Workshop #1

Harmonization of Clinical and Biological Data

Session 1

Eva Steliarova-Foucher, PhD

Serban Negoita, MD, DrPH

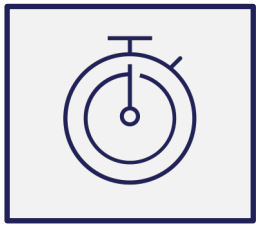
Workshop #1 Session 1

Some information for a smooth running of the session.

The audio of the session is recorded. **Please only speak in the microphone.**

Please introduce yourself every time before speaking. Do not hesitate to participate and ask questions.

Avoid using your smartphones and laptops if possible.



Please make sure to respect the time allocated for your speech & keep your interventions under 1mn.
Please be on time to the next session.

Workshop General Goals and Structure

Goal: Discuss strategies and plan an international partnership to advance the harmonization of biological and clinical data in support of childhood cancer research

Session 1: Core data elements: patient, tumor, prognostic factors

Session 2: Treatment and outcome + standards mapping

Session 3: Genetic/molecular data + challenges to harmonization

Session 4: Summary of discussions + pilot project

Intro to Session 1 Topics

- **Harmonization: effort to combine data from public health surveillance systems, observational, experimental and administrative data sources AND provide users with a comparable description of tumor biology, disease extent, treatment and outcomes**
- **Harmonization may refer to the collection, analysis and/or interpretation of data**
- **Harmonization can be achieved at various step of the process:**
  - Abstraction /extraction of row data using standard tools and formats
  - Pre-analysis recoding
  - Recoding of data for secondary use
  - Reporting standards and formats, etc.

Intro to Session 1 Topics (continued)

- **Concept of standards/standardization is central to achieving harmonization**
  - ICD-O examples of standards widely used world-wide
  - International Classification of Childhood Cancer (ICCC)
  - Standards endorsed by the International Association of Cancer Registries
  - ENCR recommendations
  - NAACCR standards used in cancer surveillance, frequently adopted by observational studies
  - SEER Recode – an example of a standard for data reporting, developed by NCI, widely used for reporting population statistics in North America

Session-Specific Questions for consideration

- Consider the perspective of a data resource
- What should be the elements of data resource
- What should be the criteria for selecting data elements of the data resource?

Session 1 Topics and Discussants

- **Dr. Gudrun Schleiermacher**

What are the core data elements and how they fit into common data models?

- **Dr. Sumit Gupta**

What are the specific needs of pediatric cancer research community regarding histology, stage and non-stage prognosticators?

Discussants

Gudrun SCHLEIERMACHER
France
Curie Institute
Practitioner and
assistant director at SIREDO center

Sumit GUPTA
Canada
Hospital for Sick Children in Toronto
Staff Oncologist and
Clinician Investigator, Division of Haematology/Oncology

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INSTITUT NATIONAL DU CANCER

Paris Conference for an International Childhood Cancer Data Partnership

Workshop 1: Harmonization of Clinical and Biological Data

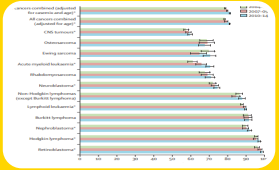
Gudrun Schleiermacher, MD PhD

Institut Curie, Paris, France

Q : What core data elements do we need?

« depth » of data

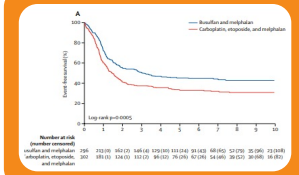
Patient numbers



Pediatric Cancer Registries

- Epidemiology : geographic repartition, evolution over time
- Survival : mortality, morbidity

Botta et al, LO , 2022



(Large-scale) pediatric oncology trials

- Survival (EFS, OS) depending on treatment
- Importance of clinical/radiological/biological prognostic markers

Ladenstein et al, LO , 2017

Molecular Characterization

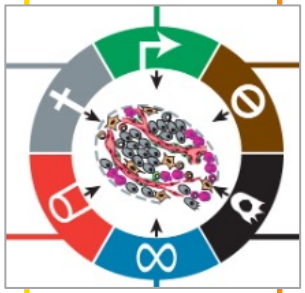
- Genomic/epigenomic tumor data; surfacome, proteomics;
- Microenvironment
- The « host », genome patient data

Gröbner et al, Nature 2018

Common data models – standardization and interoperability

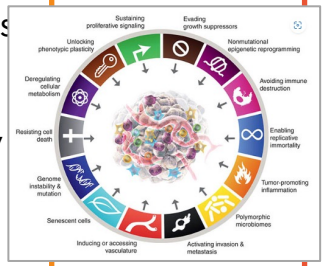
Aims : empower joint analysis across registries, trials, (genomic) characterisation

- modular, limited in size, flexible, extensible
- clinical, radiological, pathological, genomic data
- capture longitudinal changes associated with disease progression and resistance to therapeutic interventions



Methodology

- Bottom up approach : define a (first or further) data set as minimal as possible
- reach a consensus from all stakeholders involved
- using internationally established terminologies
- define implementation rules to guarantee data consistency



Output

- provide a comprehensive resource of event–based data including temporal relationships (disease progression / resistance)
- create a modular/ extensible data model : integration of omics data
  - from different experiments on the same samples
  - across studies on the same variables
  - interoperability

Guerin et al, JCO Clin Cancer Informatics, 2021
Hanahan: Hallmarks of Cancer

Prognostic and predictive elements at diagnosis / at relapse of pediatric cancer

At diagnosis : prognostic CDE

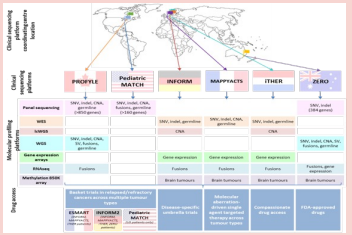
- Tumor type/ diagnosis: ICCC
- Age, Stage
- Pathology
- Tumor molecular markers

At diagnosis : additional prognostic/ predictive CDE

- Family history
- Germline variants/Cancer predisposition syndromes

At relapse : predictive > prognostic

- Pediatric« precision oncology »programs



An example: Neuroblastoma and INRG/PCDC – what have we learned

- **INRG database contains data from >25.000 neuroblastoma patients worldwide (trials and registries)**
- **Data includes baseline characteristics, limited genomic data, limited treatment data and outcomes**
- **INRG data is used to generate analyses of subgroups, studies on risk factors, risk classifier and numerous consensus publications**

Descriptions of New INRG Tumor Stages

Tumor Stage	Description
L1	Localized tumor not involving vital structures, as defined by the list of IDRFs, and confined to one body compartment
L2	Local-regional tumor with presence of one or more IDRFs
M	Distant metastatic disease (except stage MS tumor)
MS	Metastatic disease in children younger than 18 months, with metastases confined to skin, liver, and/or bone marrow

Source.—Reference 8. Complete definitions of these stages are cited in the text. IDRFs = image-defined risk factors.

INRC:


VOLUME 35 · NUMBER 22 · AUGUST 1, 2017

JOURNAL OF CLINICAL ONCOLOGY — SPECIAL ARTICLE

Revisions to the International Neuroblastoma Response Criteria: A Consensus Statement From the National Cancer Institute Clinical Trials Planning Meeting

INRG Stage	Age (months)	Histologic Category	Grade of Tumor Differentiation	*MYCN*	11q Aberration	Ploidy	Pretreatment Risk Group
L1/L2		GN maturing; GNB intermixed					A Very low
L1		Any, except GN maturing or GNB intermixed		NA			B Very low
				Amp			K High
L2	< 18	Any, except GN maturing or GNB intermixed		NA	No		D Low
					Yes		G Intermediate
	≥ 18	GNB nodular; neuroblastoma	Differentiating	NA	No		E Low
					Yes		H Intermediate
			Poorly differentiated or undifferentiated	NA			
				Amp			N High
M	< 18			NA		Hyperdiploid	F Low
	< 12			NA		Diploid	I Intermediate
	12 to < 18			NA		Diploid	J Intermediate
	< 18			Amp			O High
	≥ 18						P High
MS				NA	No		C Very low
	< 18				Yes		Q High
				Amp			R High

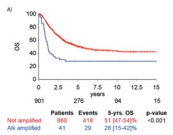
An example: Neuroblastoma and INRG/PCDC – challenges and possibilities

Challenge of integration of genomic data : in EU Importance of GDPR compliance

SIOPEN R-NET

SIOPEN Bioportal

At diagnosis : ALK, NGS panel (17genes)



British Journal of Cancer

Frequency and Prognostic Impact of *ALK* Amplifications and Mutations in the European Neuroblastoma Study Group (SIOPEN) High-Risk Neuroblastoma Trial (HR-NBL1)

Angela Bellini, PhD[1,2,3]; Ulrike Pötschger, PhD[4,5]; Virginie Bernard, PhD[6]; Eve Lapouble, PhD[7]; Sylvain Baulande, PhD[8]; Peter F. Ambros, PhD[9]; Nathalie Auger, PhD[6]; Klaus Beiske, MD, PhD[10]; Marie Bernkopf, PhD[5]; David R. Betts, PhD[11]; Jaydutt Bhalshankar, MSc[1,2,3]; Nick Bown, PhD[12]; Katleen de Preter, PhD[13]; Nathalie Clément, PhD[1,2,3]; Valérie Combaret, PhD[14]; Jaime Font de Mora, PhD[15]; Sally L. George, MD, PhD[16]; Irene Jiménez, MD[1,2,3]; Marta Jeison, PhD[17]; Barbara Marques, PhD[17]; Tommy Martinsson, PhD[18]; Katia Mazzocco, PhD[19]; Martina Morini, PhD[20]; Annick Mühlethaler-Mottet, PhD[21]; Rosa Noguera, MD[22]; Gaelle Pierron, PhD[7]; Maria Rossing, PhD[23]; Sabine Taschner-Mandl, PhD[5]; Nadine Van Roy, PhD[13]; Ales Vicha, PhD[24]; Louis Chesler, MD, PhD[25]; Walentyna Balwierz, MD[26]; Victoria Castel, MD, PhD[27]; Martin Elliott, MD[28]; Per Kogner, MD, PhD[29]; Geneviève Laureys, MD, PhD[30]; Roberto Luksch, MD[31]; Josef Malis, MD[32]; Maja Popovic-Beck, MD[33]; Shifra Ash, MD[34]; Olivier Delattre, MD[7,14]; Dominique Valteau-Couanet, MD, PhD[35]; Deborah A. Tweddle, MD, PhD[36]; Ruth Ladenstein, MD, PhD[30,37]; and Gudrun Schleiermacher, MD, PhD[1,2,3]

ARTICLE OPEN

Genetics and Genomics

Genomic *ALK* alterations in primary and relapsed neuroblastoma

Carolina Rosswog[1,2,3,4], Jana Fassunke[5], Angela Ernst[4], Birgid Schömig-Markiefka[5], Sabine Merkelbach-Bruse[5], Christoph Bartenhagen[1,2], Maria Cartolano[2], Sandra Ackermann[1,2], Jessica Theissen[1,4], Mirjam Blattner-Johnson[6,7], Barbara Jones[6,7,8], Kathrin Schramm[6,7], Janine Altmüller[9,10,11], Peter Nürnberg[2,9], Monika Ortmann[5], Frank Berthold[4], Martin Peifer[2,12], Reinhard Büttner[5], Frank Westermann[13], Johannes H. Schulte[14], Thorsten Simon[4], Barbara Hero[4] and Matthias Fischer[1,2,4]✉

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At relapse

RESEARCH ARTICLE

The European MAPPYACTS Trial: Precision Medicine Program in Pediatric and Adolescent Patients with Recurrent Malignancies

RESEARCH ARTICLE

The Pediatric Precision Oncology INFORM Registry: Clinical Outcome and Benefit for Patients with Very High-Evidence Targets

nature cancer

Article

The clinical utility of integrative genomics in childhood cancer extends beyond targetable mutations

nature medicine

ARTICLES

Molecular profiling identifies targeted therapy opportunities in pediatric solid cancer

Aim: International infrastructure to foster collaboration for clinical and translational research

Comprehensive Database comprising basic clinical and biosamples information for all patients in the SIOPEN network in GDPR compliant manner

Governance Framework for projects approval and international data sharing

SIOPEN R-NET BIOPORTAL

Harmonized Data Reporting for Specialty Committees studies

Legal Framework for data sharing and material transfer among SIOPEN members

Data Linkage Record to SIOPEN trials and national registries

Contribution to international INRG initiative

EUPID

Discussants

Gudrun SCHLEIERMACHER
France
Curie Institute
Practitioner and
assistant director at SIREDO center

Sumit GUPTA
Canada
Hospital for Sick Children in Toronto
Staff Oncologist and
Clinician Investigator, Division of Haematology/Oncology

Histology, Stage, and Non-Stage Prognosticators:

Essential or Valuable?

Simple or Complex?

Sumit Gupta, MD, PhD

Paris, France

November 7, 2023

Healthier Children. A Better World.

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Histology

- Core to childhood cancer cases in registries
- Standardly classified using ICCC-3
- How do we account for:
  - Changes in ICD-O-M coding?
  - Unknown validity of use of certain codes?
  - Variation between registries in collection methods and validity?
- As part of the US CCDI, the “Metadata Working Group” is attempting to address some of the above

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Precursor lymphoblastic lymphoma/leukemia

- B-lineage vs. T-lineage disease
  - After 2010, only 1% of US registry cases used “unknown lineage” codes (relative survival appropriate)
  - Between 1995-2009, 63% of cases used ”unknown lineage” codes (intermediate survival)
  - What about other registries?

- ALL vs LLy?
  - After 2010, ICD-O-3 combined lymphoblastic leukemia and lymphoma into single code (following WHO classification)
  - Where does this leave registries?
  - Was it even validly collected prior to 2010?

- Cytogenetics

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Stage

- Being able to compare mortality/survival between populations, either across jurisdictions or over time, requires that important prognosticators like stage be collected

- “Toronto Stage Guidelines” brought together global experts for consensus on what staging systems registries should use for 16 main childhood cancers

- Tiered system adopted; updated in 2019

Assessing the feasibility and validity of the Toronto Childhood Cancer Stage Guidelines: a population-based registry study

Prof Joanne F Aitken, PhD • Danny R Youlden, BSc • Andrew S Moore, PhD • Prof Peter D Baade, PhD • Leisa J Ward • Vicky J Thursfield, GradDip • et al. Show all authors

Published: January 23, 2018 • DOI: https://doi.org/10.1016/S2352-4642(18)30023-3 • Check for updates

International benchmarking of childhood cancer survival by stage at diagnosis: The BENCHISTA project protocol

Laura Botta[1‡], Gemma Gatta[1‡], Fabio Didonè[1]*, Angela Lopez Cortes[2], Kathy Pritchard-Jones[2], the BENCHISTA Project Working Group[¶]

The feasibility of implementing Toronto childhood cancer stage guidelines and estimating the impact on outcome for childhood cancers in seven pediatric oncology units in sub-Saharan Africa. A study from the Franco-African Pediatric Oncology Group

Brenda Mallon[1] | Rolande Kaboré[2] | Line Couitchere[3] | Fatou Binetou Akonde[4] | Mbolanirina Lala Rakotomahefa Narison[5] | Aléine Budiongo[6] | Tankélé Arsène Dackono[7] | Angel Pondy[8] | Francis Diedhiou[1] | Catherine Patte[1] | Eva Steliarova-Foucher[9] | Jacqueline Clavel[10]

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Non-stage prognosticators

- Repeated Delphi consensus in 2019 focused on NSPs
- Categorized NSPs as “Essential” vs. “Additional” vs. “New and Promising”
- Many NSPs already theoretically collected by PBCRs (e.g. histology, cytogenetics, molecular info)
- Response to treatment and host factors not considered

ALL	Age Initial WBC Lineage	Cytogenetics	-	1. Lineage can be divided into precursor B-cell vs. precursor T-cell (using ICD-O-3.2 categories) 2. Cytogenetic categories using ICD-O-3.2 classification 3. MRD not considered (response to therapy)
AML	-	Cytogenetics	-	1. Cytogenetic categories using ICD-O-3.2 classification; most relevant discussed in text. 2. MRD not considered (response to therapy)
CML	-	-	-	
HL	-	-	-	
NHL	Histology	-	-	1. Most common subtypes in childhood (see text) have unique ICD-O-3.2 codes

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Many, many, many others