

Adolescent and young adult population with cancer

Accelerating drug development through Fostering Age Inclusive Research (ACCELERATE-FAIR)

CCDF-EORTC meeting
23 September 2024



Nathalie Gaspar, pediatric oncologist

SPIAJA team, Gustave Roussy, Villejuif

GO-AJA

Co-chair ACCELERATE FAIR group

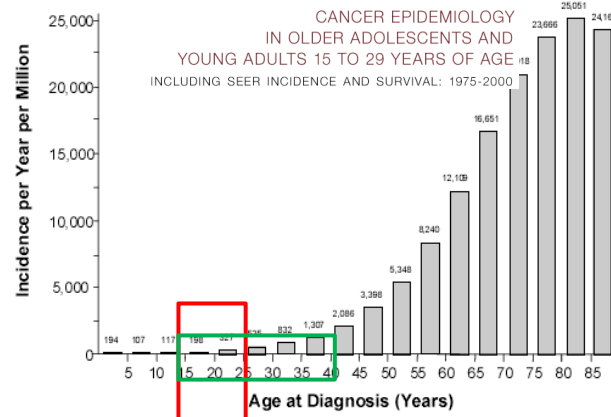
ESMO-SIOPE educational AYA group



Cancers in adolescents and young adults

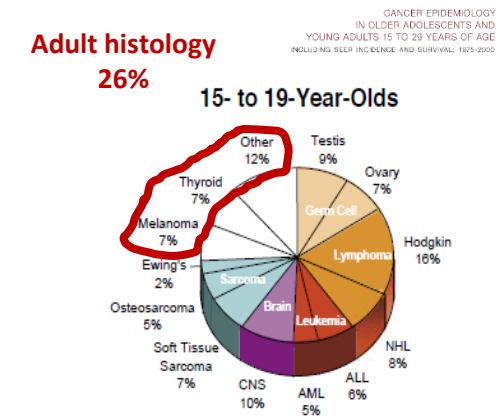
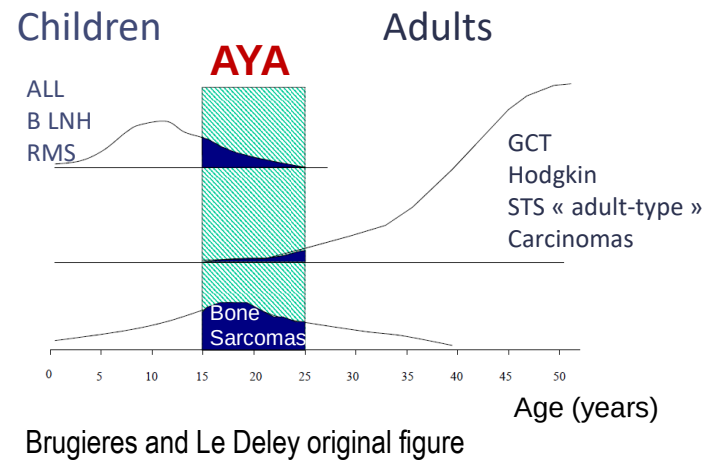
Rare diseases among rare a population

Rare disease



TYA 15-24 years in Europe
~20,000 new cases per year
 Gatta et al. EJC 2009

Wide range of histologies
 from paediatric type to adult type cancers
 and cancer with a pic incidence in AYA



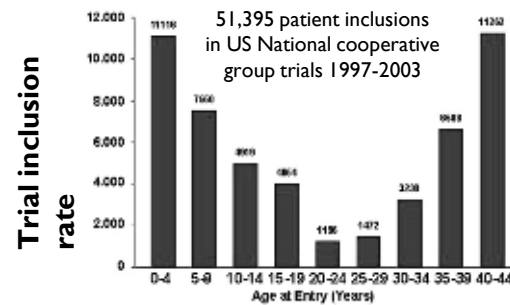
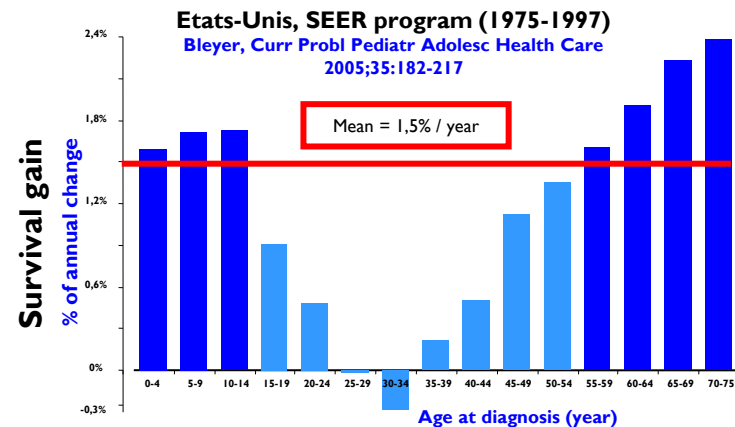
Cancer is the third cause of death in the adolescents and young adults

Persistent problems for AYA survival
 Acute leukemia, soft tissue and bone sarcoma, some brain tumours
 Some metastatic or relapsing cancer forms

Why access to clinical trial is important for AYA?

Cancer is the third cause of death in the adolescents and young adults

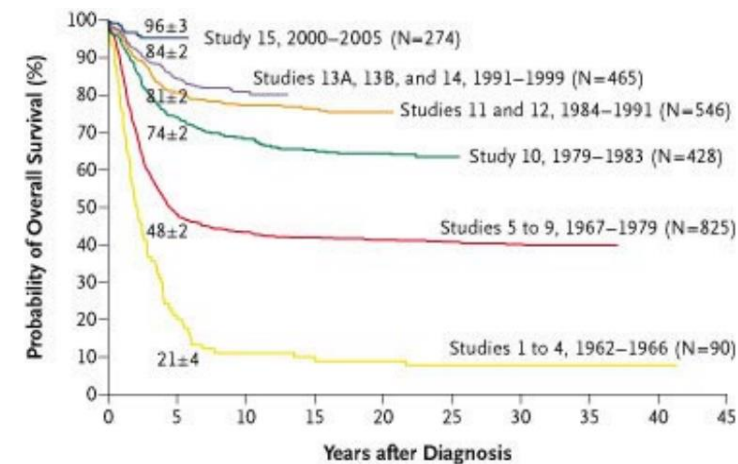
Lower AYA survival gains over years paralleled under-representation of AYA in therapeutic trials



Ferrari A and Bleyer A. Cancer Treat Rev 2007;33:603-608.

AYA survival might be improve by ...

Inclusion in therapeutic trials



Pui CH, et al. NEJM 2006;354:166-178.

Access to innovative therapies

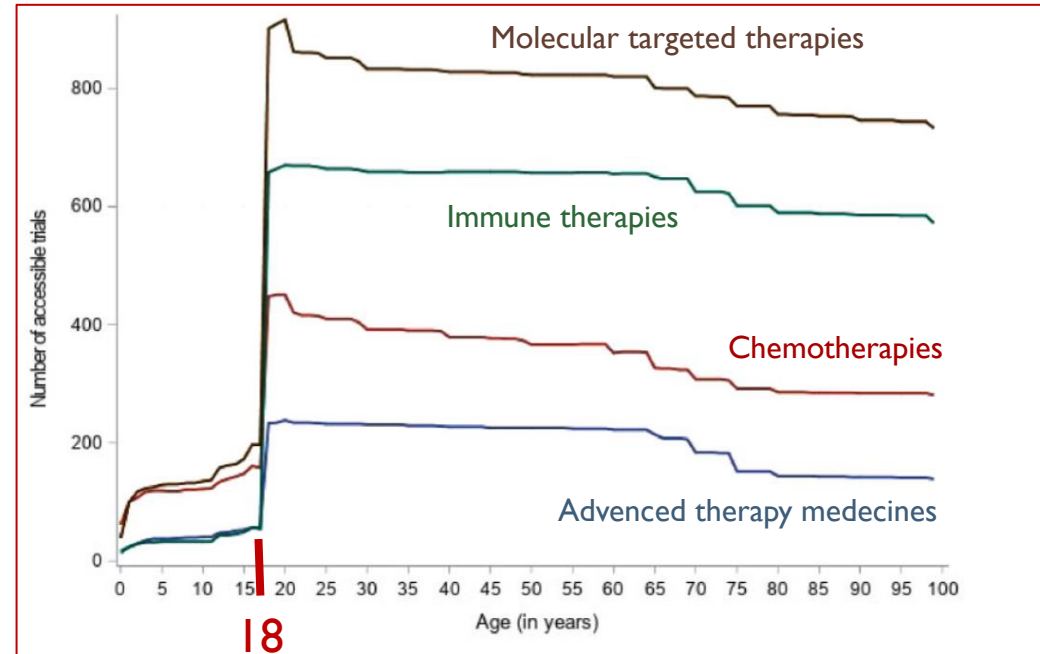
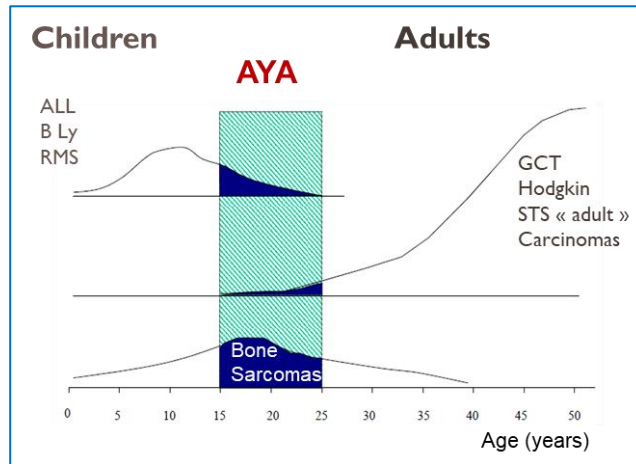
e.g. imatinib plus chemotherapy in Philadelphia chromosome-positive acute lymphoid leukaemia more often seen in AYA)

McNeer JL, et al. PBC 2018;65(6):e26989

The current landscape in clinical research

Separate pediatric and adult new drug development

Cancers in AYA have NO age barrier limit ...



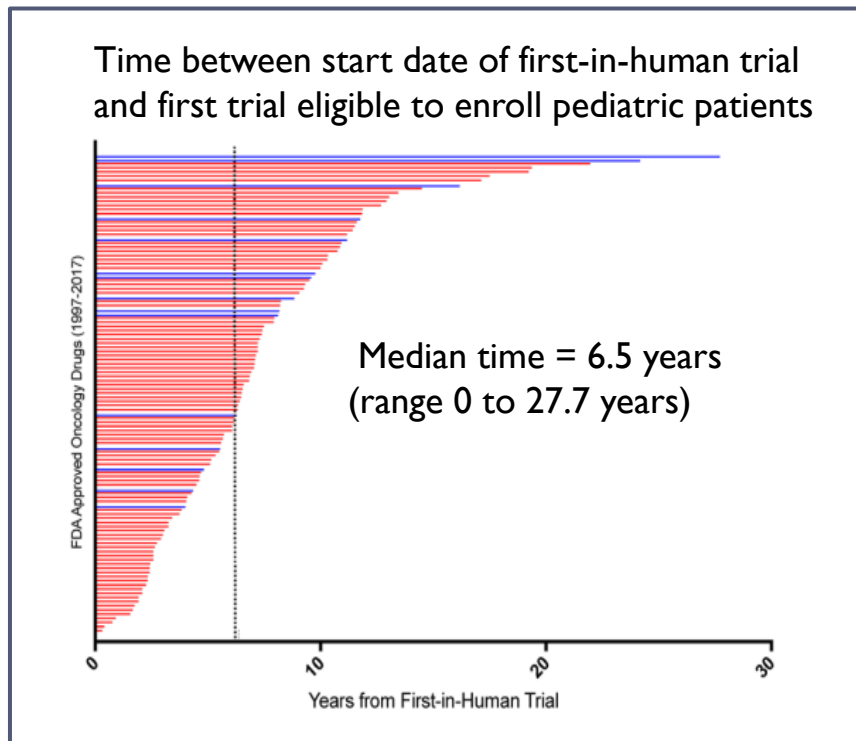
Meta-analysis
January 2007 to July 2018
10 malignancies relevant for AYAs
2176 phase I, 2 and 3 trials
79% adult
19% transitional
2% pediatric
5 AYA specific

De Rojas et al. JNCI 2019

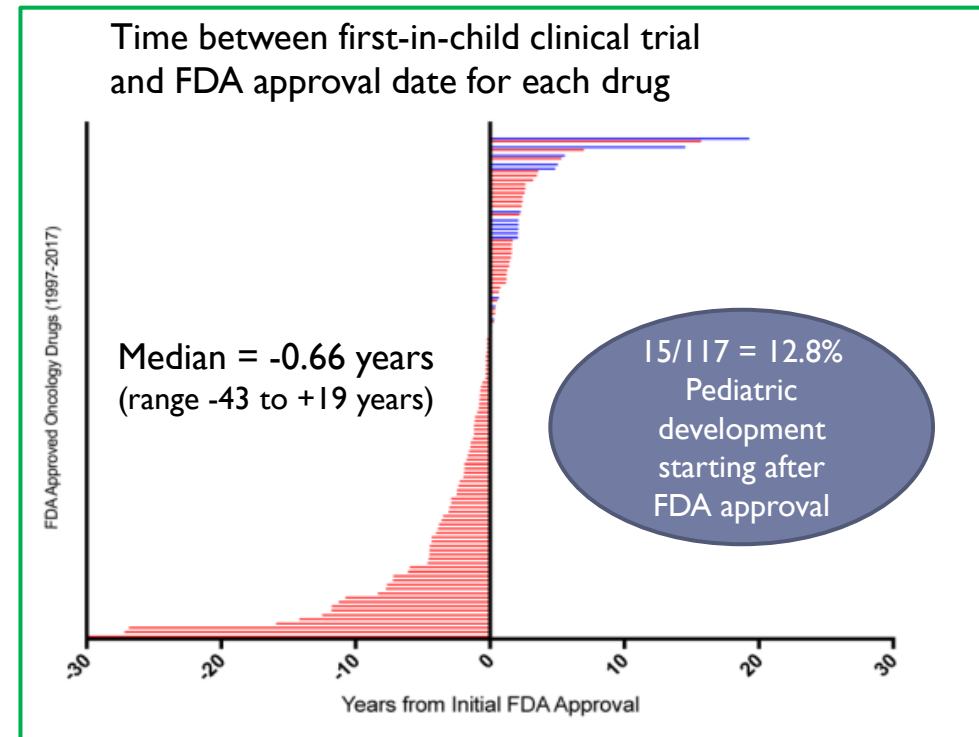
... therapeutic trials are still govern by an 18 year barrier

The current landscape

Delayed pediatric new drug development compared to adult



- At the time of initial FDA approval for oncology indication
- 5% only included children in the initial FDA approval
 - 13% did not yet have a pediatric trial open



From 1997-2017

The current landscape

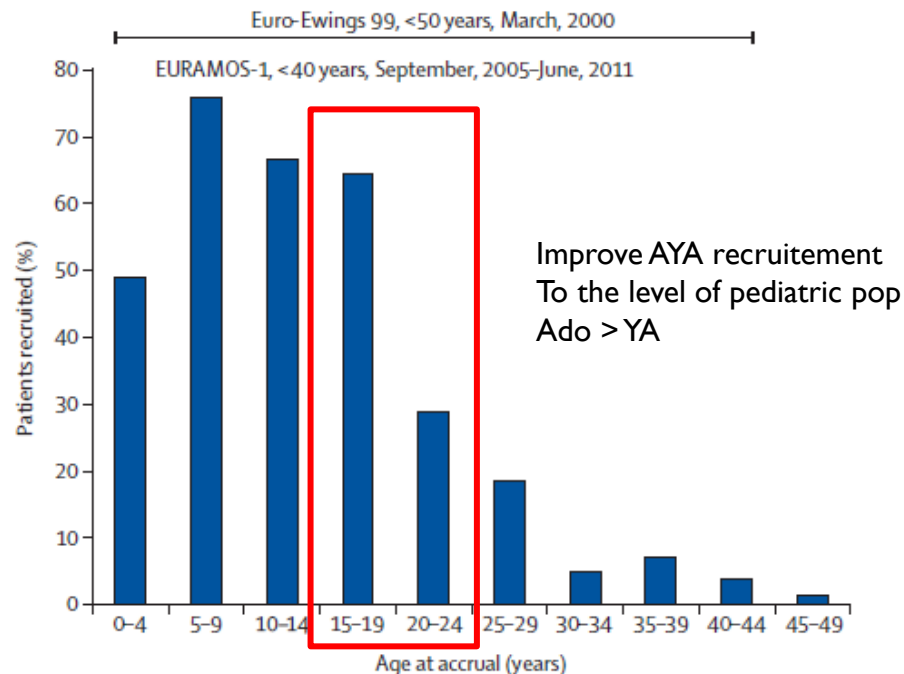
Persistent 18-year-dogma in early phases of drug development

Even in AYA disease with strong medical and pediatric oncologists collaboration

Ex Bone sarcomas

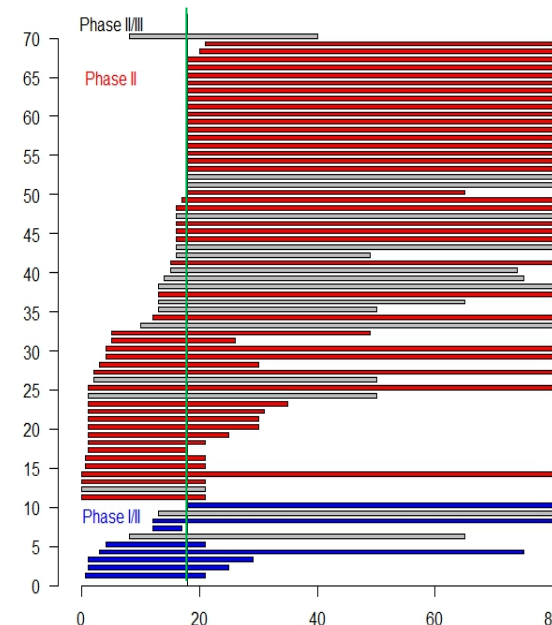
Age adapted inclusion criteria in Phase 2 trials
Rarely cover age periode of recurrence

Long history of
Joint pediatric/adult Phase 3 trials



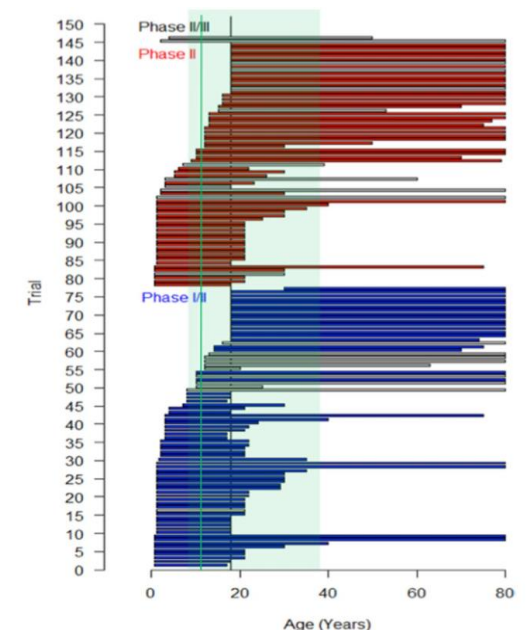
Fern et al. TLO 2014

Osteosarcoma
28% of 99 trials



Omer et al. EJC 2016

Ewing sarcoma
12% of 146 trials



Felix et al. Cancer Med. 2021

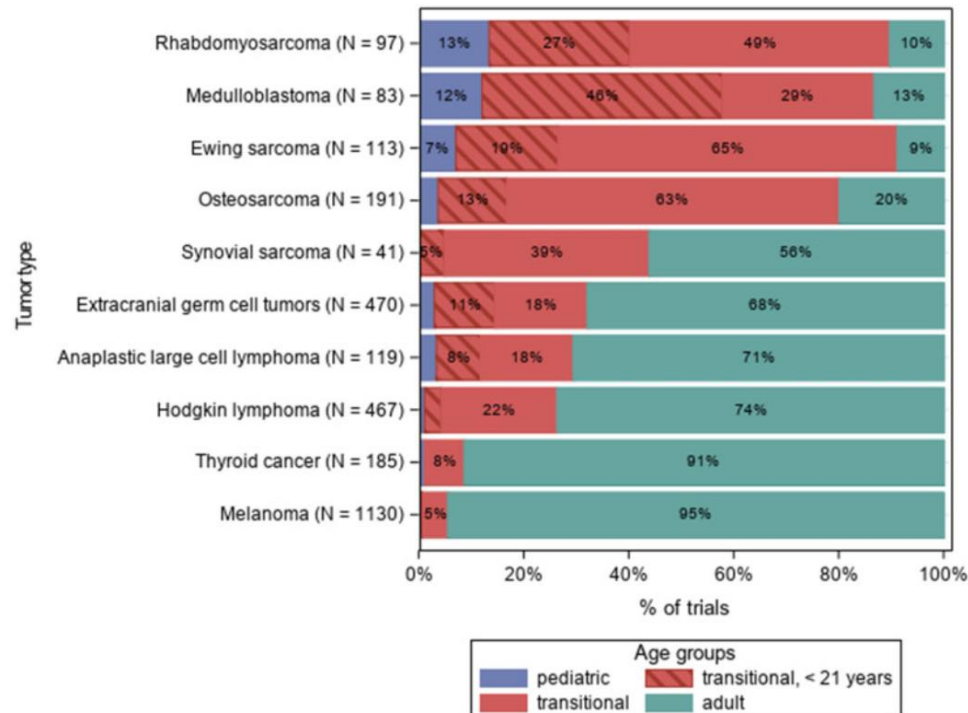
The current landscape

Lack of joint trial from phase 1 to 3 in AYA cancers

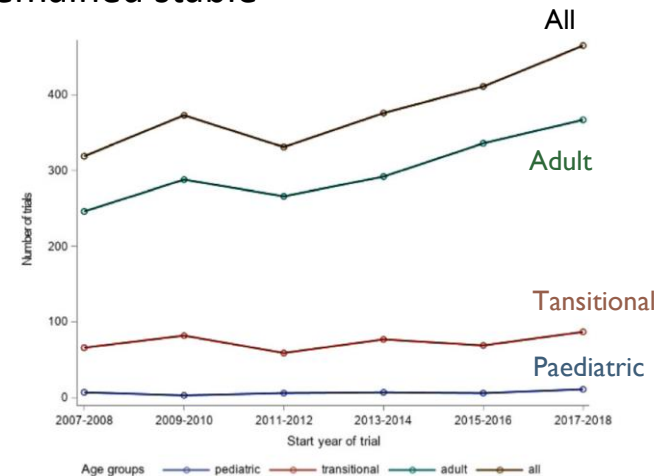
Tumors considered similar in adult and pediatric populations showed a disparate proportion of transitional trials

Trial definition according to age

- Pediatric : <18 years
- Adult: ≥18 years
- **Transitional=joint: both pediatric and adult**
- AYA-specific: lower limit 12 to 18 years, upper limit < 40 years



The total number of new trials increased over the years
Whereas the number of new pediatric and transitional trials remained stable



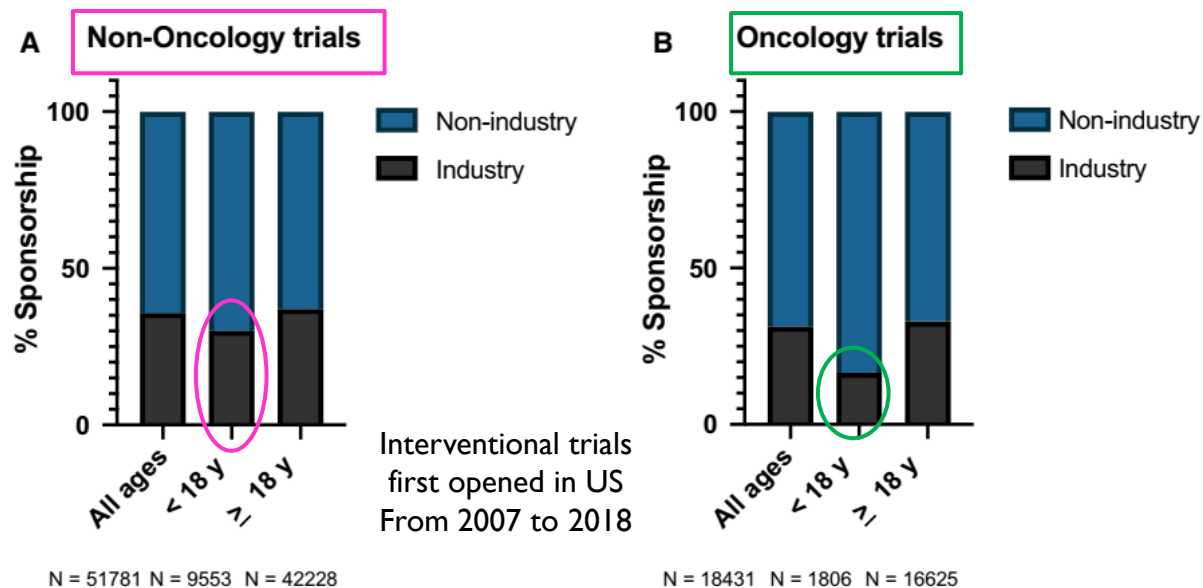
Meta-analysis
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5 AYA specific

The current landscape

Role of the trial sponsorship

Industry-sponsored trials open to patients < 18 years ($P < .001$)

- in non-oncology disciplines 15.5%
- In oncology trials 5.2%



Neel et al. Cancer Medicine 2020

Academic sponsors are more prone to widen age inclusion criteria, with only 31% of transitional trials having industry sponsors or cosponsors

De Rojas et al. JNCI 2019

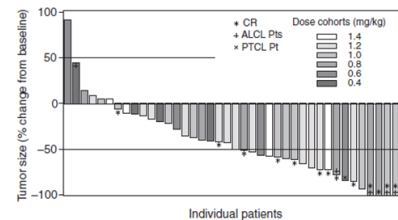
The current landscape

Delayed adolescent access to efficient drugs

Delayed pediatric development compared to adult
= **Delayed adolescent drug access to efficient drugs**
in common adolescent/adult diseases
e.g. brentuximab in Hodgkin lymphoma

Fanale MA, et al. Clin Cancer Res 2012;18:248-255.

Brentuximab vedotin



Adult Phase I trial ≥ 18 years
Relapsed or refractory CD30 positive HL
NCT00430846
Published Nov 2011

Approved
for adult
relapsed or
refractory
HL (2012)

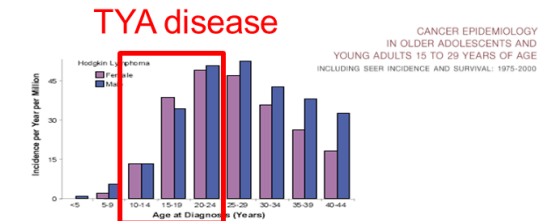
Successful trial of BV +
Chemotherapy in Adults
Stage II-IV HIV- HL,
first line TT
NCT01771107
March 2013- 2017

Approved by
FDA for front
line tt of high
risk HL
(2018)

April 2012

2018

Paediatric Phase-I/II trial of BV < 18 years for R/R HL NCT01492088
Randomized Phase 3 Study of BV for Newly Diagnosed High-Risk HL in
Children and Young Adults (<21 y)



CANCER EPIDEMIOLOGY
IN OLDER ADOLESCENTS AND
YOUNG ADULTS 15 TO 29 YEARS OF AGE
INCLUDING SEER INCIDENCE AND SURVIVAL: 1975-2000

The current landscape

European Paediatric Regulation: Paediatric Investigation Plans (PIP)

Required pediatric trial for drug efficient in adult
= **Unfeasible adolescent-specific phase I/II trials**
required within PIP, while drug already demonstrated
effective in adults with the same disease
e.g. Braf inhibitor in Melanoma

PIP

Vemurafenib

- Approved for adult melanoma V600E
- PDCO request for Melanoma V600E trial for 12-18 years

Recruiting

BRIM-P: A Study of Vemurafenib in Pediatric Patients With Stage IIIC or Stage IV Melanoma Harboring BRAFV600 Mutations

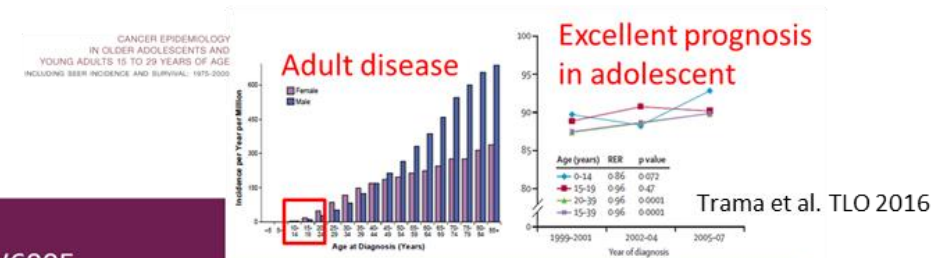
Condition: Malignant Melanoma
Intervention: Drug: vemurafenib

12-17 years
Started Jan 2013

- Unsufficient accrual worldwide
- Drug prescribed off label to ado with no data collected
- Adult studies : combination of Vemurafenib with MEK inhibitors
= better therapeutic option than single agent Vemurafenib

Ipilimumab, Same story

- Paediatric trial prematurely closed
- Standard care in adult are the combinations*



The current landscape

European Paediatric Regulation: Class waiver problem

Class waivers based on adult disease
= No drug development in pediatric disease with the same target than in adult disease

The European Paediatric Regulation (EC 1901/2006) allow paediatric class waivers for drugs developed for diseases only occurring in adults

An issue for paediatric drug development ...

From class waivers to precision medicine in paediatric oncology

www.thelancet.com/oncology Vol 18 July 2017

Andrew D J Pearson*, Stefan M Pfister, Andre Baruchel, Jean-Pierre Bourquin, Michela Casanova, Louis Chesler, François Doz, Angelika Eggert, Birgit Georger, David T W Jones, Pamela R Kearns, Jan J Molenaar, Bruce Morland, Gudrun Schleiermacher, Johannes H Schulte, Josef Vormoor, Lynley V Marshall, C Michel Zwaan, Gilles Vassal, on behalf of the Executive and Biology Committees of the Innovative Therapies for Children with Cancer European Consortium

48 (54%) of the 89 class-waivered drugs had a mechanisms of action warranting paediatric development

... but also for young adults with pediatric cancers

Restricted access of Young adults with pediatric disease to new innovative therapies, even approved in adult cancer
e.g. ALK inhibitors in ALCL

The current landscape

Pitfalls of separate pediatric and adult drug development

Class waivers based on adult disease
= No drug development in pediatric disease with the same target than in adult disease
e.g. ALK inhibitor in lung cancer; but of interest in AYA with ALCL

Delayed pediatric development compared to adult
= Delayed adolescent drug access to efficient drugs in common adolescent/adult diseases
e.g. brentuximab in Hodgkin lymphoma

+

Required pediatric trial for drug efficient in adult
= Unfeasible adolescent-specific phase I/II trials required within PIP, while drug already demonstrated effective in adults with the same disease
e.g. Braf inhibitor in Melanoma

=

Off-label use in AYA population of new efficient drugs approved in adult indications

Lost of useful information

- **For the AYA population on drug efficacy, safety and tumor biology**
- **For drug development : drug action/resistance**

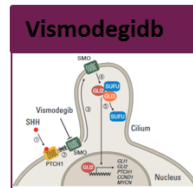
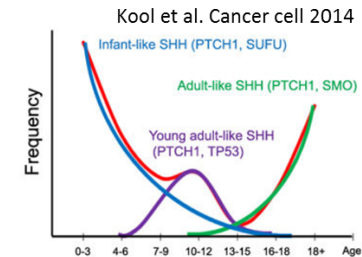
The current landscape

Risk of loss of biological information

Lost of useful information

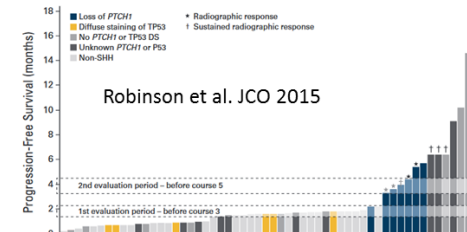
- For the **AYA** population on drug efficacy, safety and tumor biology
- For drug development : drug action/resistance

Ex Medulloblastoma and SHH inhibitors



Adult Phase I trial ≥ 18 years
NCT00607724
run 01/2007-12/2008
Response in a 26y-old MB
Published Nov 2010

Adult Phase-II
NCT00939484
ended in Dec 2012
Published 2015



Paed Phase-I trial 3-21 years
NCT00822458
01/2009-09/2013
Published 2013

Paed Phase-II
NCT01239316
ended in March 2015
Published 2015

Good example of joint development from early phase trial

What do we need for change?

To change mind



To work together



To increase awareness



To be pragmatic



The changes needed Pragmatic solutions

An agreement of all multi-stakeholders involved in pediatric early drug development in Europe

Mechanism of action biology driven early drug development
Rather than disease driven

To abolish the 18 year dogma from early drug development

European Journal of Cancer 62 (2016) 124–131

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejancer.com

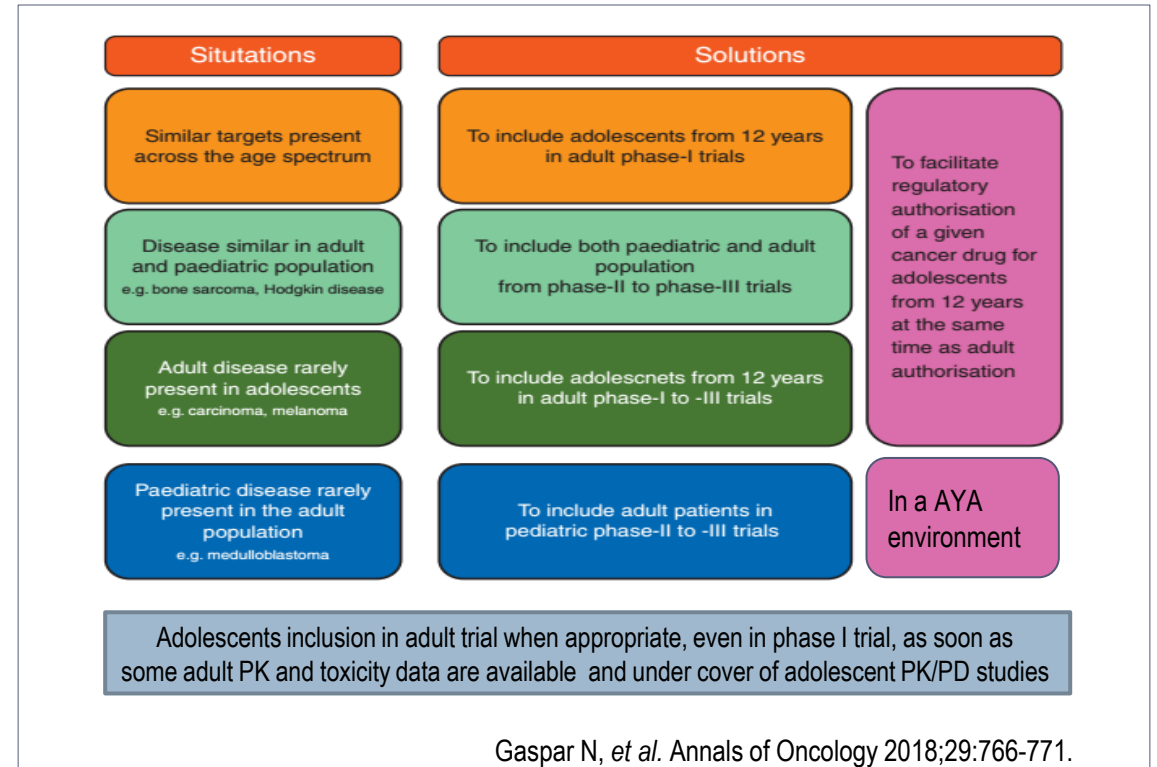
ELSEVIER

Current Perspective

Implementation of mechanism of action biology-driven early drug development for children with cancer

Andrew D.J. Pearson ^{a,*,1}, Ralf Herold ^b, Raphaël Rousseau ^c, Chris Copland ^d, Brigid Bradley-Garelik ^e, Debbie Binner ^f, Renaud Capdeville ^g, Hubert Caron ^{h,i}, Jacqueline Carleer ^j, Louis Chesler ^k, Birgit Geoerger ^l, Pamela Kearns ^m, Lynley V. Marshall ^{a,n}, Stefan M. Pfister ^o, Gudrun Schleiermacher ^p, Jeffrey Skolnik ^q, Cesare Spadoni ^r, Jaroslav Sterba ^{s,t}, Hendrick van den Berg ^b, Martina Uttenreuther-Fischer ^u, Olaf Witt ^v, Koen Norga ^w, Gilles Vassal ^x on behalf of Members of Working Group 1 of the Paediatric Platform of ACCELERATE²

CrossMark



A rational, rapid and safe solution

To include adolescents in « adults » trials from early phases (phase I/II)

No increased risk for the adolescents

Comparison of pediatric and adult phase I trial showed for adolescents ≥ 12 years and adults

- Similar PK
- Similar recommended dose
- Less acute toxicity

No legal issue

If the prerequisites to protect children in research are respected



No opposition from the industry

How to do it in practice?

Patient and parents support

As trials are the safest way to access new drugs for the adolescents



A rational, rapid and safe solution

To include adolescents in « adults » trials from early phases (phase I/II)

- ▶ No real barrier
- ▶ But not all all cost
 - ▶ When scientifically and medically justified
 - ▶ Even for first-in-human trial as long as the first patient is not an adolescent
 - ▶ Within the respect of the regulation for children in research
 - ▶ Under cover of PK, especially if no previous pediatric data
 - ▶ In an appropriate pediatric and/or AYA care environment



ACCELERATE FAIR Trial working group



Fostering Age Inclusive Research created in 2017

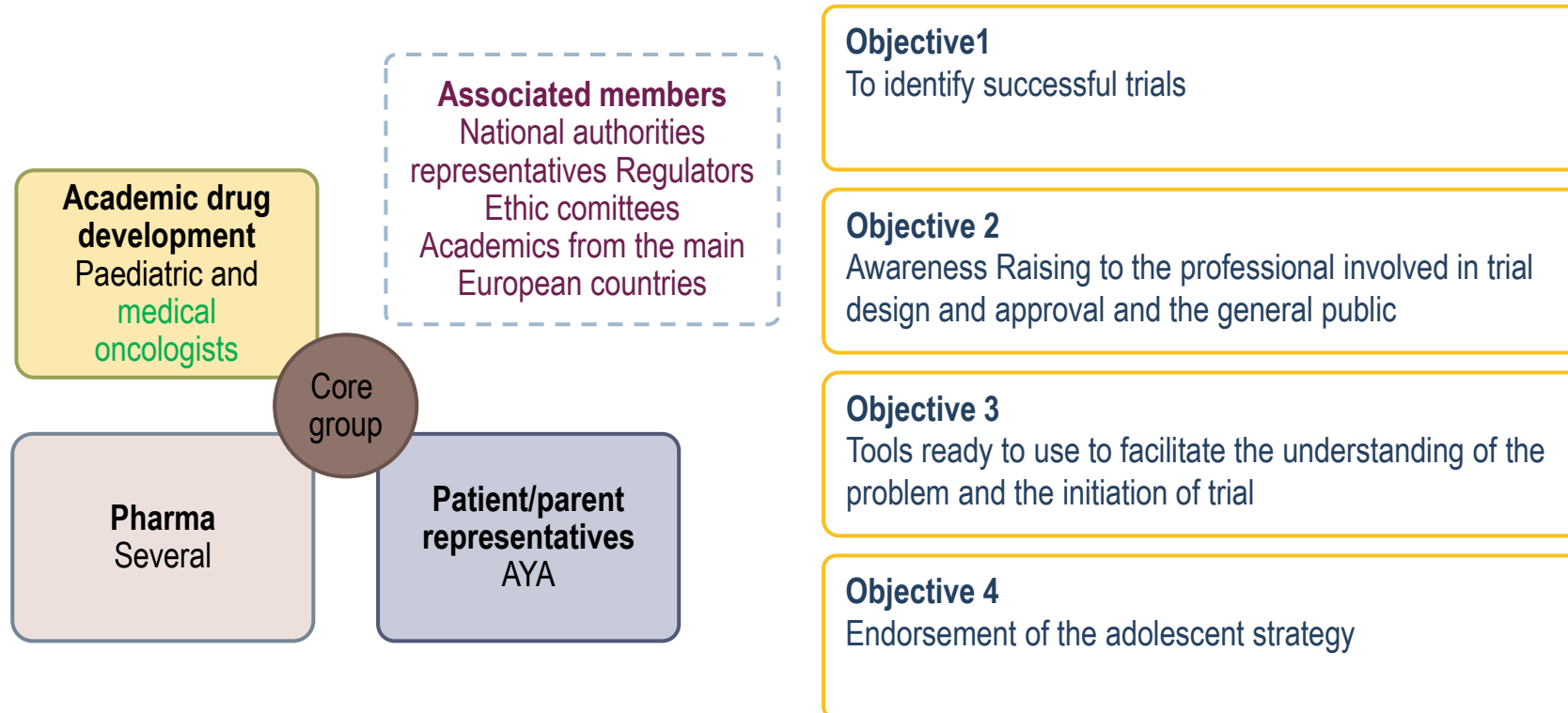
Coordination : N.Gaspar; M.Williamson

<https://www.accelerate-platform.org/fair-trials/why-fair-trials/>



2019: A broader platform

All document are freely accessible on the website



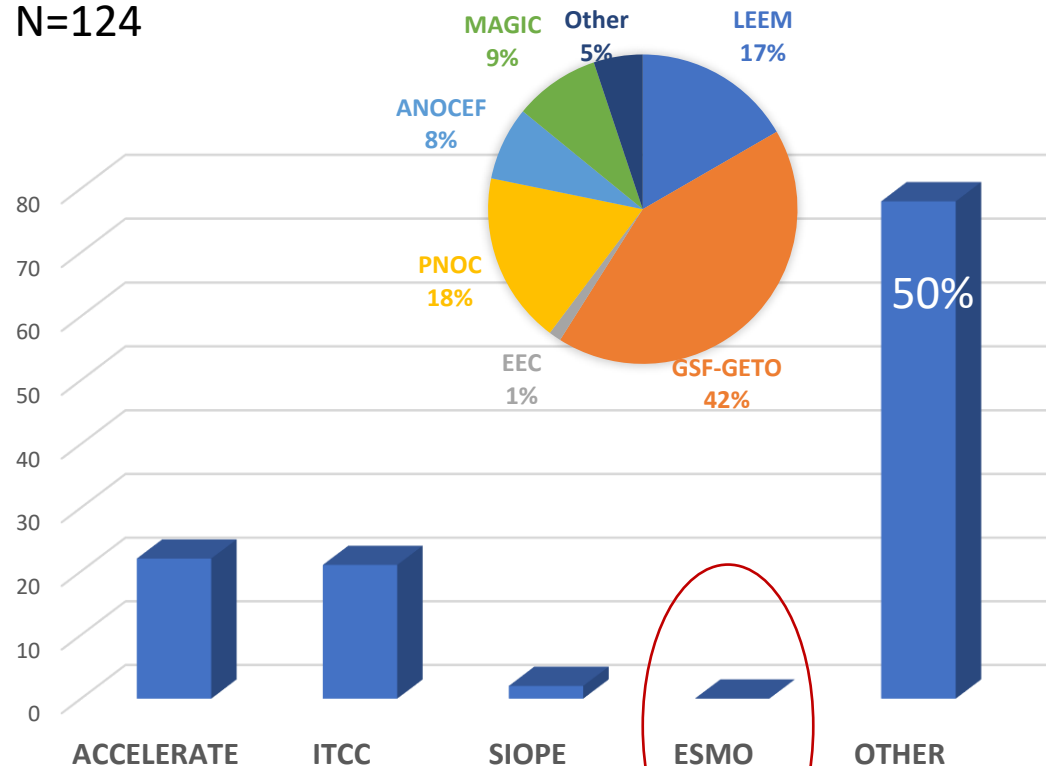
Survey on the hurdles, real or though

- on including adolescents in adult trials
- or including young adults in pediatric trials.

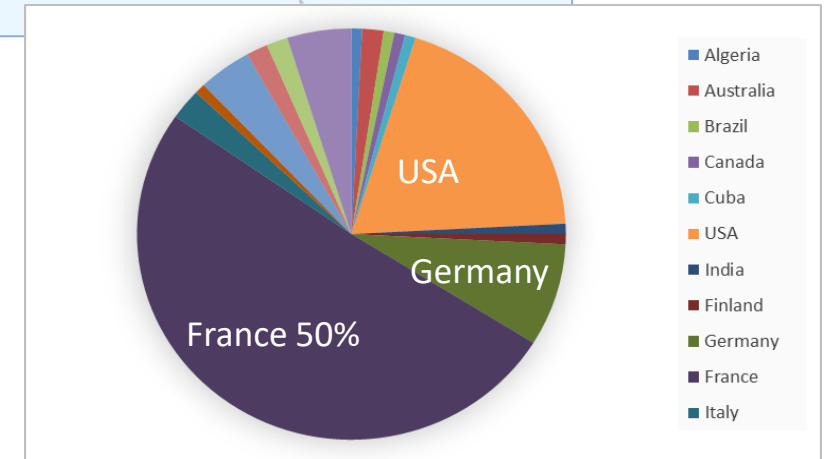
2021

Disease specific cooperative groups

N=124



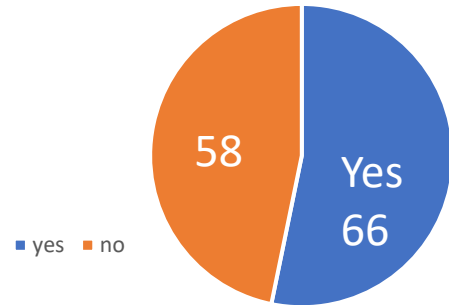
Africa	1%
Asia	1%
America	22%
Europe	75%
Oceania	2%



Medical oncologists
To improve participation ?

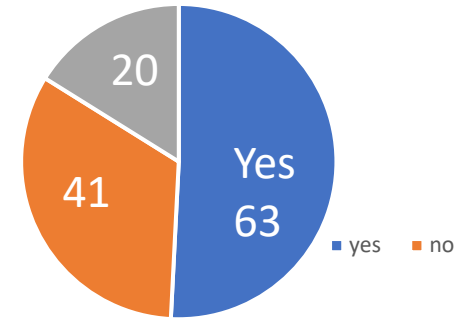
Over the last five years, have you opened ...

Any **adult phase I/II** early phase trials which permitted inclusion of **adolescent** patients?



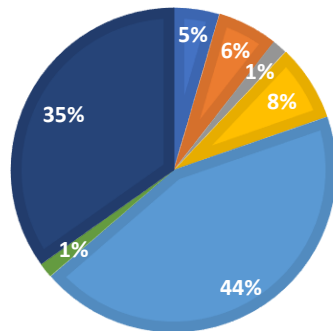
Around 50% of the trials could recruit AYA

Any **paediatric phase I/II** early phase trials which permitted inclusion of **YA** patients?



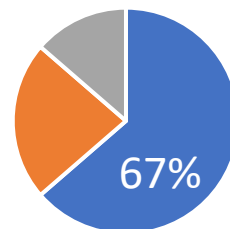
LOWER AGE LIMIT IN ADULT TRIALS

6months 2years 6years 12 years 16 years none NA



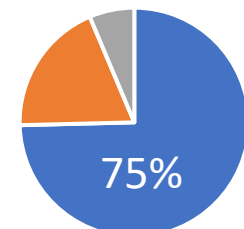
Variable age inclusion limit

adolescents (12-17 years) enrolled



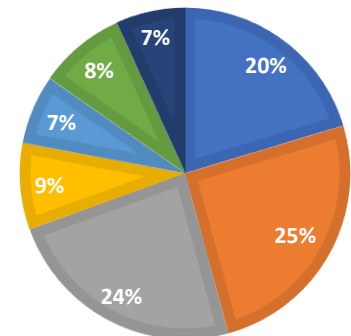
Is AYA recruitment not a problem?

young adult (18-25 years) enrolled



UPPER AGE LIMIT IN PEDIATRIC TRIALS

21 years 25 years 30 years 39 years 45 years none other



Hurdles to set-up and run joint early phase trials inclusive of AYA population

Adolescents in adult phase I/II early phase trials ?

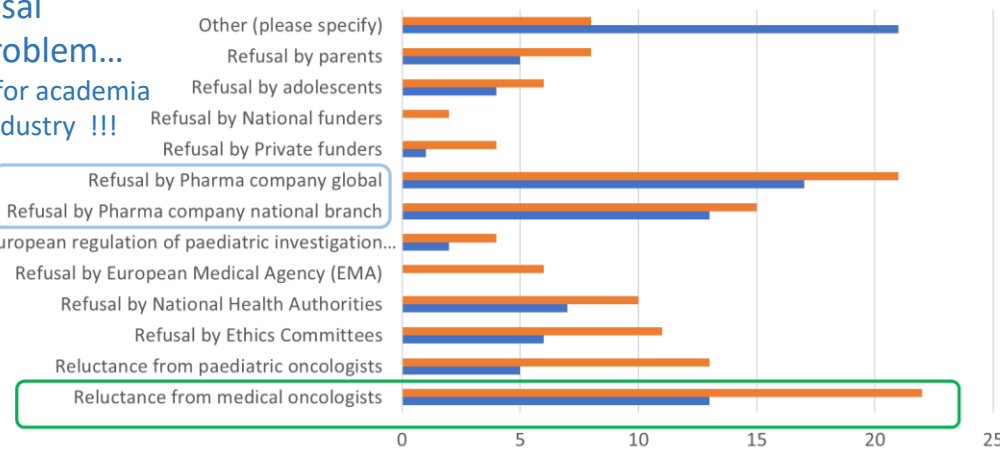
Young adults in pediatric phase I/II early phase trials ?

Pharma refusal remains a problem...

- CLEARLY for academia
- Not for Industry !!!

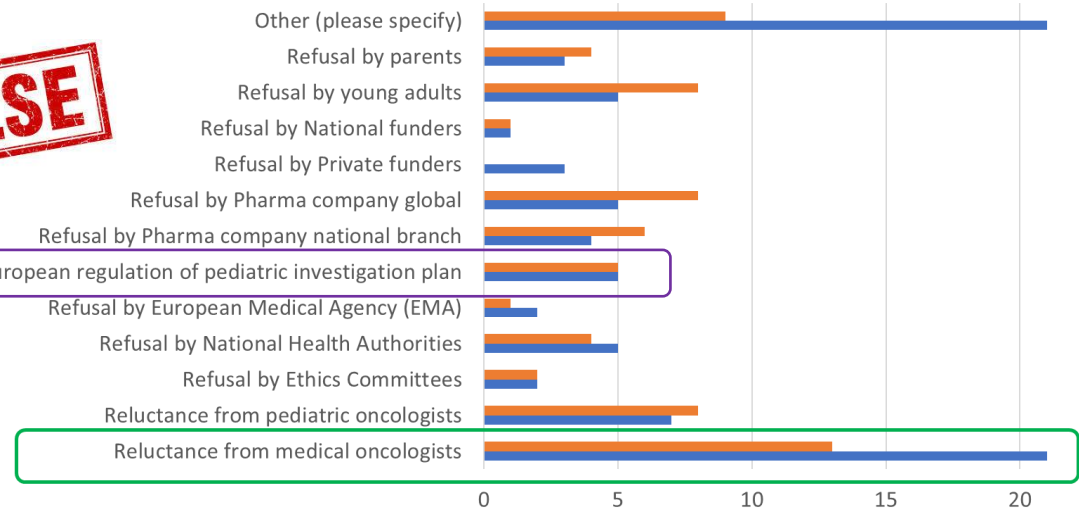
Real or Fake?

Not feasible in the European regulation of paediatric investigation...



FALSE

Not feasible in the European regulation of pediatric investigation plan



Are medical oncologists corporate? Or just unaware?

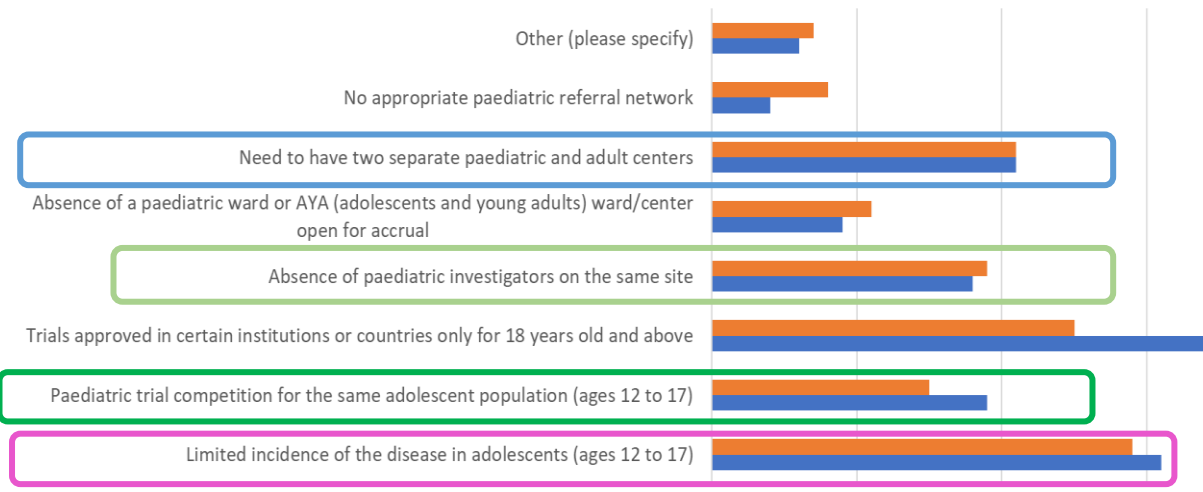
■ though ■ real

Hurdles to enroll AYA in joint early phase trials

Adolescents in adult phase I/II early phase trials ?

Young adults in pediatric phase I/II early phase trials ?

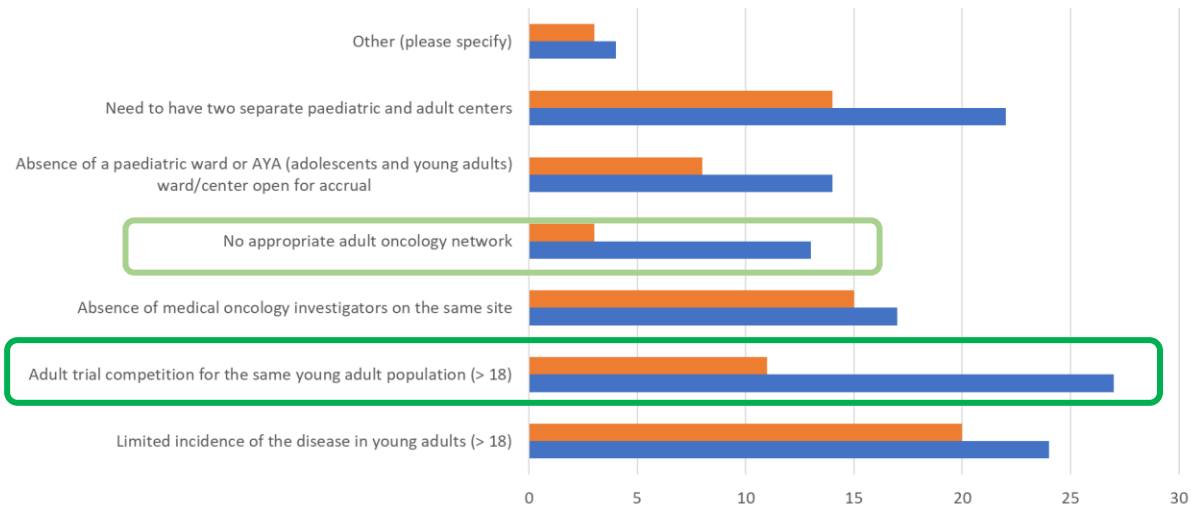
Appropriate place of care
Opening of adequate ped center/ward



Epidemiology

though real

Reasons why it could be difficult to enrol young adults in phase I/II paediatric early phase trials



Increased collaboration between
pediatric and medical oncologists

Practical toolkits

A set of practical resources to assist in designing age inclusive clinical trials.

Investigator/sponsor

Patient/parent

What can you find in the toolkit?

- [FDA Draft Guidance for Industry](#)
- [eCRF and Standard Analyses](#)
- [Patient Reported Outcomes \(PROs\)](#)
- [Assent templates for adolescents](#)
- [Protocol Elements](#)
- [Examples of HA/EC considerations on AYA](#)
- [List of AYA-clinical sites](#)

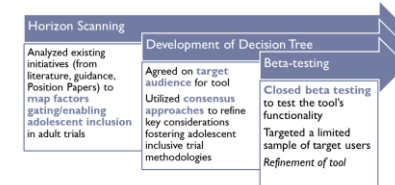


FAIR for AYA Stamp



<https://www.accelerate-platform.org/fair-trials/>

Adolescent Inclusion DECISION-TREE



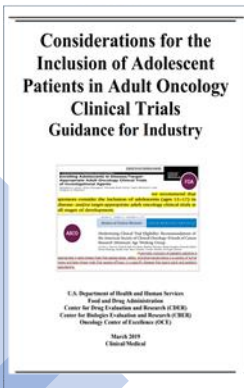
To define key considerations fostering adolescent inclusion in appropriate trials (for use by trial sponsors, investigators, health agencies, and ethics committee members)

Multi-Stakeholder support

Health authorities



FDA guidance



EMA letter of support



EFGCP letter of support



Industry

Industry organisation letter of support



AYA and their families

Patient and Parent advocates

Fostering Age Inclusive Research (FAIR) Trials for Adolescents & Young Adults



Can we identify pictures of Changes across grud development for AYA?



Pediatric investigation plan

Trial registration

Trial results

Labelling



FAIR PIP project
2017-2022

FAIR Clinical trial project
2018-2023

FAIR Labelling project
2017-2022

Reflect current changes
- In health authority decisions
- Vision of industry on trial
for pediatric development
(including AYA)

Reflect current changes
In clinical trial set-up

Real AYA
recruitment

Reflect current changes
In health authority decisions

Joint adolescent/adult trial from early drug development

Are all the problems solved?



Biology knowledge of AYA tumour

Refusal of joint trial from different stakeholders

Overlapping trials

Efficient recruitment of adolescents in adult trials

Difficulties to capture efficacy and toxicity information outside trials

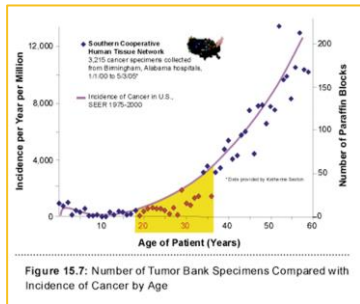
But we all have to work on it !!!!

Problems to be solved

Increase AYA tumour biology knowledge

AYA cancers might exhibit unique biologic characteristics, which may result in differences in treatment efficacy

Past insufficient biobanking
of AYA tumours



Disease specific research

Trials with biology ancillary studies

Several programmes of
tumour molecular profiling
at diagnosis and relapse

Pediatric
All tumours

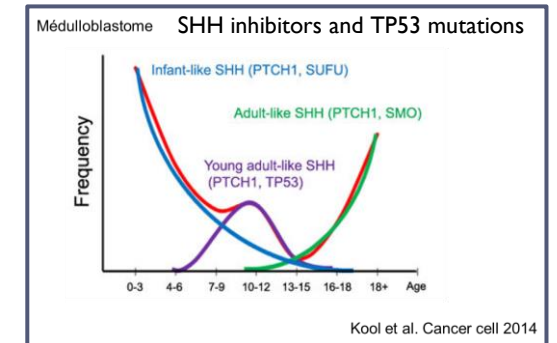
Sharing ?

Adults
Tumour specific

AYA
specific

Scattered
AYA data

EORTC SPECTA-AYA
De Rojas et al. IJC 2020



To increase molecularly driven trials
allowing the full age spectrum

BIOMEDE trial (NCT02233049)

A trial for DIPG, a very rare fatal paediatric cancer

BIOMEDE-2 trial

Enlarged inclusion criteria to mid line glioma, in AYA
disease with the same mutations

PI J.Grill, GR

Problems to be solved

Favour AYA patient access and enrolment in trial

[Lancet Oncol. 2014 Jul;15\(8\):e341-50. doi: 10.1016/S1470-2045\(14\)70113-5.](#)

Available, accessible, aware, appropriate, and acceptable: a strategy to improve participation of teenagers and young adults in cancer trials.

[Fern LA¹](#), [Lewandowski JA²](#), [Coxon KM²](#), [Whelan J³](#); [National Cancer Research Institute Teenage and Young Adult Clinical Studies Group, UK.](#)

Adolescents define themselves as the ones who have to live with the disease without current chance of cure and thus claim to understand and freely choose whether or not to participate in a trial once they have had clear explanations of expected adverse effects and uncertainties about drug efficacy. They are more than willing to participate in adult trials to increase the chance of their own disease responding, as well as for altruistic reasons, as long as they can still be treated in an age-appropriate environment. These factors are crucial for trial compliance, and data quality.

Gaspar N, *et al.* Annals of Oncology 2018

Patient
involvement

AYA care structure and support
AYA research network
Investigators trained for AYA care

Other factors to be addressed such as

- service configuration and/or place-of-care
- and recruitment methods (institutional and/or structural barriers),
- and developmental factors specific to young people, for instance, acceptability of studies (patient-related barriers).

Developing more AYA-driven trials will hopefully help overcome these obstacles.

Pediatric Innovation Research Forum

Noel et al. Therapeutic Innovation & Regulatory Science 2021

Problems to be solved

Make medical/paediatic oncologists aware of existing solutions

ESMO/SIOPE Educational Group Consensus Paper



Ferrari et al.
ESMO open 2021

REVIEW

Adolescents and young adults (AYA) with cancer: a position paper from the AYA Working Group of the European Society for Medical Oncology (ESMO) and the European Society for Paediatric Oncology (SIOPE)

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Table 3. Existing areas of consensus and future actions to optimise AYA access to care and clinical trials

	Areas of current consensus	Historical AYA challenges	Progress	Outstanding issues	Future actions
Availability of drugs and clinical trials	Improve early access to new anticancer drugs for AYA. Increase the number of early-phase trials. Simplify the process of PIPs. ³ Develop trials based on the molecular target and cancer type rather than age.	Small number of diverse cancer types. Clinical trials focused on tumour type rather than molecular pathway exclude AYA. Drug development in AYA and children is not as efficient as adult drug development. PIPs can be waived if pharmaceutical companies believe that the disease is absent in AYA.	ACCELERATE ¹⁹ initiative to favour mechanism-of-action trials, based on the biology of the disease. ACCELERATE initiative to suppress article 11b of the European Paediatric Regulation.	Companies can still apply for PIPs and not develop a drug in the child/adolescent population if the disease under study is non-existent in this population. They do not consider potential similar targets. Drugs are being used off-label in adolescents with little safety or efficacy data. Limited information about the biology of cancer in AYA and drug resistance.	- Develop drugs simultaneously across the whole age range of a disease or target pathway. - Suppress article 11b. - Do not issue waivers without scrutinising potential action in children and adolescents. - Prospective data collection for off-label use. - Identify new therapeutic targets for drug development.
Appropriateness of age eligibility criteria	Arbitrary eligibility criteria should only exist where there is a biological rationale or safety concerns/evidence. Improve access to drugs in early-phase trials.	Many AYA fall between adult and paediatric trials and are excluded based on age eligibility criteria. Pharmaceutical industry-sponsored trials predominately focus on older adults with a lower age limit of 18 years.	ACCELERATE initiative to support the inclusion of adolescents aged ≥12 years in early adult phase I/II trials including first-in-class trials. A number of joint paediatric/adult trials have been developed and have successfully recruited adolescents, and to some extent, young adults.	The number of joint paediatric/adult trials developed has been small. The lower age eligibility criterion of 18 years in trials has not been abolished, particularly in industry-sponsored registration trials. The upper age eligibility criterion in some paediatric trials remains. Trials initiated by paediatric and adult oncology researchers in the same cancer type may overlap, creating confusion for the AYA. Increased collaboration between adult and paediatric trialists is essential.	- Provide guidance to support paediatric and adult oncologists to work together. - Stop upper/lower age eligibility criteria being set in drug trials for cancers. - Support AYA recruitment into clinical trials which span both paediatric and adult populations.
Access to trials	Relevant clinical trials should include AYA and AYA-appropriate care. Adolescents ≥12 years of age should not be excluded from adult trials, based only on age criteria.	Access to trials has been affected by the place of treatment (adult versus paediatric ward). Limited access to adult early-phase trials. Special skills required to obtain consent for AYA to participate in trials.	Development of dedicated AYA hospitals and/or care networks. Allows centralisation of care, AYA expertise and access to relevant trials.	Access to specialist AYA care is not equitable. No central AYA trials register. Researchers tend to be trained in either the paediatric or adult setting and are unfamiliar with the process for consenting AYA into clinical trials.	- Establish a portal of available AYA trials and guidance on referrals to centres with open trials. - Develop a cohort of researchers competent at consenting AYA into clinical trials.
Enrolment into clinical trials	Ensure young people and patient advocates are engaged in trial design. Ensure research questions and endpoints are relevant to AYA needs. Ensure patient information and consent processes are age appropriate.	Involving young people in trial design can be resource intensive. Traditional outcomes, such as survival, are required for regulatory approval. Some AYA cancers have excellent survival rates and trials on quality of life and late toxicities are paramount.	Funding for patient and public involvement has been provided. A number of patient groups are involved in clinical trial design. Several studies have been successfully completed with quality of life and reducing treatment burden as primary endpoints.	Limited awareness among patients and physicians regarding available clinical trials for AYA.	- Educate health care providers and other disciplines regarding the benefits of participating in clinical trials for AYA patients. - Engage patient advocates.

Problems to be solved

To capture efficacy and toxicity information outside trials



To measure the feasibility of the collection of clinical safety and efficacy data of compassionate and off-label innovative anticancer therapies, with adequate pharmacovigilance declaration to inform further use and development of these medicines in pediatric and AYA patients up to 25 years

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SACHA trial



Original Investigation | Oncology

Measuring Safety and Outcomes for the Use of Compassionate and Off-Label Therapies for Children, Adolescents, and Young Adults With Cancer in the SACHA-France Study

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Conclusions

Progresses have been made
We need **MORE**

Participation of the **AYA** population
from early phases to late phases of drug development
might have a positive impact
on patients survival and on the society

But there is not, one solution fits all



What we need

- ▶ **A STRONG** collaboration between **MEDICAL** and **PEDIATRIC** oncologists
- ▶ Increase collaboration with key multistakeholders of drug development : EMA, Ethic committees, and **ONCOLOGY COOPERATIVE GROUPS**



Thanks for your attention



The changes needed

Joint adolescent/adult trials from early drug development



1. In adult early-phase anticancer drug studies, the age of entry into clinical trials should be lowered to 12 years where the agent has an MoA relevant to adolescents' unmet treatment needs, especially when the disease is rarely present in adolescents (making separate studies unlikely), unless there are well justifiable medical and/or scientific reasons not to do so.
2. For phases II and III trials, there should be no set upper or lower age limit criteria for adolescent and young adult (AYA) cancers that are present in both paediatric and adult populations with similar biology. Adolescents over 12 years of age should be included from the onset of the cancer drug development process in adults. Additional adolescent PK and toxicity studies should be undertaken in phase II studies. Children < 12 years should be studied as soon as the pRP2Dis determined.
3. Trials enrolling adolescents should always be conducted in an age-appropriate setting with clinical care provided by expert paediatric or AYA oncologists, to ensure best safety, care and compliance. This could be facilitated by having coprincipal investigators, with separate responsibilities for adults and adolescents.
4. Adolescents should be included in paediatric phase I, II and III trials where relevant (e.g. adolescents with paediatric cancers type or biological targets).
5. Young adult with paediatric cancer types should be offered to participate in paediatric phase II/III trials.
6. This approach should yield adequate data to support an adolescent indication at the time of the initial marketing authorisation application for a given anticancer drug, particularly where the disease crosses the age spectrum and has similar biological and clinical behaviour, or when diseases are histologically different but have similar targets present across the age spectrum.
Adolescent PK/safety data collected in adult trials, even within trials for different diseases, might support extrapolation of activity between diseases if the targets are the same.



To abolish the 18 year dogma: Can we do it?

Increasing numbers of joint adolescent and adult early phase trials are opening

Already some succesful exemples

A SUCCESSFUL EXAMPLE

An "age- and tumour-agnostic" drug development e.g. rare NTRK fusion positive tumours (< 1% of all tumours)

