Improving AYA access and recruitment to trials of innovative therapies

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ACCELERATE FAIR trial group co-chair

29th November 2022

GUSTAVE ROUSSY
CANCER CAMPUS GRAND PARIS

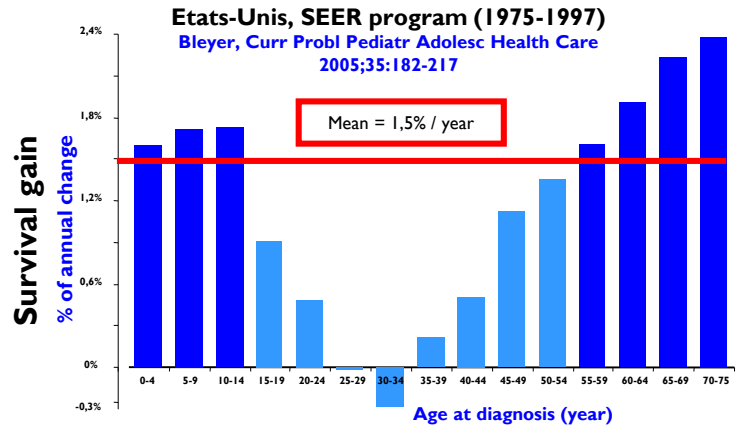
GO-AJA
Groupe Onco-hématologie Adolescents et Jeunes Adultes

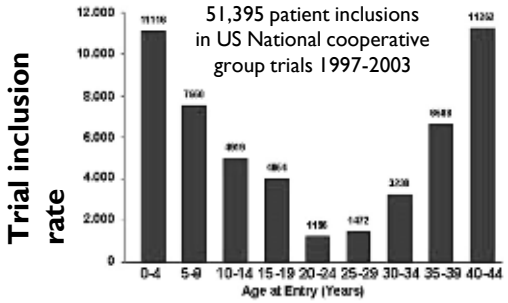
ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

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

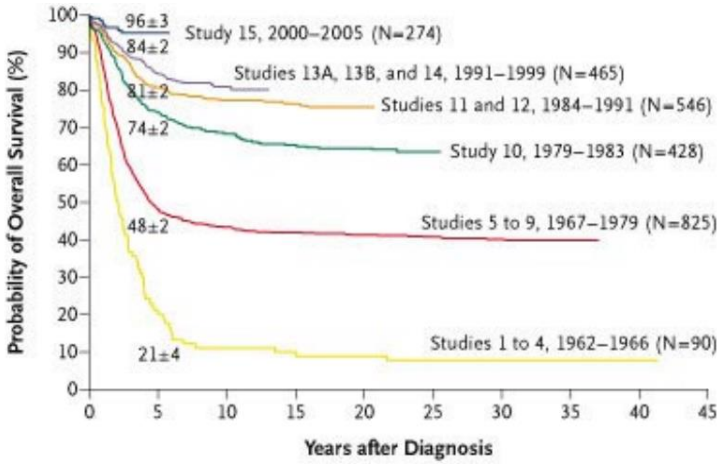




Ferrari A and Bleyer A. Cancer Treat Rev 2007;33:603-608.

AYA survival might be improves by …

Inclusion in therapeutic trials



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

Access to innovative therapies

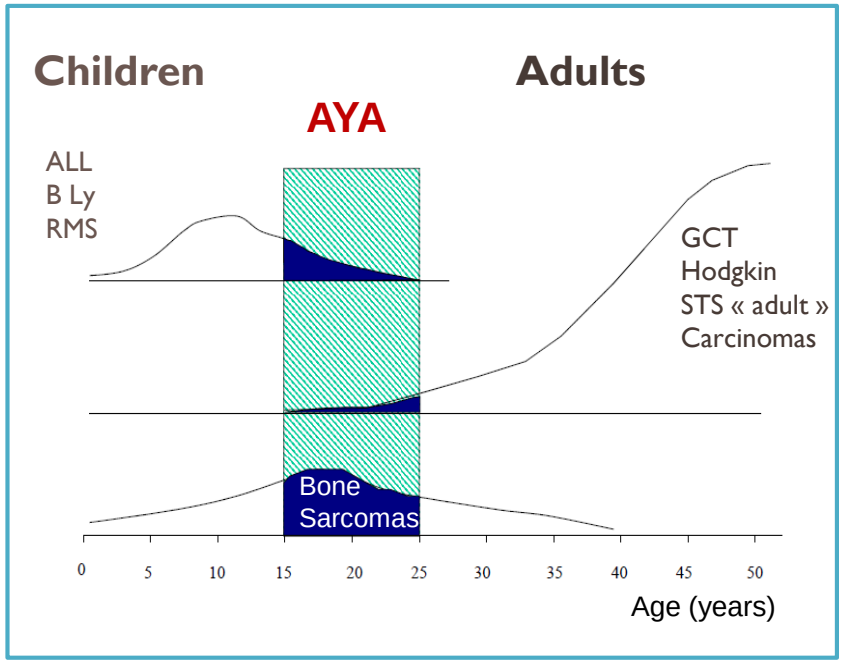
e.g. imatinib plus chemotherapy in Philadelphia chromosome-positive acute lymphoid leukaemia more often seen in AYA)

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

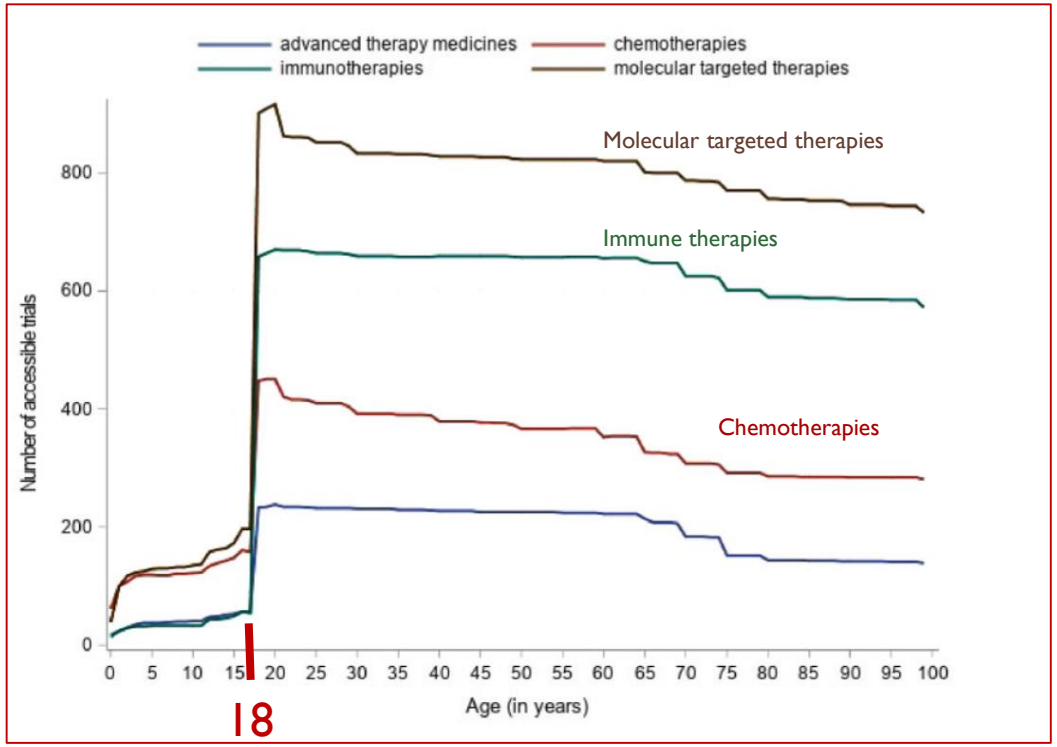
The current landscape

Separate pediatric and adult new drug development

Cancers in AYA have NO age barrier …



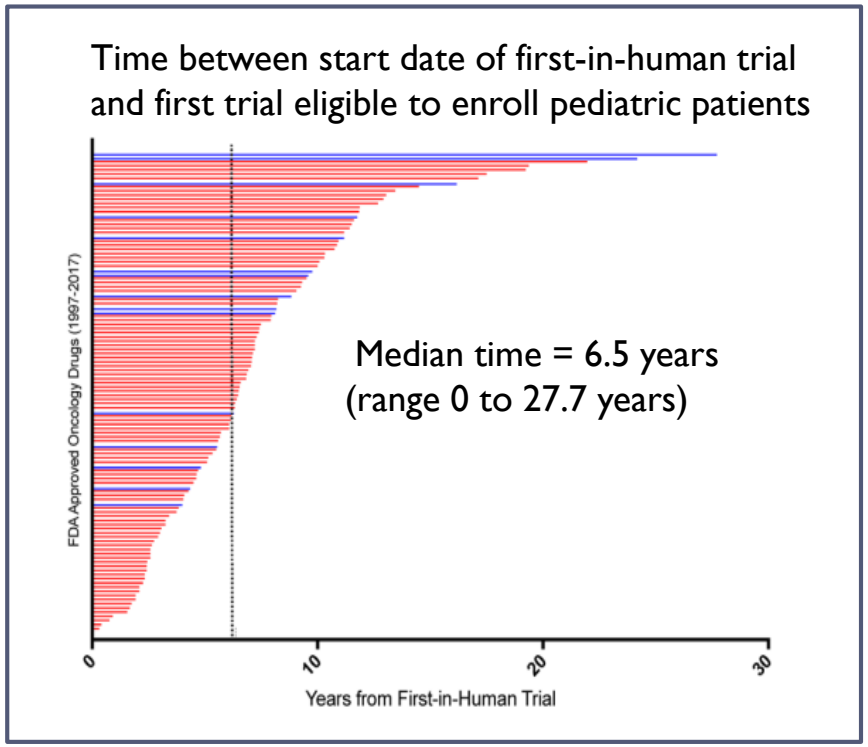
Meta-analysis
January 2007 to July 2018
10 malignancies relevant for AYAs
2176 phase 1, 2 and 3 trials
79% adult
19% transitional
2% pediatric
5 AYA specific



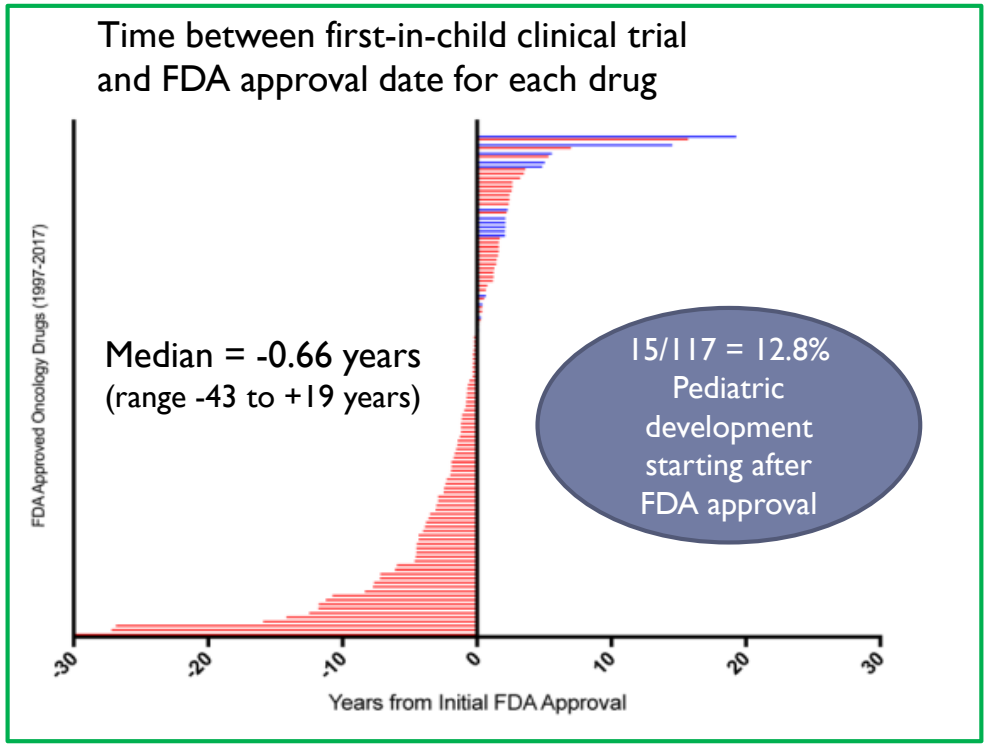
De Rojas et al. JNCI 2019

… therapeutic trials are still govern by an18 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
126 drugs initial FDA approval for oncology indication
47% small molecules, 22% antibodies, 14% chemo, -9 hormonal

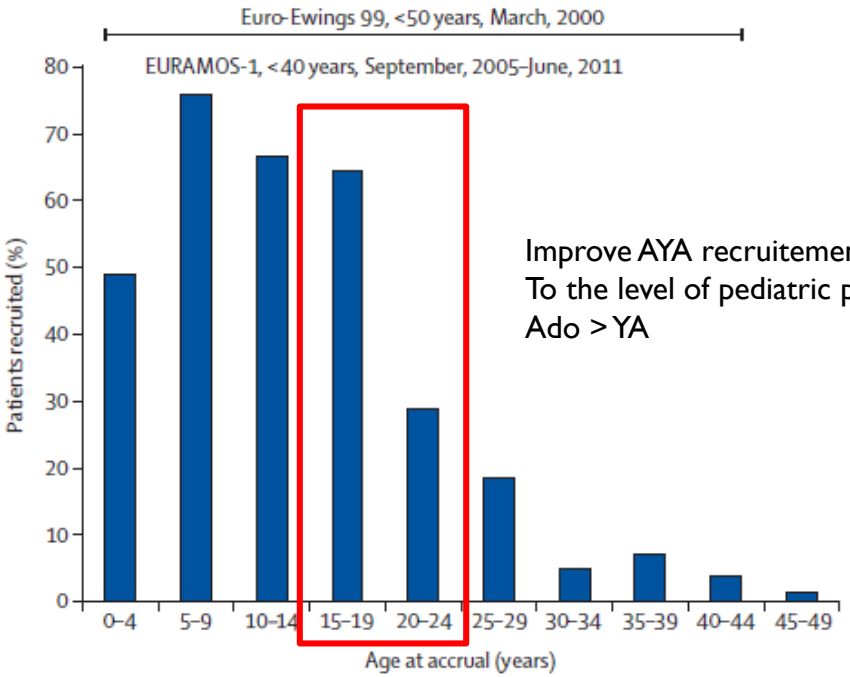
Neel et al. EJC 2019

The current landscape
Delayed pediatric new drug development compared to adult

Even in AYA diasease with strong medical and pediatric oncologists collaboration

Ex Bone sarcomas

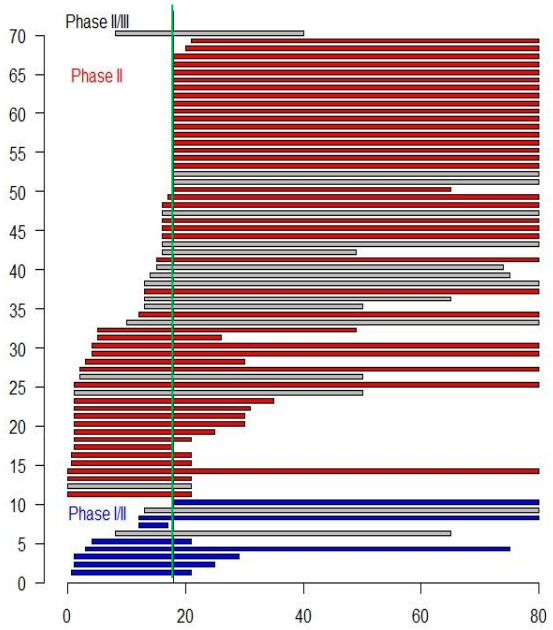
Long history of
Joint pediatric/adult Phase 3 trials



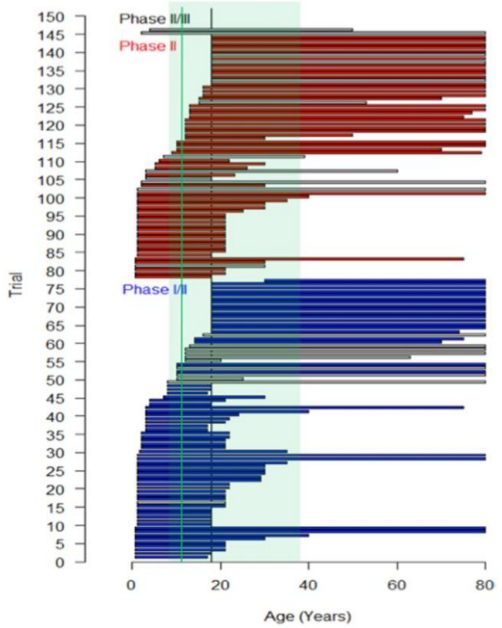
Improve AYA recruitement
To the level of pediatric pop
Ado > YA

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

Osteosarcoma
28% of 99 trials



Ewing sarcoma
12% of 146 trials



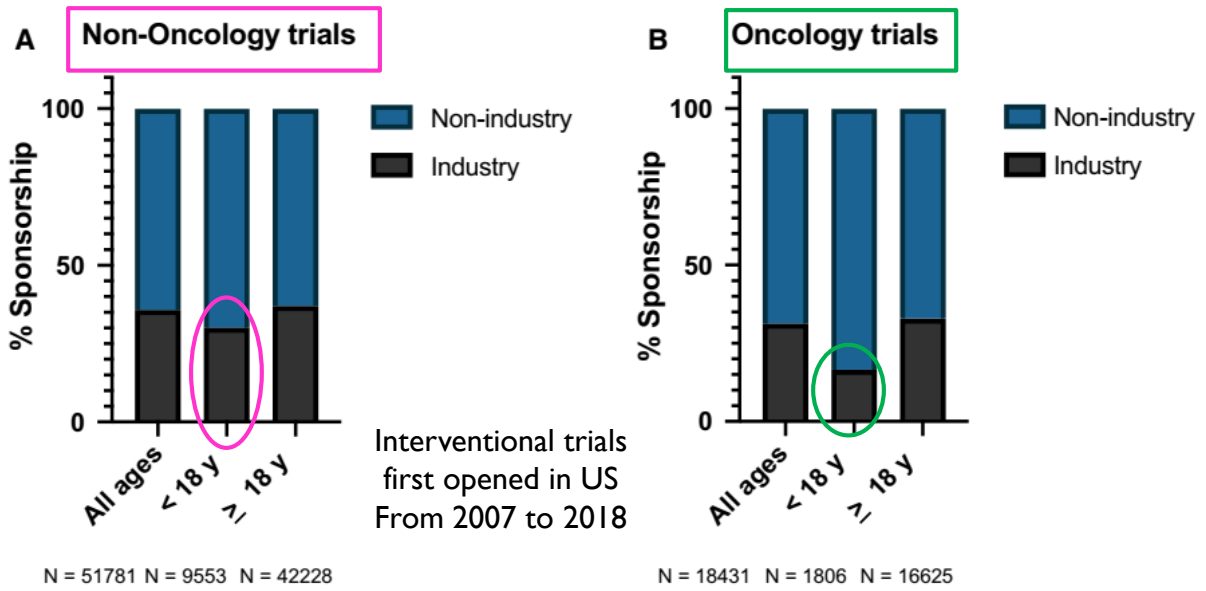
Fern et al. TLO 2014

Omer et al. EJC 2016

Felix et al. Cancer Med. 2021

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%



Interventional trials first opened in US From 2007 to 2018

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

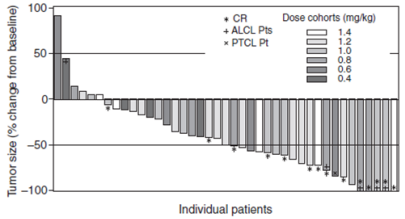
The current landscape

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

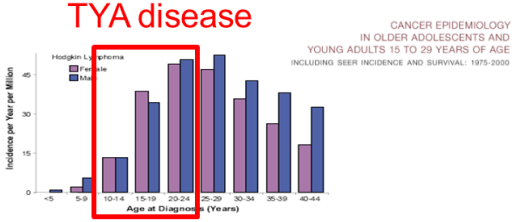
Fanale MA, *et al.* Clin Cancer Res 2012;18:248-255.

Brentuximab vedotin



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

TYA disease



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

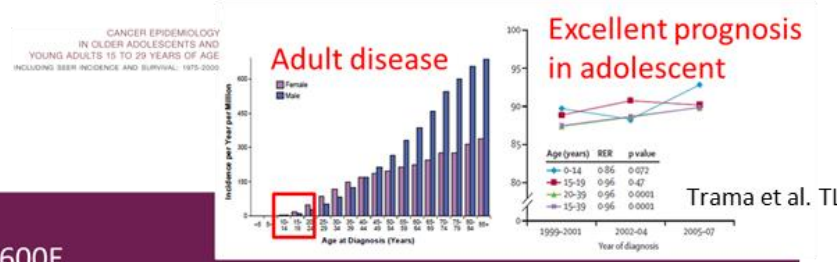
2018

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)

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



Trama et al. TLO 2016

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

- Unsuffisient acrrual 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 Geoerger, 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 approuved 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 diesease

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

=

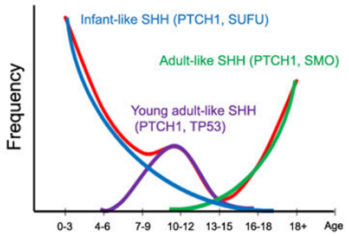
Off-label use in adolescents of new efficient drugs approved in adult indications

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

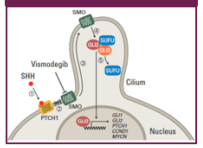
Lost of useful information
- **For the AYA population on drug efficacy, safety and tumor biology**
- **For drug development : drug action/resistance**

Kool et al. Cancer cell 2014



Ex Medulloblastoma and SHH inhibitors

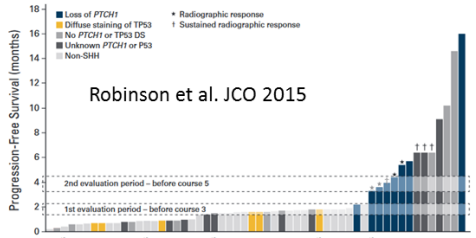
Vismodegidb



No efficacy of SHH inhibitiors if TP53 mutation presents
Mutations are age-dependant
=> The drug development can not be done in adults only

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



Robinson et al. JCO 2015

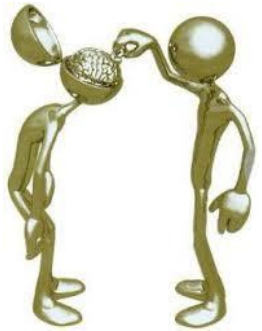
Paed Phase-I trial 3-21 years
NCT00822458
01/2009-09/2013
Published 2013

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 awarness

To be pragmatic

FAIR FOR AYA

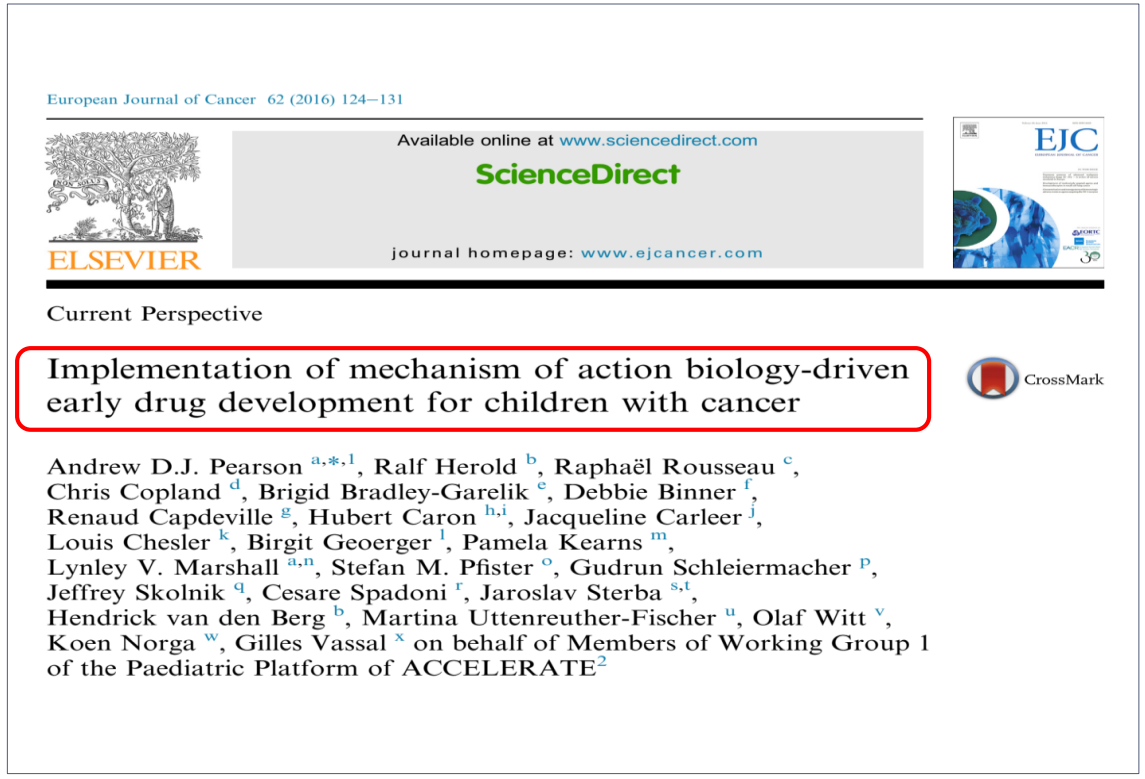
ACCELERATE

INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

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



European Journal of Cancer 62 (2016) 124–131

Available online at www.sciencedirect.com

ScienceDirect

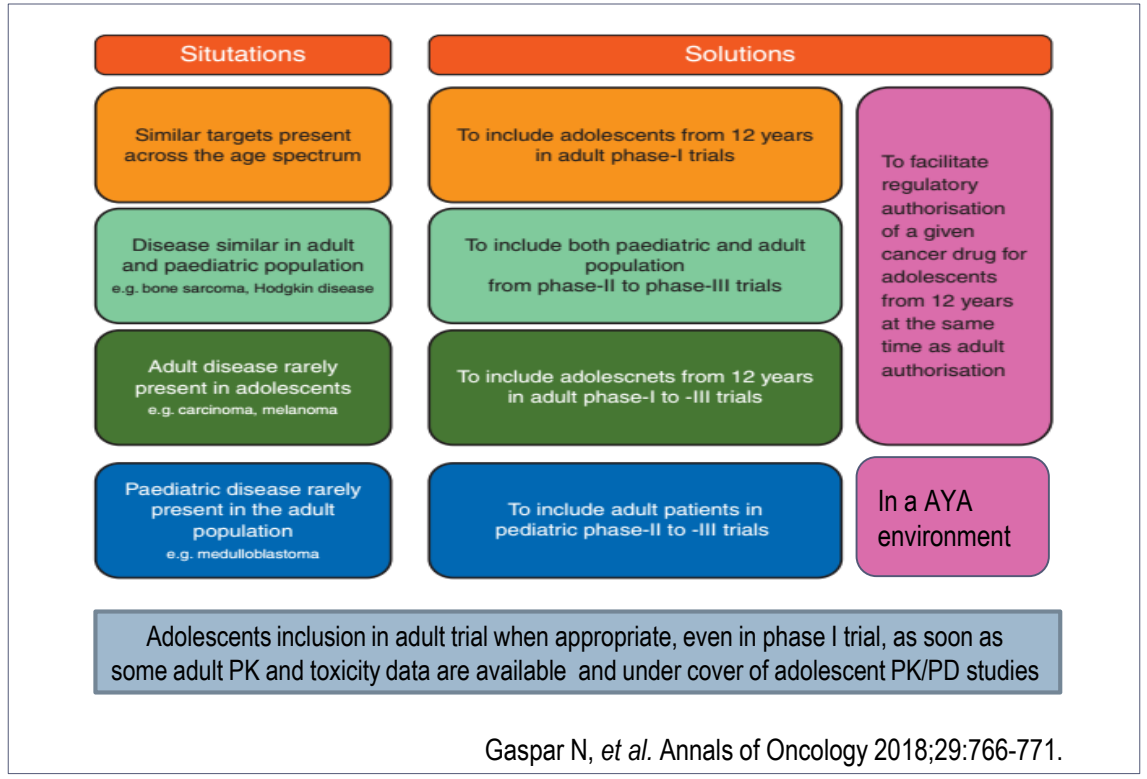
journal homepage: www.ejcancer.com

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 ACCELERATE[2]

To abolish the 18 year dogma from early drug development



Gaspar N, *et al.* Annals of Oncology 2018;29:766-771.

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 fisrt-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 environement

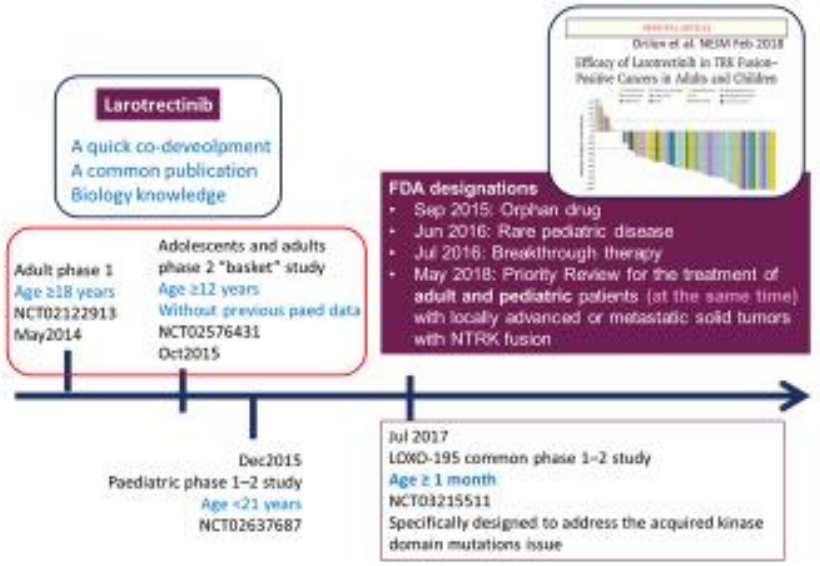
To abolish the 18 year dogma: Can we do it?

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

Already some succesful exemples

A SUCCESSFUL EXAMPLE

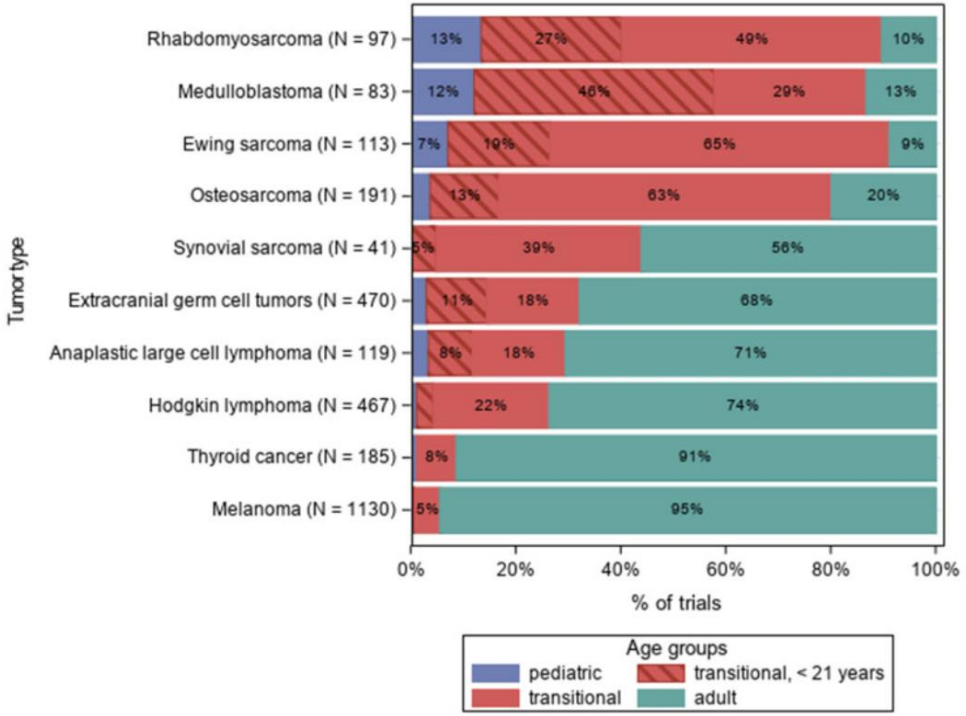
An "age- and tumour-agnostic" drug development e.g. rare NTRK fusion positive tumours (< 1% of all tumours)



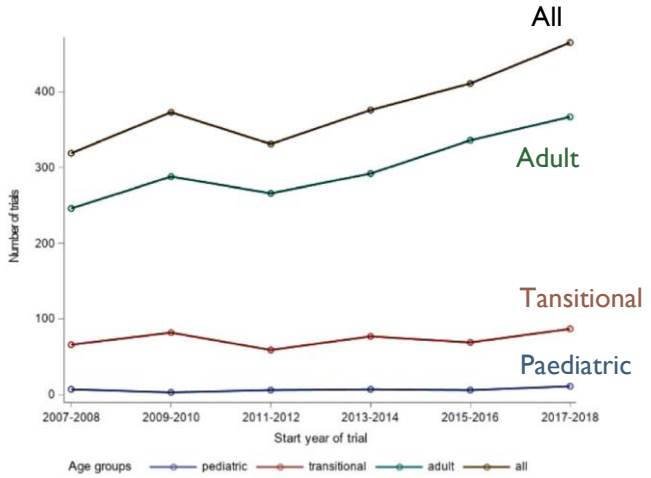
The current landscape
Lack of joint trial from phase 1 to 3 in AYA cancers

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
January 2007 to July 2018
10 malignancies relevant for AYAs
2176 phase 1, 2 and 3 trials
79% adult
19% transitional
2% pediatric
5 AYA specific

de Rojas et al. JNCI 2019

ACCELERATE FAIR Trial working group

Fostering Age Inclusive Research created in 2017

Coordination : N.Gaspar; C.Copland

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

2019: A broader platform

All documment are freely accessible on the website

Associated members
National authorities representatives Regulators
Ethic comittees
Academics from the main European countries

Academic drug development
Paediatric and medical oncologists

Core group

Pharma
Roche Genentech
BMS
Novartis

Patient/parent representatives
AYA
United2Cure

Objective1
To identify successful trials

Objective 2
Awareness Raising to the professional involved in trial design and approval and the general public

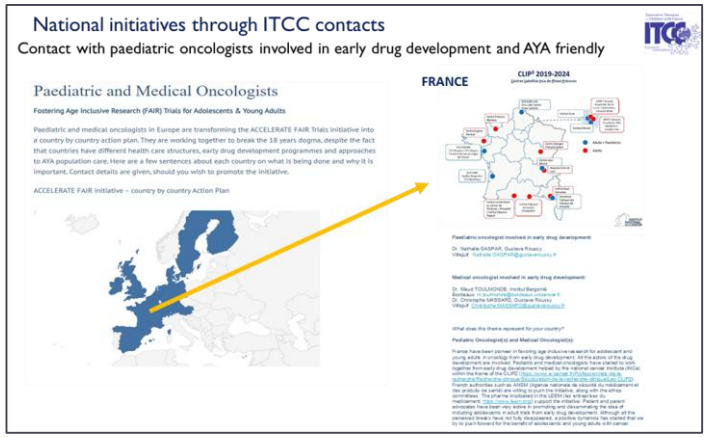
Objective 3
Tools ready to use to facilitate the understanding of the problem and the initiation of trial

Objective 4
Endorsement of the adolescent strategy

ACCELERATE FAIR trial group

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

Pediatric and medical oncologist


National initiatives through ITCC contacts

Contact with paediatric oncologists involved in early drug development and AYA friendly

Paediatric and Medical Oncologists

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

FRANCE

CLIP² 2019-2024

Health autorities

Industry

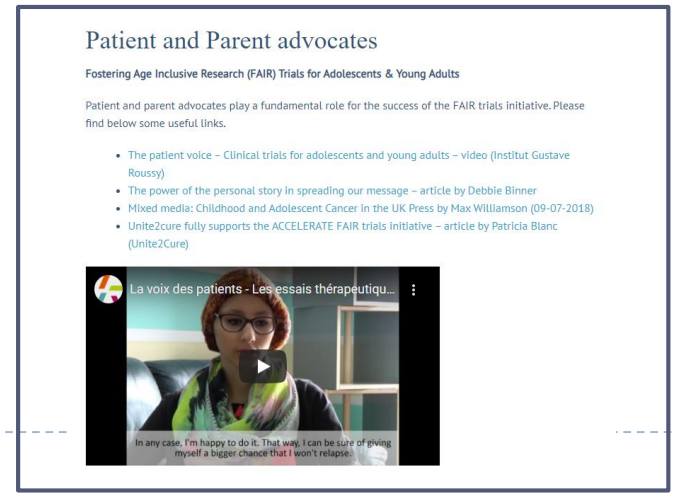

Industry organisation letter of support

June 19, 2020

RE: Fostering Age-Inclusive Research (FAIR) Trials Initiative

Dear Professor Vassal, Dr. Gaspar, and Mr. Copland,

AYA Patients et parents


Patient and Parent advocates

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

Patient and parent advocates play a fundamental role for the success of the FAIR trials initiative. Please find below some useful links.

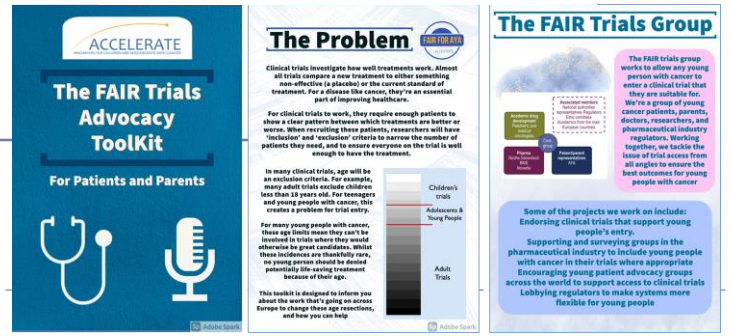
- The patient voice – Clinical trials for adolescents and young adults – video (Institut Gustave Roussy)
- The power of the personal story in spreading our message – article by Debbie Binner
- Mixed media: Childhood and Adolescent Cancer in the UK Press by Max Williamson (09-07-2018)
- Unite2cure fully supports the ACCELERATE FAIR trials initiative – article by Patricia Blanc (Unite2Cure)

ACCELERATE FAIR trial group

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

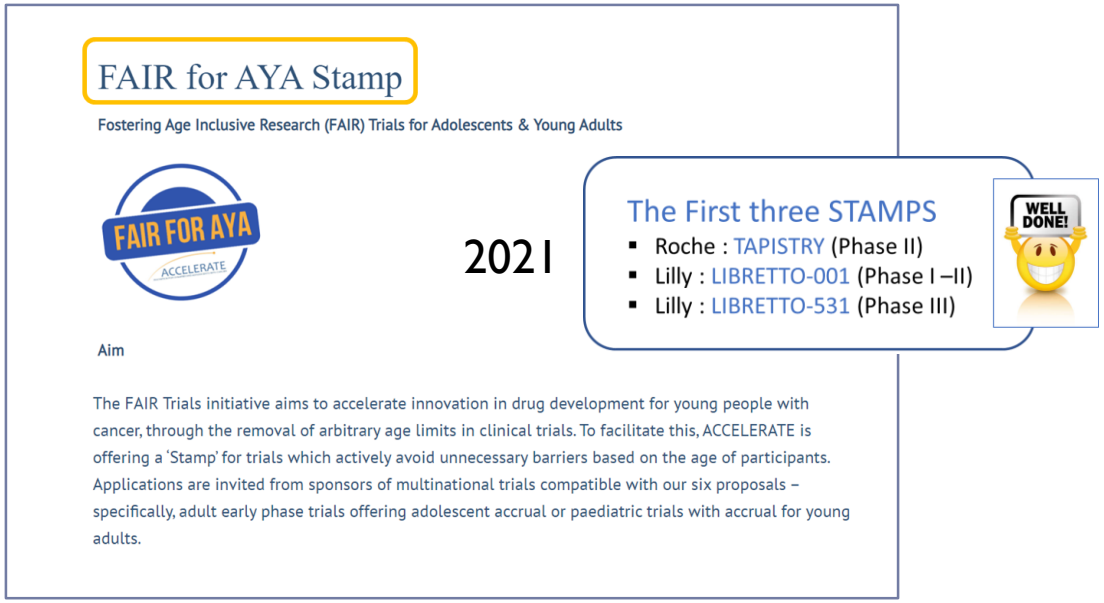
Key elements that should be present in the protocole to assure safe enrolement of adolescents in adult trials

Patient / Parent tool kit



FAIR for AYA STAMP offered for **trials** which actively avoid unnecessary barriers based on age

Structure of confidentiality set up



Joint adolescent/adult trial from early drug development

Are all the problems solved?

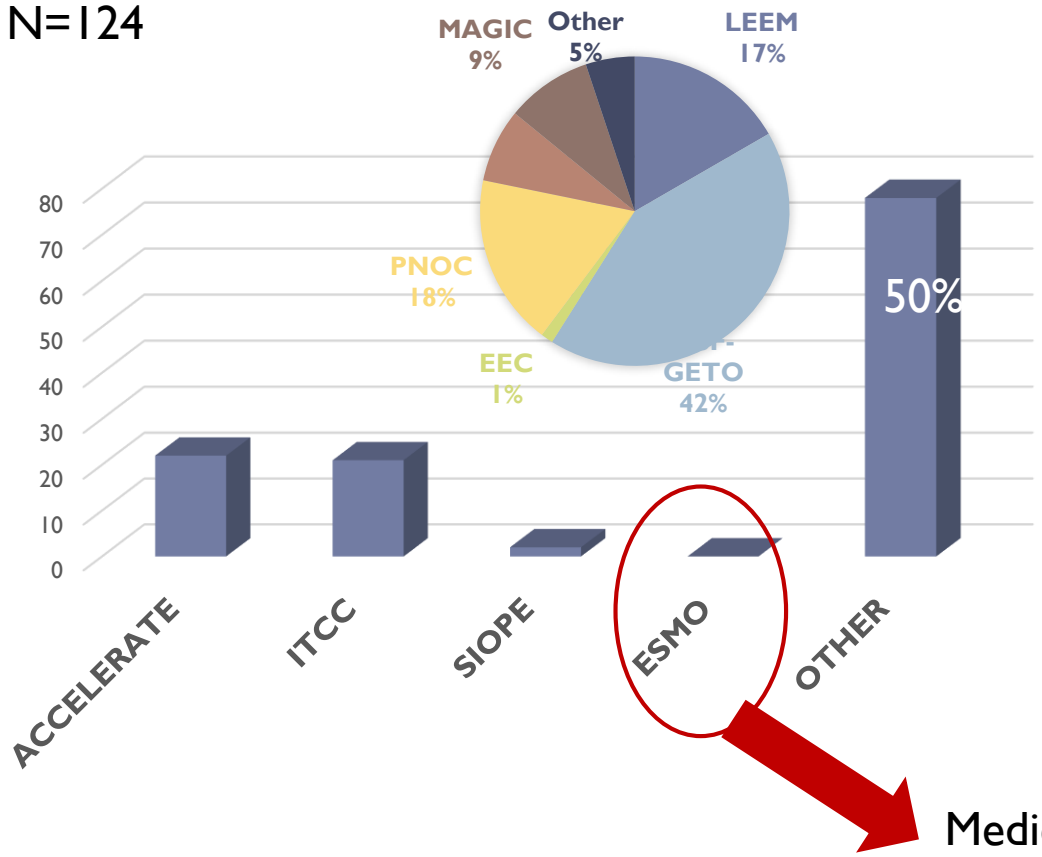
ACCELERATE FAIR Trials Survey 2021

- Survey on the hurdles, real or though on including adolescents in adult trials or including young adults in pediatric trials.
- Contacts
  - Early drug development in paediatric cancers: ITCC, ACCELERATE
  - Oncology societies: SIOPE, ESMO
  - Disease/organ specific group for AYA
    - GCT: MAGIC
    - TG: PNOC, ANOCEF
    - Lymphoma: EURONET Group, EICNHL Group
    - Bone sarcomas: EEC, FOSTER
    - EORTC

Who has answered the survey?

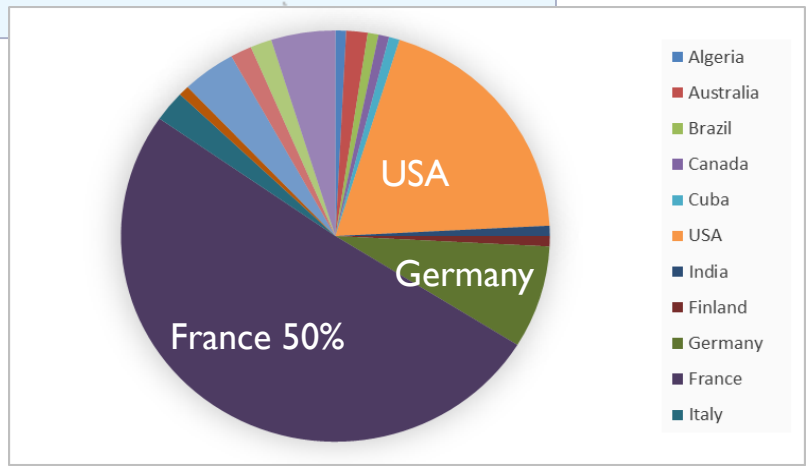
Disease specific cooperative groups

N=124



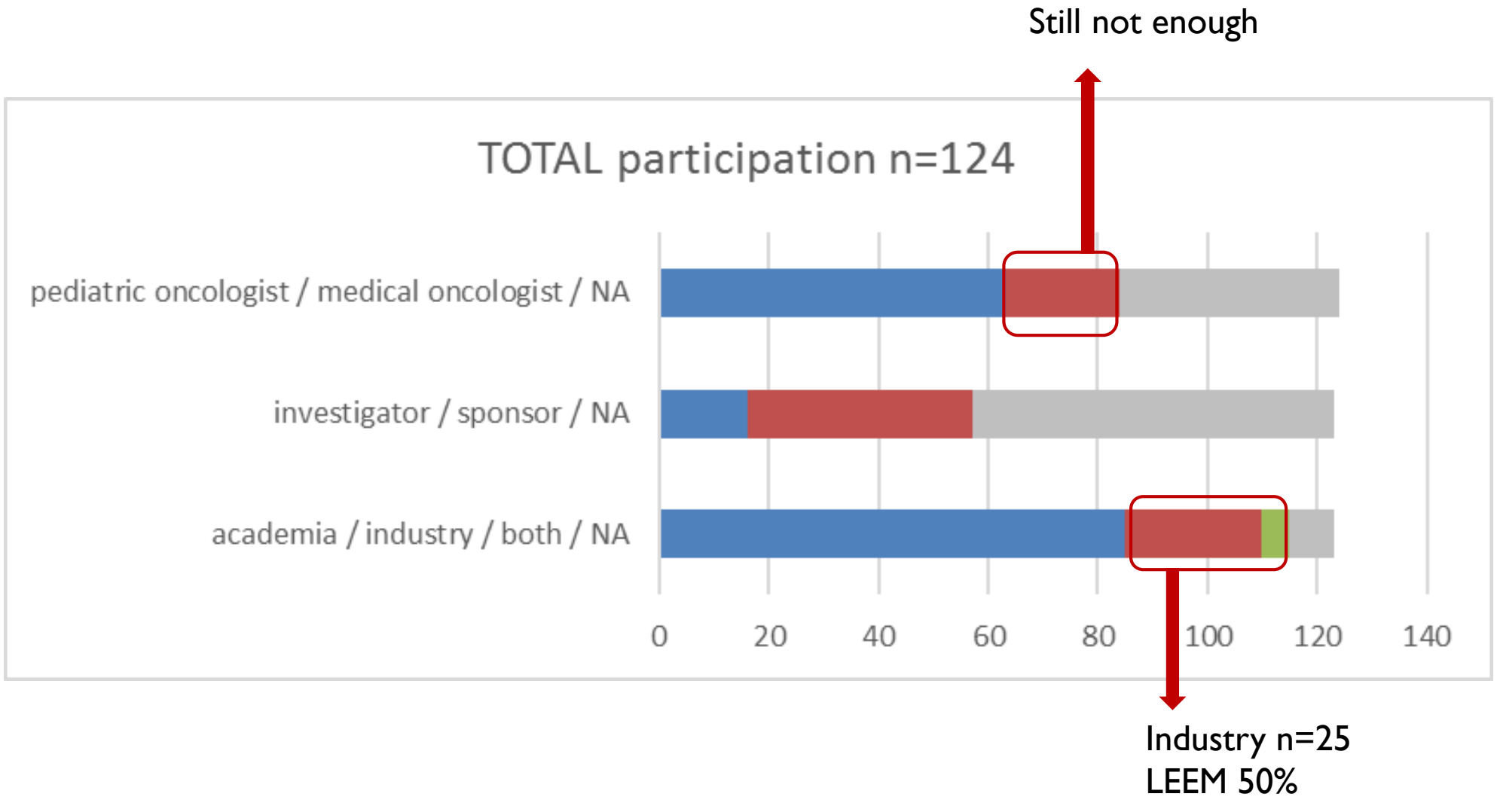
Medical oncologists
To target

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



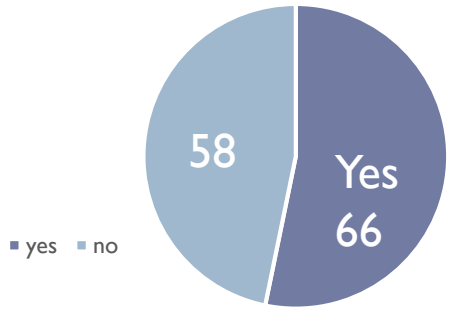
ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

Who has answered the survey?

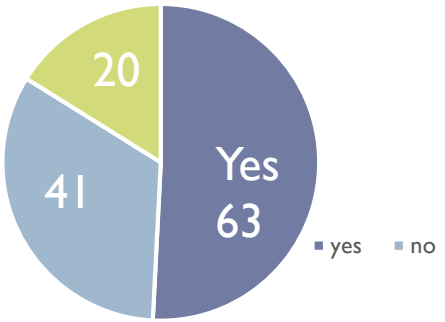


Over the last five years, have you opened …

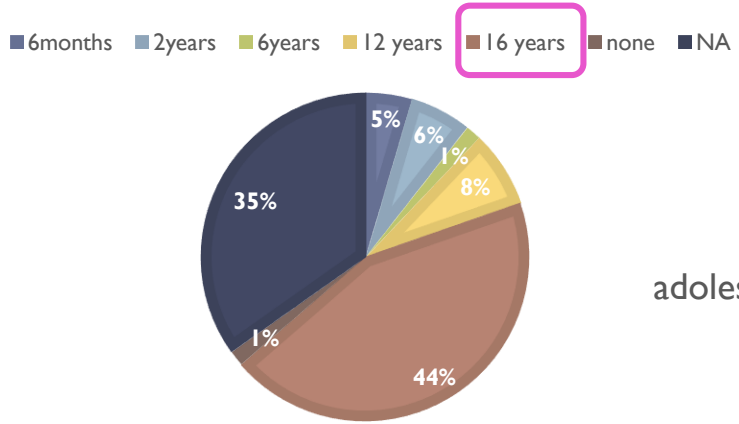
Any adult phase I/II early phase trials which permitted inclusion of AYA patients?



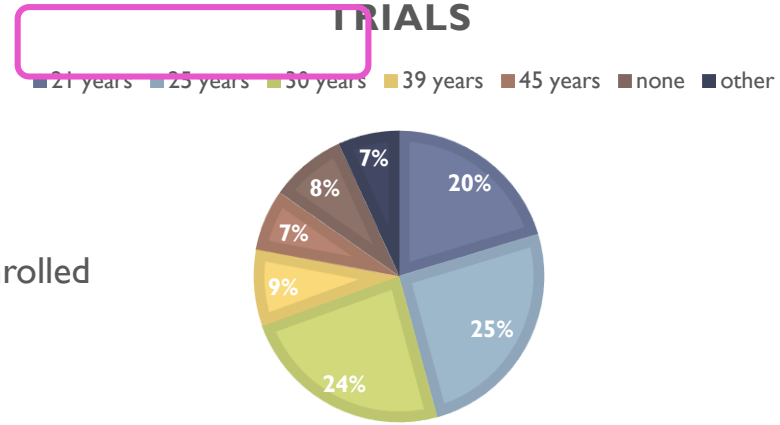
Any paediatric phase I/II early phase trials which permitted inclusion of AYA patients?



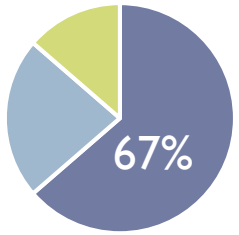
LOWER AGE LIMIT IN ADULT TRIALS



UPPER AGE LIMIT IN PEDIATRIC TRIALS

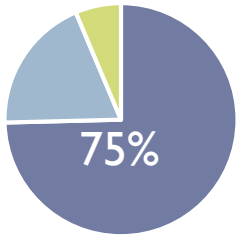


adolescents (12-17 years) enrolled



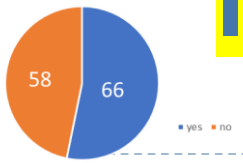
Is AYA recrutment not a problem?

young adult (18-25 years) enrolled



ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

Inclusion of adolescents 12-18 years in « adult » trial

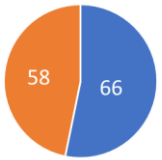


Hurdles to running joint adult-adolescent (ages 12 to 17) phase I/II early phase trials

Pharma refusal remains a problem…

- CLEARLY for academia
- Not for Industry !!!

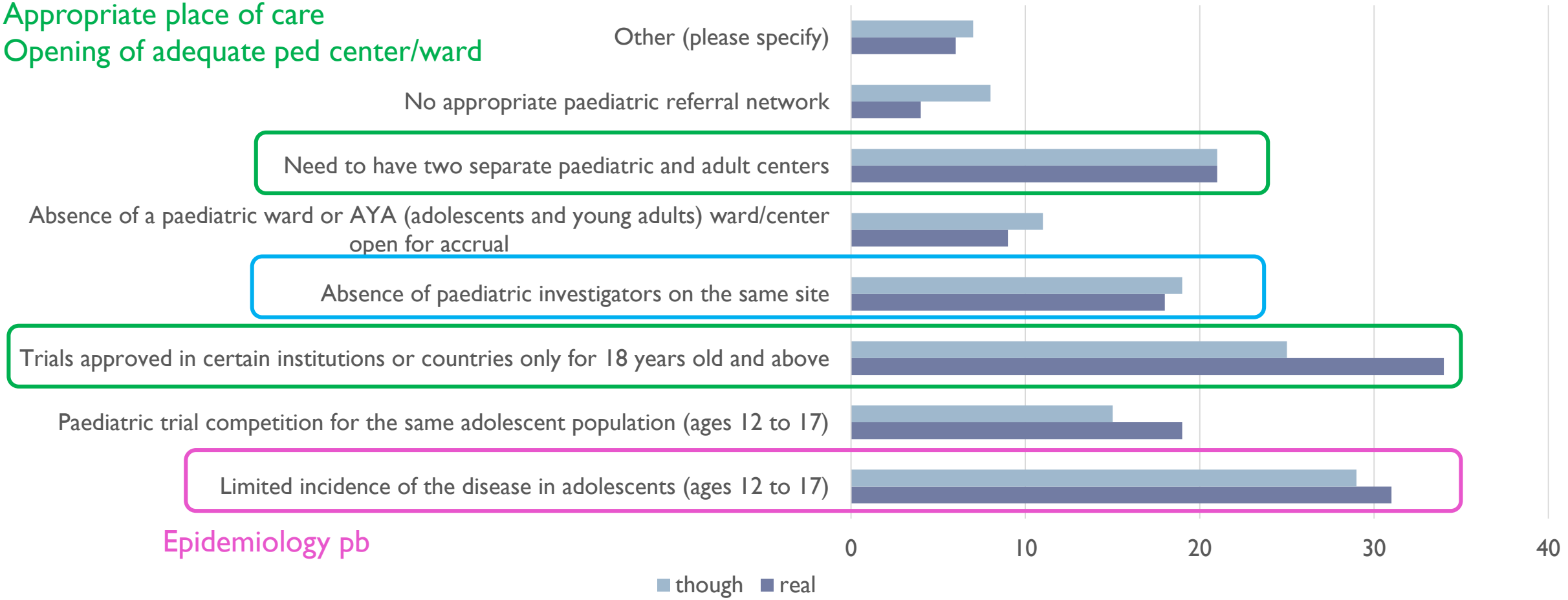
ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER



Inclusion of adolescents 12-18 years in « adult » trial

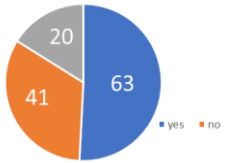
Reasons why it could be difficult to enrol adolescents in joint adult-adolescent phase I/II early phase trials

Appropriate place of care
Opening of adequate ped center/ward



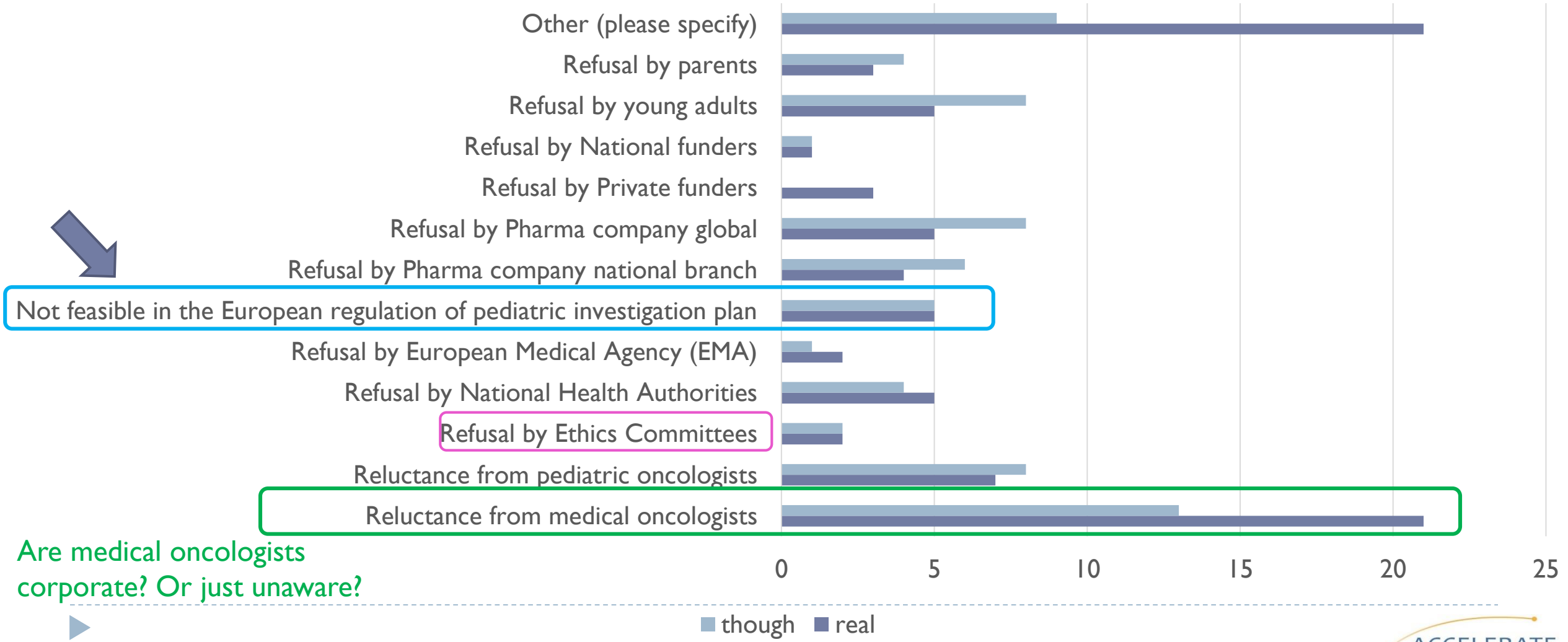
Epidemiology pb

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER



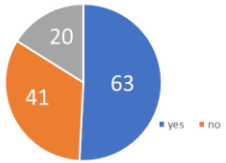
Inclusion of young adults in « pediatric » trial

Hurdles to running phase I/II paediatric early phase trials that allow inclusion of young adults age 18 and above

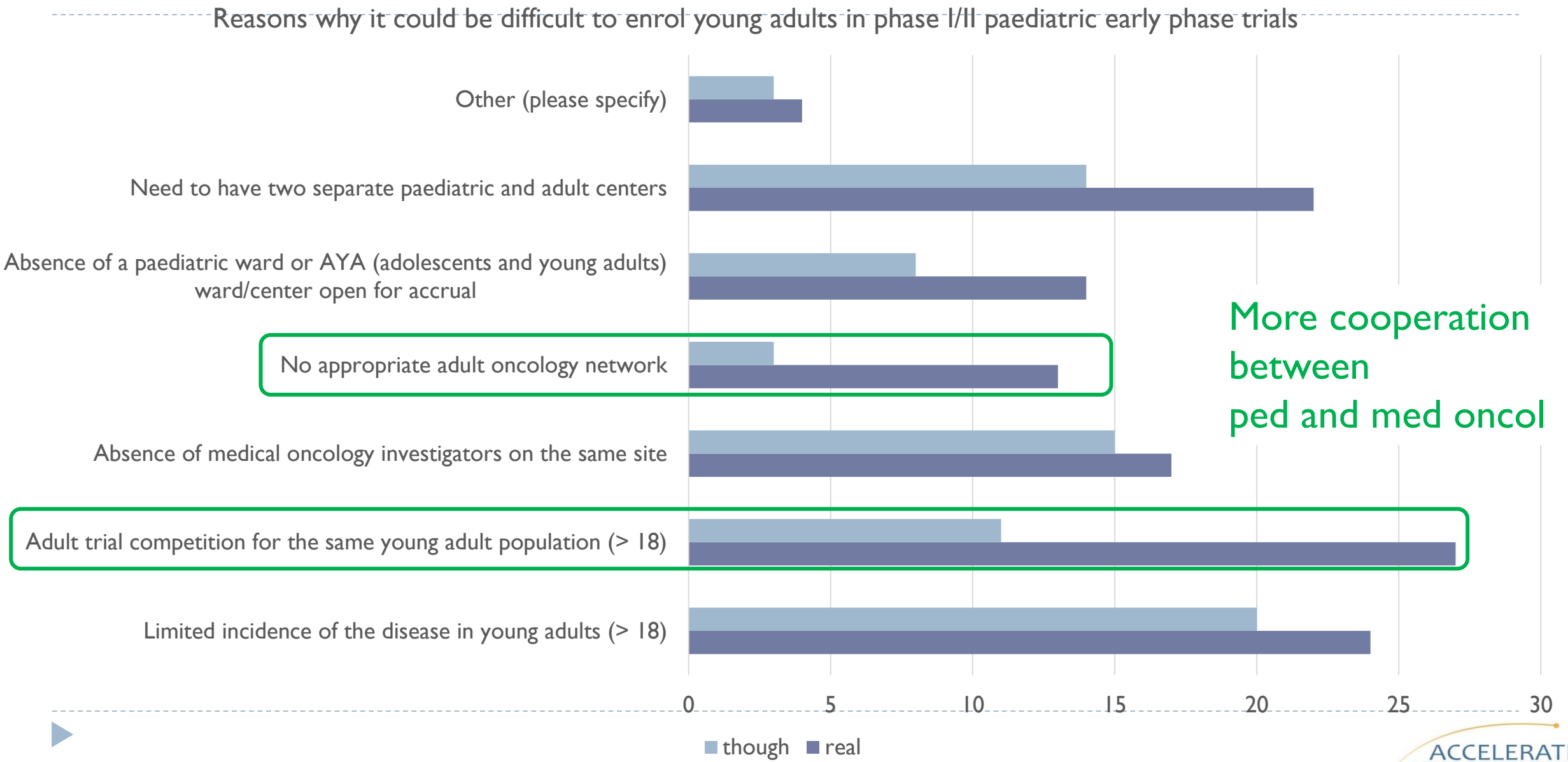


Are medical oncologists corporate? Or just unaware?

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER



Inclusion of young adults in « pediatric » trial



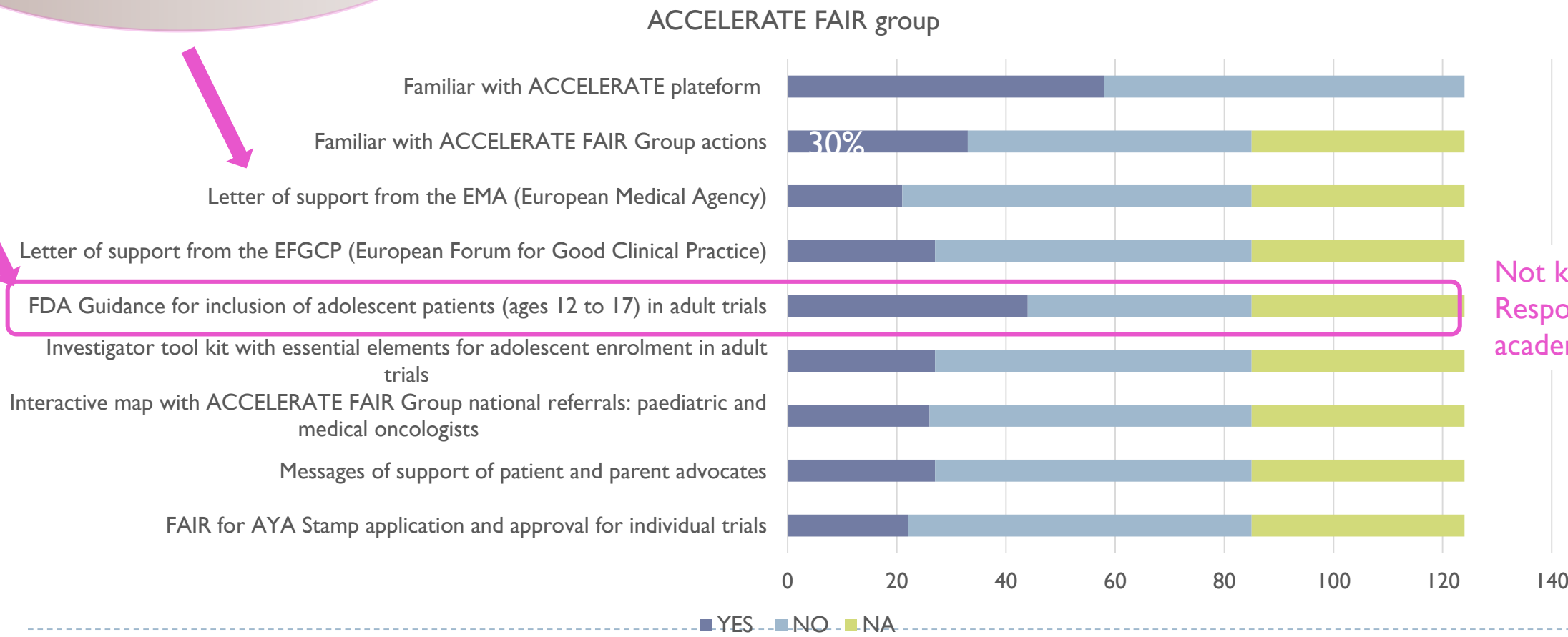
More cooperation between ped and med oncol

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

ACCELERATE FAIR trial group TOOLS

Diversify ways of communication in order to increase FAIR/ACCELERATE awareness

More communication from EMA and FDA?



Not known from Responders, both in academia/industry

Joint adolescent/adult trial from early drug development
Are all the problems solved?

Refusal of joint trial from different stakeholders
Biology knownledge of AYA tumours
Overlapping trials
Efficient recrutment 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

Make medical/paediatric oncologists aware of existing solutions

ESMO/SIOPE Educational Group Consensus Paper

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN CANCER HORIZONS

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)

A. Ferrari[1*†‡], D. Stark[2*†‡], F. A. Peccatori[3], L. Fern[4], V. Laurence[5], N. Gaspar[6], I. Bozovic-Spasojevic[7], O. Smith[8], J. De Munter[9], K. Derwich[10], L. Hjorth[11], W. T. A. van der Graaf[12], L. Soanes[13], S. Jezdic[14], A. Blondeel[15], S. Bielack[16], J.-Y. Douillard[14], G. Mountzios[17] & E. Saloustros[18†]

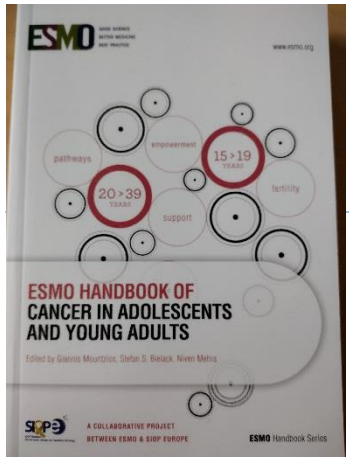
Table 3. Existing areas of consensus and future actions to optimise AYA access to care and clinical trials

	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.[a] 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[b] 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.

Ferrari et al.
ESMO open 2021

Problems to be solved

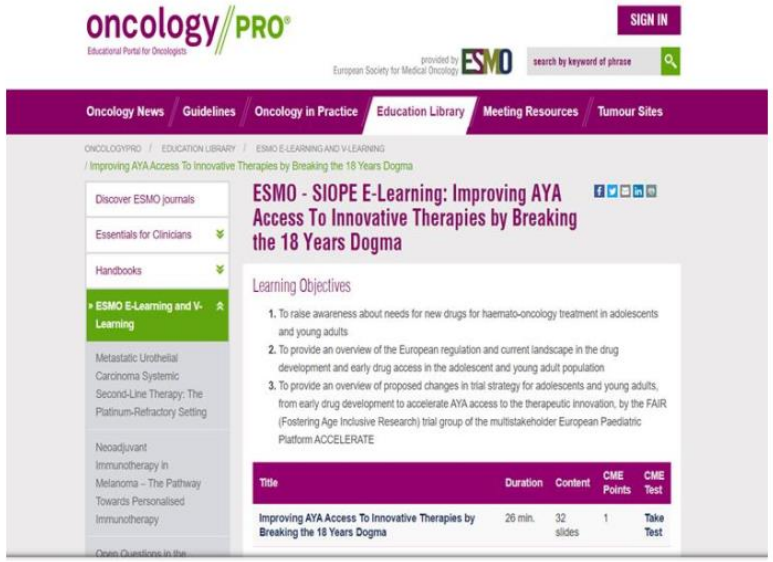
Make medical/pdediatric oncologists aware of existing solutions

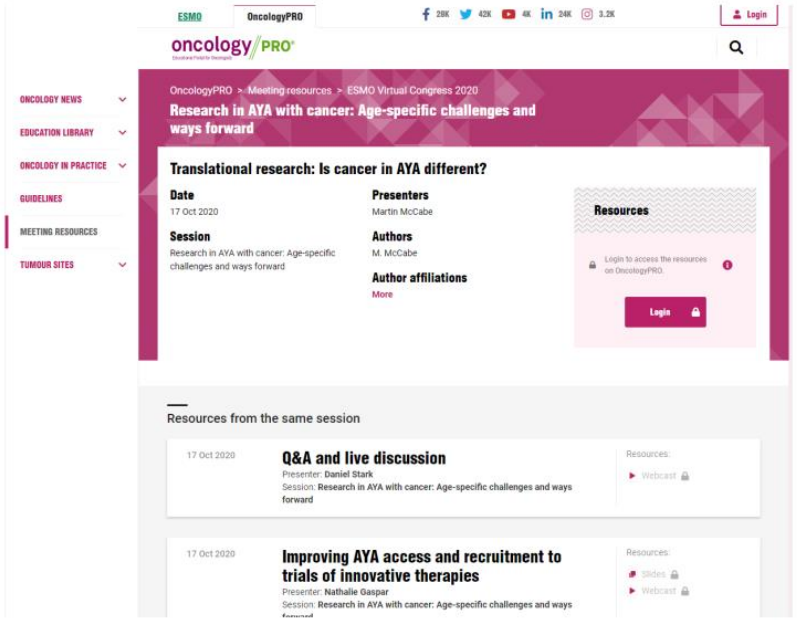


Educational tools

More to come

https://oncologypro.esmo.org/Education-Library/ESMO-E-Learning-and-V-Learning/Improving-AYA-Access-To-Innovative-Therapies-by-Breaking-the-18-Years-Dogma





https://oncologypro.esmo.org/meeting-resources/esmo-virtual-congress-2020/translational-research-is-cancer-in-aya-different

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

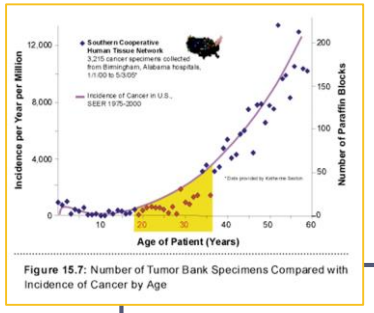
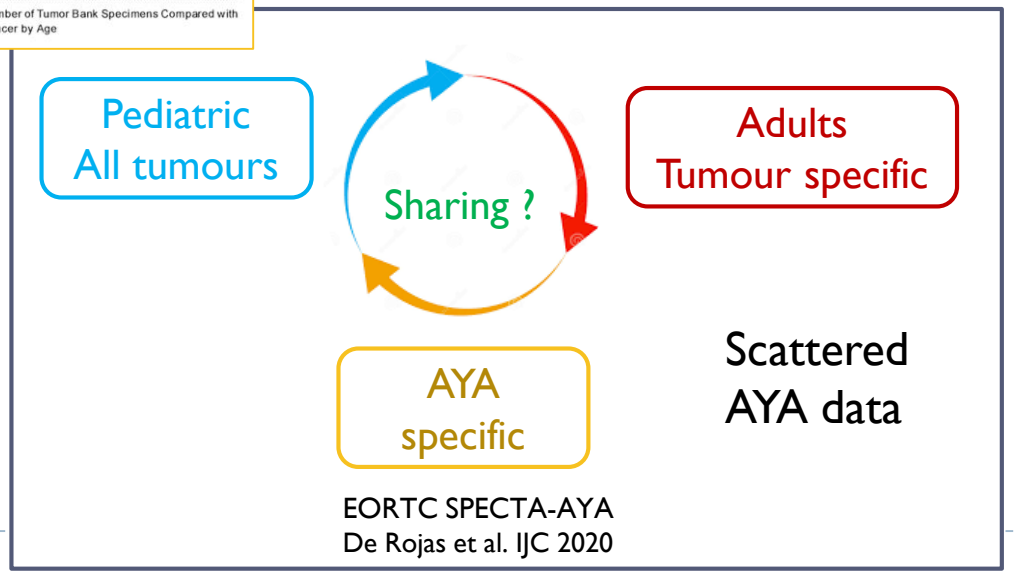


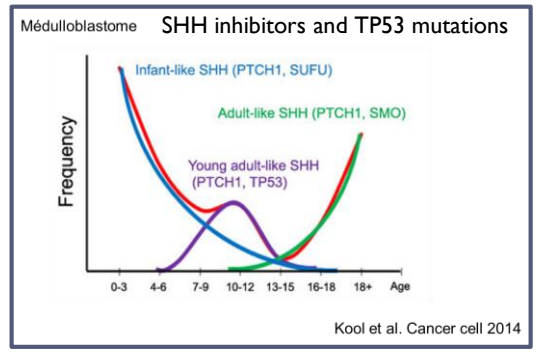
Figure 15.7: Number of Tumor Bank Specimens Compared with Incidence of Cancer by Age

Disease specific research

Trials with biology ancillary studies

Severeal programmes of tumour molecular profiling at diagnosis and relapse





To increase molecularly driven trials allowing the full age spectrum

BIOMEDE trial (NCT02233049)
A trial for DIPG, a very rare fatal paediatric tumour
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 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 LA[1], Lewandowski JA[2], Coxon KM[2], Whelan J[3]; 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

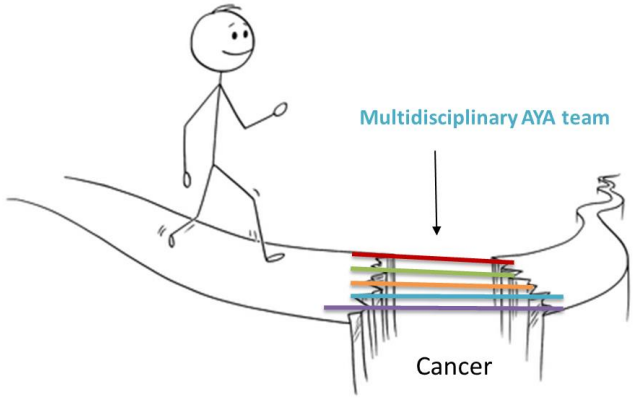
AYA care structure and support
AYA research network
Investigators trained for AYA care

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

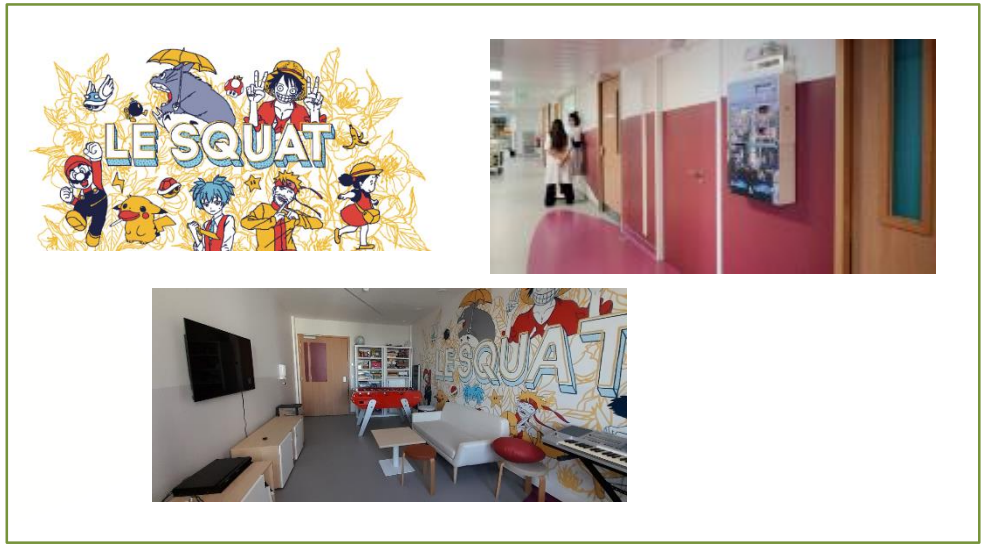
Gustave Roussy AYA care



Dedicated AYA Unit

La Montagne

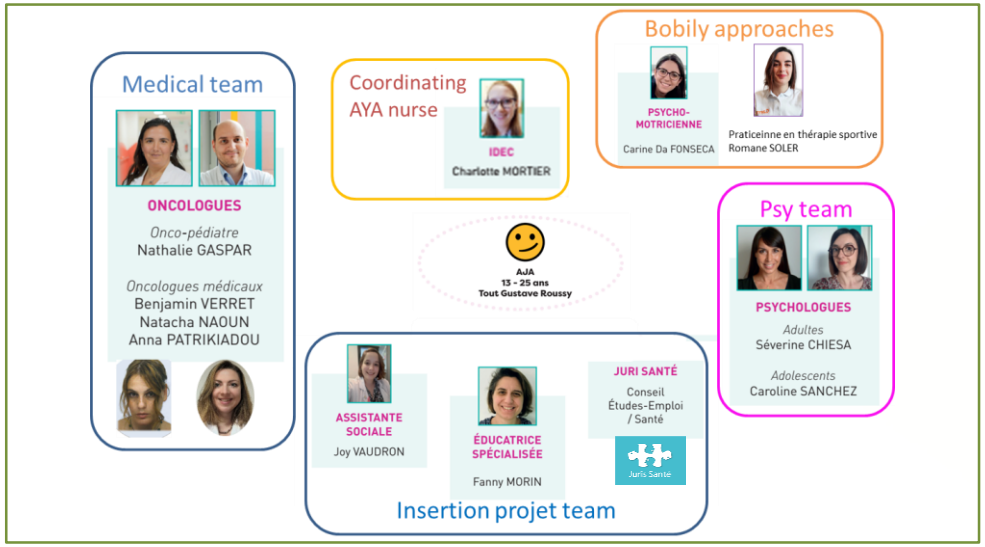
Since 2002



Dedicated AYA interdisciplinary team

SPIAJA team

Since 2012



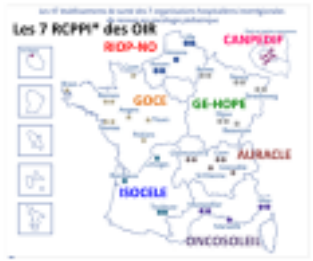
The changes needed

To not loose information on drugs used Off label

PI: Pablo Berlanga, GR

Secured Access to innovative medicines for CHildren with cAncer (SACHA)

- French observational study, prospective collection of toxicity and efficacy data of innovative therapies administered to patients ≤ 25 years-old with pediatric tumors outside their marketing authorization and the frame of clinical trials (off-label/compassionate use)
- Patients will be identified through the interregional multidisciplinary tumor boards (RCPPI) of the SFCE. Data will be collected by the validated pharmacovigilance tool VIGINOM.



SFCE New Drug Development Committee (Gustave Roussy sponsor): Nicolas André, Emilie di Carli, Nadège Corradini, Stéphane Ducassou, Natacha Entz-Werle, Anne Sophie Defachelles, Salim Laghouati, Pablo Berlanga.

To be extended
In Europe

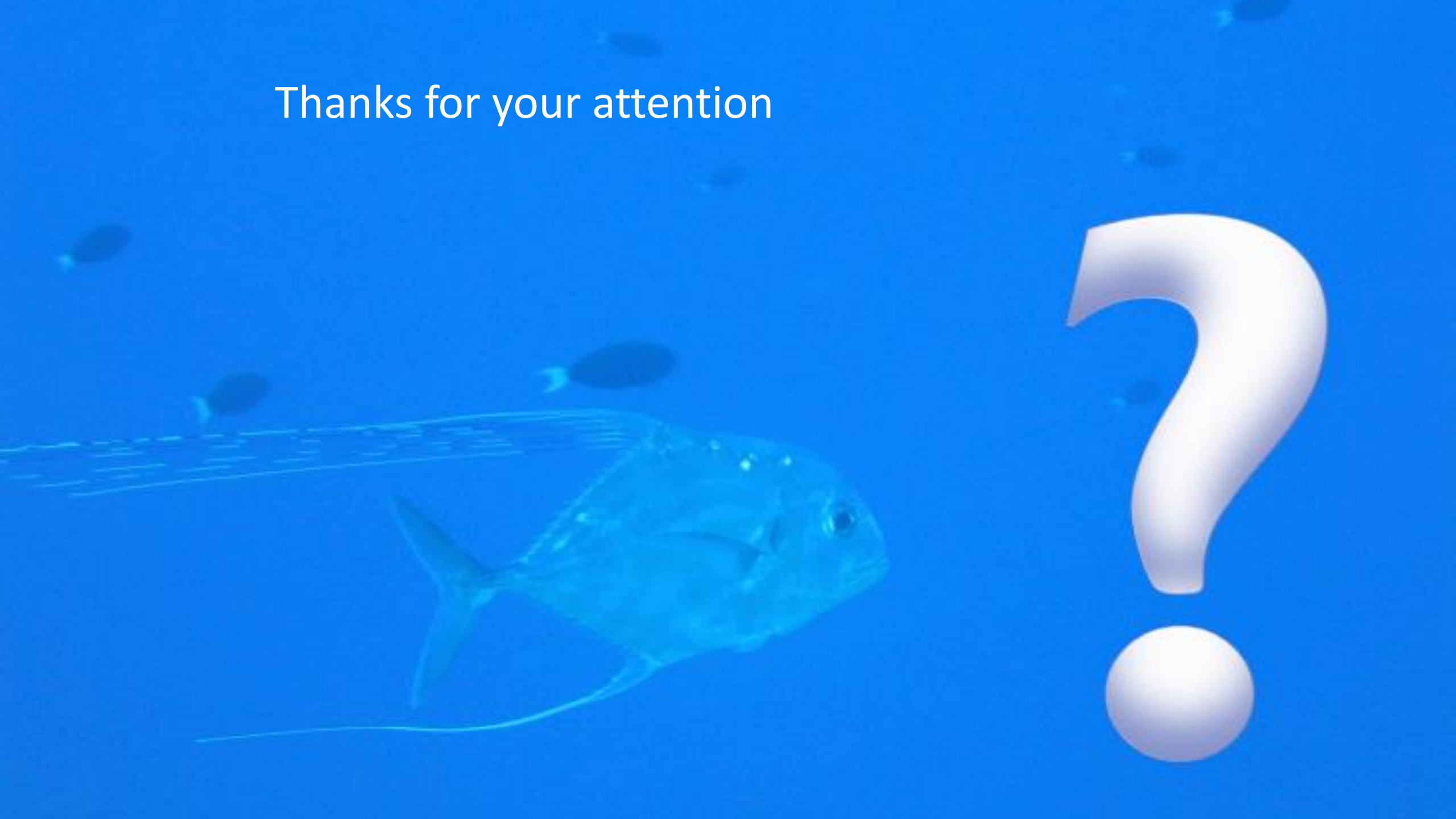
Innovative Therapies for Children with Cancer
ITCC
European Consortium

To accelerate early drug development
for adolsecents and young adults with cancer

Be ready to jump !!!

Be ready to be the generation
of medical and pediatric ongologists that WILL DO IT

Thanks for your attention



The changes needed

Joint adolescent/adult trials from ealy 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.

Gaspar N, *et al.* Annals of Oncology 2018;29:766-771.