Cancer Association of South Africa (CANSA)

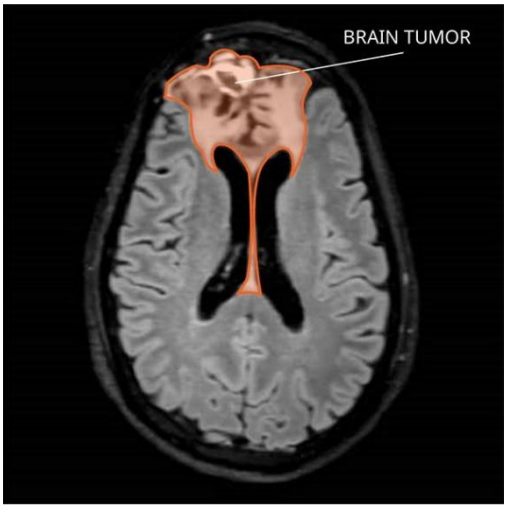
Research • Educate • Support

Fact Sheet on Oligodendroglioma

Introduction

A glioma is a type of brain tumour that grows from glial cells. Glial cells support nerve cells with energy and nutrients and help maintain the blood-brain barrier. There are various types of glial cells, each with a different function:

- Astrocyte - transports nutrients and holds neurons in place
- Oligodendrocyte - provides insulation (myelin) to neurons
- Microglia - digests dead neurons and pathogens
- Ependymal cells - line the ventricles and secrete cerebrospinal fluid



[Picture Credit: Oligodendroglioma Picture]

Glioma is an umbrella term used to describe the different types of glial tumours: astrocytoma, oligodendroglioma, and glioblastoma. Gliomas vary in their aggressiveness, or malignancy. Some are slow-growing and are likely to be curable. Others are fast-growing, invasive, difficult to treat, and are likely to recur.

Oligodendroglioma

Oligodendroglioma is a primary central nervous system (CNS) tumour. This means it begins in the brain or spinal cord. Oligodendrogliomas occur most often in people between the ages of 35 and 44, but can occur at any age. Oligodendrogliomas occur more often in males and are rare in children. They are most common in white and non-hispanic people.

Oligodendrogliomas are commonly found in the white matter and the outer layer of the brain, called the cortex, but can form anywhere in the CNS. These tumours are called oligodendrogliomas because the cells resemble oligodendrocytes, a type of brain cell that supports and insulates nerve fibres in the CNS.

Oligodendrogliomas are grouped in two grades based on their characteristics.

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1. **Grade II** oligodendrogliomas are low grade tumours. This means the tumour cells grow slowly and invade nearby normal tissue. In many cases, they form years before being diagnosed as no symptoms appear.
2. **Grade III** oligodendrogliomas are malignant (cancerous). This means they are fast-growing tumours. They are called anaplastic oligodendriogliomas.

Tork, C.A. & Atkinson, C. 2020.
"Oligodendroglioma (OG) is a type of diffusely infiltrating glioma and constitutes approximately 5% of primary intracranial tumors. They often involve the cortical gray matter and are most commonly seen in the frontal lobes. Historically OG was diagnosed based on the histological appearance of the tumor. However, in 2016 the WHO changed the criteria for the classification of CNS tumors to include both phenotypic and genotypic analysis. OGs are generally low grade WHO grade II neoplasms that are slow-growing tumors and have a favorable treatment response when compared to other gliomas. Grade III anaplastic OG is a more malignant form of the tumor which portends a less favorable prognosis and may occur de novo or as degeneration from the lower grade OG."

Hafeez, U., Menon, S., Nguyen, B., Lum, C., Gaughran, G., Pranavan, G., Cher, L., Nowak, A.K., Gan, H.K. & Parakh, S. 2019.
"There is limited information on the patterns of care and outcomes of high grade gliomas (HGGs) in young adults, in particular, the impact it has on a person's employment. We retrospectively identified young adult patients (age ≤ 40 years old) with newly diagnosed high grade gliomas treated between January 2013 and June 2018 across four major neuro-oncology centres in Australia. Patient demographics, tumour characteristics and treatment parameters were collected and outcomes determined. A total of 113 patients were identified with a median follow up of 27.0 months (range 1.0-70.2 months). The median age was 31 years, majority were male (65%) and employed (71.6%). IDH mutations were detected in 66 (62%) cases. The median progression-free survival (PFS) was 38.0 months (95% CI 23.3-52.7 months) and median overall survival (OS) was not reached. Patients with IDH wild type anaplastic astrocytoma and glioblastoma had a significantly shorter median PFS (19.3 months vs. NR, p = 0.001) and median OS (43.5 months vs NR, p = 0.007) than those with IDH mutated grade III anaplasticastrocytoma and oligodendroglioma. There was no significant difference in median OS or PFS between patients who underwent gross or subtotal tumour resection. Significantly, after diagnosis only 36 (32%) patients reported being employed. Young patients with IDH wild type astrocytomas and glioblastoma had better outcomes than reported historical controls. Most patients did not continue in employment post diagnosis."

Incidence of Oligodendroglioma in South Africa
The South African National Cancer Registry (2017) does not provide any information regarding the incidence of Oligodendroglioma.

According to the outdated National Cancer Registry (2017), known for under reporting, the following number of Brain and Central Nervous System cancer cases was histologically diagnosed in South Africa during 2017:

Group - Males 2017	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	262	1:825	0,66%
Asian males	12	1:613	1,24%
Black males	92	1:2 294	0,69%
Coloured males	40	1:530	0,83%
White males	118	1:256	0,56%

Group - Females 2017	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	215	1:1 236	0,52%
Asian females	8	1:978	0,54%
Black females	79	1:3 413	0,41%
Coloured females	26	1:822	0,57
White females	102	1:315	0,60%

The frequency of histologically diagnosed cases of Brain and Central Nervous System cancer in South Africa for 2017 was as follows (National Cancer Registry, 2017):

Group - Males 2017	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	41	23	30	36	78	46	24	4
Asian males	1	1	2	1	3	4	0	0
Black males	32	12	11	12	15	8	2	0
Coloured males	1	5	3	1	10	9	2	0
White males	7	5	14	13	30	25	20	4

Group - Females 2017	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	43	12	23	29	39	37	30	4
Asian females	2	1	0	1	1	3	0	0
Black females	27	7	10	11	12	3	8	1
Coloured females	3	0	3	3	7	4	6	0
White females	9	4	10	14	19	27	16	3

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

Risk Factors and Cause of Oligodendroglioma

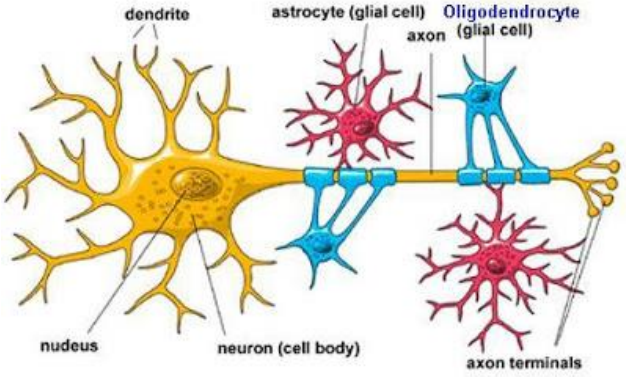
As with most tumours, the cause is not known. This can be a difficult thing to accept and can leave you feeling helpless, but there is nothing you could have done to prevent this from happening. There are no known causes of oligodendroglioma. Research that is focused around genetics is currently underway, but this has not been completed.

Signs and Symptoms of Oligodendroglioma

A person with an oligodendroglioma may display one or more of these symptoms:

- Seizures
- Headaches (not alleviated by pain killers and are worse in mornings associated with nausea and vomiting)
- Mental status change (general changes in brain function)
- Vertigo or nausea
- Visual loss (altered vision or visual hallucinations)
- Muscular weakness and loss of control of bodily movements (weakness down one side of body)
- Altered sensations (strange smells, hallucinations relating to sense of smell)

Sometimes the symptoms experienced depend on where the brain tumours are located. If they are in the frontal lobe this may cause gradual changes in mood and personality, weakness or numbness in muscles of one side of the body.



[Picture Credit: Oligodendrocyte]

If the tumour is located in the temporal lobe, this may cause problems with speech and coordination or it may affect memory.

Diagnosis of Oligodendroglioma

Tests and procedures used to diagnose oligodendroglioma may include:

- **Neurological exam.** During a neurological exam, your doctor will ask you about your signs and symptoms. He or she may check your vision, hearing, balance, coordination, strength and reflexes. Problems in one or more of these areas may provide clues about the part of your brain that could be affected by a brain tumour.

- **Imaging tests.** Imaging tests can help your doctor determine the location and size of your brain tumour. MRI is often used to diagnose brain tumours, and it may be used along with specialized MRI imaging, such as functional MRI and magnetic resonance spectroscopy.
  Other imaging tests may include CT and positron emission tomography (PET).
- **Removing a sample of tissue for testing (biopsy).** A biopsy can be done with a needle before surgery or during surgery to remove your oligodendroglioma, depending on your particular situation and the location of your tumour. The sample of suspicious tissue is analysed in a laboratory to determine the types of cells and their level of aggressiveness.

Specialised tests of the tumour cells can tell your doctor the types of mutations the cells have acquired. This gives your doctor clues about your prognosis and may guide your treatment options.

Smits, M. 2016.

"Oligodendroglioma are glial tumours, predominantly occurring in adults. Their hallmark molecular feature is codeletion of the 1p and 19q chromosome arms, which is not only of diagnostic but also of prognostic and predictive relevance. On imaging, these tumours characteristically show calcification, and they have a cortical-subcortical location, most commonly in the frontal lobe. Owing to their superficial location, there may be focal thinning or remodelling of the overlying skull. In contrast to other low-grade gliomas, minimal to moderate enhancement is commonly seen and perfusion may be moderately increased. This complicates differentiation from high-grade, anaplastic oligodendroglioma, in which enhancement and increased perfusion are also common. New enhancement in a previously non-enhancing, untreated tumour, however, is suggestive of malignant transformation, as is high growth rate. MR spectroscopy may further aid in the differentiation between low- and high-grade oligodendroglioma. A relatively common feature of recurrent disease is leptomeningeal dissemination, but extraneural spread is rare. Tumours with the 1p/19q codeletion more commonly show heterogeneous signal intensity, particularly on T2 weighted imaging; calcifications; an indistinct margin; and mildly increased perfusion and metabolism than 1p/19q intact tumours. For the initial diagnosis of oligodendroglioma, MRI and CT are complementary; MRI is superior to CT in assessing tumour

extent and cortical involvement, whereas CT is most sensitive to calcification. Advanced and functional imaging techniques may aid in grading and assessing the molecular genotype as well as in differentiating between tumour recurrence and radiation necrosis, but so far no unequivocal method or combination of methods is available."

Treatment of Oligodendroglioma

If the tumour is accessible, standard treatment for oligodendroglioma is surgical removal of as much of the tumour tissue as possible. Biopsy is typically performed on tumours that are not accessible to confirm the diagnosis and determine the grade of tumour. Recurrent low-grade oligodendrogliomas can be treated with surgery, radiation therapy (if not given initially), and chemotherapy.

- **Grade II Oligodendrogliomas**: Close follow-up with regular MRI scans is recommended following the successful removal of low-grade oligodendrogliomas. If some of the tumour remains (also called "residual" tumour), radiation treatment is recommended following surgery. The best timing for radiation therapy (i.e., immediately or when the tumour appears to be growing again), is currently being studied in clinical trials.
- **Grade III Oligodendrogliomas**: Anaplastic oligodendroglioma is typically treated with a combination of radiation therapy and chemotherapy. Recurrent anaplastic oligodendroglioma may be treated with surgery and/or chemotherapy.

Unfortunately, there are fewer clinical trials for rare forms of cancer because they are harder to organize. When a research trial is too small, the results aren't strong enough to prove that one type of treatment is better than another. So, getting enough people to participate is crucial to the success of a trial.

Hagg Torensma, R. 2018. The dilemma of cure and damage in oligodendroglioma: ways to tip the balance away from the damage. *Cancers (Basel).* 2018 Nov 12;10(11). pii: E431. doi: 10.3390/cancers10110431.
iagi, A. & Avila, E.K. 2019.
BACKGROUND: Tumor-related epilepsy (TRE) is common in patients with low-grade oligodendrogliomas. TRE is difficult to control despite multiple antiepileptic drugs (AEDs) in up to 30% of patients. Chemotherapy has been used for treatment to avoid potential radiotherapy-related neurotoxicity. This study evaluates the effect of temozolomide on seizure frequency in a homogeneous group with World Health Organization (WHO) grade II oligodendrogliomas.
METHODS: A retrospective analysis was conducted of adult patients with WHO grade II oligodendrogliomas and TRE followed at Memorial Sloan Kettering between 2005 and 2015 who were treated with temozolomide alone either as initial treatment or for disease progression. All had seizures 3 months prior to starting temozolomide. Seizure frequency was reviewed every 2 cycles and at the end of temozolomide treatment. Seizure reduction of ≥50% compared to baseline was defined as improvement.
RESULTS: Thirty-nine individuals met inclusion criteria. Median follow-up since starting temozolomide was 6 years (0.8-13 years). Reduction in seizure frequency occurred in 35 patients (89.7%). Improvement was independent of AED regimen adjustments or prior antitumor treatment in 16 (41%); of these, AED dosage was successfully reduced or completely eliminated in 10 (25.6%). Twenty-five patients (64.1%) remained on a stable AED regimen. The majority (n = 32, 82%) had radiographically stable disease, 5 (12.8%) had objective radiographic response, and 2 (5.2%) had disease progression.
CONCLUSIONS: Temozolomide may result in reduced seizure frequency, and permit discontinuation of AEDs in patients with WHO II oligodendroglioma. Improvement was observed irrespective of objective tumor response on MRI, emphasizing the importance of incorporating seizure control in assessing response to tumor-directed therapy.

Franceschi, E., Tosoni, A., De Biase, D., Lamberti, G., Danieli, D., Pizzolitto, S., Zunarelli, E., Visani, M., Di Oto, E., Mura, A., Minichillo, S., Scafati, C., Asioli, S., Paccapelo, A., Bartolini, S. & Brandes, A.A. 2019.

BACKGROUND: Patients with low-grade gliomas (LGGs) with isocitrate dehydrogenase (*IDH*) mutation (mut) and 1p19q codeletion (codel) have a median overall survival of longer than 10 years. The aim of this study is to assess the role of postsurgical treatments.

SUBJECTS, MATERIALS, AND METHODS: We evaluated patients with LGGs with *IDH* mut and 1p19q codel; *IDH1/2* was performed by immunohistochemistry and quantitative polymerase chain reaction. In all wild-type cases, we performed next-generation sequencing. 1p19 codel analysis was performed by fluorescence in situ hybridization.

RESULTS: Among the 679 patients, 93 with LGGs with IDH mutation and 1p19q codel were included. Median follow-up (FU) was 96.1 months. Eighty-four patients (90.3%) were high risk according to Radiation Therapy Oncology Group criteria. After surgery, 50 patients (53.7%) received only FU, 17 (18.3%) chemotherapy (CT), and 26 (30.1%) radiotherapy (RT) with (RT + CT, 8 patients, 8.6%) or without (RT, 18 patients, 19.4%) chemotherapy. Median progression-free survival (mPFS) was 46.3 months, 50.8 months, 103.6 months, and 120.2 months in patients with FU alone, with CT alone, with RT alone, or with RT + CT, respectively. Median PFS was significantly longer in patients who received postsurgical treatment (79.5 months, 95% confidence interval [CI]: 66.4-92.7) than patients who received FU (46.3 months, 95% CI: 36.0-56.5). Moreover, mPFS was longer in patients who received RT (alone or in combination with CT, *n* = 26, 113.8 months, 95% CI: 57.2-170.5) than those who did not (*n* = 67, 47.3 months, 95% CI: 36.4-58.2). In particular, temozolomide alone did not improve PFS with respect to FU.

CONCLUSION: RT with or without chemotherapy, but not temozolomide alone, could extend PFS in IDH mut 1p19q codel LGGs.

IMPLICATIONS FOR PRACTICE: Low-grade gliomas with high-risk features, defined according to Radiation Therapy Oncology Group criteria, receive radiotherapy and/or chemotherapy as postsurgical treatments. Radiotherapy, however, has serious long-term effects (cognitive impairment), which are to be taken into account in these young patients. Moreover, low-grade gliomas with isocitrate dehydrogenase mutation and 1p19q codeletion (oligodendrogliomas) have an extremely long survival and a better prognosis. This study suggests that postsurgical treatments prolong the time before tumor progression in patients with good prognosis as well as those with oligodendroglioma. Moreover, temozolomide alone might not be effective in prolonging progression-free survival.

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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