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The unique constellation of tumors in AYA: Not an adult, not a child

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ESMO Preceptorship on Adolescents and Young adults with cancer
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AYA Cancer: “No man’s land?”

- Cancer in Adolescents and Young Adults (AYA) represents a unique disease constellation with distinct **epidemiological, clinical** and **biological** characteristics that resemble neither to childhood cancer nor cancer in older adults.

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AYA Cancer: a unique challenge

- The lower incidence of AYA-onset cancer as compared to older adults along with the paucity of cancer clinical trials in this age group, have hampered the elucidation of the molecular biology of these tumors that is the key to the optimal therapeutic approach and improvements in clinical outcomes.

ESMO / SIOPE AYA WG

Final composition of the WG; Working as a team, monthly TCs

Giannis Mountzios, ESMO Co-Chair

Stefan Bielack, SIOPE Co- Chair

Fedro Alessandro Peccatori, ESMO

Laurence Brugières, SIOPE

Emmanouil Saloustros, ESMO

Daniel Stark, SIOPE

Juvenile Cancer: Age Definition

- AYA are best considered as the older patients in paediatric oncology or haematology practice and the younger patients in adult practice.

- At present, there are no universally accepted limits that define the age range because the interface between adult and children's services is different in different healthcare systems[1].

1. Erikson, E. Identity: Youth and Crisis New York Norton 1968

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Juvenile Cancer: Age Definition

- Teenage years are between 13 and 19 years of age, inclusive
- Older patients, 20-39 years of age, are generally considered as "young adults"
- The World Health Organization defines adolescents as those aged 10-19, whereas youth as those aged 15-24 years [1]
- The US Surveillance Epidemiology and End Results (SEER) program and few other international societies define the AYA cancer population as those aged between 15 and 29 [2]

1 http://www.who.int/topics/adolescent_health/en
2. Bleyer A, et al. National Cancer Institute, NIH Pub. No 06-5767; 2006. Cancer Epidemiology in Older Adolescents and Young Adults 15-29 Years of Age, Including SEER Incidence and Survival: 1975-2000.

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Juvenile Cancer: Age Definition

- Adolescents: 10-19 years of age
- Young adults: 20-39 years of age

AYA patient population: 10-39 years of age (broad spectrum)

1 http://www.who.int/topics/adolescent_health/en
2. Bleyer A, et al. National Cancer Institute, NIH Pub. No 06-5767; 2006. Cancer Epidemiology in Older Adolescents and Young Adults 15-29 Years of Age, Including SEER Incidence and Survival: 1975-2000.

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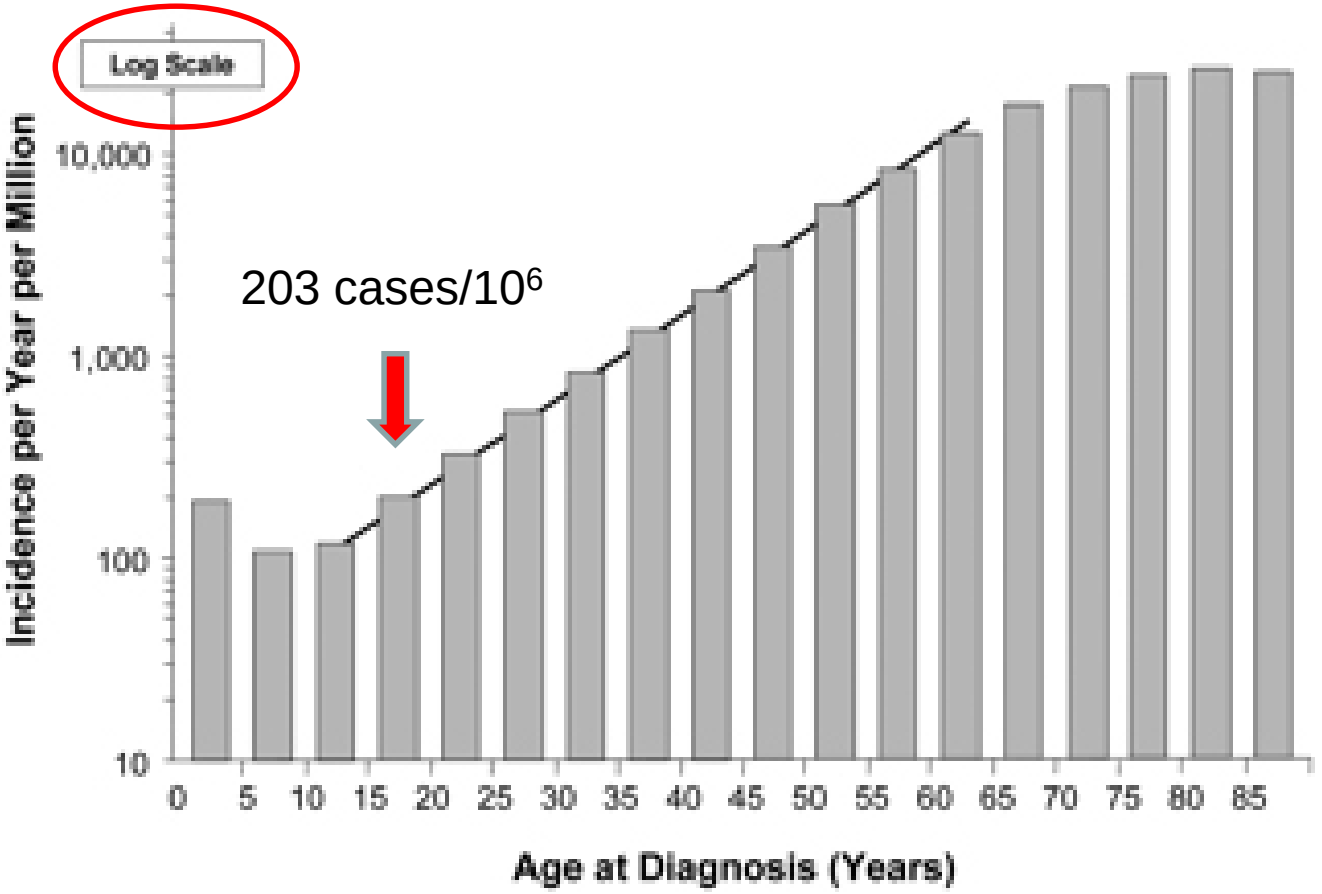
Incidence

- Annual rate: ~200-300 cases per million persons[1]
- 50% higher annual incidence comparing adolescents to younger children, and 50% higher again comparing adolescents to Young Adults[1]
- Rising cancer incidence: 0.9% per year[2]
  - The increase is mainly attributed to juvenile melanoma (5% increase), non-Hodgkin lymphomas (NHL, 2% increase) and germ-cell tumors (2% increase) [2]

1. Ries LAG et al. SEER Cancer statistics Review, NCI 2001
2. Birch JM et al. Br J Cancer 2002

Incidence according to age



Bleyer et al. Oncologist 2006

Unique Entity: Not an adult, not a child

"ADULT" type tumors

- Epithelial tumors (breast, colon, cervical etc) are seen in adolescents but significantly more often in young adults

- Epithelial carcinomas, nasopharyngeal carcinomas, thyroid cancer and melanomas are "adult type" tumors seen in AYA

Bleyer et al. Oncologist 2006

Unique Entity: Not an adult, not a child

“Pediatric” type tumors

- Embryonal Rhabdomyosarcoma, Wilms Tumours and neuroblastomas are rarely seen true “pediatric type” tumors occurring in AYA

Bleyer et al. Oncologist 2006

Unique Entity: Not an adult, not a child

- Hodgkin's disease (HD) and Germ-cell tumors are 3-6 times higher in adolescents than in the pediatric population

- NHL and CNS tumors are almost as common in adolescents as in childhood.

- ALL is less frequent, whereas osteosarcoma is most frequent in AYA.

Bleyer et al. Oncologist 2006

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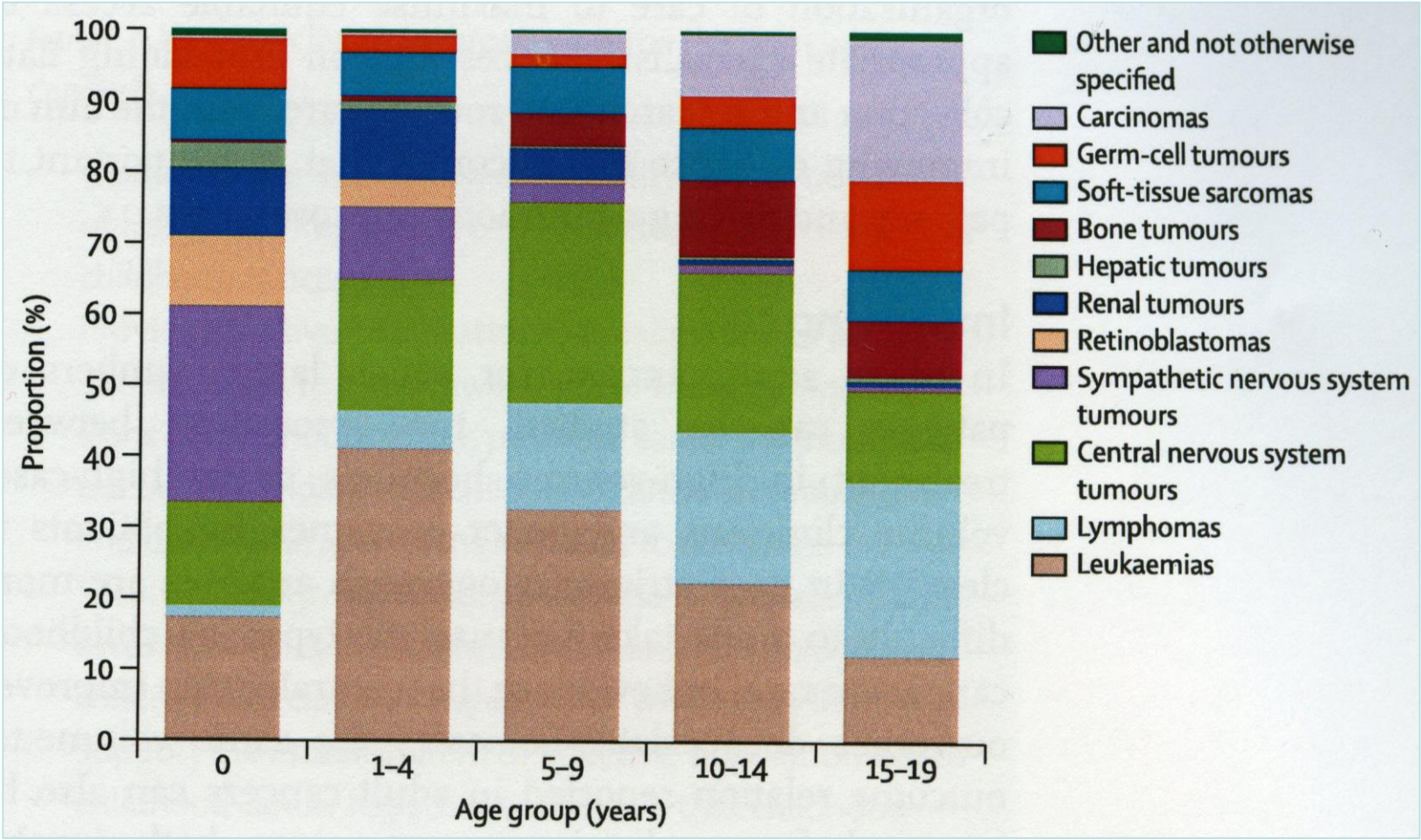
Proportions of the 12 main tumor groups in children and adolescents in Europe



Pritchard-Jones K. Et al., The Lancet Oncology, March 2013

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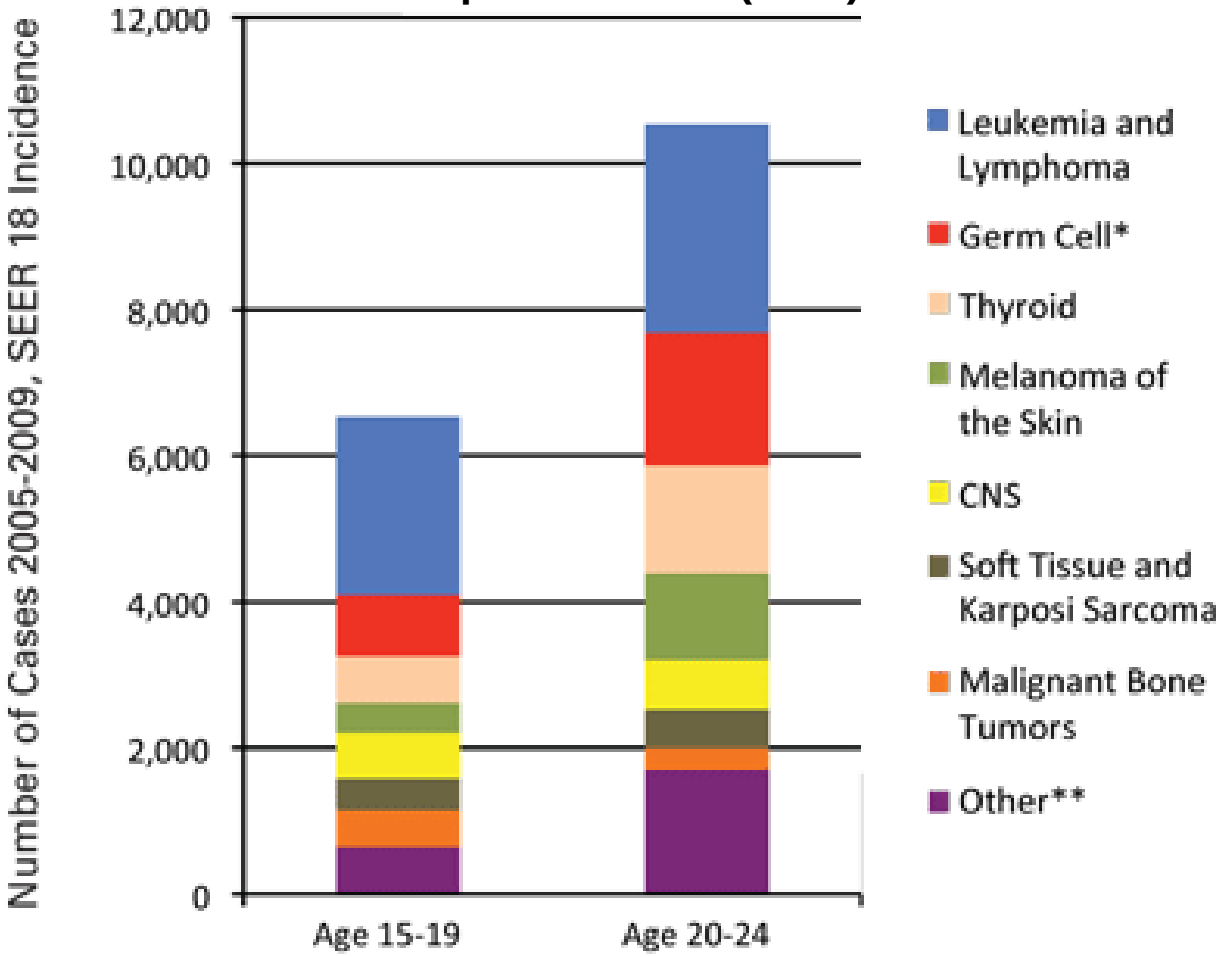
TYPES OF CANCER IN ADOLESCENT AND YOUNG ADULTS

Population USA (2012): 313.914.000



* Includes testicular cancer.

** Includes breast, cervix, colon, and other less prevalent cancers.

Data source: SEER 18, 2005-2009, ages 15-24

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Risk factors: Genetic

- The vast majority of cancers in AYA are sporadic events of unknown etiology.
- Genetic syndromes associated with increased incidence of AYA cancer represent less than 10% of all cases
- Those managing AYA cancers need expertise in taking a full family history

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Risk factors: Genetic

- Genetic syndromes associated with increased incidence of AYA cancer:
  - Neurofibromatosis (*NF1 and NF2*)
  - Li-Fraumeni syndrome (*TP53*)
  - Xeroderma pigmentosum (*XP*)
  - Ataxia-telangiectasia (*ATM*)
  - Fanconi pancytopenia
  - Hereditary dysplastic nevus syndrome
  - Turner , Beckwith-Wiedemann , Bloom and Gorlin's syndromes
  - Multiple Endocrine Neoplasia syndromes (MEN)
  - *BRCA1/BRCA2* tumor suppressor gene mutations
  - Familial Adenomatous Polyposis and Lynch syndromes

Risk factors: Environmental

In rare cases environmental factors have been observed in the pathogenesis of AYA cancer :

- Clear-cell adenocarcinoma of the vagina or cervix
  (Maternal exposure to Diethylstilbestrol during pregnancy)
- Liver tumors (Congenital exposure to HBV/HCV)
- Cervical Cancer (HPV infection)
- Kaposi Sarcoma (HIV)
- HL and Burkitt lymphoma (EBV)
- Second primary tumors (childhood exposure to chemo-radiation)
- Juvenile melanona (UV sunlight exposure)

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Classification

- AYA tumors are not best classified using an adult cancer classification system which is tumor primary-site specific. In contrast, they may be classified by a pathology-driven approach

Tumour group	Definition
Group 1	Leukaemias
Group 2	Lymphomas
Group 3	CNS tumours
Group 4	Bone tumours
Group 5	Soft tissue sarcomas
Group 6	Germ cell tumours
Group 7	Melanoma and skin carcinoma
Group 8	Carcinomas (except of skin)
Group 9	Miscellaneous specified neoplasms (including embryonal paediatric tumours)
Group 10	Unspecified malignant neoplasms

. Birch JM et al. Br J Cancer 2002

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"Take home" messages

- Unique patient population: not a child, not an adult.
- Unique range of affecting malignancies: midway between pediatric and adult tumor epidemiology
- These unique characteristics emphasize the need for an individualized approach for this group of patients with special and often unmet needs

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AYA deserve the best of both worlds!!