical Oncology Slide Deck Editors 2018



Piotr Rutkowski

Maria Skłodowska-Curie Institute – Oncology Center, Warsaw, Poland



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Eva Wardelmann

Gerhard Domagk Institute of Pathology, Münster, Germany



Axel Le Cesne

Gustave Roussy, Villejuif, Paris, France

Contents

- Soft tissue sarcoma.....
- GIST.....
- Osteosarcoma and chondrosarcoma.....
- Rarer sarcomas and desmoid tumors.....



WORLD
SARCOMA
NETWORK

20th WSN Meeting

June 2nd 2018

6:00pm - 8:00pm

The Blackstone, Chicago, IL

Agenda

- **Sarcoma of the Year**
 - Former SoY follow up
 - ES: publication
 - 2018: MDM2/CDK4 Mutated sarcoma: Intimal Sarcoma
 - Initiatives/projects feedback
 - S Stacchiotti ASCO poster, CTOS 2017 Presentation in Sarcoma of the Year Session
 - 2019: DSRCT
- **WSN Projects**
 - Trials
 - Collaborative projects
 - ImmunoSarc (LSSI-ICG) (**B Maki, JY Blay**)
 - ISKS (**D Thomas**)
 - EuroJoss (Sarcoma of the year 2014 followup) (**W Van de Graaf**)
 - Meta-analysis on adjuvant Imatinib studies in GIST (**M VonMehren**)
 - Rare Sarcoma Prospective registry: SoY (**S Stacchiotti**)
 - REgistries (**JY Blay**)
 - WSN Retrospective combined control arm data from the multiple Phase III trials in sarcomas: the Data Sphere project example (**S George**)
 - WSN-SARC database for de-identified reporting of mutation testing and the tested drugs : medical decision made based on genomics (**R Maki**)
 - GIST Frontline trial (**B Tap**)
 - Immune infiltrate in Sarcoma (**J Desai**)
 - RareCan1 (**B Hassan**)
 - ICP and immune infiltrat (**A Dufresne**)
- **GIST Task Force**
 - Non-consensus paper
- **Partnerships**
 - Lilly



WSN in brief

- Launched in 2010 (Paris)
- 38 members (10 initially)
- Involving 15 National Groups (5 initially)
- 6th year with highlighted topic
 - Uterine Sarcomas 2013
 - Synovial Sarcomas 2014
 - Angiosarcomas 2015
 - Alveolar Soft Part Sarcoma 2016
 - Epithelioid Sarcoma 2017
 - Intima Sarcoma (MDM2/CDK4 Mutated Sarcoma) 2018
 - DSRCT 2019
- Yearly labeled session in CTOS
- 2 meetings per year (90% mean attendance rate)
- New sub committee (GIST Task Force, Immuno)



SoY follow up

Sarcoma of the Year	Follow up activities
Uterine Sarcomas 2013	
Synovial Sarcomas 2014	EuroJoSS
Angiosarcomas 2015	
Alveolar Soft Part Sarcoma 2016	
Epithelioid Sarcoma 2017	S Stacchiotti registry + follow up project Contact Epysime (S Patel/G Demetri) : pathologist classification/review and molecular analysis Paper: "Anthracycline, gemcitabine and pazopanib in epithelioid sarcoma: results of a retrospective multi-institutional case series" JAMA Oncolog
Intima Sarcoma (MDM2/CDK4 Mutated Sarcoma) 2018	S Stacchiotti registry
DSRCT 2019	

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SoY action plan

- CTOS session
 - WSN abstract submission
 - WSN introductory pending questions
- Retrospective study/registry
- Sarcoma Central
 - 10 cases/WSN institution
- Key question editorial
 - Clinical Sarcoma Research



SoY follow up table

Year	Sarcoma type	CTOS session	CTOS abstract (Y/N, Name)	Retro Study	Sarcom Central Case reported (Y/N, Numbers)	Key Questions	Editorial published	Publication
2013	US							
2014	SS	Y						
2015	AS	Y						
2016	ASPS	Y						
2017	ES	Y	Y, S Stacchiotti	Y	N	Classification, molecular analysis		"Anthracycline, gemcitabine and pazopanib in epithelioid sarcoma: results of a retrospective multi-institutional case series" JAMA Oncology
2018	IS (MDM2/CDK4)			Y				
2019	DSRCT							

Sarcoma of the Year

2018: MDM2/CDK4 Mutated sarcoma: Intimal sarcoma

Science on board, neglected histology, share will for data collection

- **CTOS Session**
 - WSN contribution :
 - Key questions to be addressed
 - Abstract
- **Retrospective study/registry** (S Stacchiotti)
 - Medical Treatment of MDM2 Positive Intimal Sarcoma: **on going**
- **Other actions?**
 - Sarcoma Central contribution
 - 10 cases/WSN institution
 - **Key question editorial** (which journal?)
 - Sarcoma Foundation of America
 - Clinical Sarcoma Research



SoY 2018 key questions

- Pathological classification
- Systemic treatments?
- Targeting MDM2/CDK4



Sarcoma of the Year 2019

- **DSRCT**
 - **Pediatricians?**
 - **Key topics to be proposed**
 - **Surgery/HIPEC**
 - **Immunotherapy**
 - **Targeted treatments**



Clinical Studies

ImadGIST (**JY Blay**)

SSGXXII (**KS Hall**)

Collaborative projects

ImmunoSarc (LSSI-ICG) (**B Maki, JY Blay**)

ISKs (**D Thomas**)

EuroJoss (Sarcoma of the year 2014 followup) (**W Van de Graaf**)

Meta-analysis on adjuvant Imatinib studies in GIST (**M VonMehren**)

Rare Sarcoma Prospective registry: Follow-up (**S Stacchiotti**)

Registries (**JY Blay**)

WSN Retrospective combined control arm data from the multiple Phase III trials in sarcomas: the Data Sphere project example (**S George**)

WSN-SARC database for de-identified reporting of mutation testing and the tested drugs : medical decision made based on genomics (**R Maki**)

GIST Frontline trial (**B Tap**)

Immune infiltrate in Sarcoma (**J Desai**)

RareCan1 (**B Hassan**)

ICP and immune infiltrat (**A Dufresne**)

J Trent, P Hohenberger, B Tap, J Desai

GIST FRONTLINE TRIALS



Action plan

- 2 working groups
 - Circulating DNA (J Trent, P Hohenberger)
 - NGS Harmonisation (B Tap, J Desai)



J DESAI, B TAP, B MAKI

IMMUNE INFILTRATE IN SARCOMA



B Hassan

RARECAN1



**Preliminary Concept
(EORTC Board approval July 2017)**

**EORTC Project 1739
RareCan1: Biomarker stratified open label
Phase II trial of multiple single agents in rare
cancers of unmet need.**

Bass Hassan, Peter Dutton, Saskia Litiere, Angélique Deleersnijder,
Sandrine Marreaud, Julien Peron, Peny Zacharopoulou

RareCan1: main drivers

- Need for inclusion of rare cancers in early drug development
- Need to improve potential for license (orphan) indications for Rare Cancers (ICD-10)
- Need for cost effective discovery of signals of activity

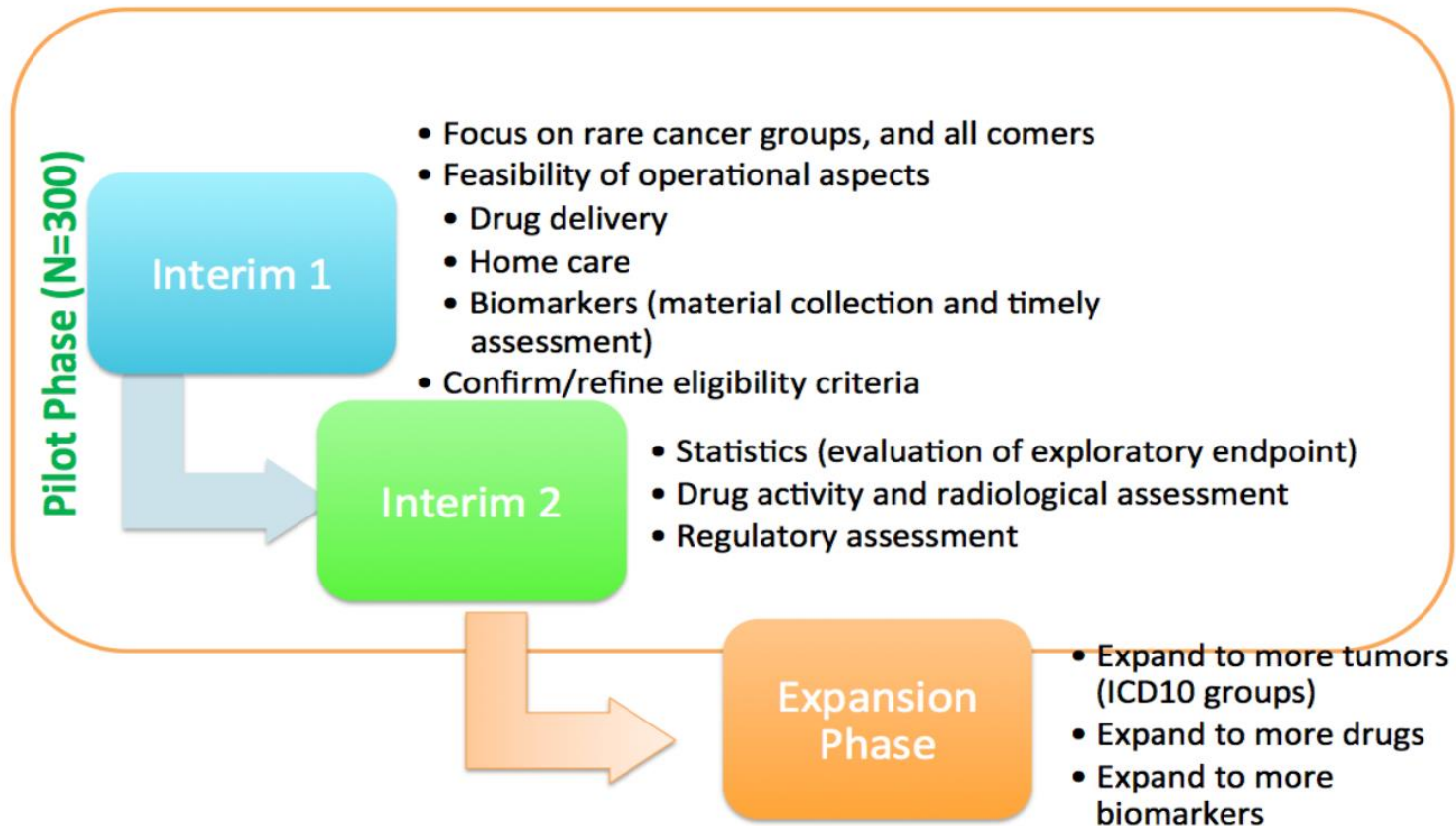
RareCan1 scientific rationale

- Target generic targets of cancer in all rare cancer ICD-10 types (basket study for angiogenesis, epigenetic, cell cycle, immune checkpoints)
- Permissive trial recruitment based on drug resistance biomarker selection (enhancing recruitment opportunity)
- Quantification of response based on the individual patient, leading to tumour growth index validation
- Quality of life secondary validation (EORTC)
- Using multiple agents, sequentially administered (3-4 agents), enhancing patient opportunity
- Consideration of access and trial delivery at home

Pilot Phase

- Confirm the operational feasibility of the model
- Evaluate whether alternative endpoints than those based on RECIST could be suitable endpoints for the screening of drug activity

Pilot Phase

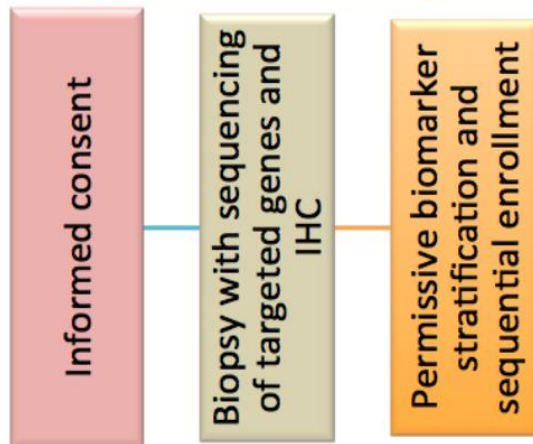


Study Design- Pilot Phase

- Patients with documented progressive disease (within 3 months)
- Primary endpoint: clinical benefit rate (CR, PR or SD) according to RECIST
- 2-step design: min number of CR, PR or SD in order to proceed to step 2

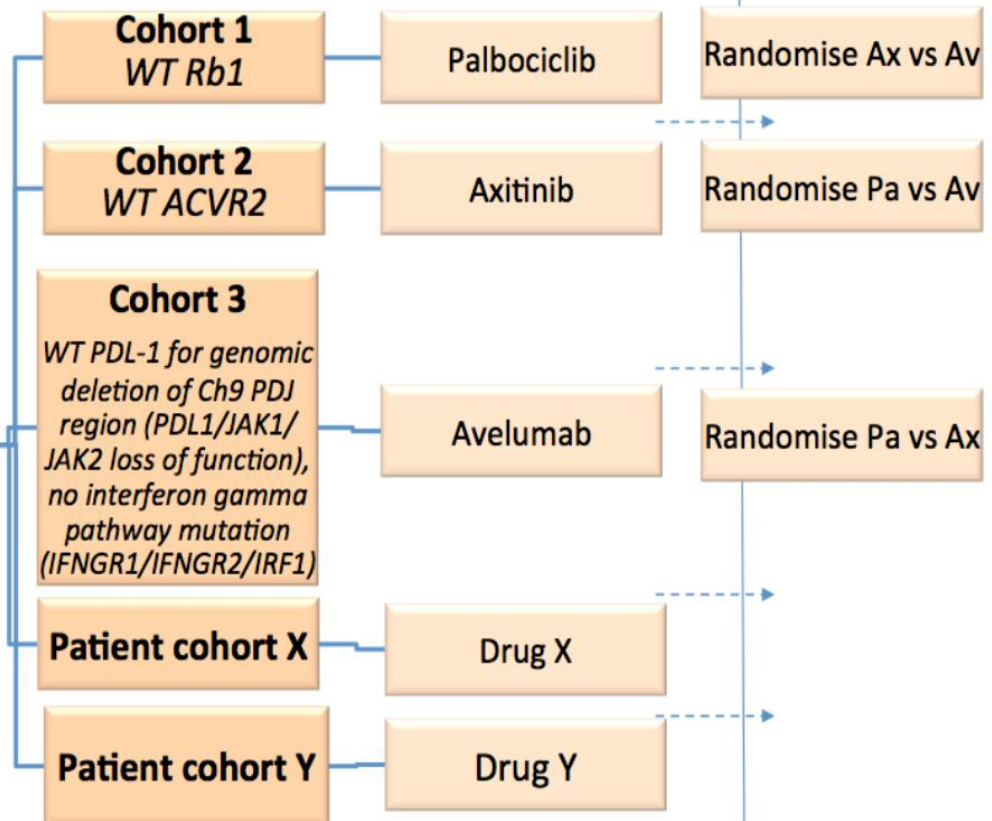
**Patients with rare cancers
ICD-10 (20-200 groups):**
- Progressed over previous
12-16 weeks
- Exhausted conventional
treatments

Max 4-8 weeks



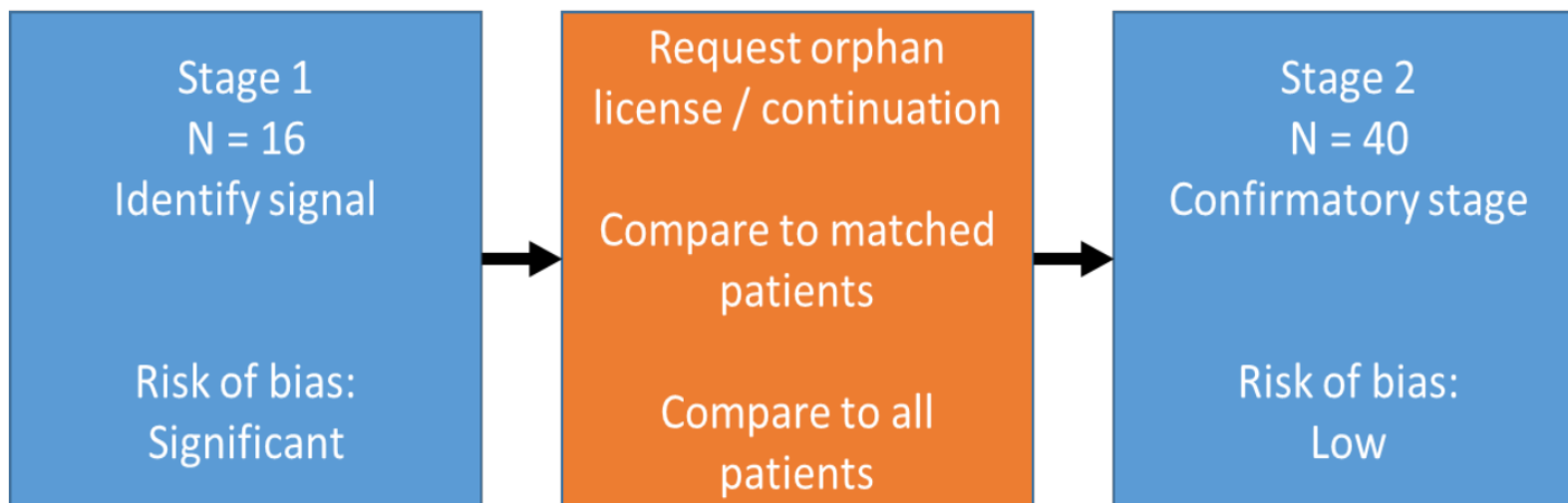
In the pilot phase, we will focus first on a smaller patient population

**Examples of agents in
Pilot Phase 300 patients**



Scans every at 6 & 12 weeks

Expansion Phase Statistical two stage design



To keep the sample size down when the treatment is ineffective in an ICD10 group stage 1 will consist of sub-stages.

These are designed to identify a signal initially and then build up some evidence of efficacy in the ICD10 group prior to requesting continuation to stage 2, whilst discarding ICD10 groups when little to no signal is observed.

Secondary Evaluation of Tumor Growth Rate (TGR)

- Heterogeneity in patterns of tumour growth of patients participating to the study will represent a challenge in response assessment
- Key aim: explore an alternative approach using the patient as his/her own control
- TGR definition: Percentage of tumor growth per unit time, between two CT/MRI evaluation every 4-8 weeks
- Pilot Phase data motivated by Clarinet Study:
 - Develop realistic simulation of tumour growth patterns
 - Test design decisions on a range of realistic scenarios.
 - Compare disease prevalence of subgroups to historical data.

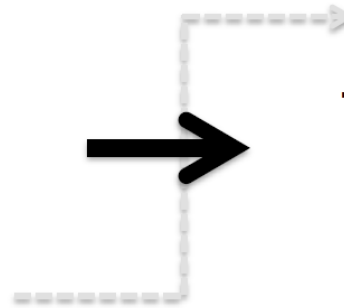
Exploratory analysis of tumor growth rate (TGR) with lanreotide depot/autogel (LAN) in patients (pts) with neuroendocrine tumors (NETs) from the CLARINET study. Martyn E. Caplin, Marianne E. Pavel, Philippe Ruzniewski, Nilani Liyanage, Christine Massien, and Clarisse Dromain *Journal of Clinical Oncology* 2016 34:15_suppl, 4096-4096

<http://www.neaeope.gr/wp-content/uploads/Ruzniewski.pdf>

End points

- **Pilot phase**

- **Primary endpoint:** clinical benefit rate according to RECIST
- **Secondary endpoint:** tumor growth rate – to be defined during the discovery phase



- **Expansion Phase***

- **Primary endpoint:** tumor growth rate
- **Secondary endpoint:** clinical benefit rate according to RECIST
- Select and validate the top ICD10s

- **Other Secondary Endpoints**

- Quality of Life
- Survival
- Safety

*If sufficient evidence available from pilot phase

Trial Governance

- This trial will be conducted in consultation with a Trial Steering Committee. The Study Steering Committee will be chaired by the EORTC study chairman and comprises:
- Study Coordinators representing the **EORTC** and **EURACAN** network
- Representative persons from the study team (EORTC and Oxford University)
- Consulting biology and therapeutic-area experts
- The Study Steering Committee will provide guidance for the treatment of each tumor type depending on the drugs under investigation, on the assessment of biomarkers, operational aspects of the trial, and make recommendations to the study team. The study steering committee will also act as a molecular tumour board for the study.



Statistical Model-*setting the bar high*

- CR+PR+SD = Responder
- PD = Non-Responder
- Based on baseline disease control rate of 20%

$$H_0: p \leq 0.2$$

$$H_1: p > 0.2 \text{ power tested at } p=0.5/0.6/0.7$$

Design Strategy

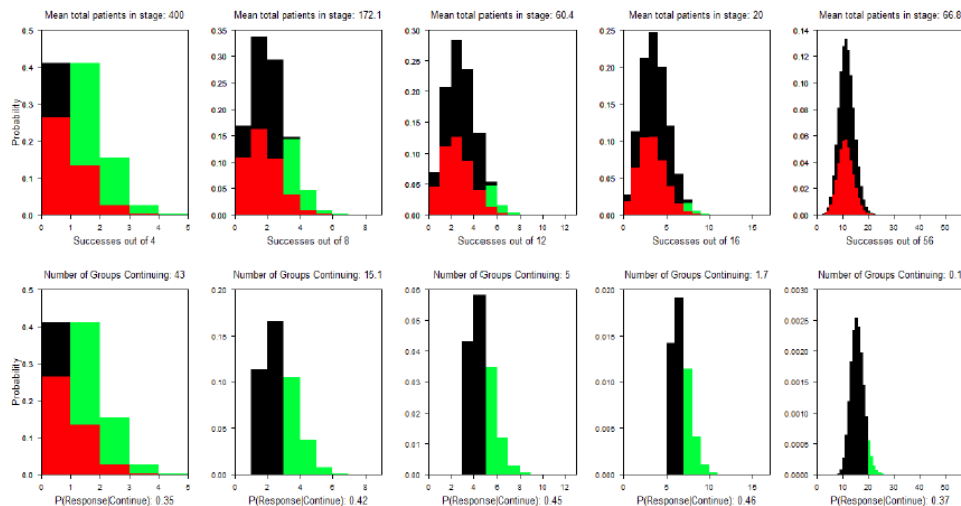
The overall power increases to 89.3% for an ICD-10 group with a 60% disease control rate and 97.6% power with a 70% disease control rate.

Table 12: The probability of passing each stage given a true probability.

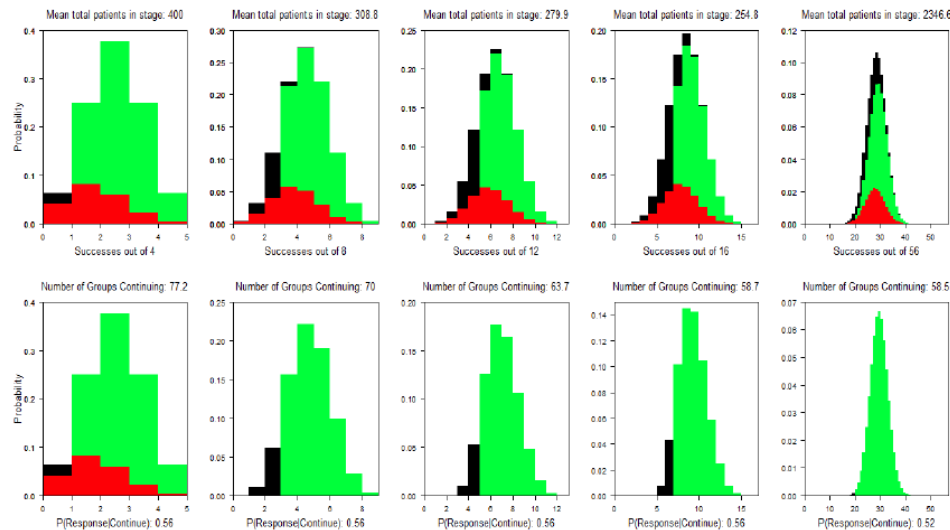
True probability	Stage 1				Stage 2	Mean sample size
	4	8	12	16	56	
0.1	0.344	0.036	0.004	<0.001	<0.001	5.55
0.2	0.590	0.192	0.062	0.020	0.001	8.19
0.5	0.938	0.836	0.756	0.693	0.691	41.84
0.6	0.974	0.938	0.912	0.893	0.893	50.99
0.7	0.992	0.983	0.979	0.976	0.976	54.86

Probability distribution of trial at each analysis point if the true probability of response is 0.2, including the global stopping rule (red) with a global response probability of 0.1 and a 1% probability of recruiting a patient to this ICD10 group

P=0.2



P=0.5

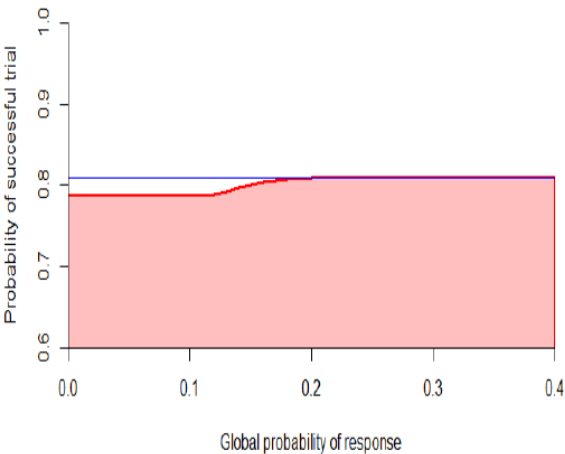


Stopping model validation

Trabectedin L sarcoma (C49)

1.4 per 100,000 (1.8%)

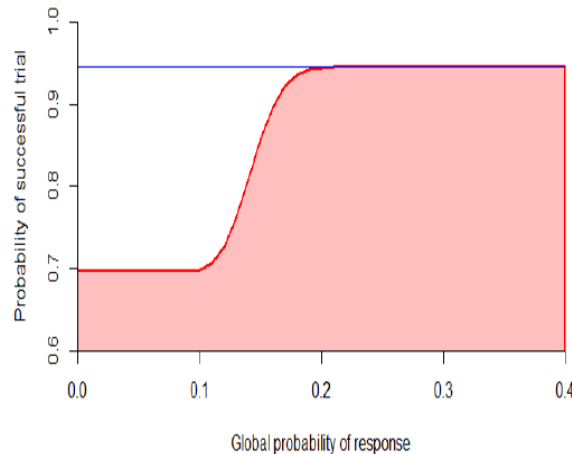
PFS @ 3m 56%



Vorinostat cTcell NHL (C84)

0.5 per 100,000 (0.65%)

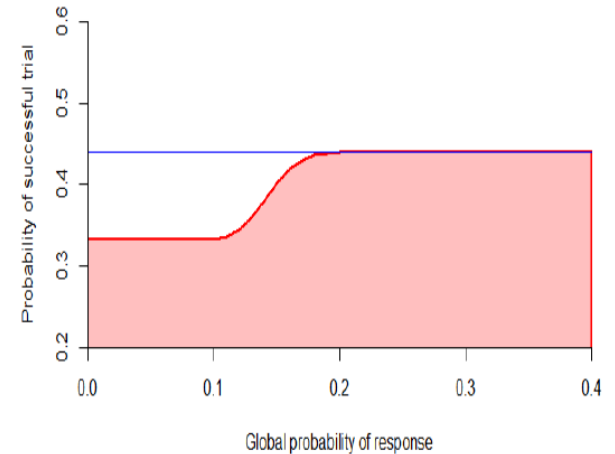
PFS @ 3m 65%



Avelumab Merkel cell (C4A)

0.6 per 100,000 (0.79%)

PFS @ 3m 42%



Key Questions/ Discussion points

- Identification of (single) agents suitable for the concept
- Initial interest from biotech as multiple agents tested in multiple indications- cost effective
- Sarcoma as a major component

A Dufresne

ICP&IMMUNE INFILTRATE



Compared descriptive analysis of immunologic landscape in soft tissue sarcoma and GIST

A. Dufresne MD PhD

ASCO 2018 #11517

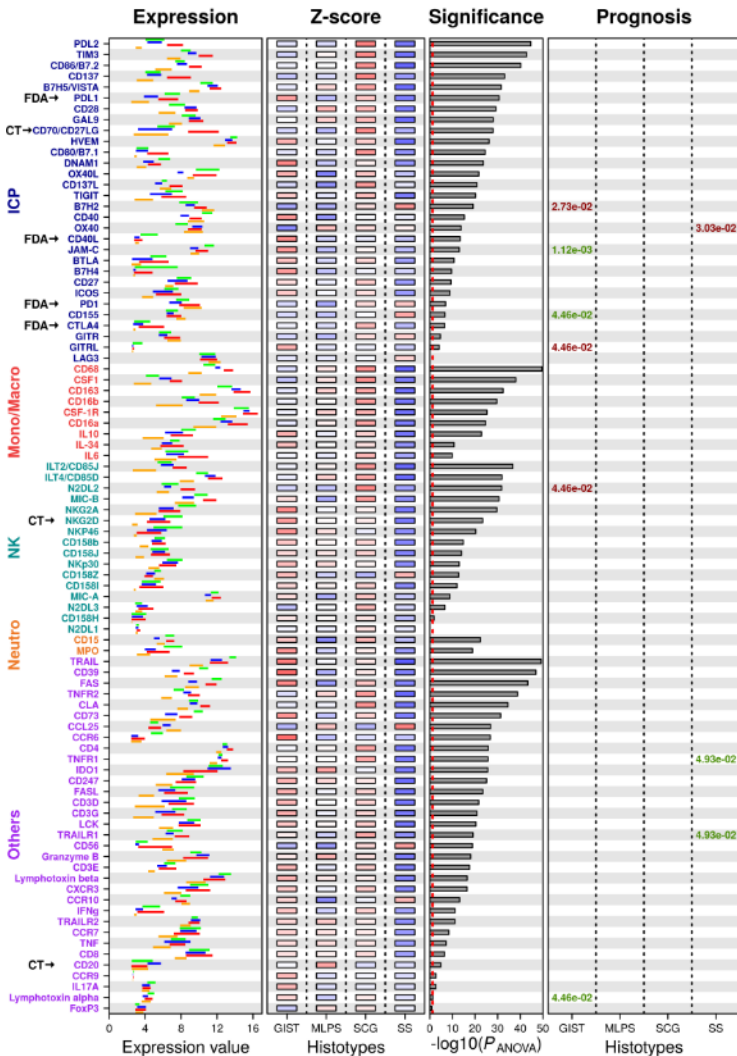
Rationale

- Development of immune therapy in sarcoma faces a high heterogeneity (different histological subtypes, molecular subtypes)
- Limited response rates in sarcomas of single agent PD1/PDL1 Ab
- Objective of this study: to provide a description of immunologic landscape of soft tissue sarcoma and GIST

Material and methods

- All patients included had soft tissue sarcoma (STS) and were managed in expert centers of the French Sarcoma Group.
- Tumor samples obtained from surgical resection of the primary tumor (treatment naïve).
- Whole cohort 255 samples with 87 STS with complex genetics (SCG),
60 GIST,
58 synovial sarcomas (SS),
50 myxoid liposarcomas (MLPS).
- Gene expression of 90 immune check point (ICP) and membrane markers (MM) of immune cells performed using **Agilent Whole Human Genome Microarrays**
- Correlation to pathological diagnosis and survival.
- CIBERSORT signature studied the distribution of immune cell population.

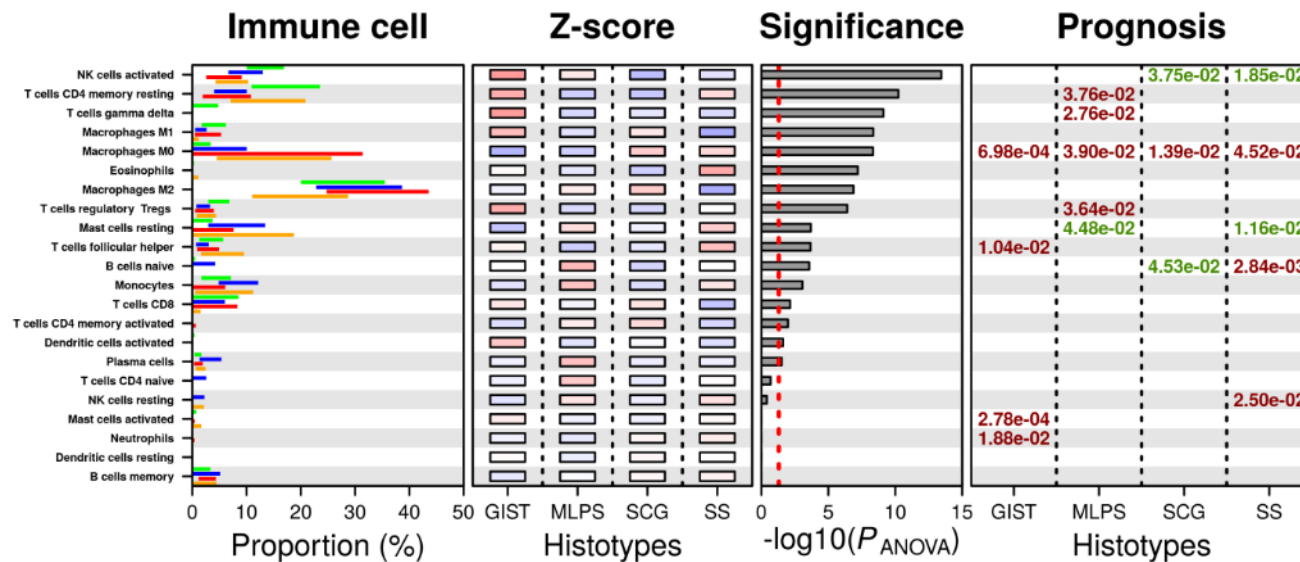
2/ Expression level of 90 ICP/MM across each sarcoma subtype



- Substantial level of expression of the majority of the ICP/MM across the 4 sarcoma sub types. Highest levels of expression reported for CSF-1R, CD163, HVEM, CD4, CD16a, and TNFR1.
 - Important variation of expression level of ICP/MM across the different sarcoma subtypes (“Significance”).
 - When differential expression level between the 4 sarcoma subtypes, lowest expression reported for SS and highest expression reported for GIST and SCG (Z-score).
 - Prognostic impact of each gene expression on metastasis-free survival in each subtype:
 - B7H2, GITRL and N2DL2 of poor prognosis in GIST,
 - CD155 and JAM-C of good prognosis in GIST,
 - OX40 of poor prognosis in SS,
 - TNFR1 and TRAILR1 of good prognosis in SS.
- **Important heterogeneity of expression of each of the 90 ICP/MM genes observed across sarcoma subtypes, and across patients within the same tumor type.**

3/ CIBERSORT signature and prognostic impact

- NK cells activated of good prognosis in SCG and SS.
- M0 macrophages are of poor prognosis in all sarcoma subtypes.
- In MLPS, T cell infiltration with T cells CD4 memory resting, T cells gamma delta and Treg were of poor prognosis.
- Mast cells resting representation is of poor prognosis in SS and good prognosis in SCG.



Conclusion

- High heterogeneity of immune profile in GIST and sarcoma subtypes
- Need for better understanding of immune environment in each sub types to design specific clinical trials of immune therapy



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GIST Task Force Project

- Non-consensus paper (**P Reichardt**)

Non-consensus/controversies in GIST paper:

Topics:

I ADJUVANT THERAPY

- Patient selection
- Impact of mutational status
- Dosing Exon 9
- KIT/PDGFR Wild type / Exotic mutations
- Duration
- Rupture

II ROLE OF SURGERY IN METASTATIC DISEASE

III TECHNICAL ISSUES OF MUTATIONAL TESTINGS (NGS)

- Who?
- When? Primary? Progression?

IV LOCAL TREATMENT IN METASTATIC GIST (Including radiation therapy)

- The role of local treatment
- Which local treatment?
- What to do in bleeding?
- What to do with liver mets?
- What to do with bone mets?

V WILD TYPE GIST

- Testing issues
- Definition: what is wild type? When allowed to say Wild type?
- Classification
- Advanced disease
- Localized disease (Adjuvant setting)

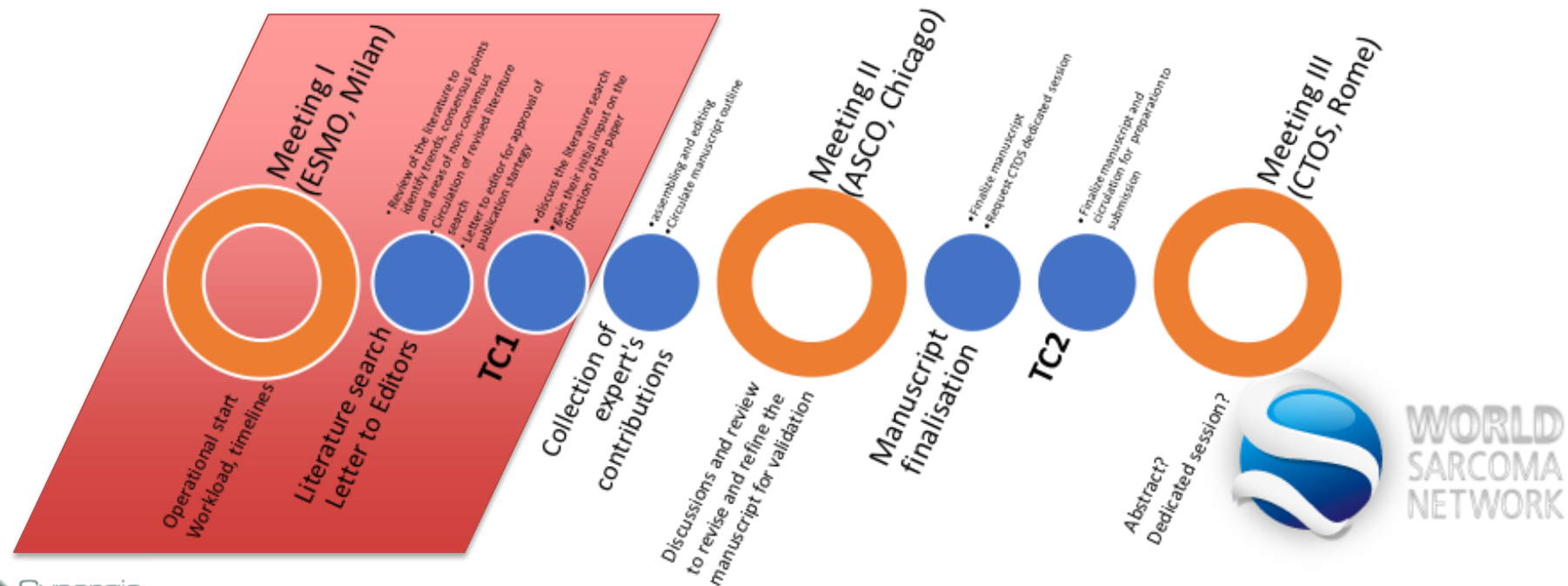


Non-consensus/controversies in GIST paper:

Editorial board

- Adjuvant Therapy: P. Reichardt, M Von Mehren/R Maki
- Role of surgery in metastatic disease: P. Rutkowski, T Nishida
- Technical issues of mutational testing (NGS): E. Wardelmann, C Antonescu
- Local treatment in metastatic GIST: R. Haas, C. Swallow
- Wild type GIST: J. Trent, Dr. Kang/M Chacon

- Medical writer: Estelle Artzner-Lecoite



Lilly

Sarcoma Highlight Slide-decks

- Outcome 2017
 - ASCO, ESMO & CTOS Slide deck are available on WSN website and Sarcoma Central



- 2018 objectives
 - 3 new slide deck (ASCO, ESMO and CTOS)
 - Editorial board presentation of the annual best-of

Lilly

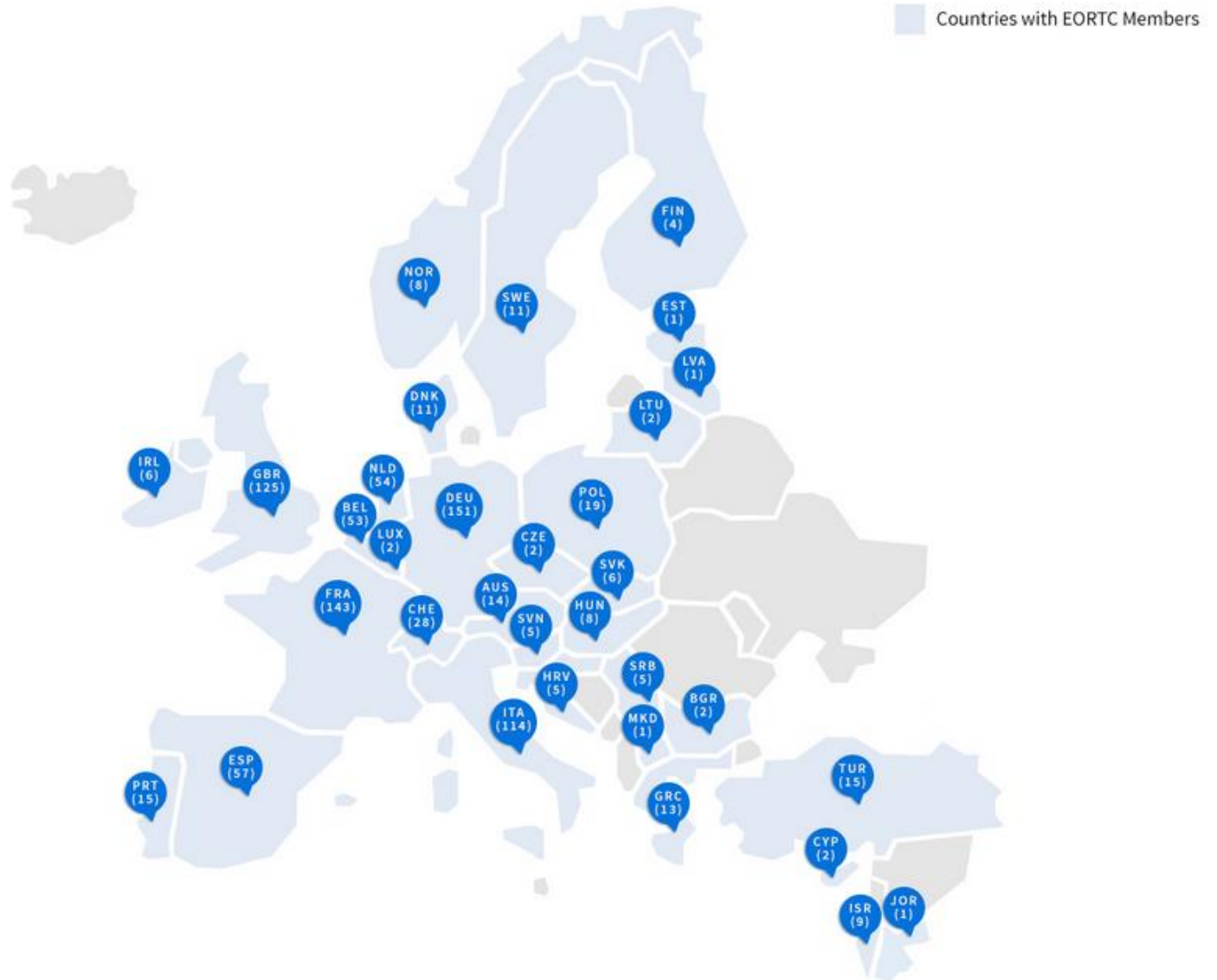


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AMERICA

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SOFT TISSUE & BONE

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Related News

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Largest trial ever performed in alveolar soft part sarcoma: results published

8 DEC

Pazopanib improves progression-free survival without impairing health-related quality of life

6 JUL

EORTC and Univ Oxford launch EUROSARC trial for patients with advanced Ewing Sarcoma

8 JUN

Recruiting Clinical Trials

[ALL CLINICAL TRIALS IN THIS RESEARCH FIELD >](#)

PHASE 2

A randomized double-blind phase II study evaluating the role of maintenance therapy with cabozantinib in High Grade Uterine Sarcoma (HGUTS) after stabilization or response to doxorubicin +/- ifosfamide following surgery or in metastatic first line treatment

PHASE 2

Phase II trial of cabazitaxel in metastatic or inoperable locally advanced dedifferentiated liposarcoma.

PHASE 3

International Randomised Controlled Trial for the Treatment of Newly Diagnosed Ewing's Sarcoma Family of Tumours – Euro Ewing 2012

PHASE 2-3

International Randomised Controlled Trial of Chemotherapy for the treatment of recurrent and primary refractory Ewing sarcoma

PHASE 2

A phase II multicenter study comparing the efficacy of the oral angiogenesis inhibitor nintedanib with the intravenous cytotoxic compound ifosfamide for treatment of patients with advanced metastatic soft tissue sarcoma after failure of systemic non-oxazaphosphorine-based first line chemotherapy for inoperable disease "ANITA"

Main Achievements

In recent years, EORTC has been involved in a number of large practice-changing clinical trials in the field of Soft Tissue and Bone, leading to the registration of drugs to treat sarcomas including gastrointestinal stromal tumors (GIST). The following compounds were investigated within this group (STBSG):

- Imatinib for GIST [↗](#)
- Trabectedin for all types of STS
- Pazopanib for non-adipocytic STS [↗](#)
- Eribulin for liposarcomas [More information ↗](#)

Multicentre trials, with large patient numbers to influence clinical practice and address important research topics, evaluated the role of adjuvant chemotherapy in soft tissue sarcoma patients [↗](#) as well as the role of single-agent doxorubicin versus the combination of doxorubicin plus ifosfamide in advanced and/or metastatic STS patients.



FP7 EUROSARC – European Clinical Trials in Rare Sarcomas within an integrated translational trial network.

EUROSARC aims to validate novel local and systemic treatment strategies in localized phase sarcomas, and innovative targeted therapies in advanced phase sarcomas based on the scientific understanding of molecular alterations driving the tumors. Several clinical trials are involved including EORTC trial 62092-22092-STRASS A phase III randomized study of preoperative radiotherapy plus surgery versus surgery alone for patients with Retroperitoneal sarcomas.

FP7 EEC EURO EWING – International Clinical Trials to Improve Survival from Ewing Sarcoma. EEC **EURO EWING** aims to improve treatment outcomes for patients with Ewing sarcoma, a rare cancer. The program comprises two clinical trials testing different chemotherapy treatments for this rare disease: trial EORTC 1402 “International Randomised Controlled Trial for the Treatment of Newly Diagnosed Ewing’s Sarcoma Family of Tumours – Euro Ewing 2012” and trial EORTC 1403 “International Randomised Controlled Trial of Chemotherapy for the treatment of Recurrent and Primary Refractory Ewing Sarcoma – rEECur”.

European Reference Networks (ERN) for rare solid tumours (EURACAN). EURACAN is involving references centers in Europe covering ten types of rare cancers. EURACAN will improve patient cares and facilitate research in rare cancers. EORTC is providing the clinical research infrastructure. (No website available yet)



Conticabase

European sarcoma database and tumour bank

SarcomaBCB

L'ANSM suspend les essais masitinib promus par AB Science. Le GSF-GETO recommande imatinib ou sunitinib en remplacement.

[Home](#) [Account request](#) [Forgot password](#) [Tools](#) ▾

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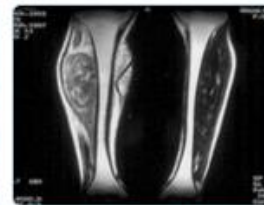
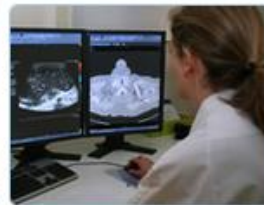
Welcome to Conticabase

The CONTICANET database and tumour bank This database contains anonymised information describing the tumour, treatment and follow-up as well as tumour sample availability and molecular biology analyses for mesenchymal tumours except GIST and bone tumours.

The tool can be used as a local center database thanks to its [rules for access](#) to patient data and material. It will be maintained and updated centrally. Please follow this [link](#) to fill the account application form.

The query tool allows users to ask questions about the overall content of the database (data dictionary) in order to evaluate the feasibility of specific collaborative studies.

We hope this database will become an important tool for increasing our knowledge on these rare tumours and for developing joint research programmes.



Content overview

Conticabase currently contains the following data :

- Patients : 20317
- metastasis : 5784
- Cell lines : 25
- Immuno-Histochemistry : 19830
- Primary tumours : 20484
- Chemotherapy lines : 9176
- Paraffins : 28435
- Molecular cytogenetics : 8771
- Local recurrences : 4879
- Samples : 28962
- Frozen tissues : 11493
- Blood samples : 1054

Last modification on 01/02/2019 19:59:44 by jean-denis.

Imagine if the best specialists from across Europe could join their efforts to tackle complex or rare medical conditions that require highly specialised healthcare and a concentration of knowledge and resources.



**THE
POWER
OF AN
IDEA**

Topics

- Recent developments in thymoma – N.Girard
- Mesothelioma : current standard practice - E.Ruffini
- Soft tissue tumors of the thorax and chest wall - W.Hartmann

- **Structural development to improve the care of Rare Cancer in Europe**
- **Guideline evaluation and creating a reference network EURACAN**



European Reference Network

for rare or low prevalence complex diseases

Network
Adult Cancers
(ERN EURACAN)

EURACAN



Melanoma Patient Network Europe

RARE SOLID ADULT CANCERS

EURACAN - Distribution of Members by Country



COUNTRIES/Towns

BELGIUM (Antwerp, Brussels, Leuven, Liège)

CZECH REPUBLIC (Brno, Prague)

DENMARK (Aarhus)

GERMANY (Berlin, Essen, Mannheim, Hamburg-Eppendorf, Marburg, Würzburg)

FINLAND (Turku)

FRANCE (Lyon, Paris, Villejuif)

HUNGARY (Budapest)

IRELAND (Dublin)

ITALY (Aviano, Bologna, Candiolo, Firenze, Genoa, Meldola, Milan, Naples, Rome, Siena, Torino, Treviso)

LITHUANIA (Kaunas)

NETHERLANDS (Amsterdam, Leiden, Maastricht, Nijmegen, Rotterdam, Gronigen)

NORWAY (Oslo)

POLAND (Warsaw)

PORTUGAL (Coimbra, Lisboa, Porto)

SPAIN (Sevilla, Barcelona)

SWEDEN (Karolinska, Uppsala)

SLOVENIA (Ljubljana)

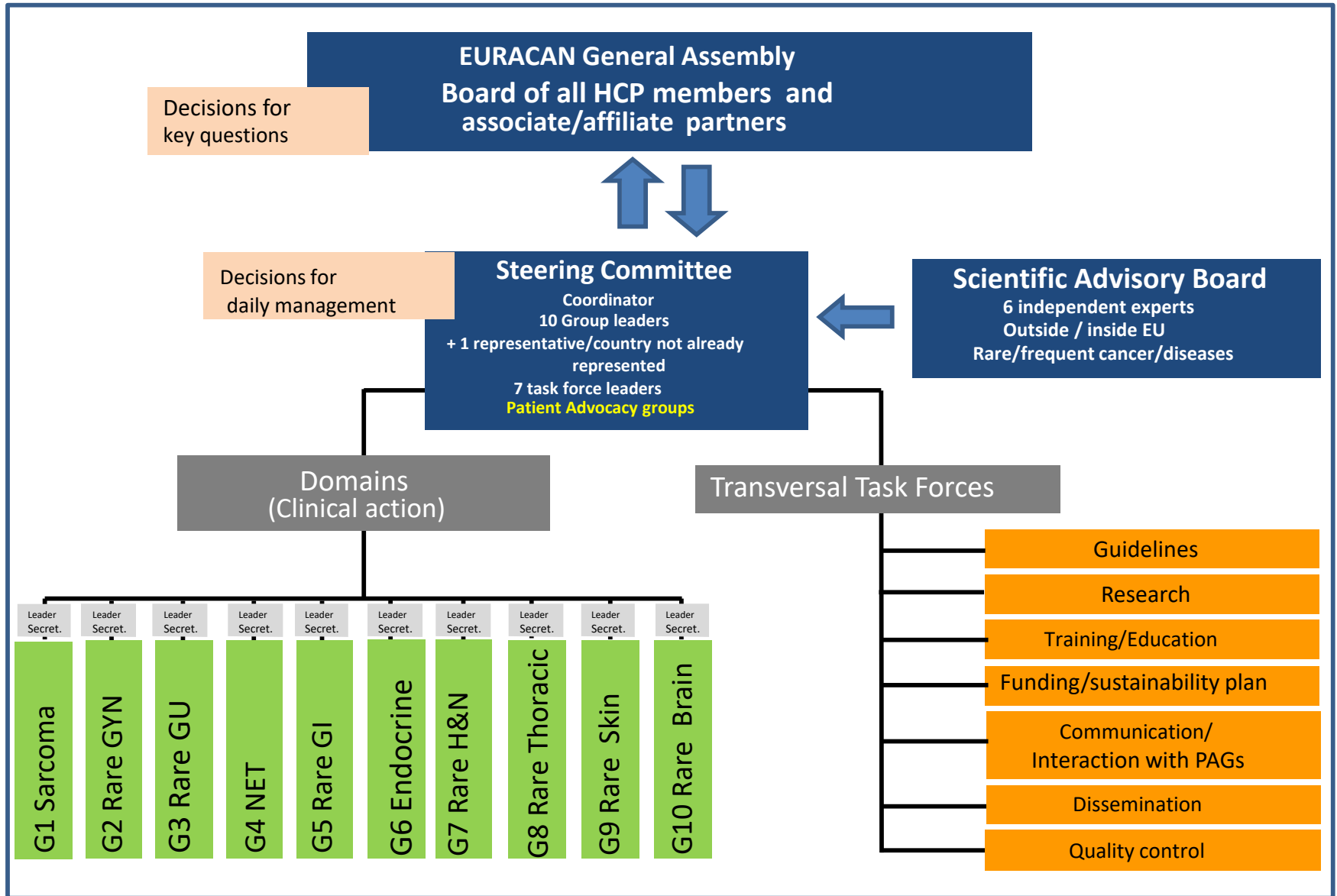
UNITED KINGDOM (Coventry, London, Oxford, Sheffield)

EURACAN - Targeted Rare Adult Cancers




- Rare adult solid cancers are grouped in 10 domains corresponding to the RARECARE classification and the ICD10
- These domains are based on pre-existing successful collaborations,
- in particular for clinical research and expert networks active in the last 10-20 years

GOVERNANCE





- **Pediatric cancers**
- **Haematologic rare neoplasms**
- **Sarcomas**
- **Rare thoracic cancers**
- **Neuroendocrine tumours**
- **Head & neck cancers**
- **Central nervous system tumours**
- **Rare female genital cancers**
- **Rare urological and male genital tumours**
- **Endocrine gland tumours**
- **Digestive rare cancers**
- **Rare skin cancers & non-cutaneous melanoma**



23%
of all
cancers

ECPC General Assembly
Friday 3 – Sunday 5 June 2016, Brussels
Advancing the rights of cancer survivors



Joint Action on Rare Cancers (JARC)

Annalisa Trama

Fondazione IRCCS Istituto Nazionale dei Tumori, Milano

JARC working packages

WP number	WP name
1	Coordination
2	Dissemination
3	Evaluation
4	Epidemiology
5	Assuring Quality
6	Clinical Trials
7	Patient empowerment and access to innovation
8	Public education
9	Childhood Cancers
10	Rare Cancer Policy

ECPC, EURORDIS

Patient empowerment and access to innovation

WP 6 Clinical practice guidelines

- Actions to assess the scenario of existing clinical practice guidelines on RCs
- To provide recommendations on how to ensure best production, dissemination and implementation of clinical practice guidelines on RCs
- at local level and within future ERNs

STATUS REPORT

WP 6: Clinical Practice Guidelines



Medizinische Fakultät Mannheim
der Universität Heidelberg

Universitätsklinikum Mannheim



WP6: Description of work

- Task 6.1 Available clinical practice guidelines at the European level on all families of rare cancers
- Task 6.2 Quality evaluation of existing clinical practice guidelines for rare cancer subtypes
- Task 6.3 Open issues about implementation of clinical practice guidelines at the local level, with special regard to their relation with local reimbursement mechanisms and to study innovative models to provide value-based rare cancer care
- Task 6.4 Solutions on how to incorporate clinical practice guidelines within ERNs.

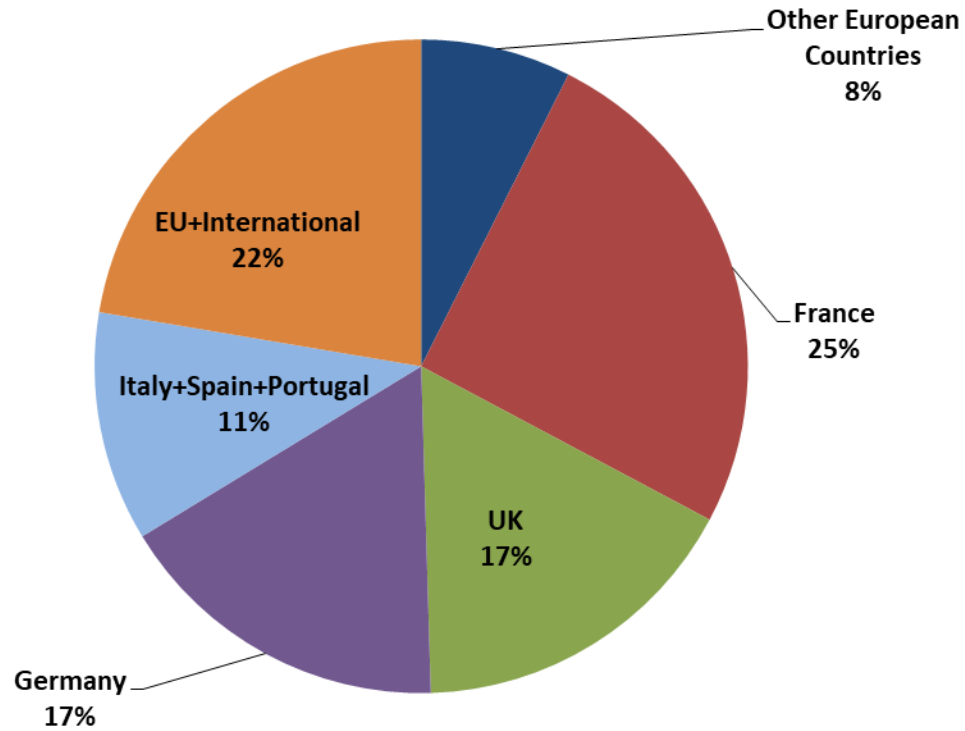
Task 6.1. Tabular representation of Guidelines Collection

COUNTRIES	CANCER FAMILY	CANCER FAMILY	CANCER FAMILY	CANCER FAMILY	CANCER FAMILY	CANCER FAMILY	CANCER FAMILY	CANCER FAMILY	CANCER FAMILY	CANCER FAMILY
	Head and neck cancers	Thoracic rare cancers	Male genital and urogenital rare cancers	Female genital rare cancers	Neuroendocrine tumours	Tumours of the endocrine organs	Central Nervous System tumours	Sarcomas	Digestive rare cancers	Rare skin cancers and non-cutaneous melanoma
	n=number Guidelines	n=number Guidelines	n=number Guidelines	n=number Guidelines	n=number Guidelines	n=number Guidelines	n=number Guidelines	n=number Guidelines	n=number Guidelines	n=number Guidelines
Austria+ Switzerland	0	1	0	1	0	0	0	0	1	0
BENELUX	3	1	3	2	7	1	0	0	12	1
Czech R.+Croatia	0	0	0	0	0	0	0	0	0	0
France	21	6	7	11	14	16	4	7	24	11
UK	25	1	5	7	2	5	4	3	7	7
Germany	6	0	2	8	3	5	5	8	9	7
Italy+Spain+Portugal	13	2	1	3	7	7	1	11	9	5
Greece+Poland+Hungary	0	0	0	0	1	0	0	0	1	0
Scandinavia	0	0	0	0	1	0	0	2	0	0
EU+International	3	10	7	8	21	17	7	8	6	7
	71	21	25	40	56	51	21	39	69	38

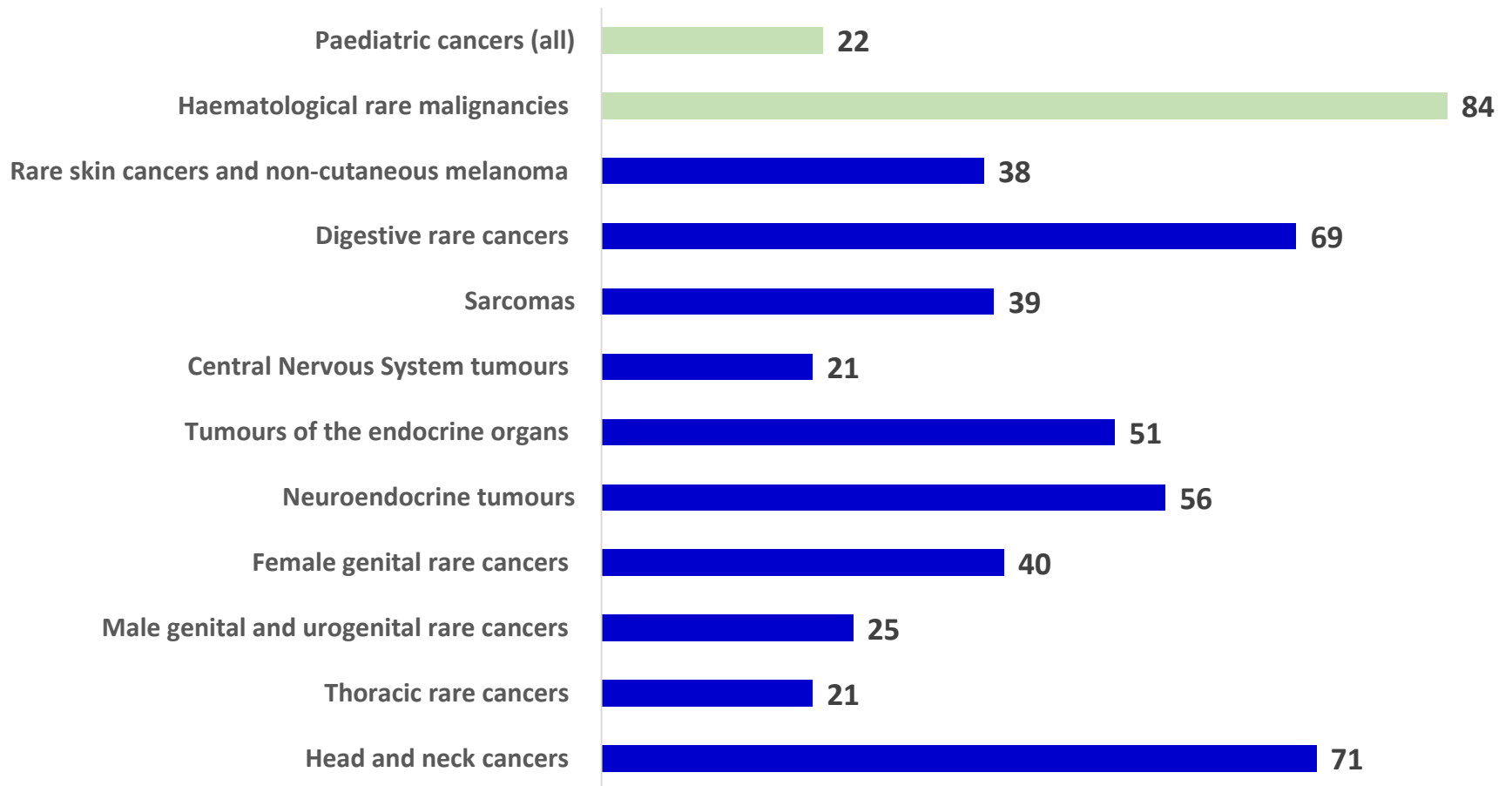
Head and neck cancers	Thoracic rare cancers	Male genital and urogenital rare cancers	Female genital rare cancers	Neuroendocrine tumours	Tumours of the endocrine organs	Central Nervous System tumours	Sarcomas	Digestive rare cancers	Rare skin cancers and non-cutaneous melanoma
71	21	25	40	56	51	21	39	69	38

Guidelines collected per EU Countries

■ Other European Countries ■ France ■ UK ■ Germany ■ Italy+Spain+Portugal ■ EU+International



Guidelines Collection



Total number of guidelines collected: 537

RESEARCH ARTICLE

Open Access



Validation and reliability of a guideline appraisal mini-checklist for daily practice use

Andrea Siebenhofer^{1,2*}, Thomas Semlitsch¹, Thomas Herborn², Ulrich Siering³, Ina Kopp⁴ and Johannes Hartig⁵

Evaluation of Guideline Quality

- **Appraisal Tool: Mix Methods**
- Using of **Cluzeau instrument** with 19 sample questions (Evaluation Criteria)
- Using of the international Centre for Allied Health Evidence (**iCAHE instrument**) for scoring (binary scored instrument) => appraisal score calculation
- Multiple choice answer, mostly the “yes/no” score
=>Yes=1; No=0
- Quality assessment rating scales:
 - 1= STRONG (total score 80% – 100%)
 - 2= MODERATE (total score 50% – 80%)
 - 3= WEAK (total score 50% or less)

scores calculation for CPGs quality evaluation

Topic: Thoracic RCs

GuidelineC ode	Q					Q1						Q1		Scoring Percentage										
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13			Q14	Q15	Q16	Q17	Q18	Q19			
EU-Int./ESMO																								
Thoracic rare cancer																								
Girard N et al.	EU/ INT	0201	1	1	1	1	1	0	0	1	0	0	0	1	1	1	1	0	0	1	0	11	58%	MODERATE
	EU/ INT	0202	1	1	1	1	1	0	0	1	0	0	0	1	1	1	1	0	0	1	0	11	58%	MODERATE
Baas et al.	EU/ INT	0203	1	1	1	1	1	0	0	1	0	0	0	1	1	1	1	0	0	1	0	11	58%	MODERATE
Husain et al.	EU/ INT	0204	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	18	95%	STRONG
V. Zandwijk et al.	EU/ INT	0205	1	1	1	1	0	0	0	1	1	0	0	1	0	0	0	1	1	0	1	10	53%	MODERATE
	Thoracic rare cancer		none																					
France																								
Thoracic rare cancer																								
Girard N et al.	FR0201		1	1	1	0	1	0	0	1	1	1	1	1	1	1	1	1	1	1	0	15	79%	MODERATE
Locatelli-Sanchez M et al.	FR0202		1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	18	95%	STRONG
HAS/ INCA-ALD 30 Meso	FR0203		1	1	0	0	1	0	0	1	1	0	1	1	1	1	1	0	1	1	0	12	63%	MODERATE

1 =STRONG (total score 80% – 100%): Green
 2 =MODERATE (total score 50% – 80%): Yelow
 3 =WEAK (total score 50% or less): red
 Yes =1; No=0

1. Rigour of guideline development (7 questions)

- Is the agency responsible for the development of the guidelines clearly identified? (**Responsibility for guideline development**)
- Did the development group contain representatives of all key disciplines? (**Guideline development group**)
- Are the sources of information used to select the evidence adequate? (**Identification and interpretation of evidence**)
- Are the methods for assessing and rating the evidence adequate? (**Formulation of recommendations**)
- Are the methods for formulating the recommendations satisfactory? (**Formulation of recommendations**)
- Is there an explicit link between the major recommendations and the level of supporting evidence? (**Formulation of recommendations**)
- Is there a date for reviewing or updating the guidelines? (**Peer review and updating**)

2. Context and content (8 questions)

- Are the reasons for developing the guidelines and their objectives clearly stated? (**Objectives**)
- Is there a satisfactory description of the patients to be covered by the guidelines? (**Context**)
- Is there a description of the circumstances in which exceptions might be made in using the guidelines? (**Context**)
- Is there a statement of how the patient's preferences should be taken into account in applying the guidelines? (**Context**)
- Are the recommendations clearly presented? (**Clarity**)
- Do the guidelines describe the condition to be detected, treated, or prevented in unambiguous terms? (**Clarity**)
- Are the different possible options for management of the condition clearly stated in the guidelines? (**Clarity**)
- Are the recommendations supported by the estimated benefits, harms and costs of the intervention? (**Likely costs and benefits**)

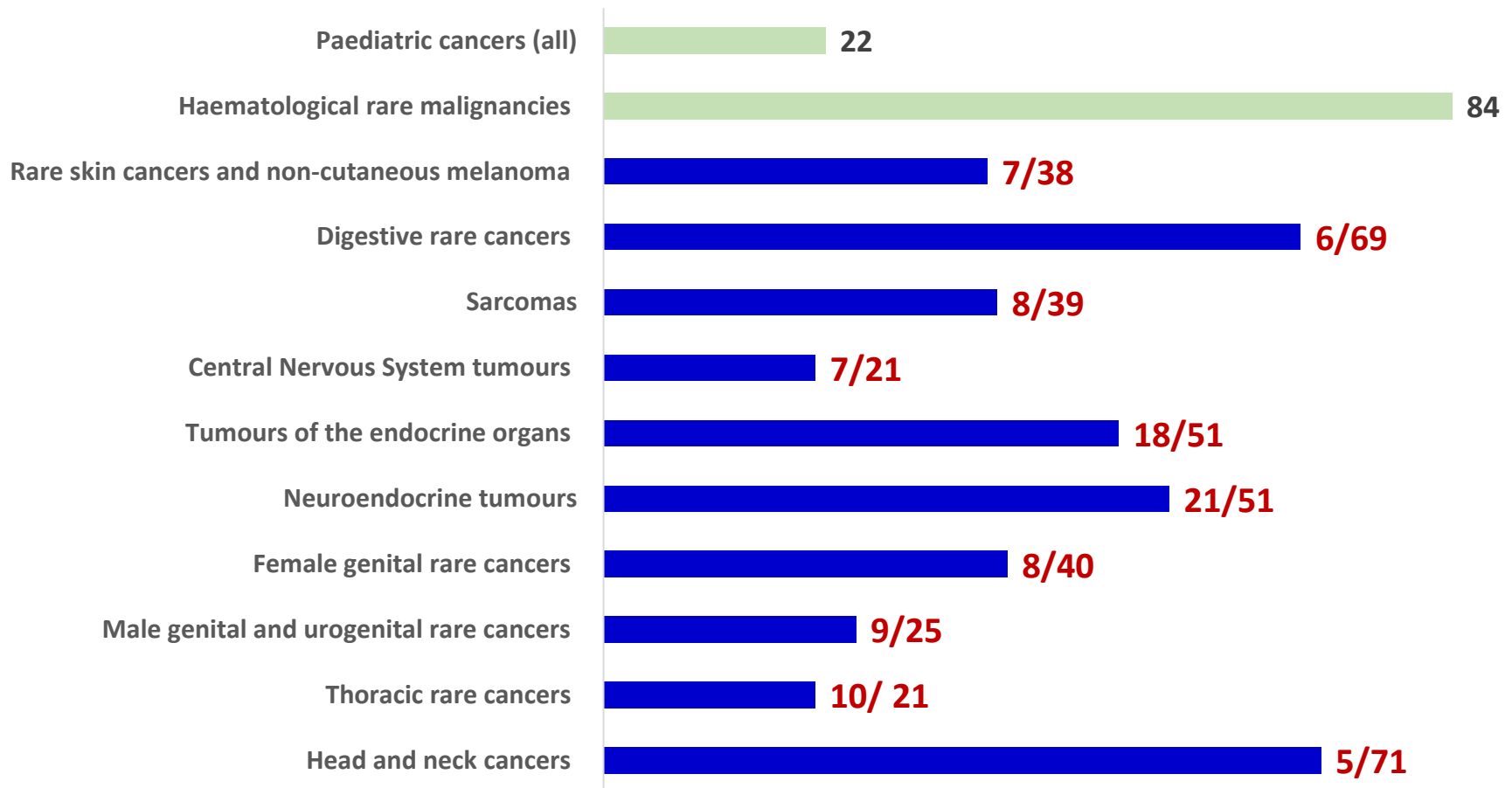
3. Application of guidelines (4 questions)

- Does the guideline document suggest possible methods for dissemination and implementation?
- Does the guideline document identify key elements which need to be considered by local guideline groups?
- Does the guideline document identify clear standards or targets?
- Does the guideline document define measurable outcomes that can be monitored?

Still missing: involvement of patient advocacy groups

**Cluzeau published in 1999
not intended for Rare Cancer !**

Guidelines Collection



**Number of guidelines on an EU-international level
fulfilling mini-checklist requirements: 99 /537**