Patient pathways and clinical governance: Patient flow knowledge generation and clinical practice

Jean-Yves Blay

(coordinator ERN EURACAN)
Rare cancers are not so rare: The rare cancer burden in Europe

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1 in 5 cancers is rare...
Rare cancers have worse prognosis

![Graph showing the comparison between rare and common cancers over years. The rare cancers show a steeper decline, indicating a worse prognosis.](image-url)
• promote good quality and safe care to patients by fostering proper diagnosis, treatment, follow-up and management of patients across the Network
• empower and involve patients
• offer and promote multi-disciplinary advice for complex cases
• develop and implement clinical guidelines and cross-border patient pathways
• exchange, gather and disseminate knowledge, evidence and expertise within and outside the Network
• promote collaborative research within the Network
• reinforce research and epidemiological surveillance, through setting up of shared registries
• exchange and disseminate knowledge and best practices, in particular by supporting national centres and networks
EURACAN governance

EURACAN General Assembly
Board of all HCP members and associate/affiliate partners

Decisions for key questions

Steering Committee
Coordinator
10 Group leaders
+ 1 representative/country not already represented
7 task force leaders
Patient Advocacy groups

Decisions for daily management

Scientific Advisory Board
6 independent experts
Rare/frequent cancer/diseases
Outside / inside EU

Domains (Clinical action)

Transversal Task Forces

- Guidelines
- Research
- Training/Education
- Funding/sustainability plan
- Communication/Interaction with PAGs
- Dissemination
- Quality control
Diagnosis
Over 80 histotypes of sarcomas...

### Comparative study in three different European regions

- **ContiCanet**: European network of excellence (Connective Tissue Cancer Network)
- **Collaboration between Aquitaine, Rhône-Alpes & Veneto**
- **Inclusion criteria**: STS and visceral
  - 3 exhaustive data bases of incident cases of sarcoma during 2 years

#### Incidence / 100,000 / yr

- **Others**
- **Osteos**
- **Solitary fibrous tumors**
- **Fibrosarcomas**
- **MPNST**
- **LG Fibromyxoid Sarcomas**
- **Angiosarcomas**
- **Ewing sarcomas**
- **Synovial sarcomas**
- **Rhabdomyosarcomas**
- **Myxofibrosarcomas**
- **MFH**
- **Uterine LMS**
- **Dermatofibros**
- **Kaposi**
- **Leiomyos non ut.**
- **Sarcoma NOS**
- **Liposarcomas**
- **GIST**
Sarcomas and aggressive connective tissue tumors

Mutations kinases
- GIST

Translocations
- DFSP
- SyS
- Ewing

Amplification
- 12q13-15
- MDM2/CDK4

TSG loss
- NF1, TSC1/2

Genomique complexe
- WDDDDLPS

MPNST

PEComas

Desmoids

Mutations
- APC/bCat

LMS, UPS
For 56% the diagnosis is not totally correct.

For 35% the diagnosis is not totally correct.
Histological discordances

Figure 1: Proportion of diagnostic discordances in three sarcoma networks
In the Evaluation Médicale et Sarcomes study, major discordances were defined as changes between two different histological types, and minor discordances as changes between two different grades. In the Conticanet and RRePPS studies, major discordances were defined as changes between benign and malignant sarcoma or between sarcoma and non-mesenchymal diagnosis (i.e., carcinoma). Minor discordances were defined as changes between two different histological types.
RRePS—Réseau de Référence en Pathologie des Sarcomes.
Guidelines
• **Biopsy first**
  - Assessment by an experienced team
• Adequate preop imaging
• En bloc surgical resection
  - Planning R0
  - If R1, consider re resection
• Post operative radiotherapy
  - (G2-3 and/or deep seated, and/or >5cm)
• Preoperative radiotherapy
Research
Research in rare cancers

- Increasing burden of clinical research
- Refined biological understanding
- Rare tumors are good models for PoC
- Numbers: new designs needed
- Health technology assessment: which rules?
- Association of reference networks with research consortium
Research methods to change clinical practice for patients with rare cancers

Lucinda Billingham, Kinga Malottki, Neil Steven


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<table>
<thead>
<tr>
<th>Cancer incidence</th>
<th>Large population</th>
<th>Extremely rare population</th>
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<tbody>
<tr>
<td>Strength of previous belief of clinical benefit to warrant undertaking study</td>
<td>Moderate (e.g., phase 2 evidence of efficacy)</td>
<td>High (e.g., clear molecular hypothesis underpinning trial)</td>
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<td>Feasibility and suitability of prospective designs</td>
<td>RCT</td>
<td>N-of-1 trials</td>
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<td>Single-group trials</td>
<td>Basket trials</td>
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<td></td>
<td>Umbrella trials</td>
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<td>Enrichment trials</td>
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<td>Validity of observational studies</td>
<td>Case reports</td>
<td>Large databases</td>
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<td>Appropriateness of outcome measures</td>
<td>Overall survival or progression-free survival</td>
<td>Biological effect</td>
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<td>Tumour response</td>
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<td>Large effect on patient-reported outcome</td>
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<tr>
<td></td>
<td>Single primary measure</td>
<td>Consistency across basket of measures</td>
</tr>
<tr>
<td>Size of treatment effect</td>
<td>Minimum clinically relevant</td>
<td>Large single benefit or multiple small</td>
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<tr>
<td>Legitimacy of statistical basis for design</td>
<td>Hypothesis testing</td>
<td>Descriptive analysis</td>
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<td>Relaxed or adaptive RCTs</td>
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<td>Bayesian analysis</td>
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*Figure 1: Research methods to change clinical practice in relation to the range of cancer incidence*
Clinical research in rare cancers?

- Histological classification
- IHC/ single gene
- Gene panel
- WES
- WGS
Patient flow knowledge generation and clinical practice
3 networks of reference for sarcomas

Label by INCa

RRePS
Pr Jean-Michel COINDRE BERGONIE
Réseau de Référence en Pathology des Sarcomes Tissus mous / viscères

ResOs
Pr François GOUIN CHU Nantes
Pr Gonzague DE PINIEUX CHU Tours
Réseau de référence Pathology/clinical Sarcomes osseux

NetSarc
Pr Jean-Yves BLAY CENTRE LEON BERARD
Réseau de Référence Clinical des Sarcomes Tissus mous / viscères

Evaluation:
- activity,
- discrepancies
- delays,
- technics used,
- Frozen/FFPE

Database shared via Internet

Activity of MDTB:
- new patients / Fup Patients
- Description traitements local phase advanced phase
- inclusions trials,

Organisation of third level MDTB

Structuration of MDTB sarcoma in France
The nationwide cohort of 26883 patients with sarcomas & connective tissue tumors treated in NETSARC reference network between 2010 and 2015 in France: major impact of multidisciplinary board presentation prior to first treatment
Patients in MDT of NetSARC

Soft tissue

Visceral

Bone
Results (3)
Better management when MDT before treatment

• A higher number of pts presented in Netsarc MDTB had
  – Adequate imaging of the tumor before treatment/surgery (87.9% vs 67.8%, $p<0.0001$)
  – Biopsy prior the first resection (87% vs 55.0%, $p<0.0001$).
Quality of initial surgery, incident patients (STS & visceral sarcomas operated)

ASCO16
Local relapse free and relapse free survival
Needed

• Improved education of practitioners and health care workers
• Easily accessible informations
• Communication tools
• Continuous medical education
• Real life analysis of the outcome of patients
• Databases
• Simple and efficient access to MDT
• Referral system intra / extra country
EURACAN
What are the objectives

• Improving the quality of care of patients with Rare cancers in EU
• Guidelines
• Communication
• Patient pathways
• Expertise for all
• Cross border
• Research
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Leader Secret.

Leader Secret.

Leader Secret.

G1 Sarcoma

G2 Rare GYN

G3 Rare GU

G4 NET

G5 Rare GI

G6 Endocrine

G7 Rare H&N

G8 Rare Thoracic

G9 Rare Skin

G10 Rare Brain

Guidelines
Research
Training/Education
Funding/sustainability plan
Communication/ Interaction with PAGs
Dissemination
Quality control
EURACAN – Domain leaders

- **G1**: Sarcoma: Paolo Casali <paolo.casali@istitutotumori.mi.it>
- **G2**: Rare GYN: Michael Seckl (m.seckl@imperial.ac.uk)
- **G3**: Rare GU: Pr J.A. Gietema, (j.a.gietema@umcg.nl)
- **G4**: NET: Martyn Caplin, (m.caplin@ucl.ac.uk)
- **G5**: GI: Lucjan Wyrwicz; (lucjan.wyrwicz@gmail.com)
- **G6**: Endocrine: Eric Baudin (eric.baudin@gustaveroussy.fr)
- **G7**: Rare Head and Neck: Lisa Licitra <Lisa.Licitra@istitutotumori.mi.it>
- **G8**: Rare Thoracic: Nicolas Girard <nggirard@gmail.com>
- **G9**: Rare Skin/Eye melanoma: Dirk Schadendorf Dirk.Schadendorf@uk-essen.de
- **G10**: Brain tumors: Martin J van den Bent m.vandenbent@erasmusmc.nl
EURACAN domains and subdomains

G1 Soft tissue / visceral sarcoma
G1 Bone Sarcoma
G2 Trophoblastic disease
G3 Rare female genital organ / placenta
G3 Rare male genital organ / urinary tract
G4 Rare neuroendocrine system
G5 Rare Digestive tract
G5 Rare Endocrine organs
G5 Rare Brain / spinal cords / meninges / cranial nerves
G5 Peritoneal
G5 Anal
G5 Biliary tract
G8 Rare thorax
G7 Rare Head and neck
G9 Rare skin / eye melanoma
G9 Skin
G9 Eye melanoma
G10 Rare brain / spinal cords / meninges / cranial nerves
G10 Rare brain / spinal cords / meninges / cranial nerves
G10 Rare brain / spinal cords / meninges / cranial nerves
Distribution of centres by country

Endorsement process – member state

Minimal set of criteria:
- Expertise
- N of patients
Conclusions

• Patient pathways must be carefully monitored
• Patients empowerment
• Communication, education
• Webbased tools
• Clinical governance
• Monitoring patient outcome in exhaustive real life populations enables measuring the impact of our action and open now questions
• The missions of the ERNs
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