# Anaplastic oligoastrocytoma

In the revised 4th edition of the World Health Organization Classification of Tumors of the Central Nervous System published in 2016, classification of especially diffuse gliomas has fundamentally changed: for the first time a large subset of these tumours is now defined based on presence/absence of IDH mutation and 1p/19q co-deletion. Following this approach, the diagnosis of anaplastic oligoastrocytoma can be expected to largely disappear [1].

Anaplastic oligoastrocytoma is a brain tumor that forms when two types of cells in the brain, called oligodendrocytes and astrocytes, rapidly increase in number to form a mass.

Because an oligoastrocytoma is made up of a combination of two cell types, it is known as a mixed glioma.

## Epidemiology

Anaplastic oligoastrocytomas (AOA) are relatively uncommon high-grade gliomas. While oligodendroglial elements are thought to be associated with better outcomes, the magnitude of the difference is not clear.

Patients with anaplastic oligoastrocytoma have distinct outcomes based upon grade (OA3 vs. OA4) and in comparison with pure astrocytoma (AA or Glioblastoma). Future trials which include more than one histologic entity need to report results by cell type and grade and account for the varying prognoses in interpreting treatment outcomes [2].

## Treatment

Surgery, radiotherapy and chemotherapy with PCV or TMZ are the first-line standard of care for AG with slight modifications according to molecular variables. A multidisciplinary team is highly recommended in the management of these tumors [3].

For the subset of patients with 1p/19q codeleted AO/AOA, PCV plus RT may be an especially effective treatment, although this observation was derived from an unplanned analysis [4].

For many years standard of treatment remained Maximum Safe Resection (MSR) followed by Radiotherapy (RT). These tumors have also been known to be sensitive to alkylator-based chemotherapy particularly the subset having 1p/19q co-deletion signature. There is robust data showing that these tumors are responsive to chemotherapy in recurrent or progressive setting. Recently, up front chemotherapy has been added to standard post-surgery RT. It has been found that subset of AO/AOA having 1p/19q co-deletion responded very well to the addition of chemotherapy. This substantial benefit in terms of median Overall Survival (OS) and median Progression Free Survival (PFS) have intrigued the personalized treatment of AO/AOA on the basis of molecular signature markers [5].

The benefit of adjuvant chemotherapy and radiotherapy (RT), given as single modalities or sequentially, is still unclear.

Early PCV, either before or after RT, appears to improve OS of participants with AO or AOA. Use of biomarkers including codeletion of chromosomes 1p and 19q with or without IDH-1 or -2 mutation identify a subset of people with increased sensitivity to combined PCV and RT. The important role of biomarkers was supported in all of the RCTs examined, and prospective evaluation should be undertaken in future studies. However, PCV was associated with significant grade 3 and 4 toxicities, and whether temozolomide can be substituted for this remains unclear [6].

## Outcome

Gousias et al. evaluated KPNA2 and CRM1, as well as the IDH1 mutation status, as possible novel biomarkers for World Health Organization grade III anaplastic oligoastrocytomas (AOA).

They analyzed nuclear expression of KPNA2 by immunohistochemistry in 72 primary anaplastic gliomas (29 AOA, 24 anaplastic astrocytomas, 19 anaplastic oligodendrogliomas). The IDH1 mutation status was also determined in patients with anaplastic astrocytomas and AOA, and AOA patients were additionally evaluated for CRM1 nuclear expression. Long term survivors (LTS; >8 years) with AOA showed lower KPNA2 expression levels compared to non-LTS (p=0.005). KPNA2 expression (⩾ 5% versus <5%, 1-<5%, median) was found to correlate inversely with overall survival (OS) and progression-free survival (PFS) in our overall series as well as in the AOA group (anaplastic gliomas: OS p=0.017; PFS p=0.033; AOA: OS p=0.017, PFS p=0.040). Mutant IDH1-R132H was detected in 69% of the AOA cohort; a combination of KPNA2 low expression and mutant IDH1-R132H was only seen in LTS (p=0.050). No differences between the histological subtypes were observed in terms of KPNA2 expression and IDH1-R132H mutation status. This is the first time it has been shown that KPNA2 expression may have potential as a prognostic biomarker for AOA as well [7].

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