

Italian pediatric and adult oncology communities join forces for a national project dedicated to adolescents and young adults with cancer

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Abstract

Adolescents and young adults with cancer have substantially different clinical and psychological needs compared to those of pediatric patients and of older adult patients. We describe the development of an Italian national project dedicated to adolescents and young adults with cancer.

Keywords

Adolescents, young adults, AYA, Italy, AIEOP, AIOM

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Adolescents and young adults (AYAs) diagnosed with cancer make up a particular group of patients whose clinical and psychological needs differ substantially from those of pediatric patients or older adult patients.¹

This editorial describes challenges of working with AYAs, goals set to improve their treatment, and what has been achieved, and describes the development of an Italian national project dedicated to AYAs with cancer.

In recent years, the international scientific community has recognized the particular problems faced by AYA patients. Several local, national, and international projects have developed with the aim of improving chances of survival and quality of life.² These programs often have different features and objectives and propose a variety of solutions.³

The definition of AYAs remains under discussion.⁴ Whereas it is generally accepted that adolescence ranges roughly from 15 to 19 years of age, with young adulthood beginning at around age 20, there is little consensus regarding the upper age limit, which has been variously set at 24, 35, and 39 years. Limiting the AYA age range to between 15 and 24 years enables a stronger focus on the psychosocial aspects shared by AYAs (e.g. fragility, immaturity,

social and sexual experimentation, and lack of a career or economic independence). Experts dedicated to AYA

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Table 1. Unique challenges for adolescents and young adults (AYAs) with cancer.

Unique epidemiology, with both pediatric-type and adult-type tumors
Specific tumor genomics and biology, which may differ for many tumors in AYAs compared with children or older adults
Specific host biology that may also differ by age, with a distinct pharmacology and a potential effect on the efficacy and toxicity of therapy
Insufficient awareness, among young people and their families, as well as physicians, that cancer can develop in this age group
Complex pathway to diagnosis, risk of diagnostic delay, and difficulty of accessing specialized care
Limited participation in clinical research (from 5% to 34% of AYA patients enter clinical trials)
Lack of improvement in survival rates compared with other age groups; for some tumor types, survival in AYAs is worse than in children with the same disease
Unique (and often unmet) psychological needs, including those relating to bodily changes and sexuality, to the development of personal identity, relationships, and independence, and privacy and risk-taking behaviors
Complex communication challenges, shared decision-making, compliance, and treatment adherence
Possible infertility
Survivorship (with potentially distinct late sequelae) and transition to adult medical management
Particular aspects of palliative care and end-of-life care (difficulty of adjusting to a short life expectancy)
Need for a holistic approach with a specific, integrated multidisciplinary team of professionals (age-specific psychologists, clinical nurses, social workers, palliative care specialists, physiotherapists, occupational therapists, experts in nutrition, fertility, and sexuality); involvement of both pediatric and adult medical oncologists/hematologists
Specialized staff training and continuous professional education
Need for age-appropriate clinical environments with dedicated facilities and programs
Need to give young people “voice and choice”; importance of partnership with patients’ advocates

projects tend to prefer a broader definition, and to consider an age range of 15–39 years, as proposed by the US National Cancer Institute/LiveStrong Foundation Progress Review Group.⁵ Including patients >25 years of age alters the epidemiology of cancer types affecting AYAs because it involves various epithelial tumors that are more commonly seen in older adults.^{6–8}

Regardless of the definition adopted, there are several ways in which AYAs inhabit a middle ground between the worlds of pediatric and adult oncology, and neither pediatric nor adult healthcare models have proved capable of meeting their particular needs.^{9,10}

Table 1 identifies unique characteristics of this group of patients, which range from a unique epidemiology (with both pediatric-type and adult-type tumors occurring within the same age group) to a complex psychological sphere, from clinical challenges such as difficulty accessing specialized care and treatment trials to the need for age-appropriate hospital environments with dedicated facilities and programs.¹¹

The European scenario

Faced with these challenges, the scientific community should adapt to the needs of AYA patients with cancer by involving diverse health professionals from different disciplines, patient advocates, and stakeholders, possibly engaging on an international level. An excellent example of cooperation between adult and pediatric oncology societies in Europe comes from the European Society for Medical Oncology (ESMO) joining forces with the European Society for Paediatric Oncology (SIOPE) to

establish a Working Group on AYAs.¹² This Working Group was initially founded for mainly educational purposes: to raise awareness and train adult and pediatric oncology communities; to enhance/exchange knowledge on specific issues in AYAs; to organize joint programs, integrating adult and pediatric oncology groups; and ultimately to improve the standard of care for AYAs with cancer all over Europe. This effort has since evolved, with both international societies recognizing the need to take shared action to influence healthcare policy regarding AYA cancer care and research in Europe by promoting schemes on a national or EU Parliament level.

One of the first actions taken by the ESMO-SIOPE Working Group was to promote a survey describing the training and different practices of European healthcare providers regarding AYAs, and the availability of specialized services for this age group. The survey revealed a severe underprovision and inequity of specialized cancer care for AYAs across Europe, with more than two-thirds of respondents (67%) reporting that their patients had no access to services specifically for AYAs with cancer, or that such services were not being developed. This figure rose to 87% in eastern and southeastern Europe, while it was 55% and 40% for western and northern Europe, respectively.¹³

The ESMO-SIOPE Working Group recently published a position paper that summarizes the challenging aspects of managing AYAs with cancer. It illustrates the vision shared by the two scientific societies on the subject, and what steps must be taken jointly to deal with the most sensitive issues. The publication of such a position paper is an important tool for raising awareness of the need for

age-appropriate specialist services to improve cancer outcomes.¹²

The ESMO-SIOPE position paper focuses on two main points:

1. Provision of and access to specialized centers or service networks built specifically for AYAs and definition of the minimal essential requirements for such centers
2. Development of clinical trials with novel therapeutics and endpoints to address the unique needs of this population

The chances of accessing the best possible treatment available remain a challenge for this group of patients, especially when compared with the advances made in the model of care for children with cancer achieved over the years. There have been several reports of adolescents having worse survival rates than children for many neoplasms, including leukemias and lymphomas, astrocytomas, and bone and soft tissue sarcomas.^{14–17} This survival gap cannot be justified by any single factor. It may partially reflect age-related differences in tumor biology and intrinsic aggressiveness, but variables related to patients' clinical management may have a role as well. The issue of improving access to clinical trials for AYAs with cancer arose from past data showing a more limited improvement in their survival and a correlation with a lower numbers of patients being enrolled in clinical trials by comparison with children or older adults.^{18–25}

The reasons why AYAs are less likely to be enrolled in clinical trials are well documented. They include, among others, a paucity of trials for cancer types common among AYAs; the place of care (children's versus adult hospitals); restrictive age eligibility criteria, with lower age limits often being set at 18 years; treating physicians' lack of awareness of available trials (in the previously cited ESMO/SIOPE survey, more than two-thirds of respondents were unaware of research initiatives for AYAs); and trial designs failing to accommodate AYA-specific life-style, education, and employment factors.²⁶

The significant improvement in survival rates seen in children with cancer over the years can be attributed to the centralization of oncologic care and patients' enrollment in well-designed national/international cancer trials. It is therefore reasonable to assume that a similar approach would have a similarly positive effect on outcomes for AYAs. A complex strategy is clearly needed to improve AYA recruitment in clinical trials, with far-reaching changes to the traditional approaches to drug development, regulation, protocol planning, and care environments. Practical examples extensively discussed in the position paper include trial designs driven by a drug's mechanism of action (rather than by eligibility criteria driven by cancer type or age), with the inclusion of adolescents in early

phase I/II clinical trials from puberty, and the inclusion of young adults in pediatric protocols for pediatric-type malignancies; and the need to revise the European Paediatric Regulation to encourage trials involving the AYA population and to reduce the risk of companies waiving approvals. It could also be beneficial to engage AYA patients with cancer in designing research projects.^{27–35}

Another crucial aspect concerns how we establish the functional and structural characteristics of centers wishing to treat AYAs; in other words, guidelines on the minimum essential requirements for such centers.¹² Ideally, AYA care should be patient-centered, taking an approach that acknowledges each patient's level of independence and maturity. Efforts should be made to provide appropriately equipped spaces and age-specific programs designed to suit AYAs' needs, enabling them to continue living as normally as possible.^{36–39} Patients should be given opportunities to voice their needs and express their choices; their experiences and opinions should be taken into account. The minimum requirements for AYA centers should therefore include flexible age ranges for access to care; a large multidisciplinary team with professionals from different clinical disciplines; the involvement of both pediatric and adult medical oncologists and hematologists; the availability of clinical trials and expertise on a variety of tumor types; age-specific environments designed around AYAs' needs (e.g. access to peers, provision of social and creative activities, education, etc.⁴⁰); age-appropriate psychosocial support; fertility preservation programs^{41,42}; age-specific palliative care services; and late effect/survivorship clinics.^{2,9,10,43,44}

In response to the increasing complexity of cancer care for AYAs, the need for wider cooperation on a European level has been approached by creating the European Network for Teenagers and Young Adults with Cancer (ENTYAC), a federation in which existing professional societies in the sphere of healthcare (ESMO and SIOPE, for example, but also others), national groups of professionals concerned with AYA patients with cancer, nongovernmental organizations, patients, and family groups can cooperate and grow.^{45,46}

The Italian program

Italy has attempted to deal with the increasing demand for AYA-specific care through a nationwide project begun in 2008, promoted by the Italian Association for Pediatric Hematology-Oncology (Associazione Italiana Ematologia Oncologia Pediatrica [AIEOP]).^{47–51} AIEOP is a national cooperative group that has been working for children and adolescents with cancer in Italy since 1975. It has created a network of 49 centers dedicated to the treatment of children and adolescents with oncologic, hematologic, or immunologic diseases. These centers are distributed all over the country and it is noteworthy that there are no pediatric oncology and hematology units in Italy that are not

AIEOP affiliates. A unique characteristic of the AIEOP is that it not only promotes scientific research, but is also directly involved in managing treatment protocols and every aspect of patient care, and has its own databases for collecting patients' clinical information.⁵²

The AIEOP Adolescents Committee was formed with the aim of improving adolescents' access to AIEOP centers, raising awareness that adolescents can have cancer, and promoting cooperation with the world of adult medical oncology.⁵⁰ The Committee established a formal cooperation with the Federation of Parents' Associations (the Federazione Italiana Associazioni Genitori Oncoematologia Pediatrica [FIAGOP]), which brings together most of the parents' organizations active around the country.

The AIEOP Adolescents Committee launched various initiatives dedicated to adolescents with some success, though some difficulties still need to be overcome. In particular, various projects aim to induce the scientific community to pay more attention to these patients and to organize educational projects designed for teenagers and their families. A few examples worth mentioning are as follows: a campaign called "There's no reason why" (to improve awareness that cancer can develop in adolescence)⁵³; the #fattivedere campaign (an Italian term with the dual meaning of "Don't hide!" and "Get a check-up") aimed at helping young people interpret any symptoms they experience, seek medical advice, and arrive at an earlier diagnosis⁵⁴; and the "Winners' Cup" (a football tournament for adolescents with cancer or a history of cancer that, in its third edition in 2019, involved young people from eight different European countries).⁵⁵

A recent survey (conducted in 2020) showed that 19 AIEOP centers have developed specific programs dedicated to adolescent patients (10 years earlier, only two centers had attempted to do so)⁵⁶⁻⁶¹ (Figure). The percentage of adolescents treated at AIEOP centers has also increased over the years, with the observed/expected ratio rising from 10% in 1989–2006 to 28% in 2007–2012, and 37% in 2013–2017.⁶²

A national project called (Società Italiana Adolescenti con Malattie Onco-Ematologiche [SIAMO] [Italian Society for Adolescents with Onco-Hematological Diseases]) was launched in 2014 as an extension of the AIEOP Committee on Adolescents.^{63,64} The aim was to create a broad-based, comprehensive national platform together with scientific societies focusing on adult oncology (and other stakeholders, such as parents' associations). Efforts to develop a genuinely effective collaboration between pediatric and adult oncologists failed, and, given the lack of support from the Italian national health service and government, the SIAMO project was abandoned in June 2018.⁶²

Efforts to achieve a closer collaboration between pediatric and adult oncologists on the topic of AYAs have continued to be made, however, and in April 2021 the Italian adult medical oncology society (Associazione Italiana di Oncologia Medica [AIOM]) joined forces with the AIEOP



Figure. A young patient of the Youth Project in Milan, a program specifically dedicated to adolescents and young adults with cancer, with the aim to overcome any obstacles affecting their quality of treatment and their quality of life, focusing on medical aspects of care as well as on a holistic approach to the patients' lives (photograph by Alice Patriccioli).

to set up a formal AIEOP-AIOM Working Group dedicated to AYAs.

The AIOM has represented the Italian medical oncology community since 1973. With more than 2500 active members, it promotes progress in clinical and experimental areas and social support; facilitates cooperation between oncologists and specialists in other disciplines; collaborates with national, regional, and local institutions; and develops clinical recommendations and guidelines for tumor types and disease settings.^{65,66}

The AIEOP-AIOM Working Group dedicated to AYAs is taking its first steps towards defining its formal structure and strategy. Its starting goals are as follows:

- To formalize collaboration between pediatric and adult oncologists
- To raise awareness regarding cancer in AYA age by producing educational projects and making them available via e-learning platforms, by publishing a newsletter, and by organizing face-to-face meetings
- To promote clinical and biological research on cancer in AYAs
- To draw up clinical recommendations or guidelines on various topics common to both societies
- To promote cooperation with potential stakeholders
- To establish (in an institutionally shared document) the essential structural and functional characteristics

for a center to be considered suitable for the clinical management of adolescent patients, with the aim of identifying a network of specifically dedicated onco-hematologic centers—be they medical oncology or pediatric oncology units—distributed all over the country

- To earn institutional recognition in order to make the program sustainable, make local programs part of a comprehensive national approach, and adopt a standard of care, the final goal being to establish a comprehensive national approach supported by the central government and the Italian national health system
- To decide on the best approach to treating adolescent patients with onco-hematologic diseases, starting from the patients' needs, from “what is best for them,” and always bearing in mind the importance of involving the patients themselves

One of the main challenges for young people with cancer is to live life as normally as possible. This means achieving developmental milestones, living the same experiences as their peers, and experiencing rites of passage that should not be postponed as a result of being diagnosed with cancer. Physicians should understand these needs and provide models of care that facilitate these experiences. For this to happen, it is fundamentally important for physicians, nurses, social support workers, and psychologists who work with AYAs with cancer to have training to help their young patients cope with the multifaceted challenges of their illness. Providers must recognize the importance of establishing an open relationship with their patients and helping AYAs with cancer find the resources they need to answer their questions, help them cope, and fulfill their psychosocial as well as physical needs.

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