FUNDACIÓN FAVALORO
HOSPITAL UNIVERSITARIO
INSTITUTO DE NEUROCIENCIAS

# Tumores del SNC cómo llegar al diagnóstico - Conducta terapéutica


## DR. ALEJANDRO MUGGERI

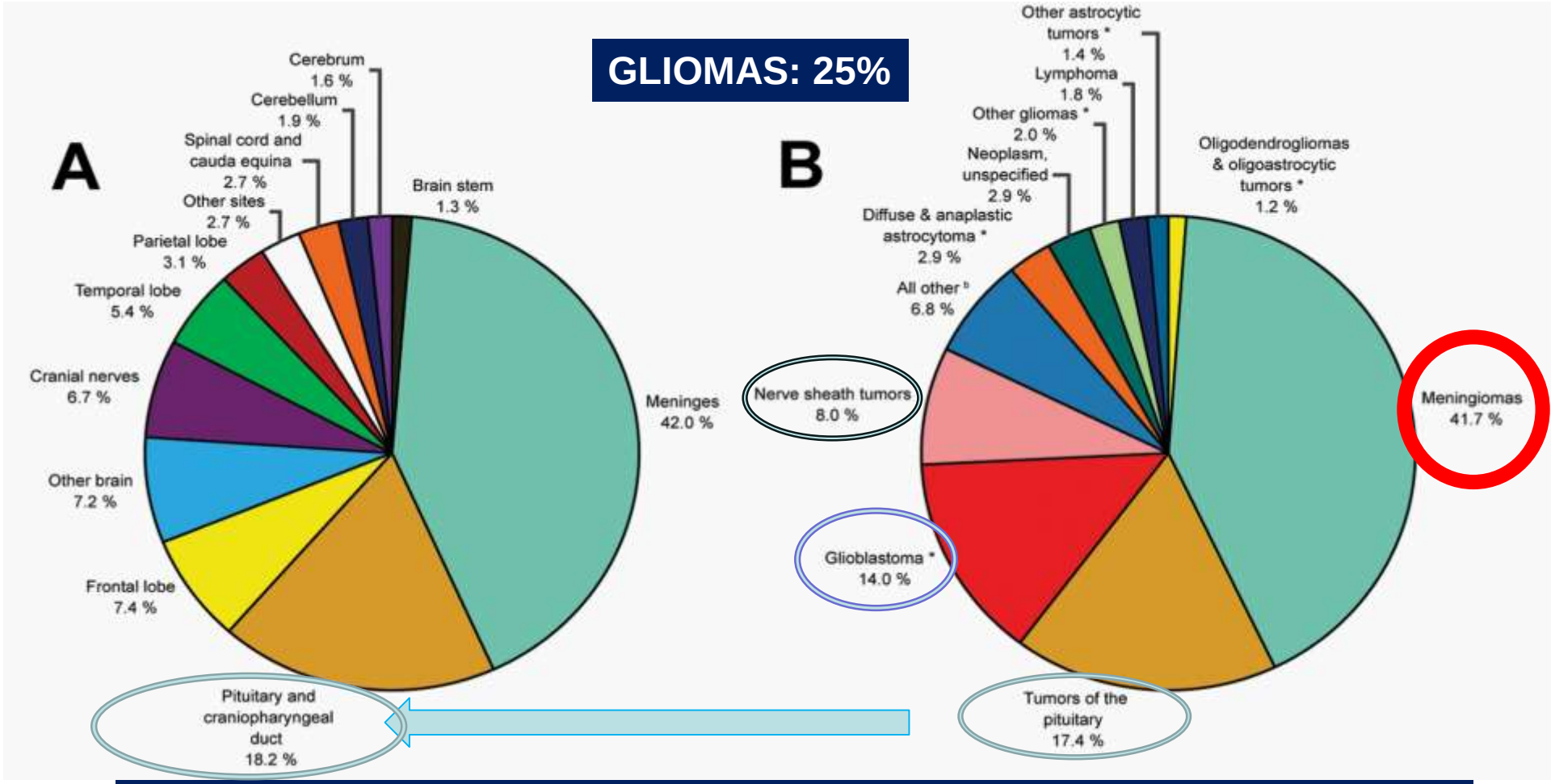
## ONCOLOGO

1. **TIPOS DE TUMORES, INCIDENCIA, ETIOLOGIA, DIAGNOSTICO CLINICO, HISTOLOGICO Y MOLECULAR**

2. **GENERALIDADES IMÁGENES DE TUMORES DE SNC (Dr Rosana Salvatico)**

3. **GENERALIDADES SOBRE EL TRATAMIENTO DE LOS TUMORES DE SNC**

# CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2017–2021



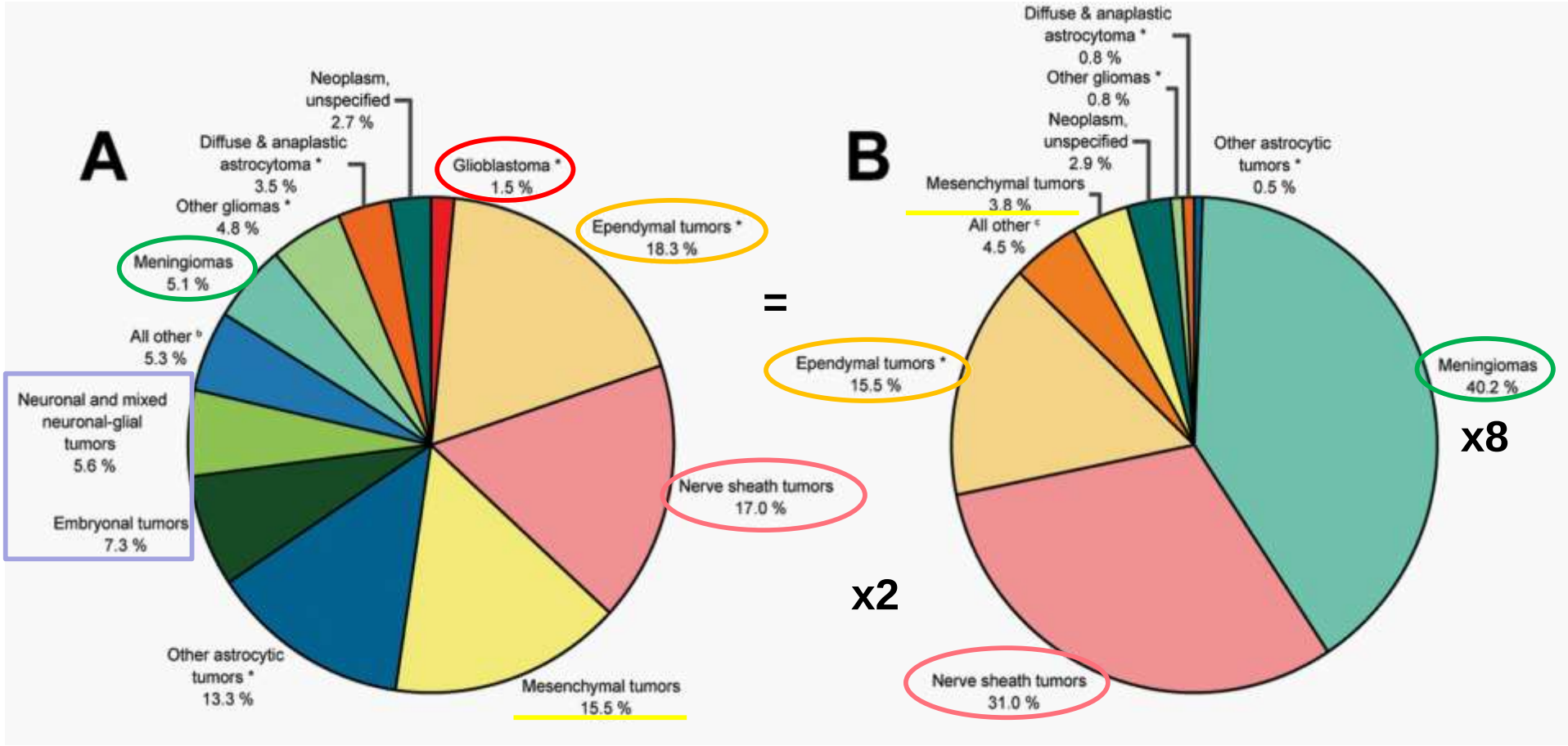

**METASTASIS CEREBRALES HASTA 7 VECES MAS FRECUENTES QUE T 1⁰**

FLENI

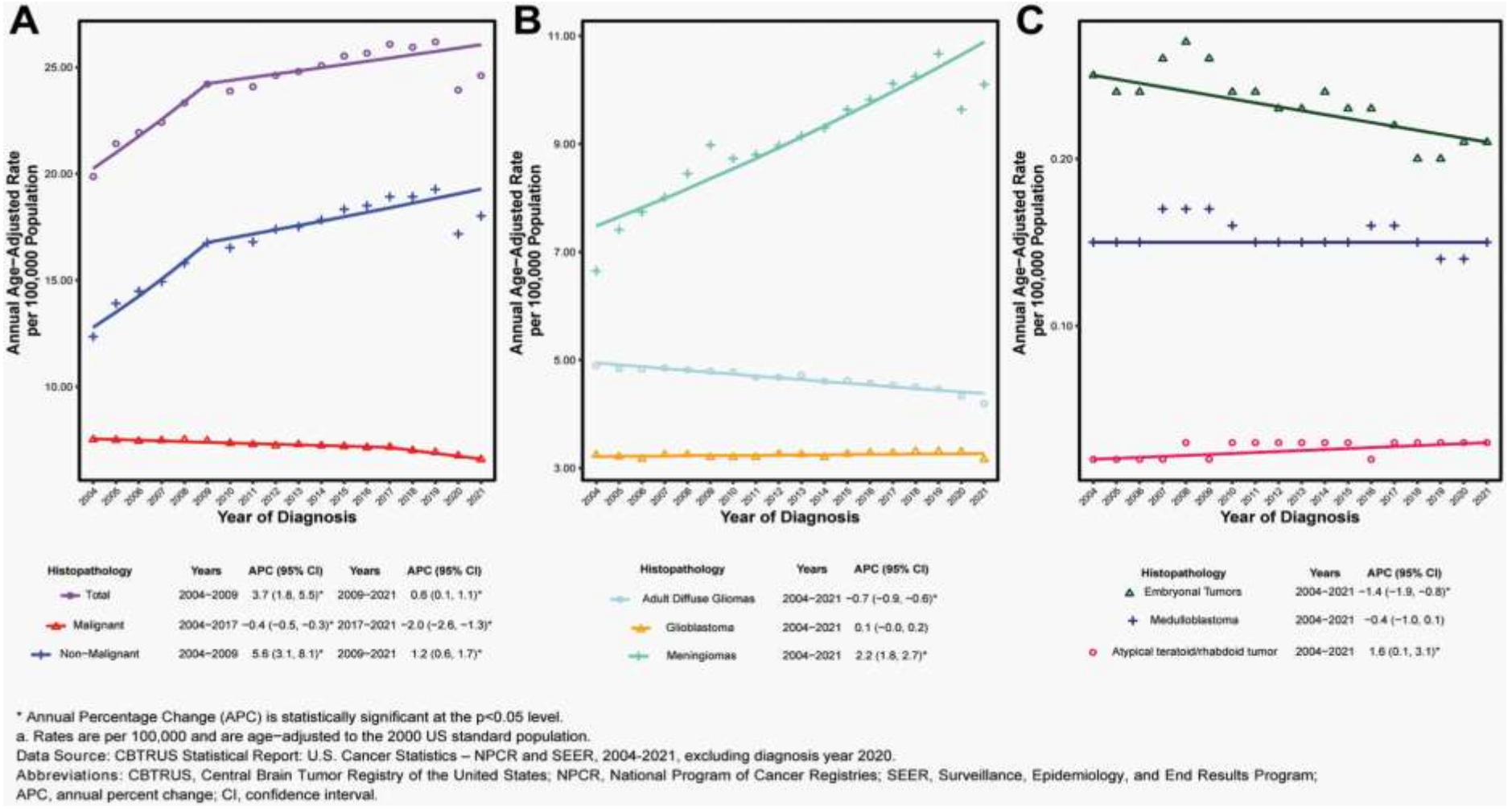
Distribution of Primary Spinal Cord, Spinal Meninges, and Cauda Equina Tumors by Histopathology in A) Children and Adolescents (Ages 0-19 Years, Five-Year Total=1,368; Annual Average Cases=274) and B) Adults (Ages 20+ Years, Five-Year Total=18,966; Annual Average Cases=3,793)

**NIÑOS Y ADOLESCENTES**

**ADULTOS**



# Annual Age-Adjusted Incidence Rates[a] and Annual Percent Change of Selected Brain and Other Central Nervous System Tumors by A) Behavior, B) Meningiomas and Select Gliomas, and C) Embryonal Tumors




* Annual Percentage Change (APC) is statistically significant at the p<0.05 level.
a. Rates are per 100,000 and are age-adjusted to the 2000 US standard population.
Data Source: CBTRUS Statistical Report: U.S. Cancer Statistics – NPCR and SEER, 2004-2021, excluding diagnosis year 2020.
Abbreviations: CBTRUS, Central Brain Tumor Registry of the United States; NPCR, National Program of Cancer Registries; SEER, Surveillance, Epidemiology, and End Results Program; APC, annual percent change; CI, confidence interval.

# ETIOLOGÍA

- Factor hereditario en 10 % de gliomas.
- 15 % historia familiar de cáncer.
- Radiaciones ionizantes (sarcomas, meningiomas y **gliomas) 2,3% PWBI**
- LPSNC (inmunodepresión, virus VEB, HIV)
- **CMV? → GB**
- ***Exposiciones prolongadas a OEM-RF? IARC 2011 posible carcinogénico***
- ***Hormonas exógenas (reemplazo hormonal, ACO) Meningiomas***

**Sind. De Turcot:** MDB, GB y poliposis gastrointestinal APC (5q).

**Sind. De Li Fraumeni:** MDB, ca de mama y sarcoma de partes blandas p53 (17p).

**Enf. De Von Recklinghausen:** glioma del óptico o del cerebelo, meningiomas, neurinomas NF1 (17q) →neurofibromina

**Neurofibromatosis tipo II:** meningiomas, gliomas, neurinomas del acústico, ependimomas, ca renal y feocromocitoma NF2→MERLINA

**Enf. De Cowden:** hamartomas en piel, encéfalo, meningiomas, ca de tiroides y mama PTEN (10q). MATCHS

**Enf de Von Hippel Lindau:** ca ce claras riñón, hemangioblastomas

**Esclerosis tuberosa:** astro subependimario de células gigantes, hamartomas cerebrales TSC1 y 2 → hamartina y tuberina vía AKT

**Sind de Gorlin:** MDB, meningiomas, ca basocelular PTCH (9q)

**NEM 1:** ADENOMAS DE HIPÓFISIS

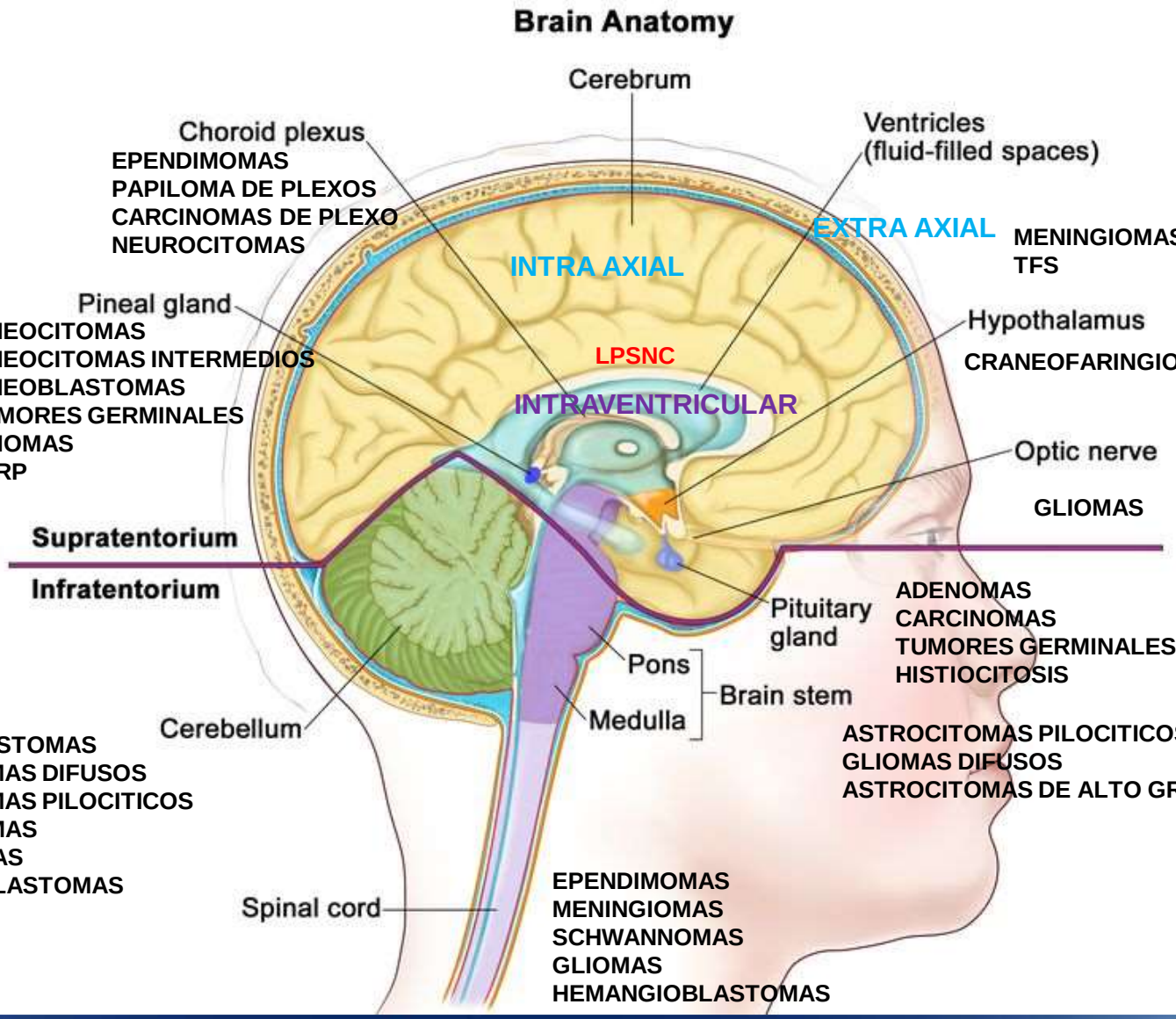
# CRITERIOS DE SOSPECHA DE SINDROME TUMORAL HEREDITARIO

- ✓ **5-10% de todos los cáncer**
- ✓ **Varios miembros de la familia afectados**
- ✓ **Edad precoz al diagnostico**
- ✓ **Afectación bilateral de tumores en órganos pares**
- ✓ **Alto riesgo de tumores primarios múltiples**
- ✓ **Alteraciones benignas o características de determinados síndromes hereditarios ya conocidos**

**TEST GENETICO → PREVENCION DETECCION PRECOZ → CONSEJO GENETICO**

# LOCALIZACION

- ✓ **BAJO GRADO**
- ✓ **ALTO GRADO**



# ANATOMÍA PATOLÓGICA

- ~~TNM~~
- TIPO DE BIOPSIA
- PERFIL MOLECULAR
- GRADOS DE LA OMS (1 – 4)
  - atipía nuclear
  - número de mitosis
  - proliferación vascular
  - necrosis

- **WHO 2016 Biología molecular: 1p19q, IDH1**

- **WHO 2021 diagnostico integrado y en capas, histología (grado), IHQ, biología molecular, perfil de metilación del ADN**

Neuro-Oncology
23(8), 1231–1251, 2021 | doi:10.1093/neuonc/noab106 | Advance Access date 29 June 2021

# The 2021 WHO Classification of Tumors of the Central Nervous System: a summary

David N. Louis, Arie Perry, Pieter Wesseling, Daniel J. Brat, Ian A. Cree, Dominique Figarella-Branger, Cynthia Hawkins, H. K. Ng, Stefan M. Pfister, Guido Reifenberger, Riccardo Soffietti, Andreas von Deimling, and David W. Ellison

**Table 1** 2021 WHO Classification of Tumors of the Central Nervous System. Provisional Entities are in Italics

| World Health Organization Classification ofTumors of the Central Nervous System, fifth edition |
|---|
| Gliomas, glioneuronal tumors, and neuronal tumors |
| Adult-type diffuse gliomas |
| Astrocytoma, IDH-mutant |
| Oligodendroglioma, IDH-mutant, and 1p/19q-codeleted |
| Glioblastoma, IDH-wildtype |
| Pediatric-type diffuse low-grade gliomas |
| Diffuse astrocytoma, *MYB*- or *MYBL1*-altered |
| Angiocentric glioma |
| Polymorphous low-grade neuroepithelial tumor of the young |
| Diffuse low-grade glioma, MAPK pathway-altered |
| Pediatric-type diffuse high-grade gliomas |
| Diffuse midline glioma, H3 K27-altered |
| Diffuse hemispheric glioma, H3 G34-mutant |
| Diffuse pediatric-type high-grade glioma, H3-wildtype and IDH-wildtype |
| Infant-type hemispheric glioma |
| Circumscribed astrocytic gliomas |
| Pilocytic astrocytoma |
| High-grade astrocytoma with piloid features |
| Pleomorphic xanthoastrocytoma |
| Subependymal giant cell astrocytoma |
| Chordoid glioma |
| Astroblastoma, *MN1*-altered |
| Glioneuronal and neuronal tumors |
| Ganglioglioma |
| Desmoplastic infantile ganglioglioma / desmoplastic infantile astrocytoma |
| Dysembryoplastic neuroepithelial tumor |
| *Diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters* |
| Papillary glioneuronal tumor |
| Rosette-forming glioneuronal tumor |
| Myxoid glioneuronal tumor |
| Diffuse leptomeningeal glioneuronal tumor |
| Gangliocytoma |
| Multinodular and vacuolating neuronal tumor |
| Dysplastic cerebellar gangliocytoma (Lhermitte-Duclos disease) |
| Central neurocytoma |
| Extraventricular neurocytoma |
| Cerebellar liponeurocytoma |
| Ependymal tumors |
| Supratentorial ependymoma |
| Supratentorial ependymoma, *ZFTA* fusion-positive |
| Supratentorial ependymoma, *YAP1* fusion-positive |
| Posterior fossa ependymoma |
| Posterior fossa ependymoma, group PFA |
| Posterior fossa ependymoma, group PFB |
| Spinal ependymoma |
| Spinal ependymoma, *MYCN*-amplified |
| Myxopapillary ependymoma |
| Subependymoma |

- Choroid plexus tumors
  - Choroid plexus papilloma
  - Atypical choroid plexus papilloma
  - Choroid plexus carcinoma
- Embryonal tumors
  - Medulloblastoma
    - Medulloblastomas, molecularly defined
      - Medulloblastoma, WNT-activated
      - Medulloblastoma, SHH-activated and *TP53*-wildtype
      - Medulloblastoma, SHH-activated and *TP53*-mutant
      - Medulloblastoma, non-WNT/non-SHH
    - Medulloblastomas, histologically defined
  - Other CNS embryonal tumors
    - Atypical teratoid/rhabdoid tumor
    - *Cribriform neuroepithelial tumor*
    - Embryonal tumor with multilayered rosettes
    - CNS neuroblastoma, *FOXR2*-activated
    - CNS tumor with *BCOR* internal tandem duplication
    - CNS embryonal tumor
- Pineal tumors
  - Pineocytoma
  - Pineal parenchymal tumor of intermediate differentiation
  - Pineoblastoma
  - Papillary tumor of the pineal region
  - Desmoplastic myxoid tumor of the pineal region, *SMARCB1*-mutant
- Cranial and paraspinal nerve tumors
  - Schwannoma
  - Neurofibroma
  - Perineurioma
  - Hybrid nerve sheath tumor
  - Malignant melanotic nerve sheath tumor
  - Malignant peripheral nerve sheath tumor
  - Paraganglioma
- Meningiomas
  - Meningioma

- Mesenchymal, non-meningothelial tumors
  - Soft tissue tumors
    - Fibroblastic and myofibroblastic tumors
      - Solitary fibrous tumor
    - Vascular tumors
      - Hemangiomas and vascular malformations
      - Hemangioblastoma
    - Skeletal muscle tumors
      - Rhabdomyosarcoma
    - Uncertain differentiation
      - *Intracranial mesenchymal tumor, FET-CREB fusion-positive*
      - *CIC*-rearranged sarcoma
      - Primary intracranial sarcoma, *DICER1*-mutant
      - Ewing sarcoma
  - Chondro-osseous tumors
    - Chondrogenic tumors
      - Mesenchymal chondrosarcoma
      - Chondrosarcoma
    - Notochordal tumors
      - Chordoma (including poorly differentiated chordoma)
- Melanocytic tumors
  - Diffuse meningeal melanocytic neoplasms
    - Meningeal melanocytosis and meningeal melanomatosis
  - Circumscribed meningeal melanocytic neoplasms
    - Meningeal melanocytoma and meningeal melanoma
- Hematolymphoid tumors
  - Lymphomas
    - CNS lymphomas
      - Primary diffuse large B-cell lymphoma of the CNS
      - Immunodeficiency-associated CNS lymphoma
      - Lymphomatoid granulomatosis
      - Intravascular large B-cell lymphoma
    - Miscellaneous rare lymphomas in the CNS
      - MALT lymphoma of the dura
      - Other low-grade B-cell lymphomas of the CNS
      - Anaplastic large cell lymphoma (*ALK+*/*ALK–*)
      - T-cell and NK/T-cell lymphomas
  - Histiocytic tumors
    - Erdheim-Chester disease
    - Rosai-Dorfman disease
    - Juvenile xanthogranuloma
    - Langerhans cell histiocytosis
    - Histiocytic sarcoma
- Germ cell tumors
  - Mature teratoma
  - Immature teratoma
  - Teratoma with somatic-type malignancy
  - Germinoma
  - Embryonal carcinoma
  - Yolk sac tumor
  - Choriocarcinoma
  - Mixed germ cell tumor

- Tumors of the sellar region
  - Adamantinomatous craniopharyngioma
  - Papillary craniopharyngioma
  - Pituicytoma, granular cell tumor of the sellar region, and spindle cell oncocytoma
  - Pituitary adenoma/PitNET
  - Pituitary blastoma
- Metastases to the CNS
  - Metastases to the brain and spinal cord parenchyma
  - Metastases to the meninges

- **Importante grado de discrepancia en el diagnóstico patológico (20-50%), en 9% la discrepancia es mayor**

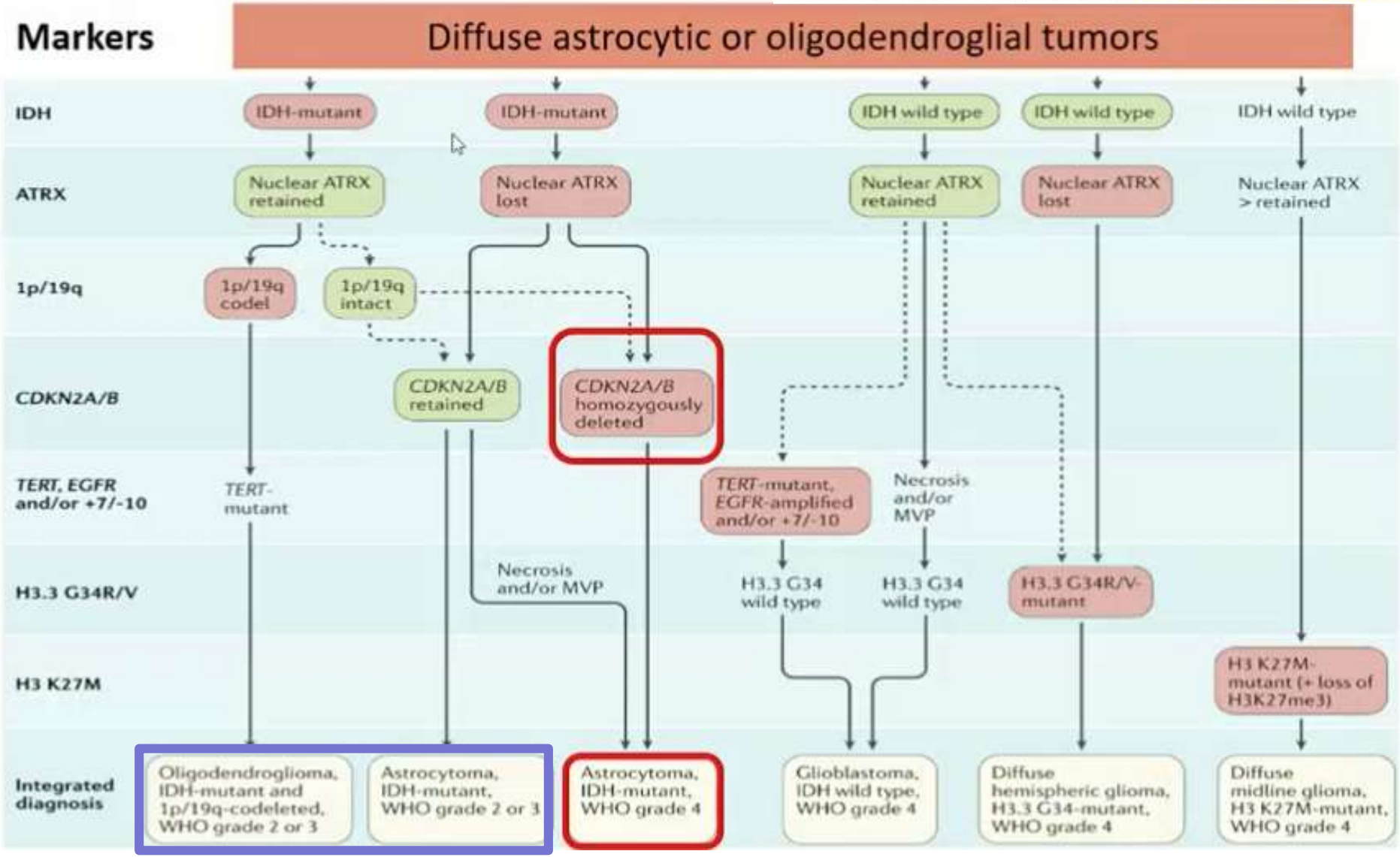
- **En general las muestras son revisadas por 3 patólogos en los trabajos randomizados y aún así hay discrepancias.**

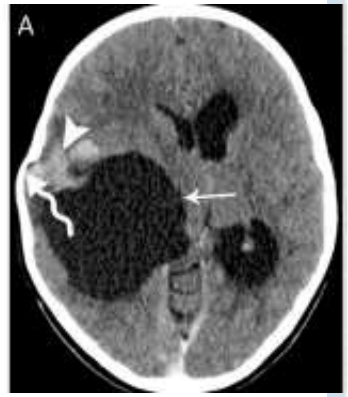
- **Cómo se traslada eso en la practica diaria?**

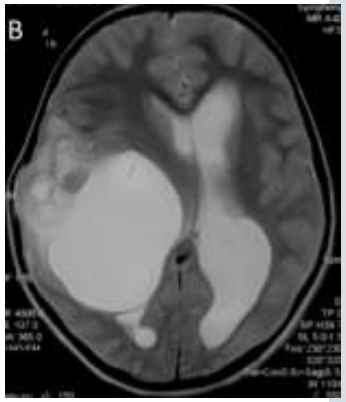
| Tumor Type | Genes/Molecular Profiles Characteristically Altered[a] |
|---|---|
| Astrocytoma, IDH-mutant | *IDH1, IDH2, ATRX, TP53, CDKN2A/B* |
| Oligodendroglioma, IDH-mutant, and 1p/19q-codeleted | *IDH1, IDH2,* 1p/19q, *TERT* promoter, *CIC, FUBP1, NOTCH1* |
| Glioblastoma, IDH-wildtype | IDH-wildtype, *TERT* promoter, chromosomes 7/10, *EGFR* |
| Diffuse astrocytoma, *MYB*- or *MYBL1*-altered | *MYB, MYBL1* |
| Angiocentric glioma | *MYB* |
| Polymorphous low-grade neuroepithelial tumor of the young | *BRAF,* FGFR family |
| Diffuse low-grade glioma, MAPK pathway-altered | *FGFR1, BRAF* |
| Diffuse midline glioma, H3 K27-altered | H3 K27, *TP53, ACVR1, PDGFRA, EGFR, EZHIP* |
| Diffuse hemispheric glioma, H3 G34-mutant | H3 G34, *TP53, ATRX* |
| Diffuse pediatric-type high-grade glioma, H3-wildtype, and IDH-wildtype | IDH-wildtype, H3-wildtype, *PDGFRA, MYCN, EGFR* (methylome) |
| Infant-type hemispheric glioma | NTRK family, *ALK, ROS, MET* |
| Pilocytic astrocytoma | *KIAA1549-BRAF, BRAF, NF1* |
| High-grade astrocytoma with piloid features | *BRAF, NF1, ATRX, CDKN2A/B* (methylome) |
| Pleomorphic xanthoastrocytoma | *BRAF, CDKN2A/B* |
| Subependymal giant cell astrocytoma | *TSC1, TSC2* |
| Chordoid glioma | *PRKCA* |
| Astroblastoma, *MN1*-altered | *MN1* |
| Ganglion cell tumors | *BRAF* |
| Dysembryoplastic neuroepithelial tumor | *FGFR1* |
| Diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters | Chromosome 14, (methylome) |
| Papillary glioneuronal tumor | *PRKCA* |
| Rosette-forming glioneuronal tumor | *FGFR1, PIK3CA, NF1* |
| Myxoid glioneuronal tumor | *PDFGRA* |
| Diffuse leptomeningeal glioneuronal tumor | *KIAA1549-BRAF* fusion, 1p (methylome) |
| Multinodular and vacuolating neuronal tumor | MAPK pathway |
| Dysplastic cerebellar gangliocytoma (Lhermitte-Duclos disease) | *PTEN* |
| Extraventricular neurocytoma | FGFR (*FGFR1-TACC1* fusion), IDH-wildtype |
| Supratentorial ependymomas | *ZFTA, RELA, YAP1, MAML2* |
| Posterior fossa ependymomas | H3 K27me3, *EZHIP* (methylome) |
| Spinal ependymomas | *NF2, MYCN* |
| Medulloblastoma, WNT-activated | *CTNNB1, APC* |
| Medulloblastoma, SHH-activated | *TP53, PTCH1, SUFU, SMO, MYCN, GLI2* (methylome) |
| Medulloblastoma, non-WNT/non-SHH | *MYC, MYCN, PRDM6, KDM6A* (methylome) |
| Atypical teratoid/rhabdoid tumor | *SMARCB1, SMARCA4* |
| Embryonal tumor with multilayered rosettes | C19MC, *DICER1* |
| CNS neuroblastoma, *FOXR2*-activated | *FOXR2* |
| CNS tumor with *BCOR* internal tandem duplication | *BCOR* |
| Desmoplastic myxoid tumor of the pineal region, *SMARCB1*-mutant | *SMARCB1* |
| Meningiomas | *NF2, AKT1, TRAF7, SMO, PIK3CA; KLF4, SMARCE1, BAP1* in subtypes; H3K27me3; *TERT* promoter, *CDKN2A/B* in CNS WHO grade 3 |
| Solitary fibrous tumor | *NAB2-STAT6* |
| Meningeal melanocytic tumors | *NRAS* (diffuse); *GNAQ, GNA11, PLCB4, CYSLTR2* (circumscribed) |

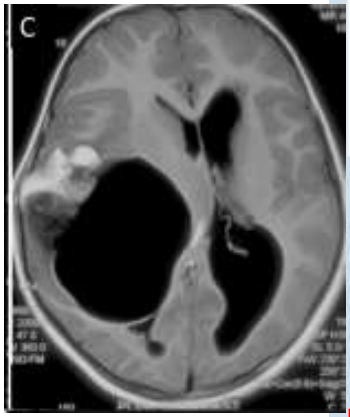
# WHO CNS5*

*Louis *et al.* Neuro Oncol, 2021 doi: 10.1093/neuonc/noab106





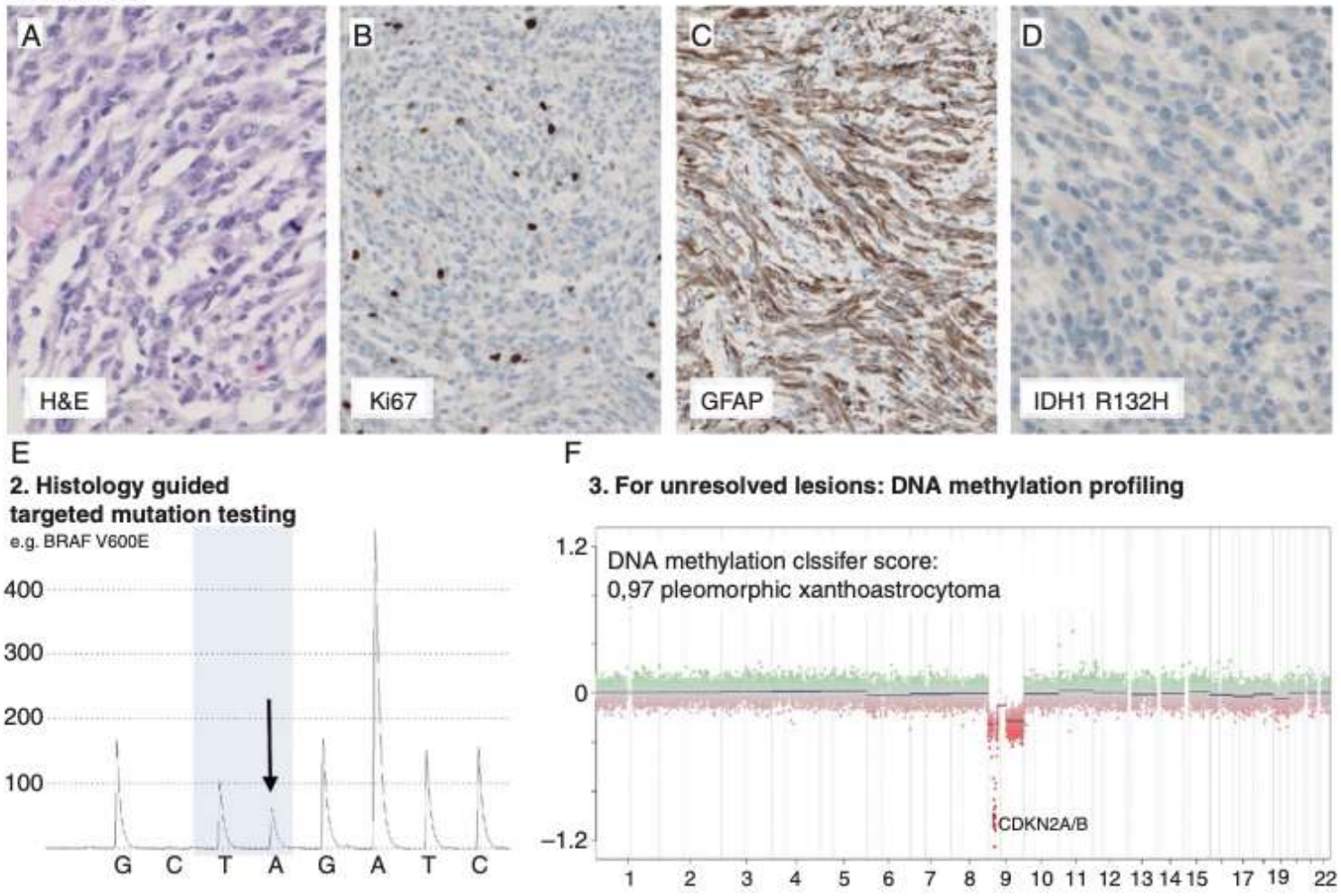
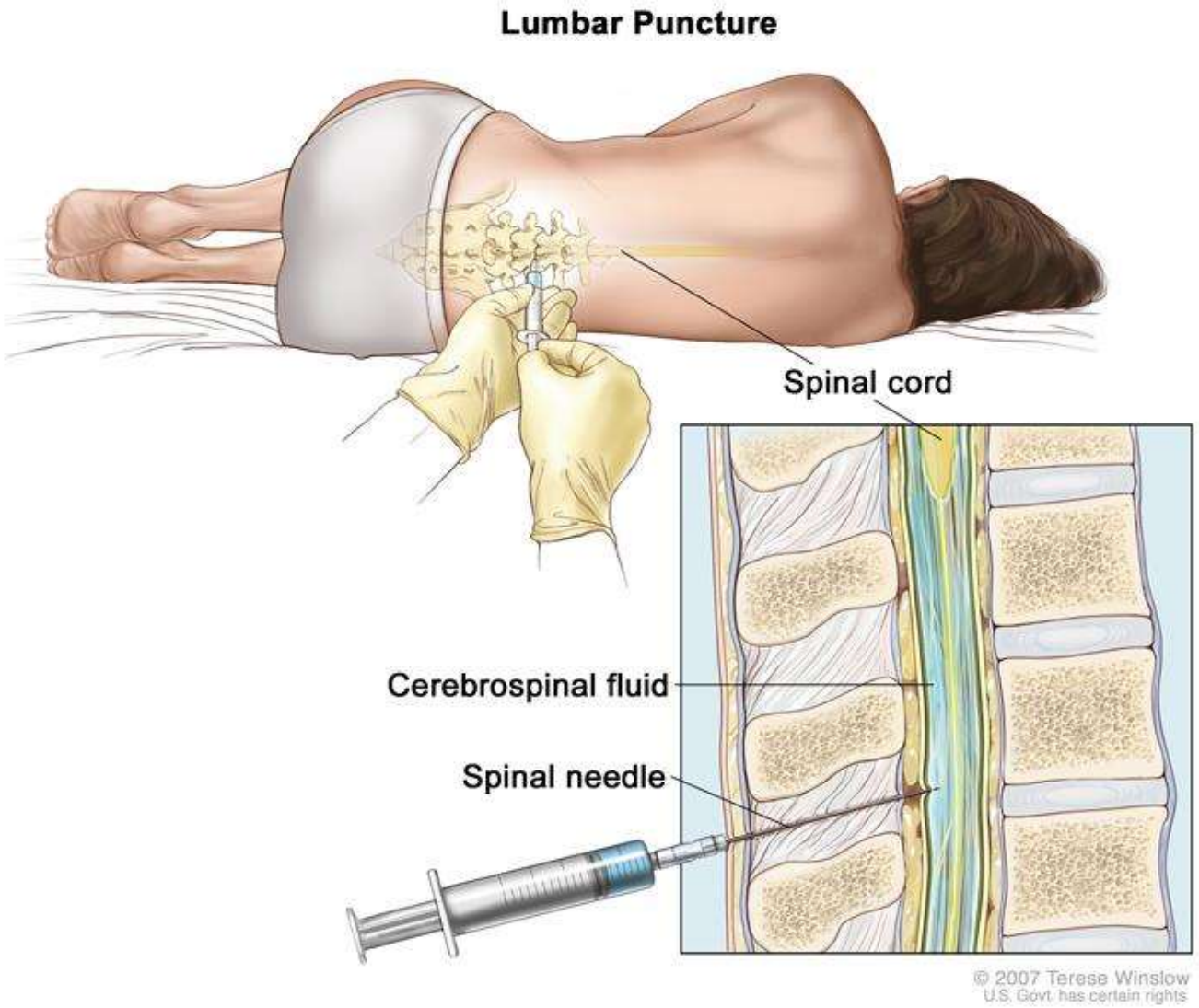




**Fig. 1** Suggested pathological processing of tumors of circumscribed astrocytic gliomas, glioneuronal and neuronal tumors. Diagnostic workup typically starts with histological evaluation of an H&E slide (example of a PXA, (a), followed by immunohistochemical analyses of proliferation markers (b), differentiation markers (eg, GFAP; c) and mutation specific immunohistochemistry (e.g. IDH1 R132H; d). For many tumor types the histological evaluation will guide further molecular testing that may either be desirable or essential for diagnosis (e). In this example the tumor was tested for BRAF because histology represented PXA that frequently harbor BRAF V600E mutation. For cases that are not resolvable by histology (eg, histological features compatible with more than one tumor type) and targeted molecular testing (eg, testing result not clear or testing not established) DNA methylation profiling and consecutive copy number analysis may aid for the classification (f).




**LPSNC, TUMORES GERMINALES, EPENDIMOMAS, CARCINOMA DE PLEXO COROIDEOS, NEUROCITOMA ATIPICO O ANAPLASICO, CARCINOMATOSIS MENINGEA, PNET, MEDULOBLASTOMAS**

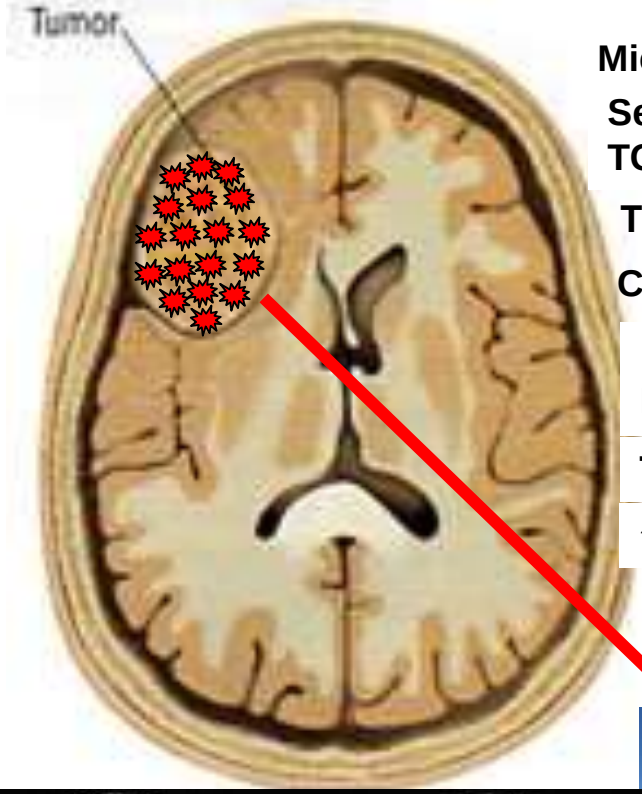
# GLIOMAS GENERALIDADES

- Grupo heterogéneo de tumores altamente infiltrantes con amplio rango de sobrevida (2 GAG – 20 años GBG).
- Pico de incidencia entre la 2º - 3º década (toda la vida por delante).
- GBG: NO ESTABLES: Crecimiento 4 mm por año
- GBG: CONVULSIONES 80-90%: Tendencia a invadir estructuras funcionales cortico subcorticales
- Mayor tendencia en los tumores de bajo grado en localizarse en zonas elocuentes.
- La SLP es muy variable de meses (Glioblastomas) a años (GBG).
- GENETICAMENTE INESTABLES: 50% sufrirán transformación a formas mas agresivas a los 5 años del dgo
- GBG (NO BENINGNOS): Mediana de SV 6 a 20 años

**CRECIMIENTO, MIGRACION Y TRANSFORMACION**

catabolismo del triptófano
indoleamine 2,3-dioxygenase-1
Triptofano dioxigenasa

# TUMORES ALTAMENTE INFILTRANTES




**Microambiente desfavorable**

**Señales inmunosupresoras**
**TGFB, IL-10, VEGF, PGE,CDF15**

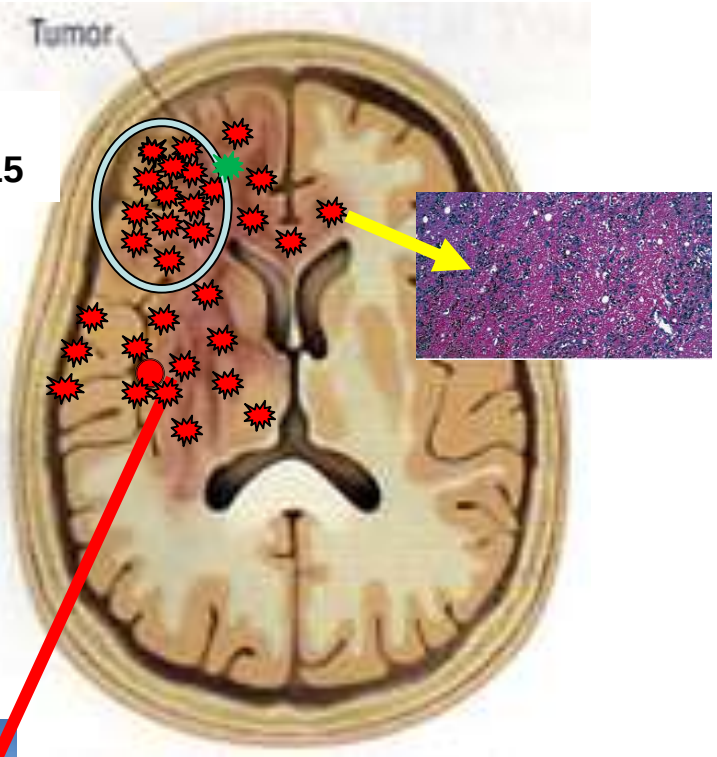
**TIL↓**

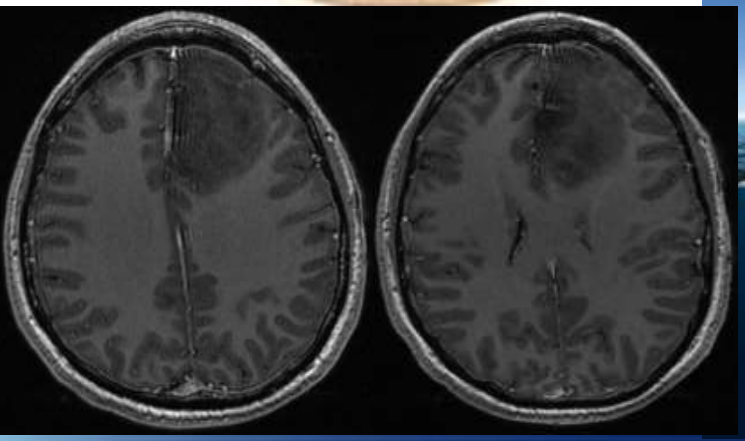
**Ce T exhaustas**

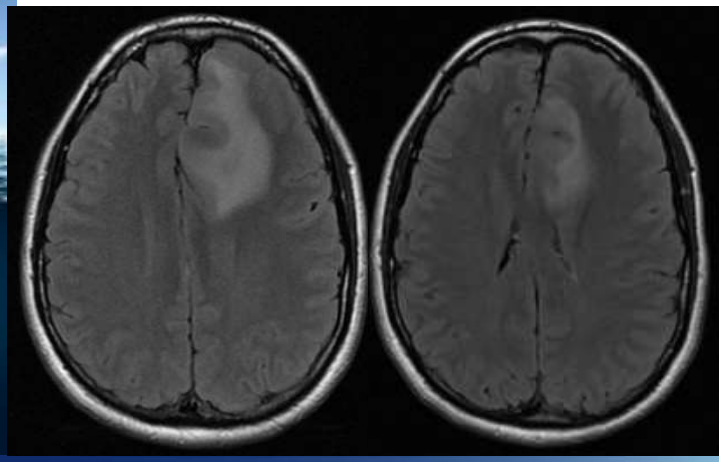
**↑Expresión**
**IDO y TDO**

**Trp→Kym**

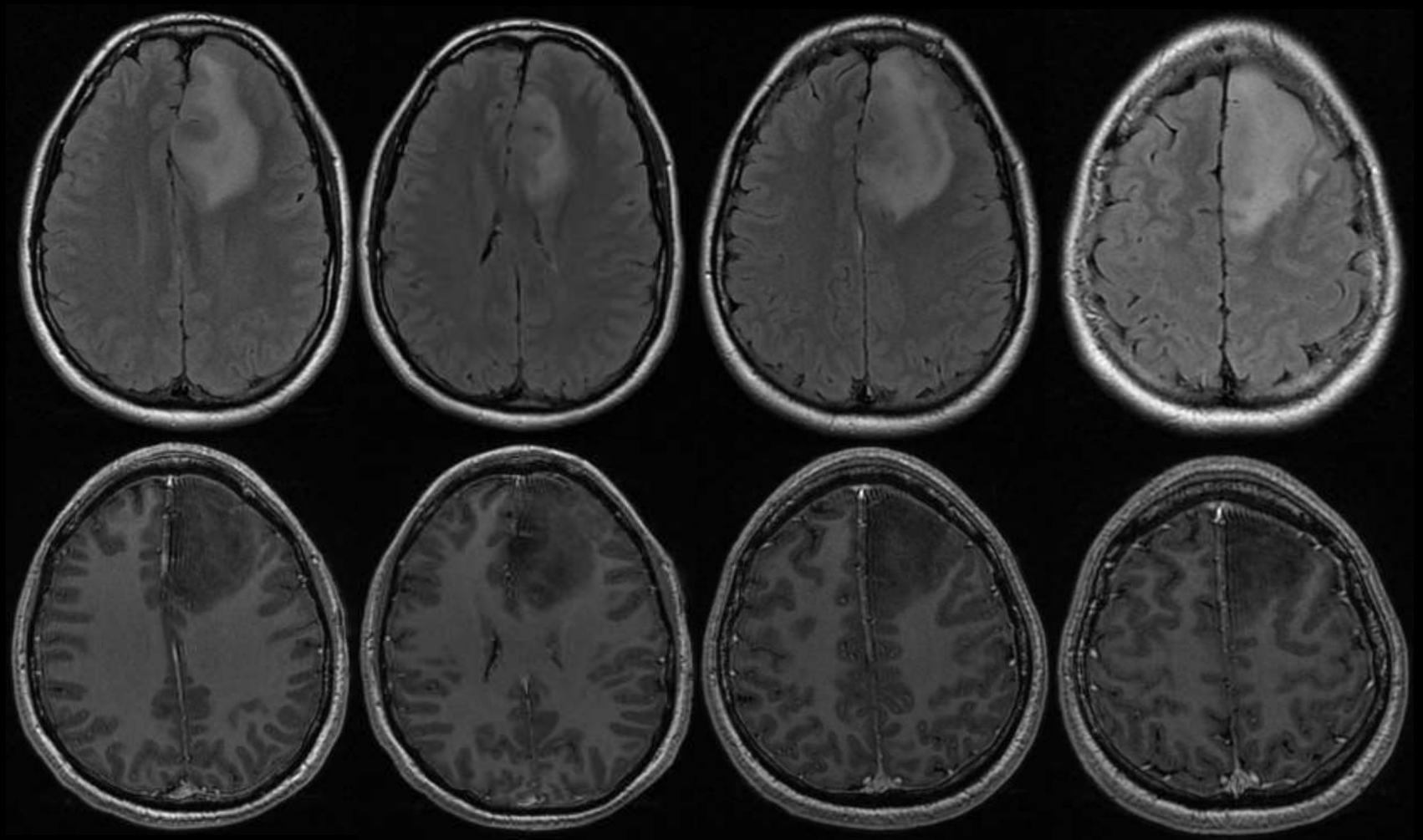
**↑VIA STAT3**





*No todo lo que realza es alto grado y no todo lo que no realza es bajo grado.*



**ASTROCITOMA 1p19q NOCODEL, IDH1 mutado, MGMT metilado, CDK2NA/B delecionado**

# PRESENTACION CLINICA

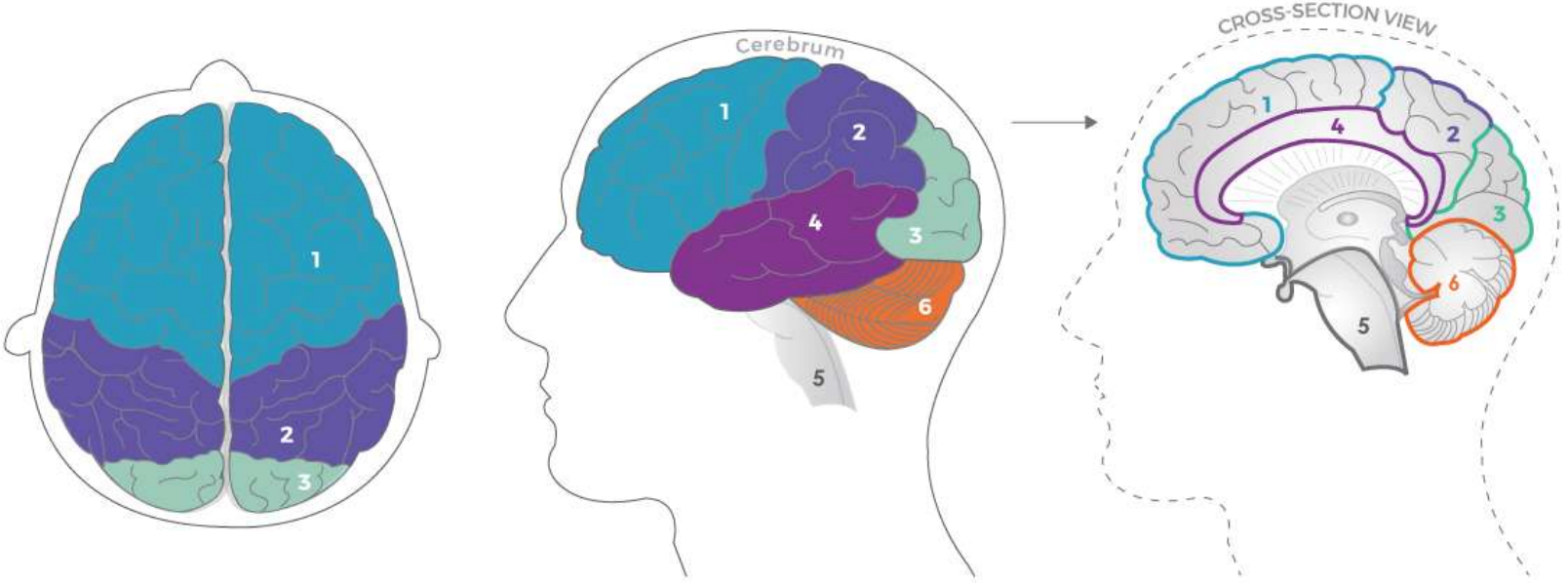
- HTE Y SIGNOS FOCALES
- HTE SIN SIGNOS FOCALES
- SIGNOS FOCALES SIN HTE
- FORMA PSEUDOICTAL

| | GBG | GAG |
|---|---|---|
| EDAD | 2 - 3 | > 3 |
| Cefalea | 40% | 50% |
| Convulsiones | 65 - 95% | 15 - 25% |
| Hemiparesia | 5 - 15% | 30 - 50% |
| Cambios del estado mental | 10% | 40 - 60% |
| TASA DE CRECIMIENTO | + | +++ |
| GADOLINIO | ---/+ | +++ |
| PERFUSION | -/+ | +++ |
| CAVIDAD | --- | +++ |
| ZONA ELOCUENTE | +++ | + |
| SOBREVIDA | 3-20 años | <3 años |

**NO SON TUMORES BENIGNOS!!!**

NATIONAL CANCER INSTITUTE

# Brain Anatomy & Functions




**1 Frontal Lobe**

Controls executive functions like concentration, thinking, problem solving and judgment; motivation, emotions, muscle strength, and behavior

**2 Parietal Lobe**

Controls feeling on the opposite side of body, ability to understand spoken language, ability to express yourself with language, and processing sensory information such as texture, temperature, and position in space

**3 Occipital Lobe**

Controls sight and processing information from the eyes, such as recognizing images

**4 Temporal Lobe**

Controls processing feelings of pain and hunger, fight-or-flight stress response, short-term memory, emotion, understanding words and directions

**5 Brainstem**

Controls heart rate, breathing, blood pressure, swallowing and digestion. May also affect the nerves that come directly from the brain, movement, and the function of any of the senses

**6 Cerebellum**

Controls speech, balance and coordination of movement of the body, arms and legs

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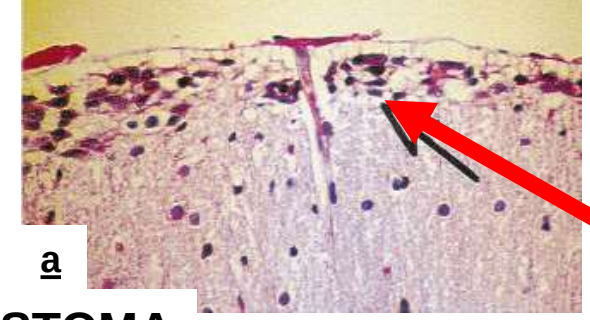
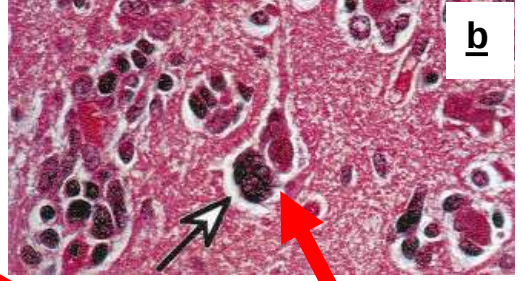
FLENI

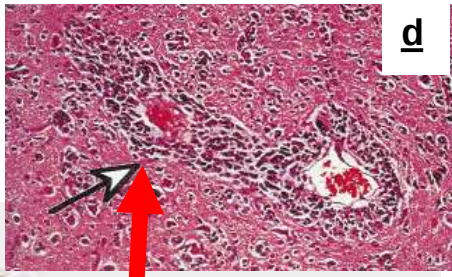


a



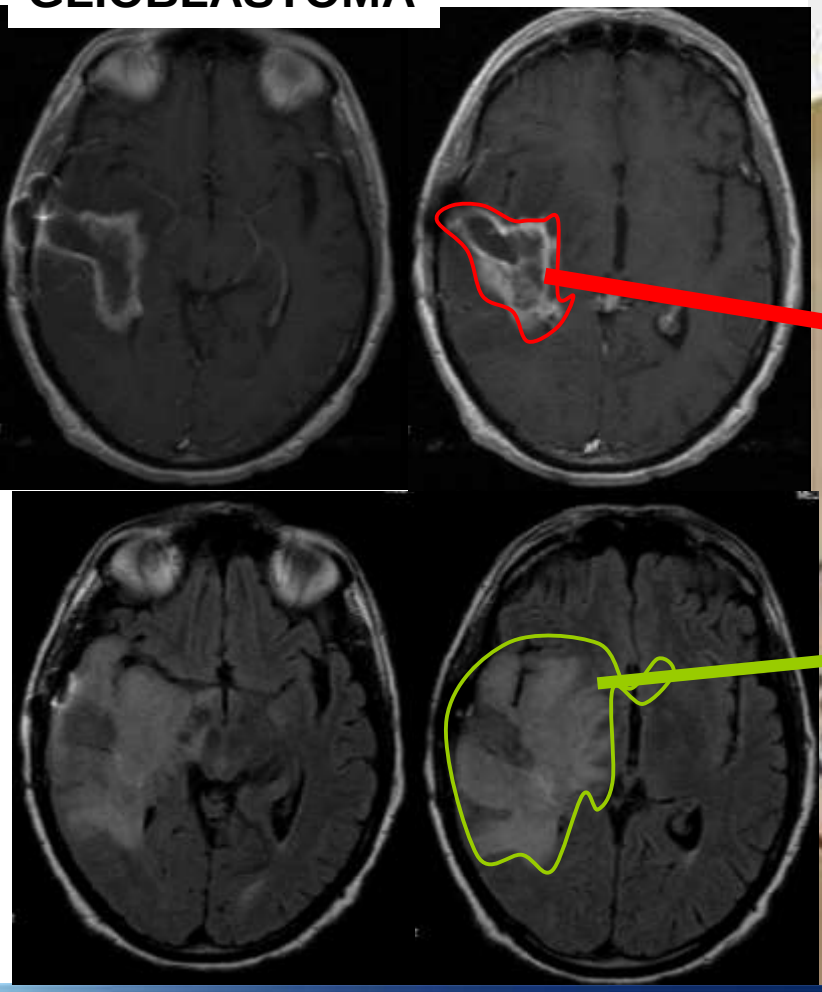
b

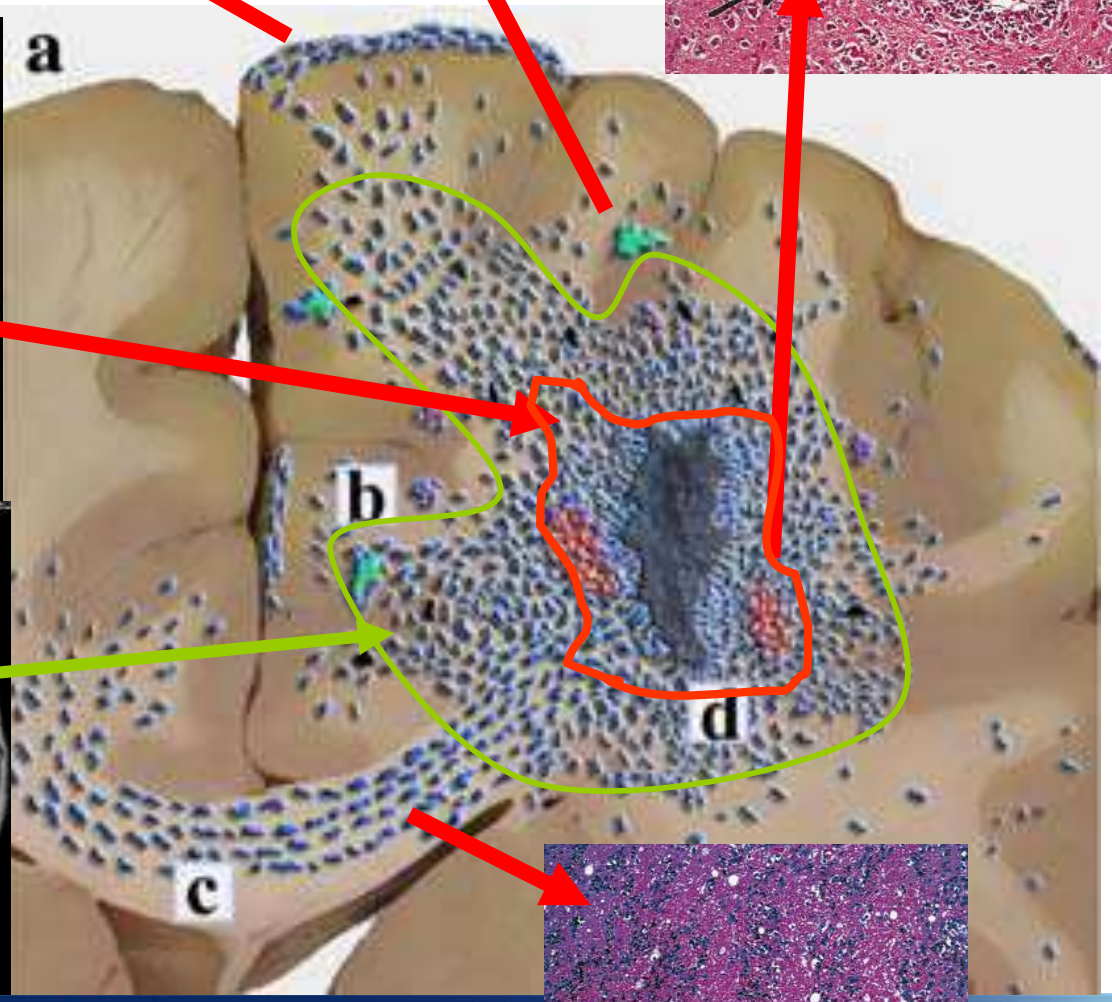
TUMORES ALTAMENTE INFILTRANTES



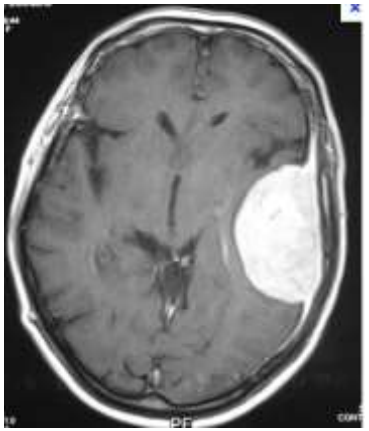
d

## GLIOBLASTOMA





# MENINGIOMAS



- Radiaciones ionizantes: más de 6 a 10 veces más de riesgo

- Obesidad 1,48 (IC: 1.3-1.69) más de riesgo de desarrollar meningiomas

  Estado de inflamación crónica señales mediadas por aumento de adipokininas e IGF

- Terapia de reemplazo hormonal estudios de casos y control y dos metaanálisis mostraron incremento del riesgo de desarrollar meningiomas

Alergias factor protector IgE biomarcador de atopia: ptes con meningiomas bajos niveles de IgE

Síndromes familiares asociados: **NF2, SMARCB1 y SMARCE1, sind de predisposición tumoral BAP1, Cowden, Gorlin, Werner,** Li-Fraumeni, Turcot, Gardner, EVHL, MEN1, Síndrome Rubinstein-Taybi

# PRESENTACION CLINICA

- ✓ No específicos
- ✓ Específicos de localización o compresión de estructuras vasculares, cerebrales o nerviosas
  Cefalea 35%, déficit de nervios craneales 30%, convulsiones 20%, trastornos cognitivos 14%, vértigo/mareos 10%, ataxia 6%,
- ✓ Asintomáticos 5-10%

Meningioma locations with associated mutations.

| Location | Frequency (%) |
|---|---|
| Convexity | 20–37% |
| Parasagittal (*NF2*) | 13–22% |
| • Falcine (*NF2*) | 5% |
| Spine (*AKT1*) | 7–12% |
| Skull Base | 43–51% |
| • Frontobasal (*TRAF7, AKT1, POLR2A, PIK3CA, SMO*) | 10–20% |
| • Sphenoid and Middle Cranial Fossa (*TRAF7, AKT1, PIK3CA*) | 9–36% |
| • Posterior Fossa (*NF2*) | 6–15% |
| ○ Tentorium Cerebelli | 2–4% |
| ○ Cerebellar Convexity | 5% |
| ○ Cerebellopontine Angle | 2–11% |
| ○ Foramen Magnum (*AKT1*) | 3% |
| ○ Petroclival (*PIK3CA*) | <1–9% |
| Intraventricular (*NF2*) | 1–5% |
| Orbital | <1–2% |
| Ectopic locations | <1% |

**Convulsiones**

Crisis Jacksonianas miemb inf, cefalea, papiledema, hemianopsia

Dorsales: paresia espástica progresiva con o sin dolor radicular o nocturno
Cervical: cuadriparesia espástica, con o sin signos bulbares

**Déficit focales**

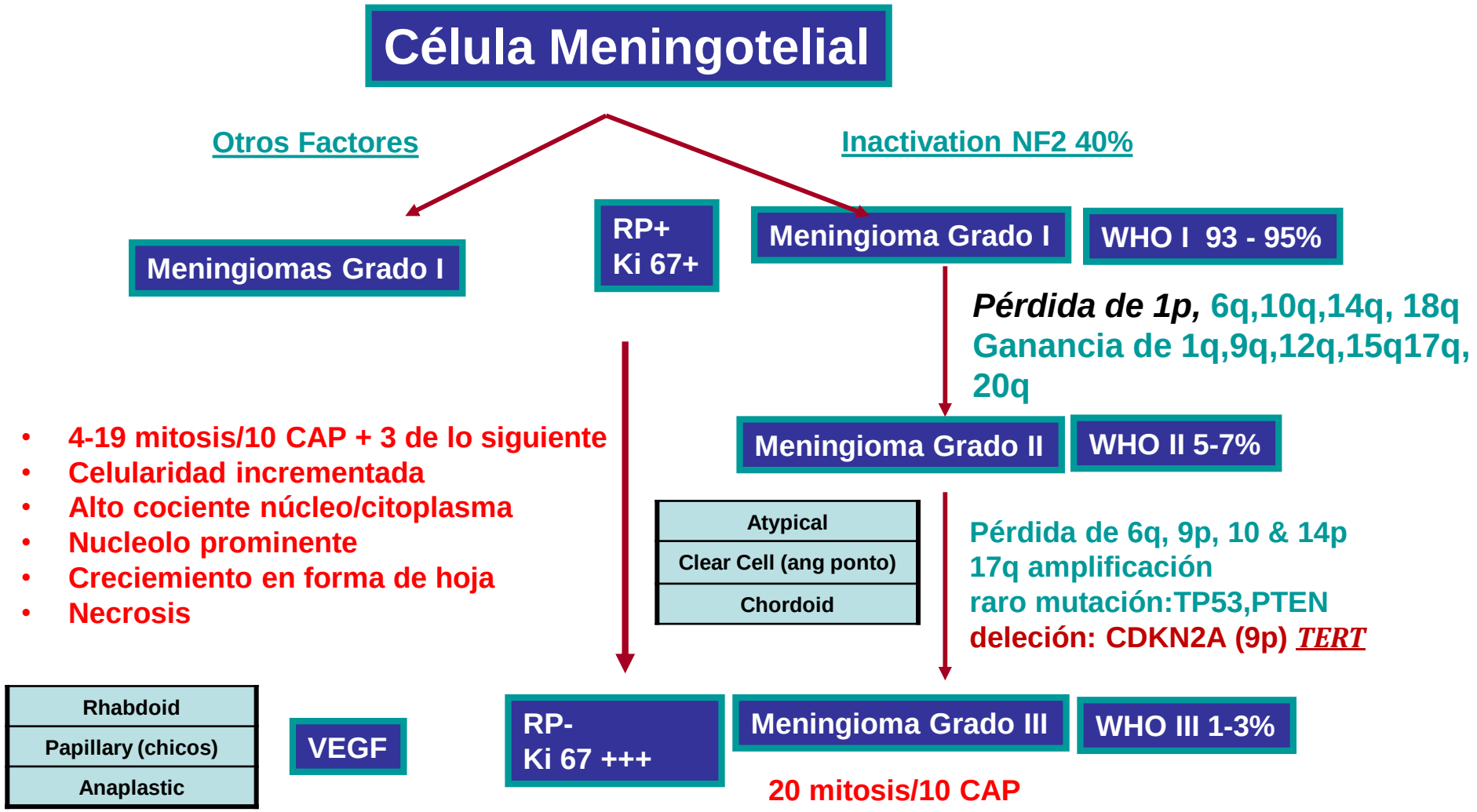
Visión, cefalea, anosmia, co, síntomas psicomotores, trast comportamiento

Exoftalmos, perdida de la visión

Hidrocefalia obstructiva, papiledema, cefalea matinal

Ataxia, neuropatías nervios craneales (v)

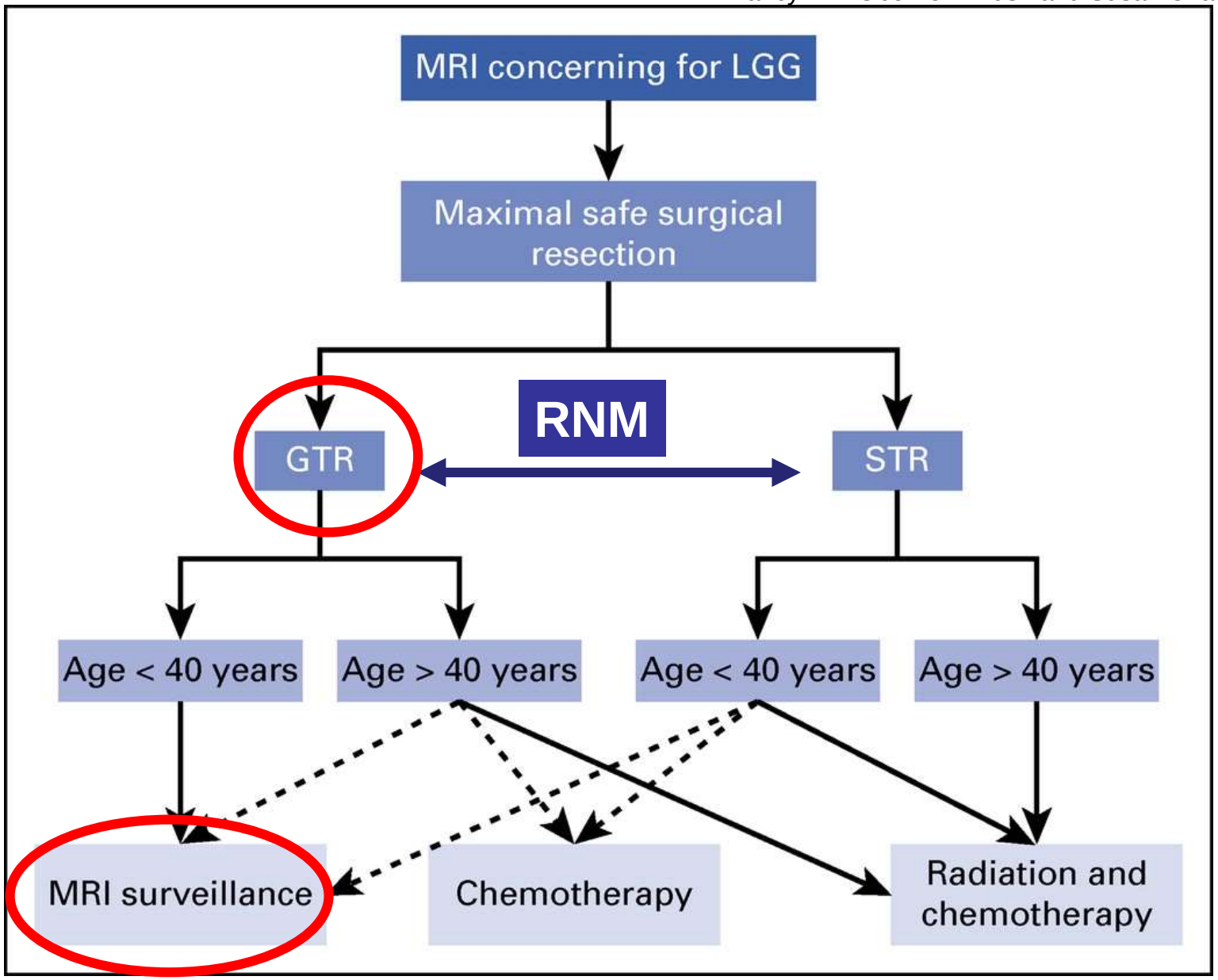
# Modelo de progresion tumoral



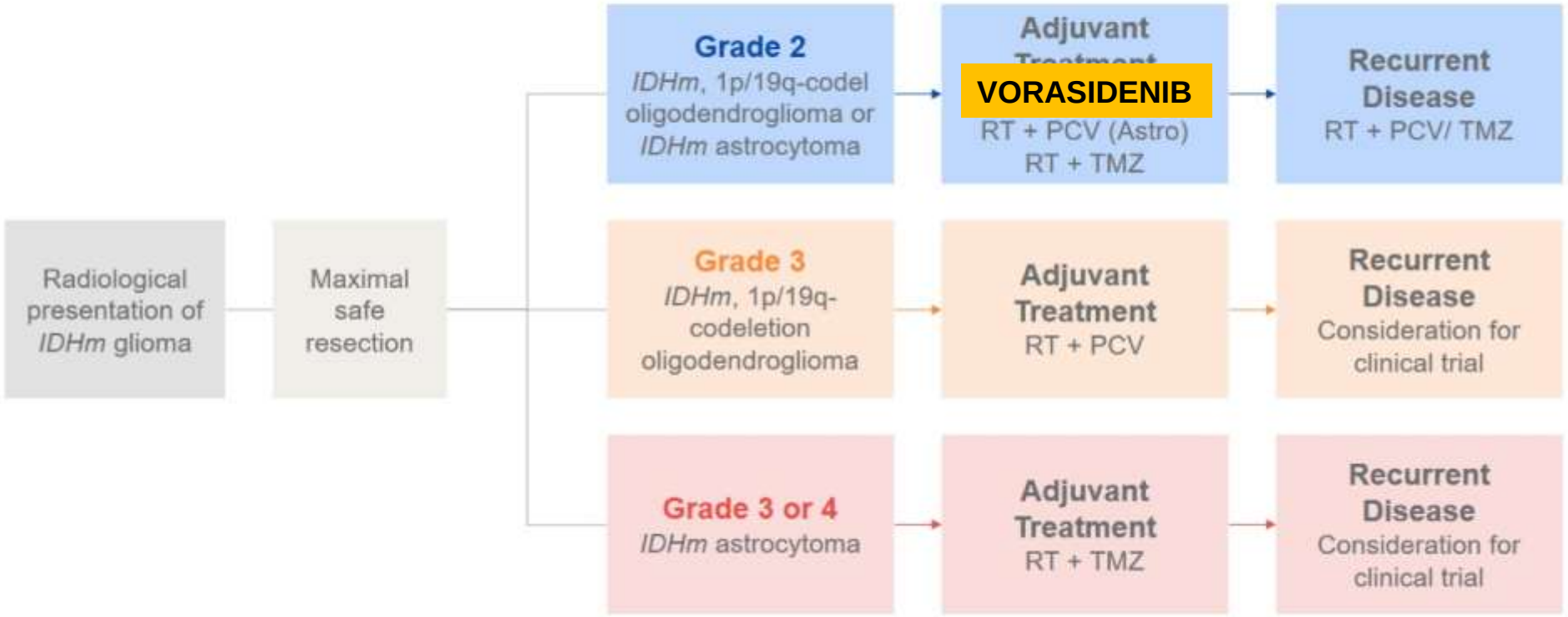
# TRATAMIENTO GENERALIDADES

- **GLIOMAS BAJO Y ALTO GRADO**
- **GLIOMAS DE TRONCO**
- **MEDULOBLASTOMA**
- **EPENDIMOMAS**
- **TUMORES DE LA REGION PINEAL**
- **LPSNC**
- **MENINGIOMAS**

Treatment Strategies for Low-Grade Glioma in Adults
Nancy Ann Oberheim Bush and Susan Chang,



# Glioma Diagnosis: Transformation From Histological to Molecular Classification Influences Surgical Management Goals




*IDHm*, *IDH*-mutant; NCCN, National Comprehensive Cancer Network; PCV, procarbazine; RT, radiotherapy; TMZ, temozolomide.

NCCN Guidelines Version 1.2023 Central Nervous System Cancers; Louis DN, et al. Neuro Oncol. 2021;23:1231-1251; Kim YZ, et al. Brain Tumor Res Treat. 2022;10:83-93.

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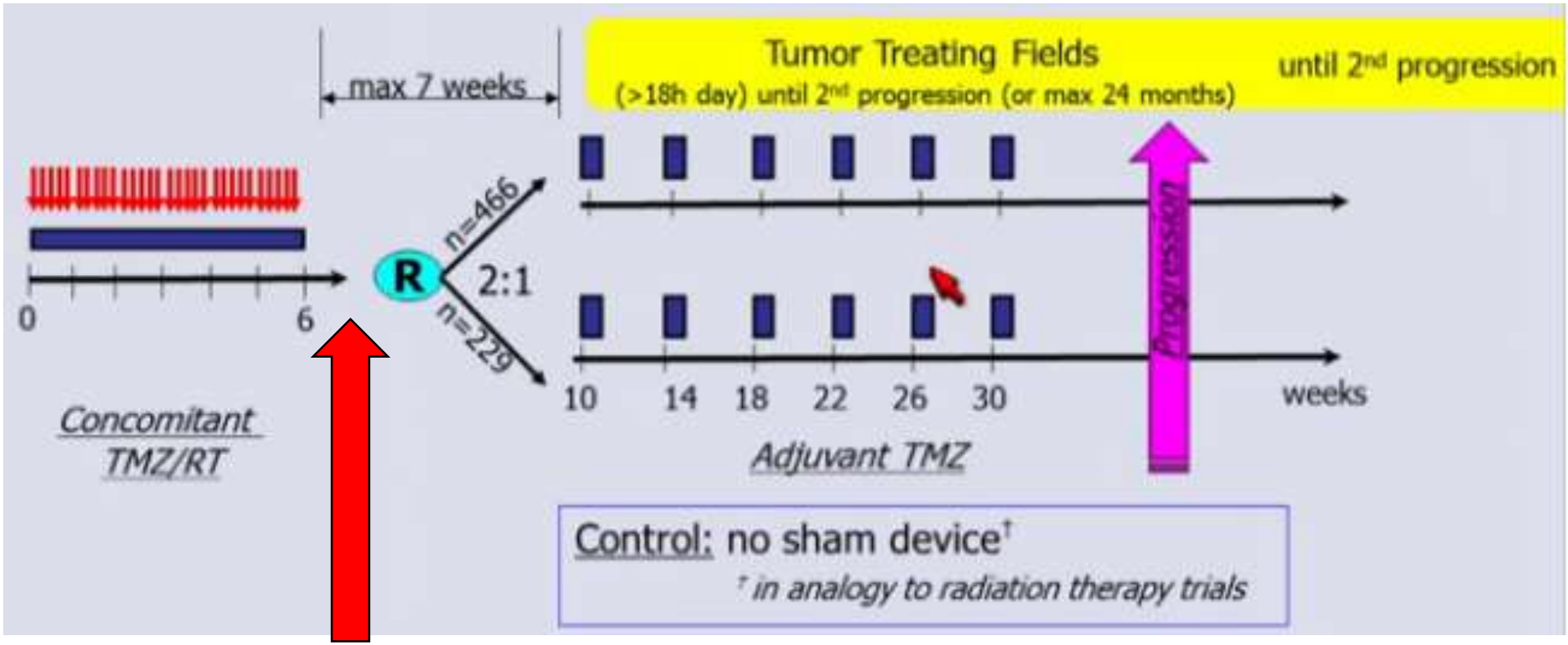
# GLIOBLASTOMAS

**KPS≥70,**
**Sin dispositivos implantables,**
**CORTI estables o en descenso últimos 7 días**

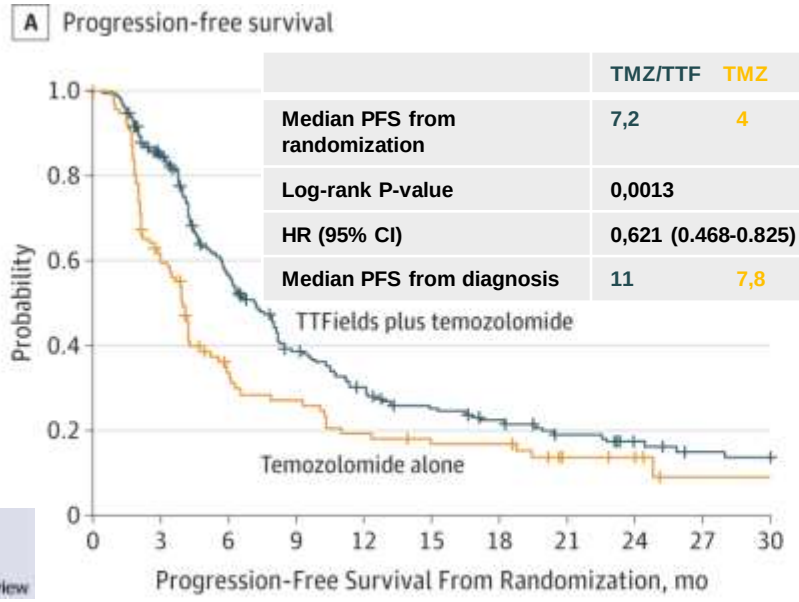



**Sin progresión**

**SEGUIMIENTO MINIMO 18 MESES**

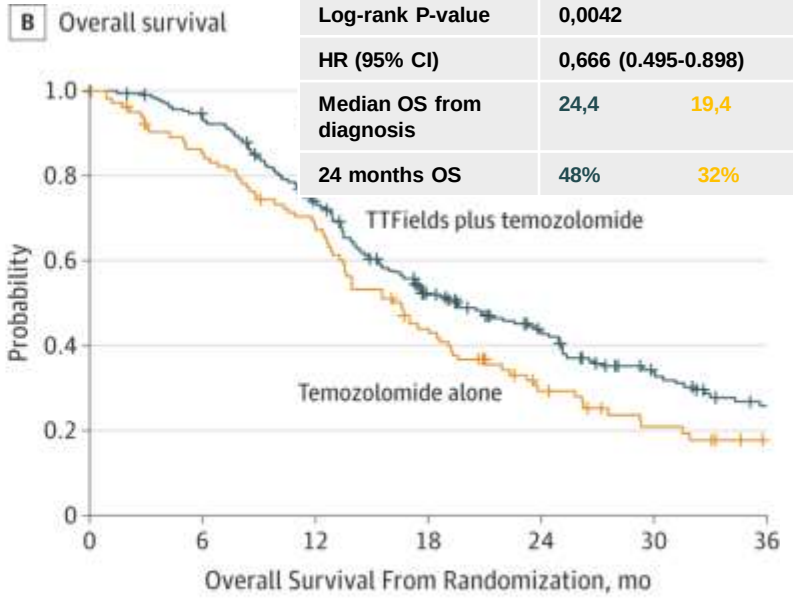
**Cutt of Dec 29, 2014**

## END POINT 1º




| | TMZ/TTF | TMZ |
|---|---|---|
| Median PFS from randomization | 7,2 | 4 |
| Log-rank P-value | 0,0013 | |
| HR (95% CI) | 0,621 (0.468-0.825) | |
| Median PFS from diagnosis | 11 | 7,8 |

Progression defined per Macdonald criteria:
- MRI q 2 months
- Blinded central radiology review




| | TMZ/TTF | TMZ |
|---|---|---|
| Median OS from randomization | 20,5 | 15,6 |
| Log-rank P-value | 0,0042 | |
| HR (95% CI) | 0,666 (0.495-0.898) | |
| Median OS from diagnosis | 24,4 | 19,4 |
| 24 months OS | 48% | 32% |

No. at risk

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| TTFields plus temozolomide | 210 | 149 | 94 | 60 | 45 | 35 | 29 | 22 | 16 | 12 | 11 |
| Temozolomide alone | 105 | 55 | 26 | 21 | 15 | 12 | 12 | 6 | 5 | 1 | 1 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 210 | 195 | 147 | 94 | 65 | 43 | 28 |
| 105 | 86 | 68 | 42 | 23 | 14 | 8 |

**Two-thirds (n = 141) of patients in the TTFields plus temozolomide group continued treatment with TTFields after first tumor progression.**

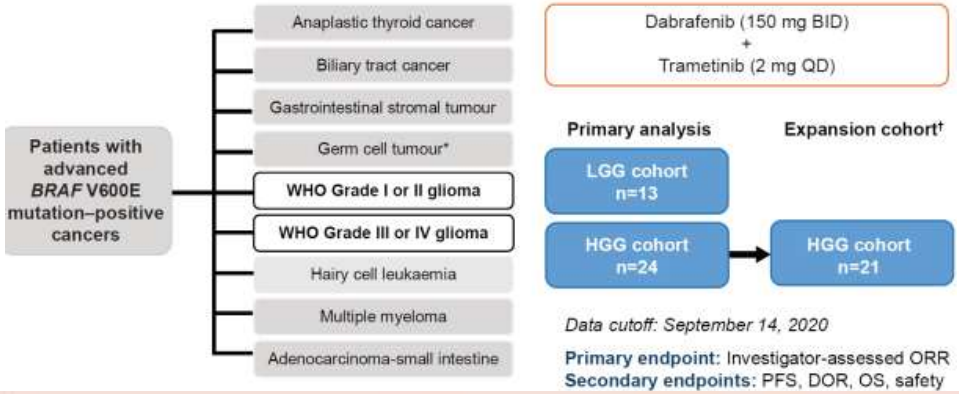
**Second-line treatments, such as nitrosoureas, temozolomide rechallenge, and bevacizumab, were received by 67% of the patients in the TTFields plus temozolomide group compared with 57% in the temozolomide alone group; about 40% of second-line therapies included bevacizumab and about 40% included nitrosoureas. The type of chemotherapy used at recurrence was balanced between treatment groups.**

*JAMA.* 2015;314(23):2535-254

FLENI

# Dabrafenib plus trametinib in patients with *BRAF*$^{V600E}$-mutant low-grade and high-grade glioma (ROAR): a multicentre, open-label, single-arm, phase 2, basket trial

*Patrick Y Wen, Alexander Stein, Martin van den Bent, Jacques De Greve, Antje Wick, Filip Y F L de Vos, Nikolas von Bubnoff, Myra E van Linde, Albert Lai, Gerald W Prager, Mario Campone, Angelica Fasolo, Jose A Lopez-Martin, Tae Min Kim, Warren P Mason, Ralf-Dieter Hofheinz, Jean-Yves Blay, Daniel C Cho, Anas Gazzah, Damien Pouessel, Jeffrey Yachnin, Aislyn Boran, Paul Burgess, Palanichamy Ilankumaran, Eduard Gasal, Vivek Subbiah*




| Histology† | HG | LG |
|---|---|---|
| Glioblastoma | 31 (69%) | 0 |
| Anaplastic pleomorphic xanthoastrocytoma | 5 (11%) | 0 |
| Anaplastic astrocytoma | 5 (11%) | 0 |
| Anaplastic ganglioglioma | 1 (2%) | 0 |
| Anaplastic oligodendroglioma | 1 (2%) | 0 |
| Astroblastoma | 1 (2%) | 0 |
| tiated | 1 (2%) | 0 |
| oma | 0 | 4 (31%) |
| rocytoma | 0 | 2 (15%) |
| ic xanthoastrocytoma | 0 | 2 (15%) |
| exus papilloma | 0 | 1 (8%) |
| oma or ganglioglioma | 0 | 1 (8%) |
| strocytoma, WHO | 0 | 1 (8%) |
| trocytoma | 0 | 1 (8%) |
| ntiated astrocytoma | 0 | 1 (8%) |

| | Grade III (n=13) | Glioblastoma (n=31) | Age 18–39 years (n=22) | Age ≥40 years (n=23) |
|---|---|---|---|---|
| Objective response rate by investigator, % (95% CI) | 38 (13·9–68·4) | 32 (16·7–51·4) | 50 (28·2–71·8) | 17 (5·0–38·8) |
| Patients responding at 12 months by investigator assessment, % (95% CI) | 100 | 67 (28·2–87·8) | 89 (43·3–98·4) | 50 (5·8–84·5) |
| Median progression-free survival by investigator, months (95% CI) | 3·8 (1·7–NR) | 2·8 (1·8–13·7) | 18·5 (5·5–41·4) | 1·7 (0·9–2·5) |
| Median overall survival, months (95% CI) | 45·2 (6·3–NR)* | 13·7 (8·4–25·6) | 45·2 (17·9–NR)† | 8·7 (3·7–11·7) |

NR=not reached. *Six deaths among 13 patients. †Eight deaths among 22 patients.

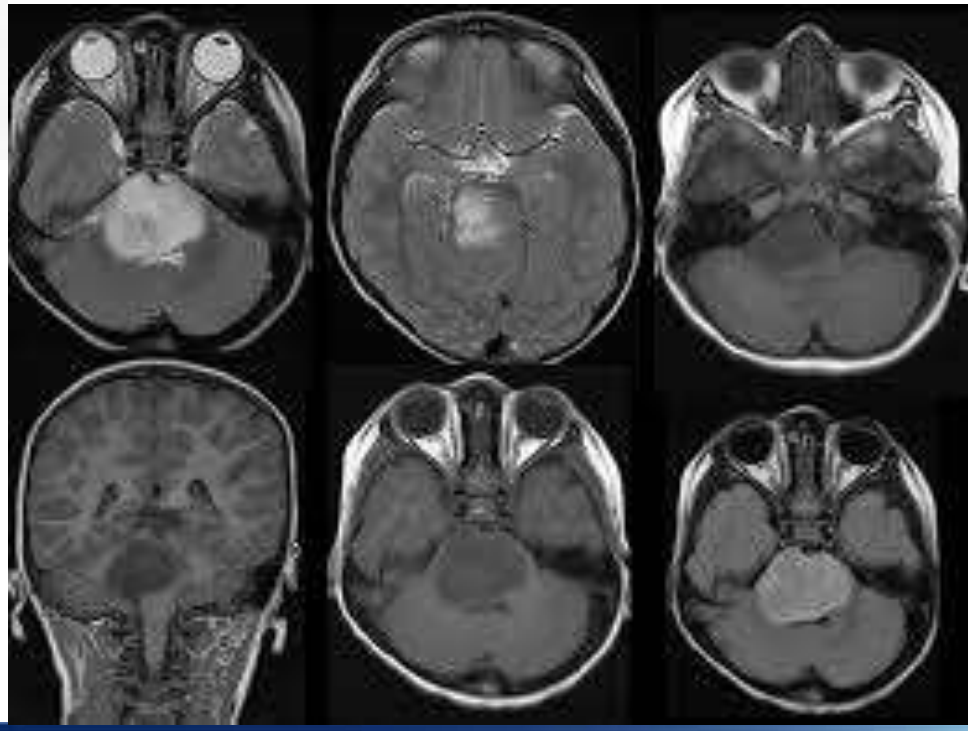
**Table 3: Post-hoc subgroup analysis of the high-grade glioma cohort**

# GLIOMAS DE TRONCO

- Approx. 1 % of all primary brain tumours, 10-20% of pediatric brain tumours
- 75% occur in children, 25 % in adults
- Median age at presentation-6.5 yrs, adults- 3rd -4th decade
- M=F
- Approx. 75% diffuse, 25 % focal
- Most focal tumours occur in midbrain
- Pontine tumours are usually diffuse and high grade

**Tratamiento**
**ALTO GRADO**
**IMRT 50-60 Gy + nimotuzumab + vinorelbine**

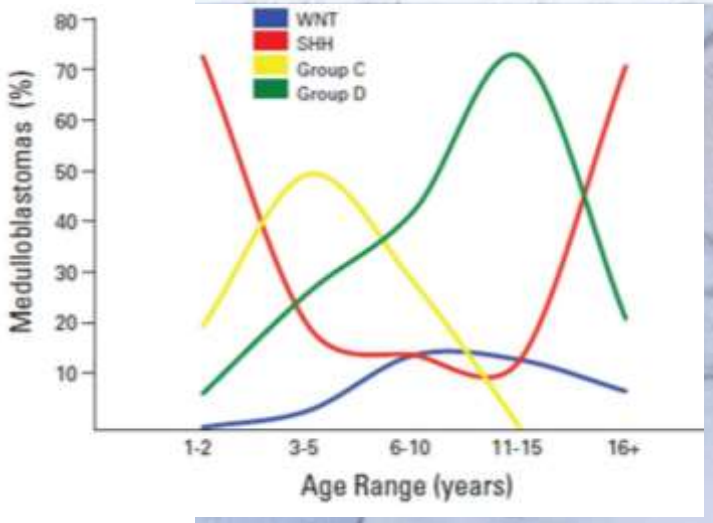
**DIFUSOS (75-80%)**
**CERVICOMEDULARES (10-15%)**
**FOCALES (20-25%)**
**EXOFITICO DORSALES**



**Biopsia!!!**

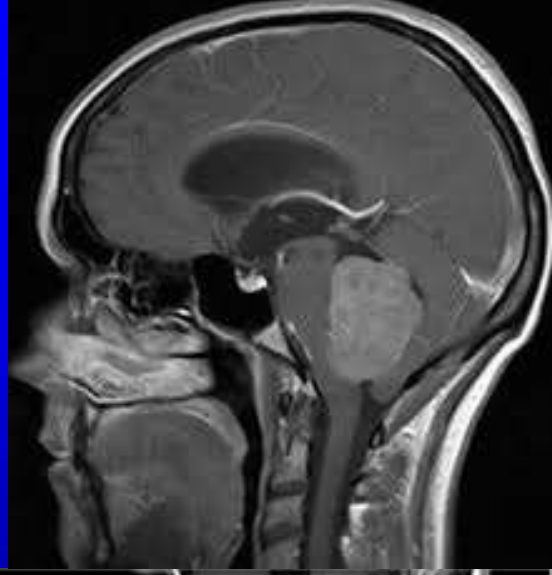
**Mutación H3K27M chicos mal pronostico**

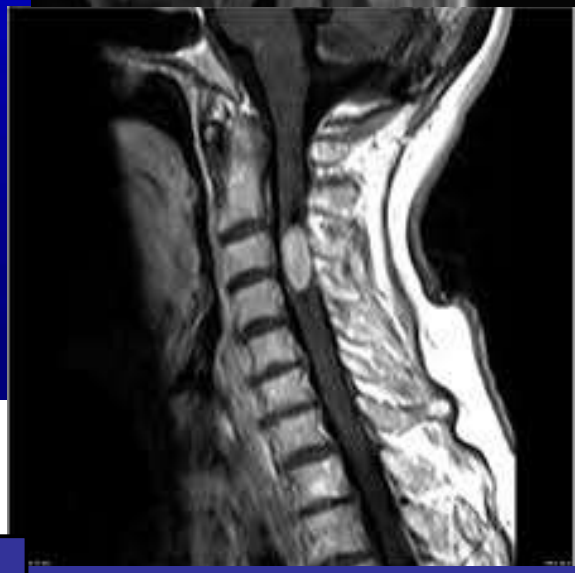
# MEDULLOBLASTOMA



# EPENDYMOMA

- Presumed cell of origin: ependymal cells
- Relatively common in children, also occur in adults
- Intra- or paraventricular location
- Posterior fossa in children, spinal cord in adults most common
- Median survival: 5-10 years
- Grossly well demarcated tumors, histologically showing dense cellularity, perivascular pseudorosettes, ependymal rosettes
- WHO grade II tumors
- Malignant degeneration to anaplastic ependymoma = WHO grade III



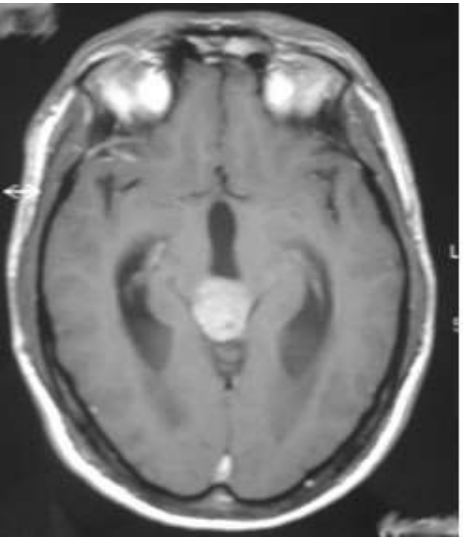


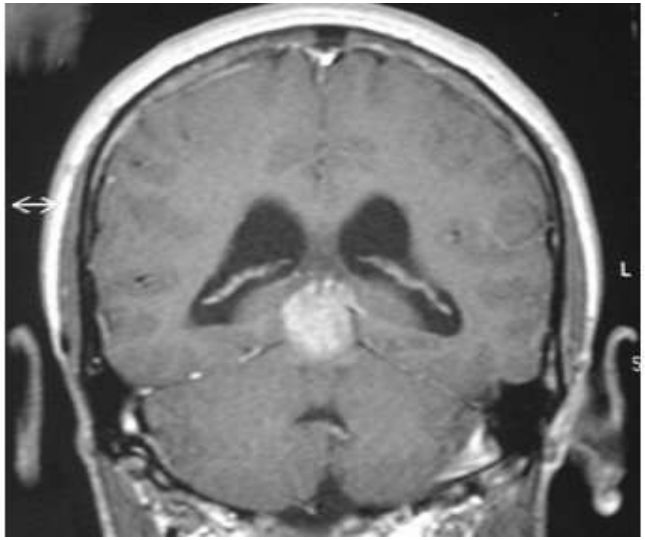
**22q, 6q Loss, 9q33-34 progresión y trans maligna, HER2 + 75%**

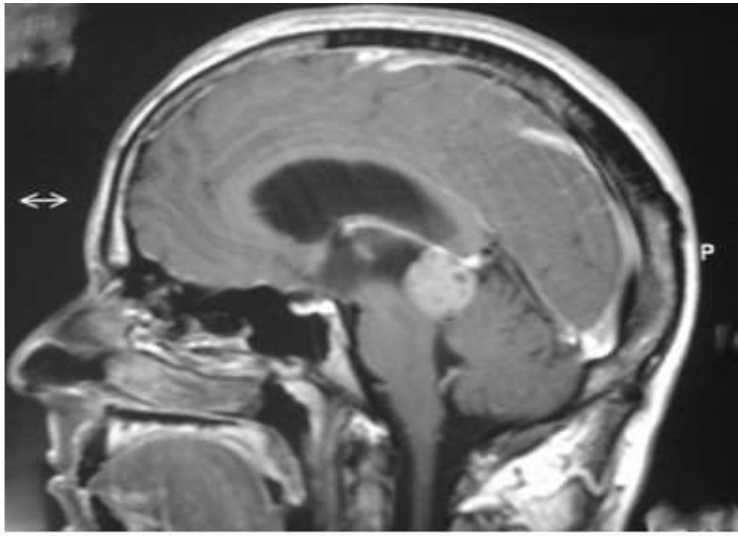
**60% infratentoriales Ca+ (10% diseminación LCR)**
**40% supra 1,6% LCR (50% ventriculares, 50% parénquima)**
**Mixopapilares cono, filum o cola de caballo**

**RT local 54-60 gy**
**QT CDDP-VP16, CC-VCR, TMZ, LAPATINIB**

# TUMORES DE REGIÓN PINEAL



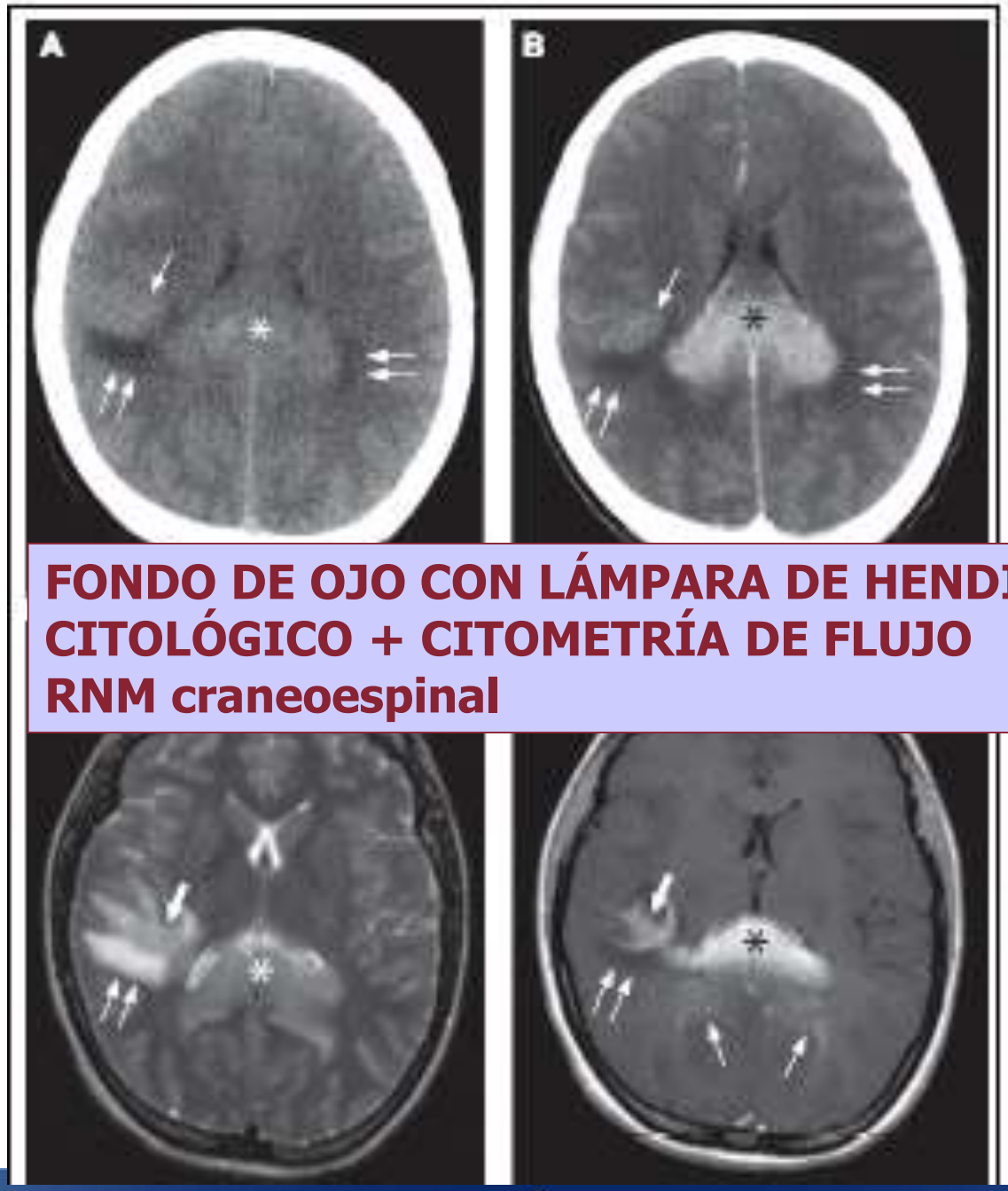




**Pineocitoma**
**TPRP**
**Pineoblastoma = PNET**
**Gliomas**

**Tumores germinales** - Germinomas → RT 40 Gy + 20 Gy ventrículos
- No germinomas → QT (PEI x 4) → RT

# LPSNC

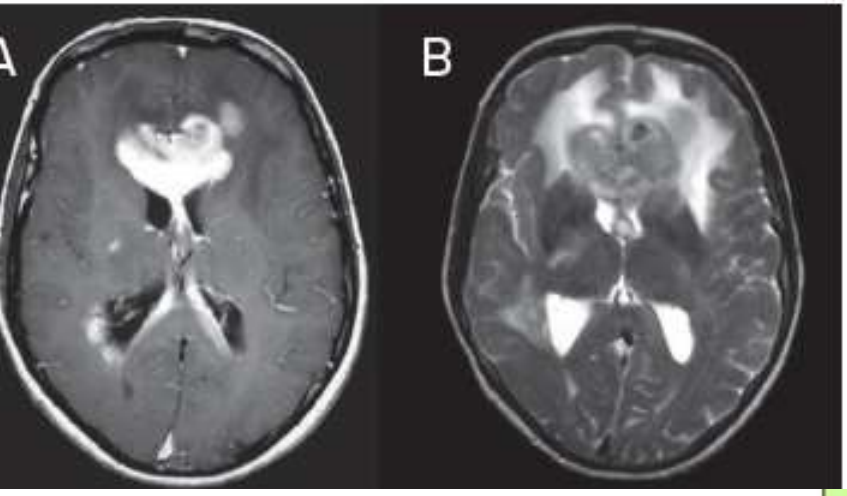



**FONDO DE OJO CON LÁMPARA DE HENDIDURA**
**CITOLÓGICO + CITOMETRÍA DE FLUJO**
**RNM craneoespinal**

80 % SUPRATENTORIALES
65 % ÚNICOS
38 % HEMISFÉRICOS
16 % PROFUNDOS
14 % CUERPO CALLOSO
12 % REGIÓN VENTRICULAR
9 % CEREBELO

20 % COMPROMISO OCULAR
15 % CÉLULAS EN LCR

# LPSNC




**Presenting symptoms**
focal deficits (70%),
neuropsychiatric sym. (43%),
high intracranial pressure (33%),
seizures (14%), headache,
ocular symptoms,
confusion, and lethargy.

**Sites of disease**
Brain hemispheres (38%),
thalamus/basal ganglia (16%),
corpus callosum (14%),
periventricular region (12%),
cerebellum (9%), eyes (5-20%),
meninges (16%), spinal cord (1%),
cranial and spinal nerves (<1%).

**Neuroimaging (MRI)**
Lesions are hypointense in T1,
isointense to hypointense on T2,
reduced ADC,
variable surrounding edema,
strong enhancement.

**PCNSL suspicion**

**NO CORTICOIDES!!!**

**Stereotactic biopsy**

**Diffuse large B-cell lymphoma**

**Staging**
Physical examination,
routine blood studies,
Whole-brain MRI,
Contrast total body CT scan,
Ophthalmologic evaluation[1],
CSF examination[2]
Bone marrow biopsy
Testicular ultrasonography
18FDG-PET (investigational).

**Baseline evaluations**
Neurological examination
Biochemical serum profile
Neuropsychiatric tests
Renal functionality tests
Hepatic functionality tests
Cardiac functionality tests
HIV, Hepatitis B & C virus.

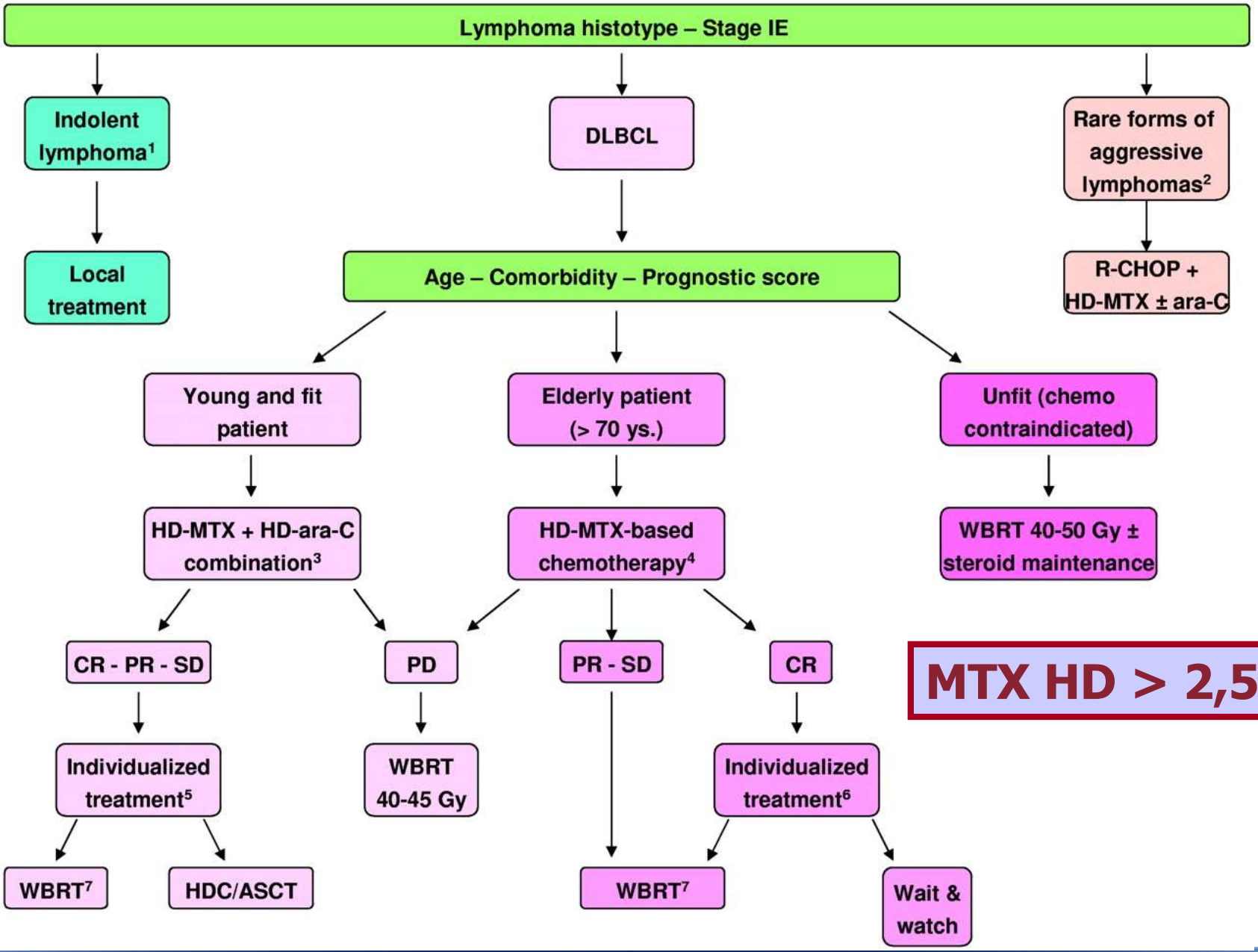
**Prognostic factors**
Age (≤60 vs. >60 ys.)
Performance status (0-1 vs. ≥2)
LDH (normal vs. elevated)
CSF protein (normal vs. elevated)
Deep regions (no vs. yes)

**Exclusion of systemic disease.**
**Extension: eyes, CSF, etc**

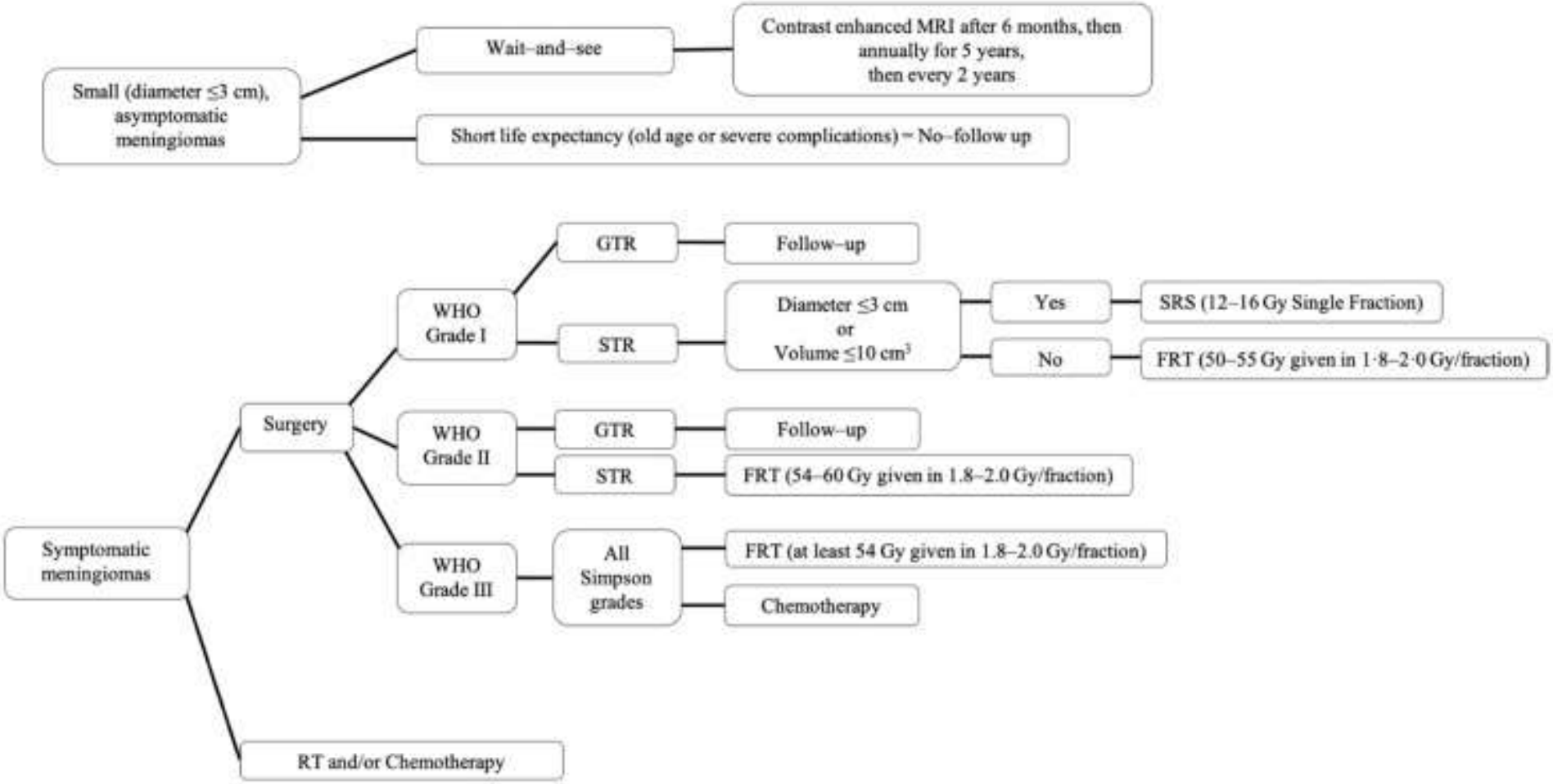
**Treatment feasibility.**

**Risk**

**Therapeutic decision**


Lymphoma histotype – Stage IE
Indolent lymphoma[1]
DLBCL
Rare forms of aggressive lymphomas[2]
Local treatment
Age – Comorbidity – Prognostic score
R-CHOP + HD-MTX ± ara-C
Young and fit patient
Elderly patient (> 70 ys.)
Unfit (chemo contraindicated)
HD-MTX + HD-ara-C combination[3]
HD-MTX-based chemotherapy[4]
WBRT 40-50 Gy ± steroid maintenance
CR - PR - SD
PD
PR - SD
CR
Individualized treatment[5]
WBRT 40-45 Gy
Individualized treatment[6]
WBRT[7]
HDC/ASCT
WBRT[7]
Wait & watch
MTX HD > 2,5 gr

# TRATAMIENTO MENINGIOMA




*Biomedicines* **2021**, *9*(3), 319; https://doi.org/10.3390/biomedicines9030319

# MUCHAS GRACIAS POR SU ATENCION

Las batallas ganadas son las que nos permiten seguir adelante, las perdidas son las que duelen, nos hacen aprender, corregir y reflexionar pero todas deben ser dadas en equipo donde nadie es más importante que otro (clínico, imagenologo, radioterapistas, cirujanos, enfermeras y paliativistas)

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