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The molecular profile of gliomas in adolescents and young adults

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Abstract

Adolescents and young adults (AYAs), defined as individuals aged 15-39, represent a distinct and underrepresented population in glioma research and clinical care. Gliomas are the most common central nervous system (CNS) tumors in this population and span both pediatric and adult molecular subtypes, making diagnosis and treatment particularly complex. While the 2021 WHO classification of CNS tumors underscores key molecular differences across age groups, there remain limited standardized, age-specific guidelines for AYA patients. Molecular profiling is especially critical in this demographic, as more than 80% of AYA gliomas harbor potentially targetable alterations, including IDH mutations and *RAS/MAPK* pathway abnormalities. Optimizing outcomes for AYA patients requires multidisciplinary collaboration across pediatric and adult specialties. Currently, low clinical trial participation and fragmented care contribute to significant disparities in treatment and outcomes. To overcome these challenges, there is an urgent need for dedicated AYA treatment frameworks, expanded clinical trial eligibility, and the routine integration of comprehensive molecular diagnostics. These efforts are essential to closing the care gap and enhancing both survival and quality of life for this vulnerable population.

Key Points

- AYA gliomas prepresent a distinct group with overlapping pediatric and adult molecular features.
- Many AYA gliomas harbor actionable molecular alterations supporting routine molecular profiling.
- Multidisciplanary AYA-focused care models are needed to address fragmented care.
- A Expanding clinical trial access is critical to improving outcomes.

Gliomas are the most common type of central nervous system (CNS) tumor and contribute significantly to morbidity and mortality among adolescents and young adults (AYA).[1,2] While the AYA age range is commonly defined as 15-29 y by organizations such as the National Cancer Institute (NCI), this definition encompasses substantial biological heterogeneity, reflecting a transitional period between pediatric and adult tumor biology. This demographic faces distinct challenges in disease management. Medical care for AYA patients is often fragmented between pediatric and adult healthcare systems, and their unique psychosocial, biological, and economic characteristics contribute to diagnostic delays, inconsistent medical follow-up, heightened sensitivity to treatment toxicities, fertility preservation issues, limited participation in clinical trials, and a lack of standardized treatment protocols. These factors result in widely variable approaches to care.

The 2021 World Health Organization (WHO) classification of CNS tumors integrated molecular profile with histopathologic characteristics, grouping gliomas into 6 categories. Several categories are specifically associated with pediatric or adult age groups.[3] Glioma tumor biology and clinical prognosis differ among age groups, and patient management is vastly different in the pediatric and adult populations due to considerations of treatment toxicities and the impact on potential future life-years. While considerable progress has been made in understanding the molecular landscape of gliomas in younger children and

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older adults, the AYA group remains underrepresented in the medical literature. Gliomas in the AYA population span both pediatric and adult molecular subtypes, making their molecular profiles more diverse and complex. Despite this complexity, data specific to AYA prognoses and treatment responses remain limited, rendering this group particularly vulnerable to inconsistencies in care and underscoring the need for targeted research and standardized treatment strategies. Inadequate management of these patients can lead to suboptimal outcomes and avoidable treatment-related toxicities. An improved understanding of glioma biology and optimal treatment approaches in adolescent and adult patients is critically needed. Herein, we review the molecular landscape of gliomas in the AYA population, highlighting their therapeutic and prognostic implications.

Molecular Profile of Gliomas in AYAs

Recent advancements in the molecular characterization of CNS tumors have identified critical oncogenic drivers that are key for classifying distinct glioma subtypes. These molecular alterations carry strong prognostic significance and are now integral to the current WHO grading paradigm, complementing traditional histopathologic criteria.[3] In the AYA population, gliomas account for approximately 29% to 35% of all CNS tumors, with an incidence rate of 3.41 per 100 000.[1,4] Notably, some reports suggest that mortality from gliomas may be increasing within this group.[5,6] In the AYA population, gliomas comprise 25% of all CNS tumors and represent approximately 83% of malignant brain tumors within this age group.[1,7]

In addition to next-generation sequencing, DNA methylation profiling has emerged as a critical diagnostic tool in contemporary neuro-oncology and is increasingly incorporated into routine clinical practice. Methylation-based classification is particularly valuable in the AYA population, where histologic overlap between pediatric-type and adult-type gliomas is common. Several entities introduced in the 2021 WHO classification—such as diffuse pediatric-type high-grade glioma, *H3*-wild-type and *IDH*-wild-type, and high-grade astrocytoma with piloid features—are defined or refined by distinct methylation signatures rather than by a single recurrent genetic alteration. In diagnostically challenging cases, methylation profiling can improve classification accuracy, inform prognosis, and influence eligibility for molecularly driven clinical trials. Its expanding clinical utility underscores the need for integrated molecular and epigenetic diagnostics when evaluating gliomas in AYA patients.

The spectrum of genetic alterations and glioma subtypes varies across the age continuum, with certain tumor types more commonly diagnosed in pediatric populations and others in adults. However, these distinctions are not absolute—adults can present with pediatric-type gliomas, and children may develop tumors typically seen in adults. Adolescents and young adults (AYA) occupy a unique transitional age range in which either tumor type may occur. As such, a comprehensive diagnostic approach that considers the full range of glioma subtypes is essential when evaluating brain tumors in this population.

Observed molecular differences within the AYA population—such as the higher prevalence of IDH mutations in individuals over 18 y of age—likely reflect the gradual biological shift from pediatric-type to adult-type gliomagenesis rather than discrete age cutoffs. Historically and across institutions, AYA definitions have varied, with upper age limits ranging from 25 to 39 y, further complicating comparisons across studies. These inconsistencies highlight the need for age-stratified analyses within the AYA population rather than treating it as a biologically uniform group.[8,9]

Adult-Type Gliomas

IDH-Altered Gliomas.—In the AYA population, adult-type diffuse gliomas are the most common glioma subtype, accounting for approximately 15.2% of all brain tumors.[1] These tumors are typically defined by the presence or absence of isocitrate dehydrogenase (*IDH*) mutations, a key molecular feature now central to glioma classification.[3]

Isocitrate dehydrogenase mutations are rare in the younger pediatric population but occur at significantly higher frequencies in AYA individuals—especially those over 18 y of age—reported in 35%-57% of cases.[10,11] While *IDH1* and *IDH2* mutations are infrequent in pediatric gliomas and have limited clinical impact on pediatric treatment protocols, they carry important prognostic and therapeutic implications in adult gliomas, where their presence is associated with improved survival compared to *IDH*-wild-type tumors.[12] The prognostic relevance of *IDH* mutations in the AYA population remains incompletely characterized, reflecting the broader challenges in optimizing treatment approaches for this transitional population.

Isocitrate dehydrogenase-mutant astrocytomas are frequently associated with *ATRX* mutations, while *IDH*-mutant oligodendrogliomas are defined by concurrent *1p/19q* codeletion and *ATRX* wild-type status.[3] Molecular features such as these not only guide classification but also inform grading under the current WHO CNS framework. For example, homozygous deletion of *CDKN2A/B* now defines WHO grade 4 *IDH*-mutant astrocytomas, regardless of histological features. Similarly, the co-occurrence of an *IDH* mutation and *1p/19q* codeletion defines oligodendroglioma (WHO grade 2 or 3, depending on additional features).[3]

Lim-Fat et al. conducted a large multi-institutional study of *IDH*-mutant gliomas, revealing that the AYA population had a slight predominance of low-grade tumors (57.8%), with 42.2% classified as high-grade.[12] *IDH1* was the predominant mutation (96%), and nearly all tumors were located in the supratentorial compartment. Notably, these tumors exhibited a high rate of malignant transformation (~56%), and AYA patients had shorter progression-free survival (PFS) and time to transformation than both pediatric and older adult cohorts—though no significant differences in overall survival were observed.[10]

Clinical Management and Treatment Considerations.—Treatment of adult-type diffuse gliomas generally begins with maximal safe resection followed by adjuvant radiation and systemic therapy. However, management strategies in the AYA population are nuanced due to unique considerations around long-term treatment toxicity, neurocognitive outcomes, fertility, and quality of life.

For WHO grade 2 *IDH*-mutant gliomas in younger AYA patients, radiation may be deferred following gross total resection, especially given the extended survival typically expected in this age group. Isocitrate dehydrogenase inhibitors such as ivosidenib and vorasidenib have shown promise in *IDH*-mutant gliomas, with ongoing studies in adult populations.[13,14] Given the occurrence of *IDH* mutations in the AYA group, it is crucial to include these patients in clinical trials evaluating these agents.

In the phase III INDIGO trial, vorasidenib significantly improved PFS compared with placebo in patients with residual or recurrent grade II *IDH1/2*-mutant gliomas (median PFS not reached vs 11.1 months), with a favorable toxicity profile and delayed need for radiation therapy. Although the trial predominantly enrolled adults, adolescent and young adult patients were included, supporting the relevance of these findings to the AYA population.[5,10,15] Earlier-phase studies of ivosidenib have also demonstrated radiographic stability and prolonged disease control in *IDH*-mutant gliomas, further supporting the role of *IDH* inhibition as a disease-modifying strategy that may be particularly attractive for younger patients in whom deferral of radiation is desirable.[16]

While *IDH* inhibitors have demonstrated the greatest benefit to date in low-grade *IDH*-mutant gliomas, their role in higher-grade tumors remains less well defined. Early-phase studies have suggested limited single-agent activity in enhancing-grade disease, and ongoing trials are evaluating *IDH* inhibitors in combination with radiation and alkylating chemotherapy to determine whether they may delay progression or mitigate treatment-related toxicity in higher-grade *IDH*-mutant gliomas.[17,18]

ASCO-SNO guidelines recommend 54 Gy radiotherapy with either temozolomide or PCV for *IDH*-mutant astrocytomas.[19] However, they allow for deferred adjuvant therapy in AYA patients <40 y old after gross total resection. For grade 3 or 4 *IDH*-mutant astrocytomas, 59.4 Gy radiation plus adjuvant temozolomide remains the standard.[20]

An additional consideration in *IDH*-mutant gliomas is temozolomide-induced hypermutation, a phenomenon associated with prolonged alkylator exposure and linked to aggressive recurrence and treatment resistance. This is particularly relevant in AYA patients, who may receive extended courses of temozolomide over long survivorship periods. Awareness of this risk has prompted interest in treatment de-escalation strategies and the integration of targeted therapies where appropriate.[21]

***Evolving Classification of Glioblastoma.*—** The diagnosis of WHO grade 4 glioblastoma now includes *IDH*-wild-type gliomas with specific molecular features—*EGFR* amplification, *TERT* promoter mutation, or combined gain of chromosome 7 and loss of chromosome 10 (+7/–10).[3] The absence of *H3* alterations is also required to confirm adult-type glioblastoma and distinguish it from pediatric-type high-grade glioma, particularly in younger AYA patients.[3]

Prognosis for *IDH*-wild-type glioblastoma remains poor, with a median overall survival of 15-18 months.[22] In the absence of robust, age-specific data, treatment paradigms for AYA patients largely reflect those established for older adults. The current standard first-line therapy consists of maximal safe resection followed by 60 Gy of radiotherapy with concurrent and adjuvant temozolomide.[23] Given the limited therapeutic advances in this setting, clinical trial enrollment following standard treatment should be prioritized for AYA patients when available. This highlights the urgent need for standardized, evidence-based management strategies specifically designed for the unique clinical and biological characteristics of the AYA population.

EGFR amplification, commonly observed in adult high-grade gliomas, is rare in patients under 35. Targeted therapies like gefitinib and erlotinib have shown limited efficacy.[24]

Immunotherapeutic strategies—such as checkpoint inhibitors, tumor vaccines, and oncolytic viruses—are under active investigation. Thus far, checkpoint inhibitors have not significantly improved OS or PFS in pediatric or adult glioma cohorts.[25-27] An exception includes patients with Lynch syndrome, who are more prevalent among AYA individuals compared to younger children or older adults, and who may benefit from *PD-1* blockade.[11]

Pediatric-Type Gliomas

Pediatric-type gliomas encompass a wide range of histopathologic and molecular entities that are most common in the pediatric population but also significantly affect AYA patients. These include both low-grade and high-grade gliomas, many of which are biologically and clinically distinct from adult-type tumors.

***Pediatric-Type Low-Grade Gliomas.*—** Pediatric-type low-grade gliomas (pLGGs) are primarily driven by genetic alterations in the *Ras/MAPK* pathway, including *BRAF V600E* point mutations, *BRAF::KIAA1549* fusions, and *FGFR1* mutations or fusions.[3] These tumors are histologically diverse and can occur throughout childhood and into young adulthood. Molecular profiling is a key component of diagnosis and therapy selection in AYA patients, as it allows for the integration of targeted therapies.

Targeted therapy has become increasingly important for pLGGs. *BRAF* inhibitors such as vemurafenib and dabrafenib have demonstrated efficacy in *BRAF V600E*-mutated low- and high-grade gliomas.[4,22] *MEK* inhibitors, including selumetinib and trametinib, are effective in both *BRAF*-altered and *NF1*-associated gliomas.[28] Tovorafenib, a second-generation pan-*RAF* inhibitor, has shown promise in recurrent or progressive pLGGs and has been studied in trials including AYA patients up to age 25.[29] While these therapies are promising, the optimal therapeutic timing and combinations with standard treatments like carboplatin and vincristine are still under investigation.

Importantly, several of the targeted therapy trials have enrolled AYAs, either explicitly or through expanded pediatric eligibility criteria. In studies of *BRAF V600E*-mutant gliomas, response rates to *BRAF* inhibition (alone or in combination with *MEK* inhibition) have ranged from approximately 40%-70%, with durable disease control observed across both pediatric and AYA cohorts. Combination *BRAF*/*MEK* inhibition has demonstrated improved response durability and reduced paradoxical *MAPK* activation

compared to *BRAF* monotherapy and is increasingly favored in clinical practice. These outcomes suggest that AYAs derive comparable benefit from *MAPK*-targeted therapies, supporting their routine consideration in molecularly selected patients.[30-32]

FGFR alterations, including mutations and rearrangements, are found in pediatric low-grade gliomas, adult high-grade gliomas, and in *IDH*-wild-type gliomas among *AYA* patients, where the reported incidence is as high as 16%.[33] The type of *FGFR* alteration varies by age group: *FGFR* fusions are more common in younger children, while point mutations predominate in AYA patients. *FGFR*-altered gliomas in the AYA population are also more likely to be high-grade compared to those in younger children. Targeted *FGFR* inhibitors are being studied across age groups, and further trials are necessary to clarify the efficacy and optimal use of these therapies in the AYA demographic.[34,35]

Pediatric-Type Diffuse Low-Grade Gliomas.—Pediatric-type diffuse low-grade gliomas are defined by the absence of *IDH* and histone *H3* mutations. These include diffuse astrocytoma with *MYB*- or *MYBL1*-alterations, angiocentric glioma typically altered by *MYB::QKI* fusion, polymorphous low-grade neuroepithelial tumor of the young (*PLNTY*), which often harbors *FGFR* fusions or *BRAF* mutations, and diffuse low-grade glioma, *MAPK*-altered.[3] This category underscores that activating *MAPK* pathway alterations, including *BRAF V600E* mutations, may also be present in diffusely infiltrative gliomas and are not restricted to circumscribed pediatric tumors. These tumors generally occur in early adulthood and are characterized by indolent behavior and excellent prognosis. Gross total resection is often curative, while chemotherapy is reserved for nonresectable tumors.

Pediatric-Type High-Grade Gliomas.—Pediatric-type high-grade gliomas (pHGGs) are aggressive CNS tumors defined by distinct molecular and biological features. A major subset, *diffuse midline glioma* (DMG), *H3K27*-altered, is driven by mutations in histone *H3* variants—either *H3.1* (*HIST1H3B*) or *H3.3* (*H3F3A*)—or by *EZHIP* overexpression, which functionally mimics *H3K27M* mutations through *PRC2* inhibition and global hypomethylation.[3] These tumors show a strong midline predilection, with location patterns influenced by age: brainstem (pons) involvement is most common in younger children, while thalamic tumors are more frequently seen in adolescents, young adults (AYAs), and adults.[7]

Although histone-mutant DMGs occur across all age groups, clinical behavior and prognosis differ. Adult DMGs more often involve the thalamus and show a modestly improved prognosis compared to pediatric cases, with a median overall survival of approximately 28 months.[36] Despite these differences, no consensus guidelines exist for the management of DMGs in adults or AYA patients, creating a therapeutic gap in this population. In addition to histone alterations, a subset of DMGs harbors *EGFR* and *PDGFRA* alterations, which represent promising therapeutic targets that may be integrated into future treatment strategies.[3]

Given the poor outcomes associated with DMGs, particularly in children, there is growing interest in epigenetic and targeted therapies. Histone deacetylase (*HDAC*) inhibitors, such as panobinostat, have shown preclinical efficacy, and next-generation agents like quisinostat and romidepsin are under evaluation.[11] Additionally, imipridones, including *ONC201* and *ONC206*, are being studied in early-phase trials for *H3K27*-altered gliomas, with *ONC201* recently receiving FDA approval based on emerging clinical efficacy in this molecular subgroup.[37,38]

Emerging clinical efforts are increasingly focused on the AYA population, with particular emphasis on thalamic DMGs, which represent a biologically and clinically distinct subgroup. These investigations underscore the urgent need for age- and mutation-specific therapies to improve outcomes in this challenging disease.

An important diagnostic tumor category in AYA patients is diffuse pediatric-type high-grade glioma, *H3*-wild-type and *IDH*-wild-type, a molecularly defined entity distinct from both diffuse midline glioma and adult-type glioblastoma. These tumors lack *IDH* and histone *H3* alterations and are frequently defined by characteristic DNA methylation profiles. Notably, a subset may harbor *EGFR* or *PDGFRA* alterations, underscoring that such alterations are not exclusive to glioblastoma or DMG. Accurate classification is critical as misdiagnosis as glioblastoma may impact prognosis estimation, therapeutic decision-making, and clinical trial eligibility, particularly in the AYA population.

Diffuse Hemispheric Gliomas, H3 G34-Mutant.—Diffuse hemispheric gliomas, H3 G34-mutant, are rare tumors overall but occur with increased frequency in the AYA population. Although they represent less than 1% of all gliomas across age groups, their incidence rises to approximately 15% in AYAs.[39] These tumors are defined by *H3.3 G34R* or *G34V* mutations and typically localize to the cerebral hemispheres, distinguishing them from midline *H3K27*-altered gliomas.[40,41] Their higher prevalence in AYAs compared to pediatric or older adult patients underscores their clinical relevance in this age group.[42] Prognosis remains poor, with a median overall survival of approximately 17 months.

Infant-Type Hemispheric Glioma.—Infant-type hemispheric glioma is, by definition, a tumor of early childhood; however, *NTRK*, *ALK*, *ROS1*, and *MET* fusions may also be identified in histologically and biologically distinct gliomas arising in AYAs. These fusion-driven tumors in AYAs should not be automatically classified as infant-type hemispheric glioma, as they may represent different diagnostic entities with variable clinical behavior, emphasizing the importance of integrated histologic, molecular, and epigenetic evaluation. Despite their rarity in older populations, these fusions should be routinely screened for in AYA patients given their significant therapeutic implications.[43,44]

Circumscribed Astrocytic Gliomas.—Circumscribed astrocytic gliomas typically exhibit a more solid growth pattern, making them more amenable to surgical resection. Although this group of gliomas is not defined by age, certain subtypes show age-related trends. For instance, pilocytic astrocytoma occurs in young adults in approximately 25% of cases and is most commonly associated with the *BRAF::KIAA1549* fusion, a molecular alteration linked to

favorable prognosis.[3] Infratentorial tumors are more frequent in children, while supratentorial tumors are more common in adults. In supratentorial, optic pathway, and other extracerebellar locations—particularly in AYA patients—pilocytic astrocytomas increasingly harbor alternative alterations such as *BRAF V600E* mutations or *NF1* alterations rather than *BRAF::KIAA1549* fusions. Long-term survival is excellent in pediatric populations, with 10-y survival rates around 90%, but somewhat lower in adults, at approximately 70%.[7] Pleomorphic xanthoastrocytoma (PXA) is more commonly seen in AYAs and often harbors *BRAF V600E* mutations along with *CDKN2A/B* deletions.[3] Prognosis is grade-dependent, with about 80% survival for grade 2 tumors and a significantly worse outlook for grade 3.[7] High-grade astrocytoma with piloid features (HGAP) is a molecularly and epigenetically defined entity characterized by *MAPK* pathway alterations, *CDKN2A/B* deletions, and *ATRX* mutations, and a distinctive DNA methylation profile and occurs with increased frequency in AYAs. Astroblastoma, *MN1*-altered, is a rare glioma that predominantly affects AYAs. It has a relatively favorable prognosis, with a 5-y survival rate of 89% and a 10-y survival rate of 55%.[3,7]

Emerging molecularly defined glioma entities further complicate classification and management in the AYA population. Neuroepithelial tumors with *PATZ1* alterations, gliomas harboring *BCOR* gene fusions (distinct from *BCOR* internal tandem duplication), and gliomas with *NTRK* alterations represent rare but increasingly recognized entities that span pediatric and AYA age groups. Unlike infant-type hemispheric gliomas—where *NTRK* fusions are common and associated with a distinct clinicopathologic entity—or adult tumors, in which *NTRK* alterations are often associated with glioblastoma, these alterations in older children and AYAs can present with heterogeneous histology and uncertain biological behavior. As a result, tumor grading can be challenging, and standardized treatment guidelines are lacking, often necessitating individualized management strategies and reliance on molecular tumor boards. Recognition of these emerging entities highlights the need for continued refinement of molecular classification frameworks and prospective studies to guide optimal therapy in this population.

Cancer Predisposition

Gliomas have been associated with several hereditary cancer syndromes, including Li-Fraumeni syndrome (*TP53* mutations), constitutional mismatch repair deficiency (CMMRD), Lynch syndrome, and other DNA replication/repair deficiency syndromes. In cases involving CMMRD or Lynch syndrome, there may be an expanded role for immunotherapy, offering a potential therapeutic benefit based on the tumor's underlying biology.

Neurofibromatosis type 1 (NF1) is another important cancer predisposition syndrome linked to glioma, particularly pediatric low-grade gliomas affecting the optic pathway. However, in the AYA population, non-optic pathway gliomas are more common and carry a higher risk of being high-grade. These may include transformed pilocytic astrocytomas harboring alterations in *CDKN2A/B* or *ATRX*.[45]

Adolescents and young adults diagnosed with glioma should be evaluated for germline genetic testing as part of their diagnostic workup. Germline mutations are more frequently observed in younger patients, with cancer predisposition syndromes identified in approximately 10% of children and adolescents with cancer.[46,47] While precise data on prevalence in the AYA population are limited, germline testing is particularly important in patients with a strong family history of cancer or with somatic alterations suggestive of underlying hereditary syndromes. These individuals should be referred for genetic counseling and considered for comprehensive germline screening.

Discussion

The 2021 WHO Classification of CNS tumors emphasizes the biological distinctions between gliomas across age groups, particularly between pediatric and adult populations. Adolescents and young adults fall into a transitional space between these groups yet lack dedicated diagnostic and therapeutic guidelines. This absence creates a critical gap in clinical care and research.

Molecular profiling is essential in the AYA population, where gliomas may exhibit features of both pediatric-type and adult-type tumors. Despite limited age-specific data, studies suggest that over 80% of AYA gliomas harbor potentially actionable molecular alterations, including IDH mutations (58%) and *RAS/MAPK* pathway alterations (24%).[9,10] Capturing these drivers may not only improve therapeutic outcomes but also reduce reliance on more toxic therapies such as radiation and cytotoxic chemotherapy—an important consideration in a population with long-term survivorship potential.

Treatment approaches and prognosis can vary substantially within the 15-39 y age range. Younger AYAs are more likely to be treated using pediatric-type protocols that emphasize chemotherapy and targeted therapies to minimize radiation-associated toxicity, whereas older AYAs are often managed according to adult treatment paradigms that incorporate earlier use of radiotherapy. These differences may influence not only survival outcomes but also long-term neurocognitive function, endocrine health, fertility, and quality of life. Emerging data suggest that molecular subtype, rather than chronological age alone, may be a more accurate predictor of outcome in AYAs, underscoring the importance of individualized, biology-driven treatment strategies within this heterogeneous population.

Effective care for AYA patients requires multidisciplinary collaboration between pediatric and adult neuro-oncology teams. This may include joint tumor boards, transitional care clinics, and dedicated AYA programs that address age-specific concerns such as fertility preservation, psychosocial support, and long-term toxicity management. Brain tumors are the second leading cause of cancer-related death in AYAs, underscoring the need for improved, tailored care.

Despite these advancements, AYA enrollment in clinical trials remains low, due in part to age-restricted eligibility criteria, limited trial access, and the absence of dedicated AYA teams in many institutions. Expanding eligibility criteria and creating trial arms specifically for AYA patients will help close this gap. In parallel, research must also address barriers to participation, including socioeconomic disparities and institutional limitations.

Conclusion

The AYA population represents a distinct clinical entity within neuro-oncology. Improving outcomes will require intentional integration of AYA patients into both pediatric and adult clinical frameworks, supported by multidisciplinary care, robust molecular diagnostics, inclusive clinical trials, and a strong focus on survivorship and quality of life. As precision medicine continues to evolve, so too must our approach to this critical and underserved age group.

Keywords

AYA (adolescents and young adults) | BRAFgliomas | H3K27MIDH | molecular | WHO CNS5

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