# When Benign Tumors Go Bad: Emerging Medical Treatments

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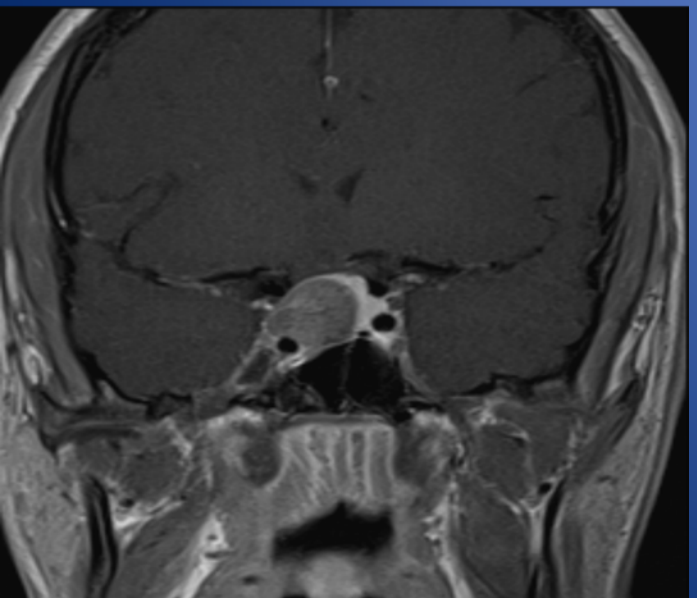
Piedmont Brain Tumor Center



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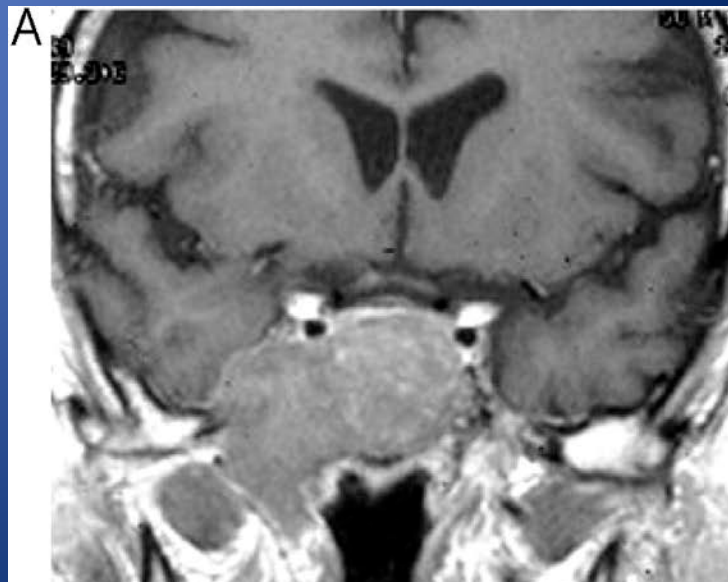

# No Relevant Disclosures

**Slides are Available for Your Reference**

**CME Objectives are in you Conference Materials**

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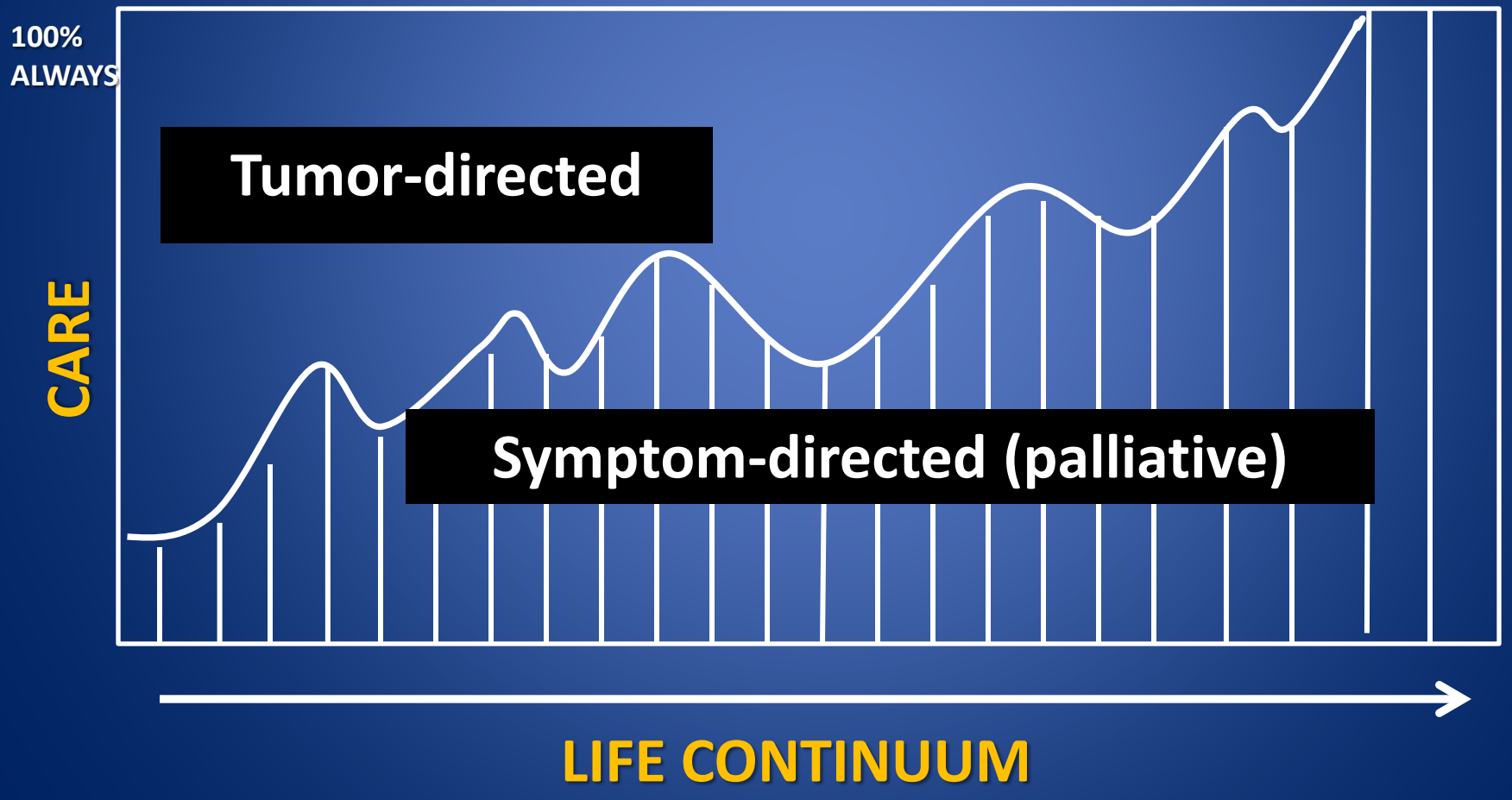
# Overarching Principle


# Paucity of Evidenced-Based Medical Therapy

## FOCUS: Using Best-Available Evidence For Individualized Goals of Care



# Symptom-directed Treatment

- Interdisciplinary Team!
- Infertility – counsel, grants
- Vision – monitor VF & VA
- Endocrine Treatments
- Cranial Nerve deficits
- Mass effect and vasogenic edema
- Seizures
- Thrombosis and hemorrhage
- Depression, coping
- Iatrogenic side-effects (from treatment)

# First Things First
# R/o Malignant Tumors

- Consider Tumor Boards
  - H&N, CNS
- Example: Sella
  - Germ cell tumors (ectopic pinealomas)
  - Chordomas
  - Primary CNS lymphoma
    - Must rule out metastatic systemic lymphoma
  - Metastatic disease (1-2% sellar masses)
    - Rarely, the 1st or only location
    - Migration alone nerves

# Also, R/o Non-Tumors

- Cysts — Rathke's cleft, arachnoid, dermoid cysts
- Abscess — rare
- Arteriovenous fistula of the cavernous sinus
- Lymphocytic hypophysitis — Lymphocytic infiltration
  - Usually occurs in late pregnancy or the postpartum period
  - infrequently in men

# Select "Benign" Tumors with Emerging Medical Tumor-Directed Therapies

## Refractory to, or not Amenable to, Traditional Treatments

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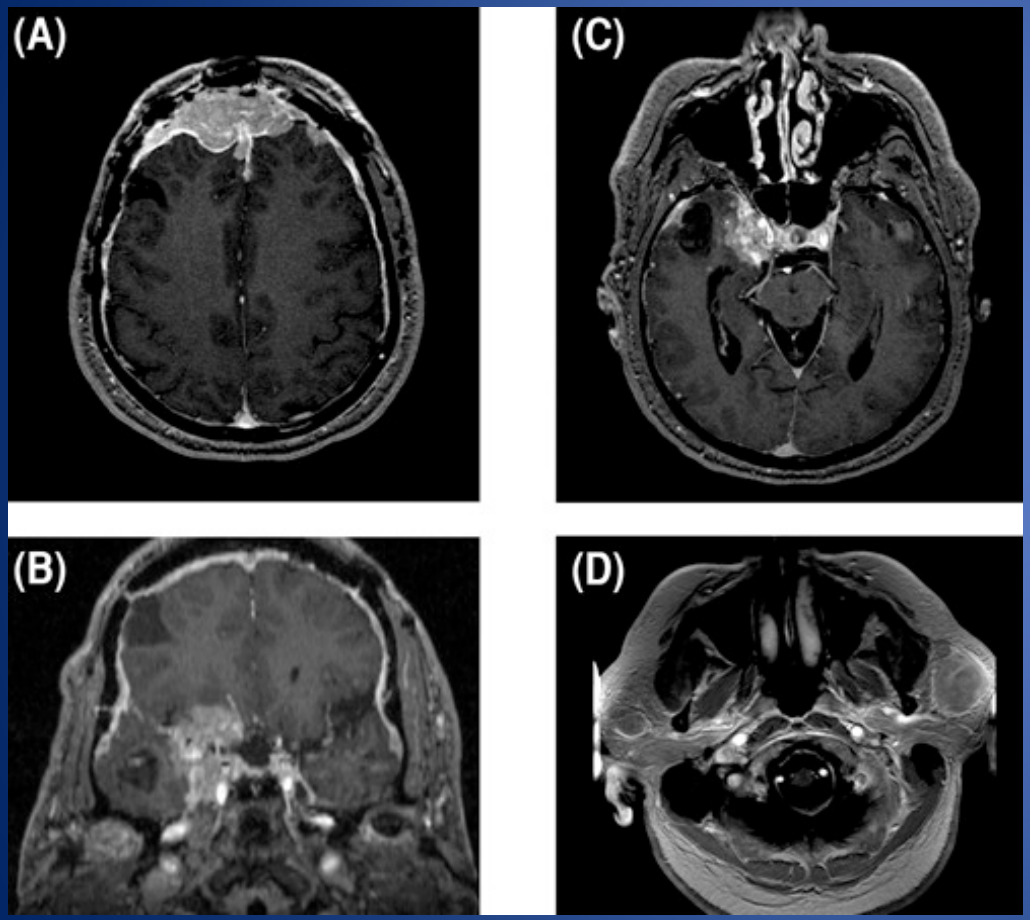
# Olfactory Neuroblastoma Case Report




Pre-treatment maximal disease at the frontal lobes (A), cavernous sinus (B, C), and parotid lymph node (D), best imaged on T1-w MRI

- Palliative Avastin (targeting venous congestion) +/- TMZ
- Palliative Ommaya Reservoir

Dunbar, EM et al, Rare Tumors, 2012

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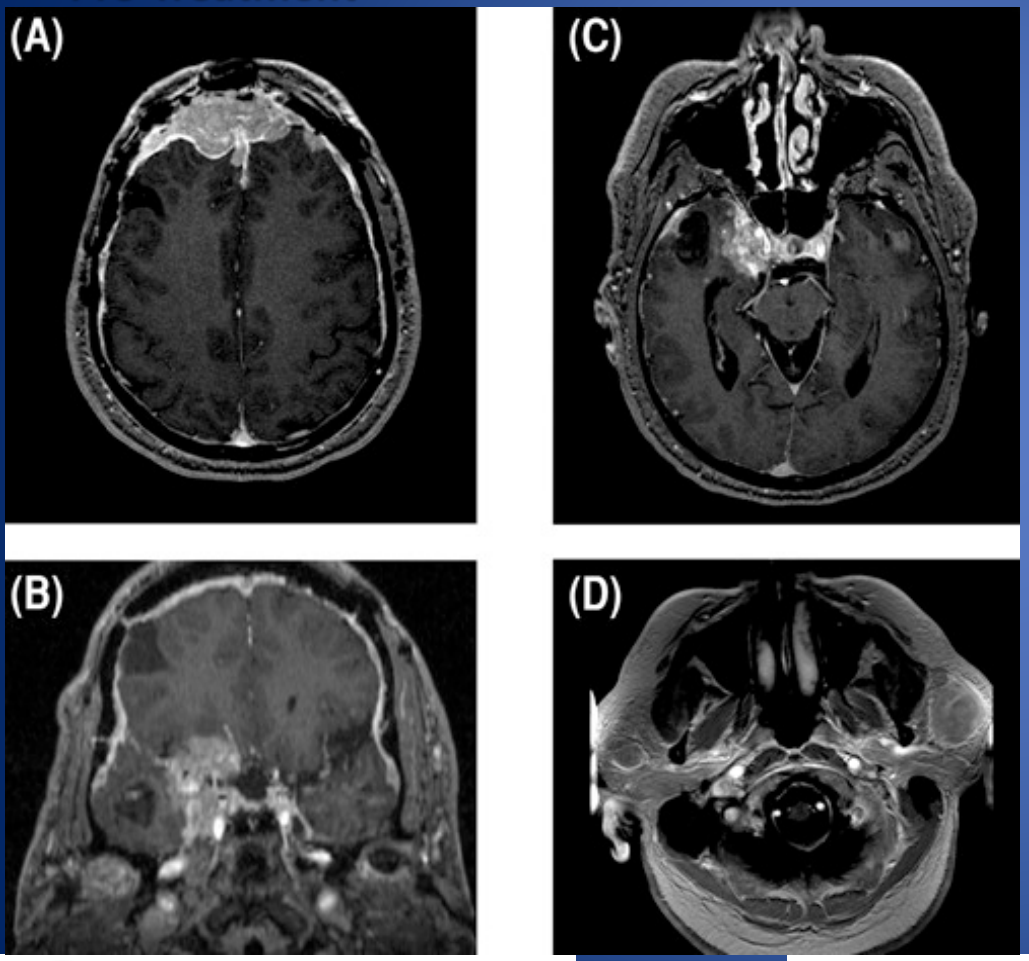
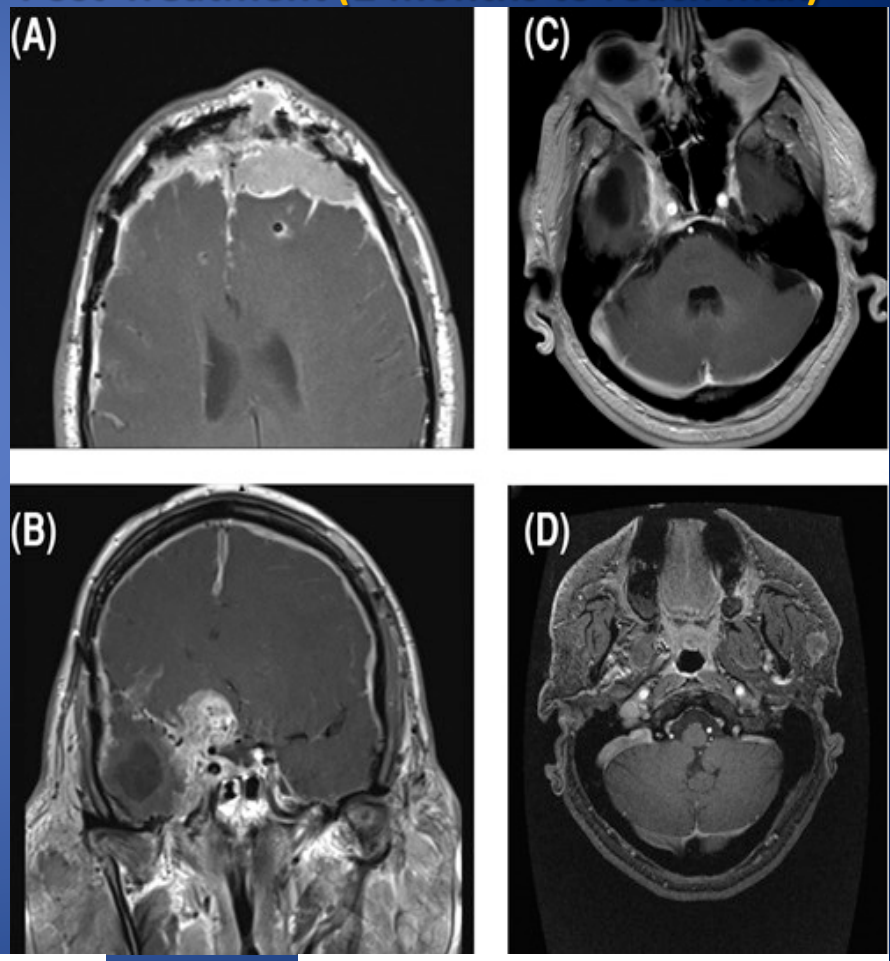
# Olfactory Neuroblastoma

**Pre-Treatment**




**Post-Treatment (2 months to reach max)**

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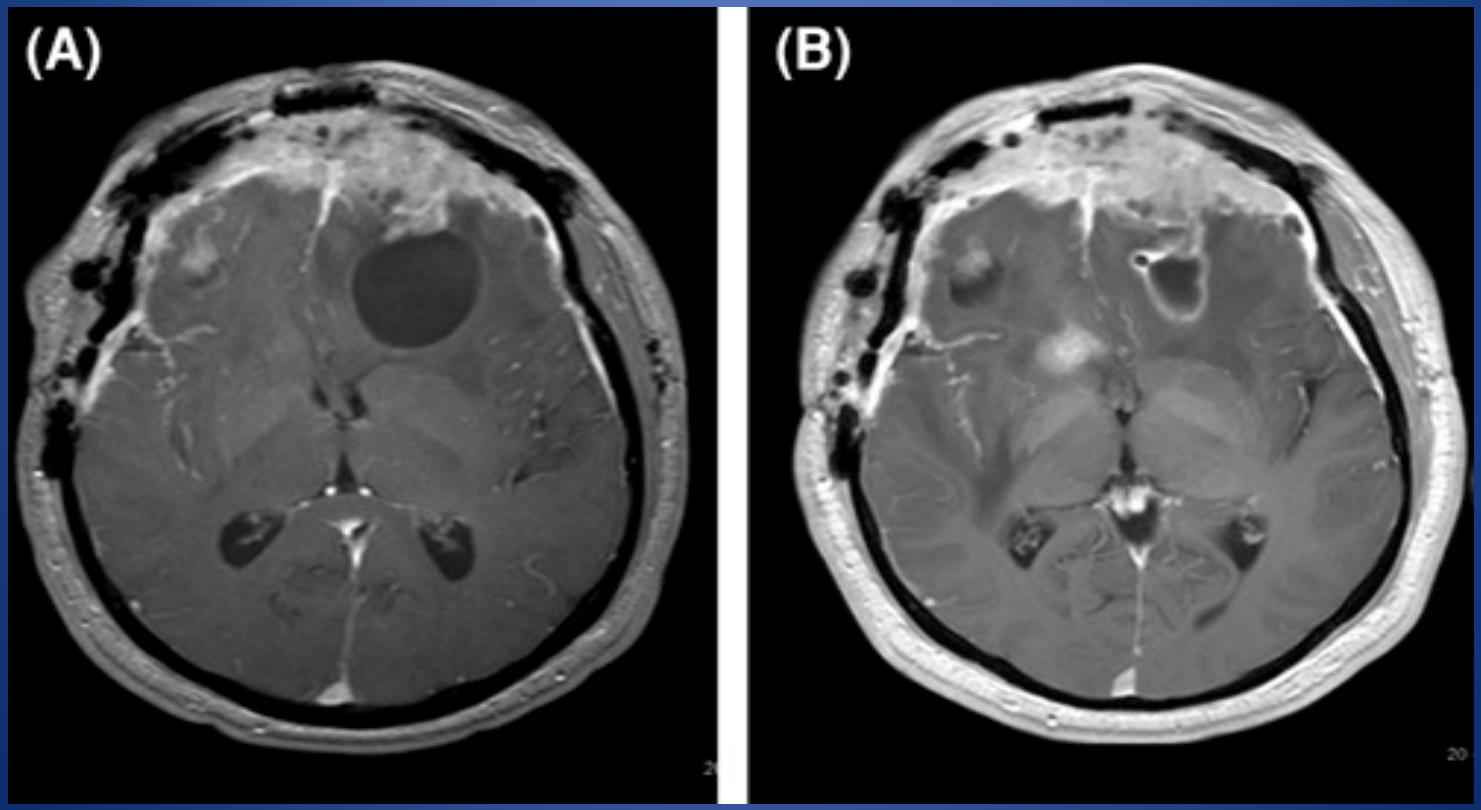
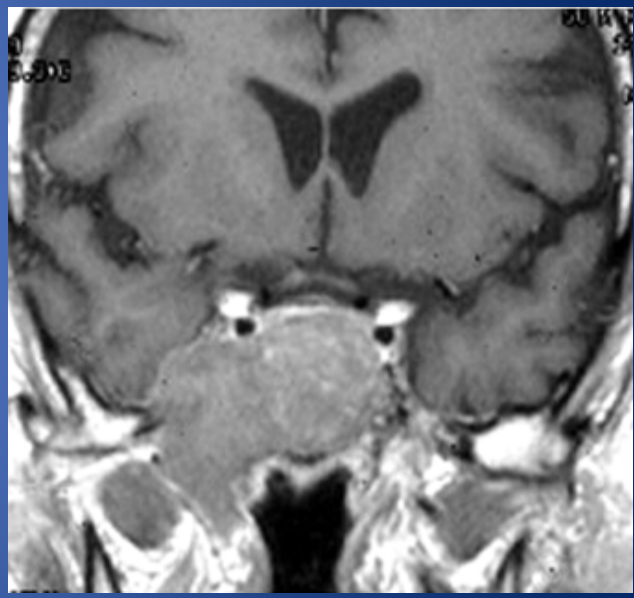
# Olfactory Neuroblastoma

Pre- and post-placement of Ommaya reservoir demonstrating maximal encephalocele size (A) and representative minimization (B) after cerebrospinal fluid draw.



# Pituitary Adenomas or Carcinomas +/- secreting Case Series

- Watch precipitous endocrine effects (central DI)
- Temozolomide
  - Especially if Meth-MGMT, +MSH6
- Capecitabine (oral 5-FU) & Temozolomide
- Avastin
  - Especially if venous congestion or edema



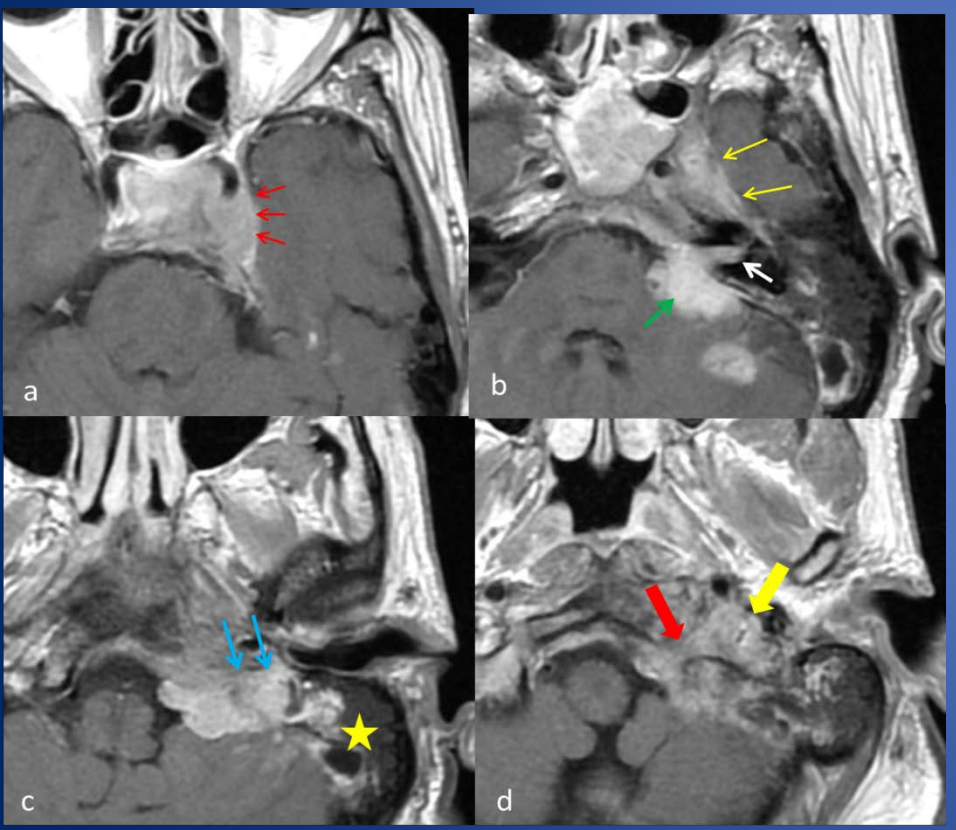
Faje AT, 2013; Chen W, 2013; Matsuno A, 2013; Jiang XB, 2013; Zacharia BE, 2013; Ortiz

# Atypical or Malignant Meningioma Case Series

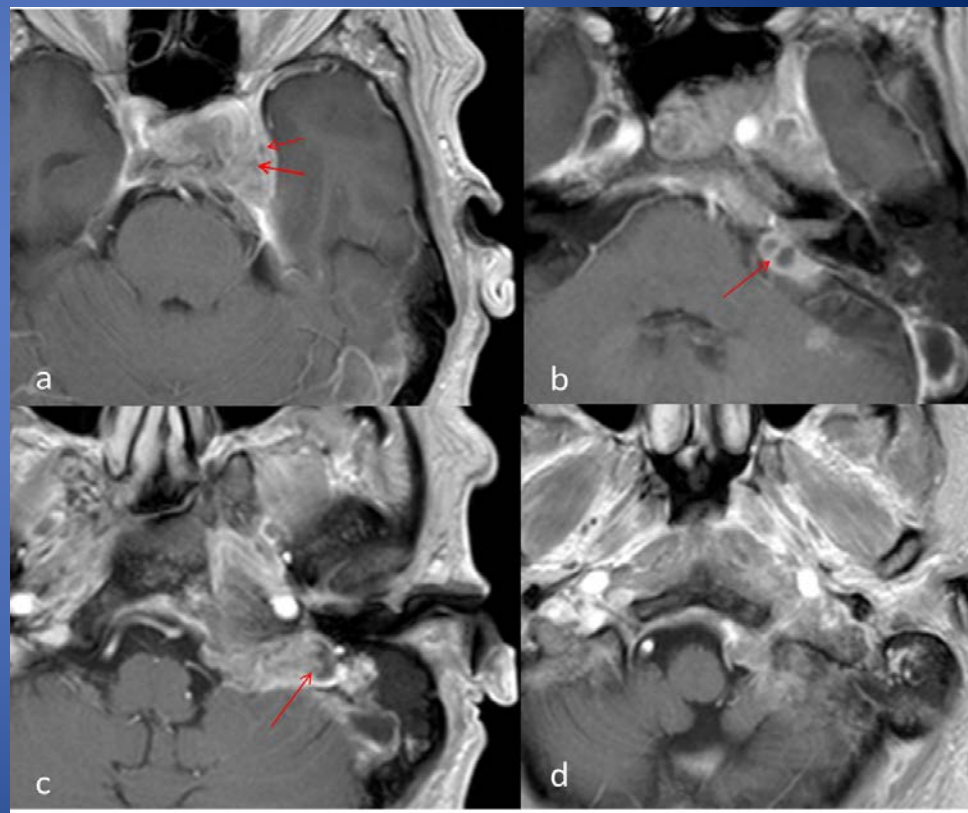
- Consider staging neck (LNs), spine (macroscopic), lungs
- No establishes systemic agent
- No significant activity with progesterones, interferon alfa-2b, Temozolomide, hydroxyurea, and chemo combos
- Somatostatin receptor analogs under investigation
  - Octreotide – stable disease > partial responses
- Molecularly Targeted Agents under investigation:
  - Anti-angiogenesis (PO, IV) – stable disease > partial responses – especially because of other effects
  - Platelet derived growth factor (PDGF)
  - Epidermal growth factor receptor (EGFR)

# Rhabdoid Meningioma Case Report

**Pre-Treatment**




**Post-Tx (max clinical: 2 mo; max rad.: 3 mo)**

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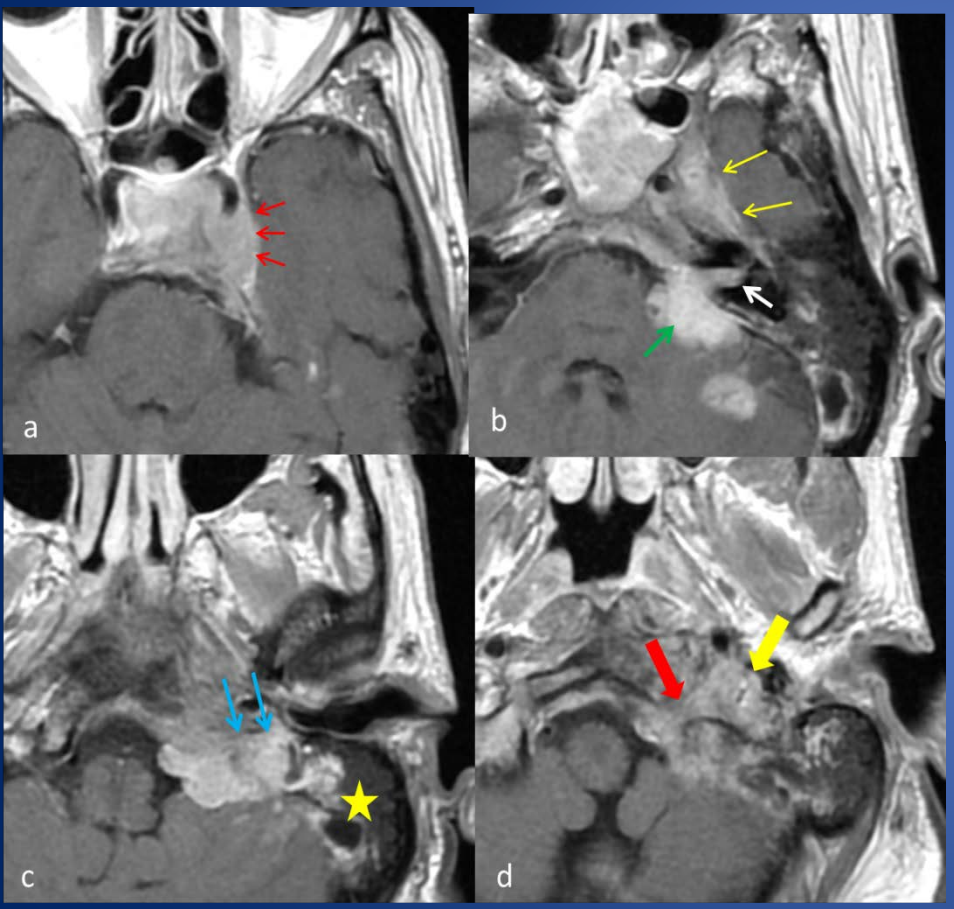
# Rhabdoid Meningioma Case Report

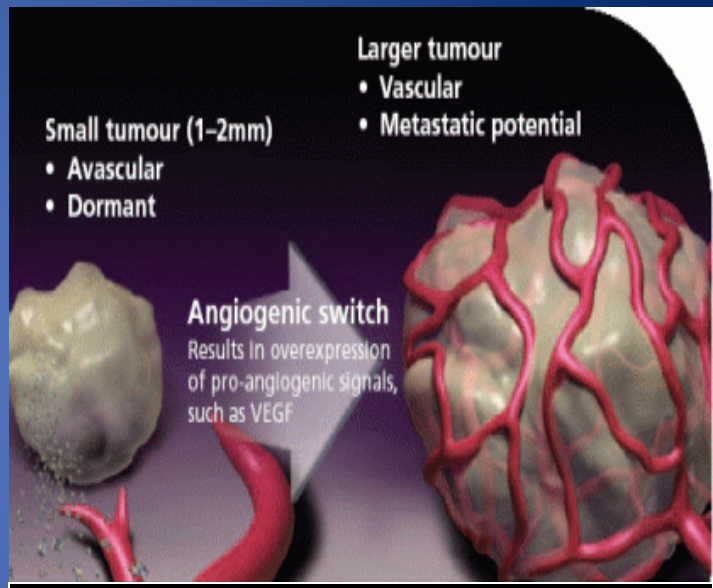



- Palliative Avastin +/- TMZ
- Significant and Durable Response
- Off narcotics
- Gabapentin, Lyrica, Lidocaine patches….

Dunbar, EM, EJCMO 2011

# Anti-angiogenic Agents Safety in CNS tumors

- Toxicities:
  - Extrapolated: Mets, Gliomas
  - (baseline % vs. AA for ~ 6-12 mo.)
- Arterial/venous thromboses (~2, <5%)
- Arterial/venous hemorrhage (~8,<10%)
- "Accelerates" CAD, CVD, PVD, Hypertension, Renal (protein, Cr.)
- Delayed wound healing/breakdown
- Fatigue
- Rare: reversible posterior leukoencephalopathy syndrome




FDA 2007: Bevacizumab (Avastin, VEGF-R monocloncal Ab) for progressed GBM[15-17]

Widely extrapolated to recurrent, progressive tumors, radiation-necrosis, etc.!

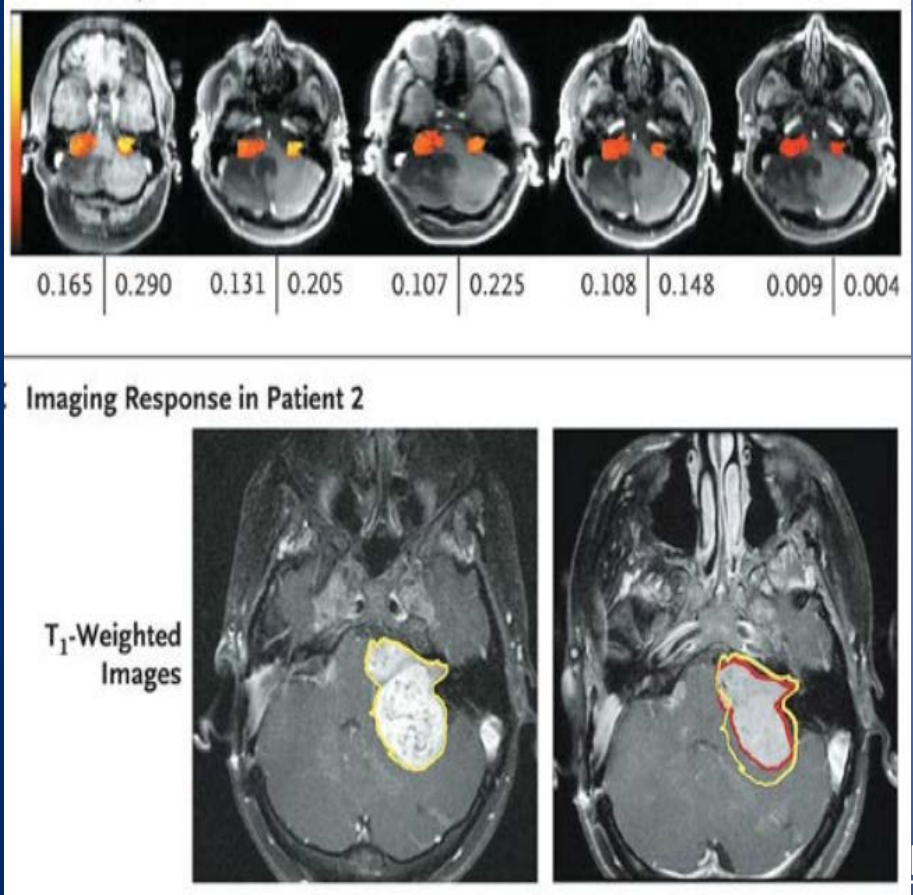
# Anti-angiogenic Agent Safety in CNS Tumors

- Surgical/Procedural safety: ASK about AAs and ACs!
- Elective: Hold for ~28 days for major, ~14 days for minor surgery/procedures (based on ½ life).
- Urgent/emergent: No reversal or antidote
- Usually no intra-op issues
- Consider conservative closure
- Close post-op monitor for delayed sequela (end of ½ life)
- Prophylaxis: Surveillance and avoid over AC

# Temozolomide (Temodar, TMZ) Safety

- Remarkably well-tolerated
- Oral, various regimens
- cbc/diff, close communication
- **Thrombocytopenia - RARE** (essentially no anemia!)
- **Immuno-suppression – QUALITATIVE > quantitive** (lymphocytes >> neutropenia)
  - PJP prophylaxis (i.e., bactrim (sulfa allergy), dapsone, pentamadine)
- Nausea
- Constipation
- Fatigue
- Headache

# Vestibular Schwannomas in NF2
# Numerous retro/prospective case series




- **Bevacizumab (Avastin)**
- ~70% stable or retained hearing
- > 50% hearing improvement
- ~ 50% some tumor shrinkage in most lesions
- Delayed hearing loss, time to surgery,
- ? Neo-adjuvant, refractory?

R, NEJM, 09

# NF-2: Meningioma, Schwannoma (Scwhannomatosis), Plexiform Neurofibromas, PNSTs Retrospective Case Series

- Schwannomas (VS, ? Others)
  - Bevacizumab (Avastin) as prior
  - VEGF pathway likely dominant driver of angiogenesis
- Meningiomas
  - Bevacizumab (Avastin)
  - Radiogrphic response in 29% of the meningiomas, but only avg. 3.7 months
  - VEGF pathway NOT dominant driver of angiogenesis
  - Comparable to sporadic meningiomas

Nunes, FP 2013; Urban T, 2012

# NF-2: Meningioma, Schwannoma (Scwhannomatosis), Plexiform Neurofibromas, PNSTs Retrospective Case Series

- Consider Tumor Boards
- Consider  Specialty Centers
- Consider Trials and Patient/Tissue Registries
- Possible synergy with surgery, SRS, RFA, u/s , etc.
- Watch for malignant transformation
- Whole-Body MRI and 18F-FDG-PET

Nunes, FP 2013; Urban T, 2012

# Medical Treatment Selection

## When/What New Treatment to Start:

1. General Science
2. General Safety
3. Goals/Wishes/Fears
4. Strategy

   i.e., Order of Therapy
5. Logistics
   - Oral, IV, Outpatient, inpatient
   - Cost/insurance
   - Frequency
   - Interested in a Trial? **See next slide**
   - Support required by others (drivers?)
   - Where located,  available elsewhere?

Relatively, equally likely to be safe or work

# What/When New Treatment to Stop:

1. Do you want it?
2. Is it Safe?
   - General medical or tumor/treatment-related
3. Is it getting the job done?
   - Based on pre-selected goals of care

# Interested in a Trial?

## A trial is a good idea that is unproven

- Types
  - Therapeutic
  - Supportive, quality of life
  - Outcome and risk factors
  - Tissue analysis
- Phases (Therapeutic)
  - Phase 1 – Safe?
  - Phase 2 – Work?
  - Phase 3 – Compare two existing therapies
- The overwhelming number of trials in brain cancer are negative, which means patients on the investigational arm of the trial either do “as well as” or “less well” than those on the standard arm

# National Trial Listing

- 1. www.clinicaltrials.gov
- 2. www.cancer.gov
-

**Helpful instructions for performing a search:**

- Click on “Search for Clinical Trials”
- Click on “Advanced Search”
- Scan down to **Recruitment** and choose “Open Studies” in the drop down menu
- Scan down to **Study Type** and choose “interventional studies” in the drop down menu
- Scan down to **Conditions** under “Targeted Search” and type in **brain tumor**
- You can then limit search by area (state) and by phase of study, as well. Please click on the highlighted word “Phase” for further definition of this term. After you have chosen all of your key terms/limits, you can click on “Search” at the bottom of the screen.

# THE END

# THANK YOU

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