

Brain tumours: when to refer to oncology and adjuvant treatment

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For neurosurgeons: primary brain tumours

Referral to oncology and adjuvant treatment by integrated diagnosis: specific indications, timing, what to send

Almost every patient with a malignant primary brain tumour needs radiotherapy, chemotherapy or both after surgery, and several decisions depend on what is done (and saved) at the operation. Final plans are made at the neuro-oncology MDT.

1 Before and at surgery: discuss with oncology when

1 Lymphoma is possible

Periventricular, homogeneous, diffusion-restricting, or immunosuppressed patient: stereotactic biopsy only, and hold steroids if the patient is stable.

2 A metastasis is likely

Known cancer, multiple lesions, or a smoker over 40: stage the body first; resect only large, symptomatic or diagnostic lesions.

3 Pineal or suprasellar mass

Serum and CSF AFP and β -hCG and a spine MRI before any operation: germ cell tumours may need no resection.

4 Deep, multifocal or frail

Agree biopsy versus resection, and the questions the tissue must answer (IDH, MGMT, H3).

5 Spine staging needed

Children, medulloblastoma, ependymoma, germ cell tumours: spine MRI before surgery avoids post-operative artefact.

6 After the operation

MRI within 24–48 hours; keep enough tissue and the paraffin blocks for the full integrated diagnosis.

2 Adjuvant management by integrated diagnosis: specific indications

Always / urgent refer every patient, usually before definitive treatment · **Yes** refer when the situation applies ·

Usually no specialist follow-up only

Glioblastoma, IDH-wildtype, age ≤70, KPS ≥70

Always

PLAN RT 60 Gy in 30 fractions with daily temozolomide, then 6 monthly cycles (EORTC/NCIC); tumour-treating fields optional (EF-14); lomustine–temozolomide for selected young, fit, MGMT-methylated patients (CeTeG/NOA-09)

POINTS **Referral:** As soon as histology is known (do not wait for all molecular results. Start RT about 3–6 weeks after surgery once the wound has healed (common practice). Send MGMT. Weekly counts; PJP prophylaxis if on steroids.

Glioblastoma, age >70 or KPS 50–70

Always

PLAN Short-course RT (40 Gy/15 or 25 Gy/5) with temozolomide if fit (Perry 2017); MGMT-methylated and frail: temozolomide alone (Nordic, NOA-08); unmethylated: short-course RT alone

POINTS **Referral:** Choice depends on MGMT and function. Biopsy is enough when resection is unsafe; ask for MGMT on the biopsy. KPS <50: supportive and palliative care; discuss before surgery.

Astrocytoma, IDH-mutant, grade 2 — gross total resection

Yes

PLAN Watchful waiting (MRI every 3–6 months) **or** vorasidenib

POINTS **Referral:** For a shared decision. IDH sequencing if IHC negative and age <55; CDKN2A/B status needed.

IDH-mutant glioma, grade 2 (astrocytoma or oligodendroglioma) — residual tumour, seizures controlled, no mass effect

Yes

PLAN Vorasidenib to delay RT and chemotherapy (INDIGO: PFS 27.7 vs 11.1 months)

POINTS INDIGO patients had non-enhancing measurable disease, no steroids, KPS ≥80. Monthly LFTs at first.

IDH-mutant glioma, grade 2 — uncontrolled seizures, growth, mass effect or enhancement

Yes

PLAN RT (50.4–54 Gy) **plus** chemotherapy: PCV (RTOG 9802, median survival 13.3 vs 7.8 years) or 12 cycles of temozolomide

POINTS **Referral:** Promptly. Chemotherapy alone only when the RT field would be very large (bihemispheric oligodendroglioma).

Astrocytoma, IDH-mutant, grade 3

Always

PLAN RT 59.4 Gy, then 12 cycles of adjuvant temozolomide (CATNON final); concurrent temozolomide adds little

POINTS No role for vorasidenib outside trials at grade 3.

Astrocytoma, IDH-mutant, grade 4 (including CDKN2A/B-deleted)

Always

PLAN RT with temozolomide (glioblastoma-style, or 12 adjuvant cycles)

POINTS Report CDKN2A/B status: it changes the grade even without necrosis.

Oligodendroglioma, IDH-mutant, 1p/19q-codeleted, grade 3

Always

PLAN RT 59.4 Gy plus PCV (or temozolomide if PCV cannot be given) (EORTC 26951/RTOG 9402: survival about doubled)

POINTS Whole-arm 1p/19q by NGS/methylation preferred to FISH alone.

Diffuse midline glioma, H3 K27-altered (thalamus, brainstem, cord)

Always

PLAN Focal RT (about 54–60 Gy); clinical trials; dordaviprone at progression (ONC201)

POINTS Resection usually not possible; stereotactic biopsy in an experienced centre.

Ependymoma, adult

Yes

PLAN Grade 3, or grade 2 with residual: focal RT. Grade 2 after gross total resection: RT or observation, individualised

POINTS Stage with MRI of the whole spine (ideally before surgery) and CSF cytology about 2 weeks after surgery.

Meningioma, grade 1

Usually no

PLAN Gross total resection: observe. Subtotal: observe, or RT/radiosurgery if growing or symptomatic

POINTS **Referral:** Neurosurgical follow-up. MRI at 3–6 months, then yearly; per EANO meningioma guidance.

Meningioma, grade 2 (atypical)

Yes

PLAN Subtotal resection: adjuvant RT. Gross total resection: RT or close MRI surveillance (randomised trials ongoing)

POINTS **Referral:** Radiation oncology. Discuss at MDT; no proven chemotherapy.

Meningioma, grade 3 (anaplastic)

Always

PLAN Adjuvant RT (about 60 Gy) whatever the extent of resection

POINTS High recurrence risk; trials for recurrence.

Circumscribed gliomas: pilocytic astrocytoma, PXA, ganglioglioma

If residual or recurrent

- PLAN** Gross total resection: observe. Residual or progressive: re-resection, RT, or targeted therapy if BRAF V600E (ROAR)
- POINTS** Ask for BRAF V600E (VE1) and BRAF fusion testing.

Primary CNS lymphoma (suspected)

Urgent

- PLAN** Stereotactic biopsy only; then methotrexate-based chemotherapy and consolidation (autologous transplant or RT) under haemato-oncology
- POINTS** **Referral:** Before definitive surgery. Withhold steroids before biopsy if the patient is stable; resection does not help. HIV test, eye (slit-lamp) and CSF studies.

Medulloblastoma or other embryonal tumour (adult or child)

Always

- PLAN** Craniospinal RT with boost plus cisplatin-based chemotherapy (risk-adapted); infants: chemotherapy to delay RT
- POINTS** Spine MRI and CSF staging; molecular group (WNT, SHH, group 3/4); germline testing for SHH.

Pineal or suprasellar mass (possible germ cell tumour)

Before surgery

- PLAN** Germinoma: chemotherapy and/or RT, no radical resection; raised serum/CSF AFP or markedly raised β -hCG: chemotherapy first without biopsy
- POINTS** Check serum and CSF AFP and β -hCG and spine MRI before any operation.

Resected brain metastasis

Always

- PLAN** Cavity SRS rather than whole-brain RT (Mahajan, N107C), plus systemic therapy for the primary
- POINTS** **Referral:** Radiation and medical oncology. Cavity SRS within about a month of surgery (3–4 weeks may lower side effects). Send tissue for EGFR/ALK/HER2/BRAF as relevant.

Any brain tumour in a child

Always

- PLAN** By type: focal or craniospinal RT, chemotherapy, BRAF/MEK inhibitors for BRAF-altered LGG (Bouffet 2023)
- POINTS** **Referral:** To a paediatric neuro-oncology team. Avoid RT under 3 years where possible; fertility, endocrine and school planning.

3 What to send with the referral

- ✓ Integrated pathology report: histology, CNS WHO grade, IDH (sequencing if IHC negative and under 55), ATRX, p53, 1p/19q, CDKN2A/B, Ki-67
- ✓ MGMT for every glioblastoma; H3 K27M (midline), H3 G34 (young, hemispheric), BRAF V600E where relevant; blocks kept available

- ✓ Pre-operative MRI and post-operative MRI within 24–48 hours (images, not just reports) for radiotherapy planning
- ✓ Operation note: extent of resection, residual tumour and its location, eloquent areas, CSF leak or wound concerns
- ✓ KPS or ECOG, deficits, seizures and the current antiseizure drug, steroid dose and taper plan, VTE prophylaxis or events
- ✓ What the patient and family understand; for young adults, whether fertility has been discussed

Do

- Refer high-grade tumours the same week the diagnosis is known; molecular results can follow.
- Taper dexamethasone to the lowest dose that controls symptoms; H2-blocker rather than routine PPI.
- Use levetiracetam for patients who have had seizures; stop perioperative prophylaxis if there were none (SNO/EANO).
- Give post-operative VTE prophylaxis; treat clots with a DOAC or LMWH after CT excludes bleeding.
- Start radiotherapy about 3–6 weeks after surgery once the wound has healed (common practice).
- Write driving advice after any seizure.

Avoid

- Steroids before biopsy when lymphoma is possible and the patient is stable.
- Enzyme-inducing antiseizure drugs (phenytoin, carbamazepine, phenobarbital): they lower temozolomide, targeted drug and dexamethasone levels.
- A late post-operative MRI (after about 72 hours): surgical enhancement hides residual tumour.
- Reporting "glioma grade 2" without IDH and 1p/19q, or using up all tissue on frozen section.
- Re-operating for early new enhancement within 3–6 months of chemoradiation without MDT review: often pseudoprogression.

Refer back, or re-discuss at the MDT, when

- New or enlarging enhancement after treatment (pseudoprogression, recurrence or radiation necrosis).
- Recurrence that may be resectable: re-resection, re-irradiation and systemic options are planned together.
- Growth or new enhancement of a low-grade glioma under surveillance or on vorasidenib.
- Steroid dependence or refractory oedema (bevacizumab option), uncontrolled seizures, or new VTE.
- Hydrocephalus or a wound problem during radiotherapy.