PRACTICE AID

Treatment Recommendations for Glioblastoma: NCCN Guidelines Summary[1]

PeerView Neuro-Oncology

American Brain Tumor Association® Providing and pursuing answers®

MLI Medical Learning Institute, Inc.

Aged ≤70 y + good PS (KPS ≥60)[a]

MGMT methylated

Adjuvant treatment

- Consider clinical trial (preferred for eligible patients) ***or***
- Standard brain RT + concurrent temozolomide and adjuvant temozolomide + TTFields therapy (category 1) ***or***
- Standard brain RT + concurrent temozolomide and adjuvant temozolomide (category 1)

MGMT unmethylated or indeterminate

Adjuvant treatment

- Consider clinical trial (preferred for eligible patients) ***or***
- Standard brain RT + concurrent temozolomide and adjuvant temozolomide + TTFields therapy (category 1) ***or***
- Standard brain RT + concurrent temozolomide and adjuvant temozolomide (category 1) ***or***
- Standard brain RT alone

Aged >70 y + good PS (KPS ≥60)[b]

MGMT methylated

Adjuvant treatment

- Consider clinical trial (preferred for eligible patients) ***or***
- Hypofractionated brain RT + concurrent and adjuvant temozolomide (category 1) ***or***
- Standard RT + concurrent temozolomide and adjuvant temozolomide + TTFields therapy (category 1) ***or***
- Standard RT + concurrent temozolomide and adjuvant temozolomide ***or***
- Temozolomide ***or***
- Hypofractionated brain RT alone

MGMT unmethylated or indeterminate

Adjuvant treatment

- Consider clinical trial (preferred for eligible patients) ***or***
- Hypofractionated brain RT + concurrent and adjuvant temozolomide ***or***
- Standard RT + concurrent temozolomide and adjuvant temozolomide + TTFields therapy (category 1) ***or***
- Standard RT + concurrent temozolomide and adjuvant temozolomide ***or***
- Hypofractionated brain RT alone

Follow-up: brain MRI 2-6 wk after RT, then every 2-4 mo for 3 y, and then every 3-6 mo indefinitely

Recurrence

Diffuse or Multiple → **Treatment**

- Consider clinical trial (preferred for eligible patients) ***or***
- Palliative/best supportive care if poor PS ***or***
- Systemic chemotherapy ***or***
- Surgery for symptomatic, large lesion ***or***
- Consider TTFields therapy for glioblastoma (category 2B)

Local

- Resectable → Consider clinical trial or resection → Brain MRI → **Treatment**
- Unresectable or resection not recommended/elected → **Treatment**

Treatment

- Consider clinical trial (preferred for eligible patients) ***or***
- Palliative/best supportive care if poor PS ***or***
- Systemic chemotherapy ***or***
- Consider reirradiation (category 2B) ***or***
- Consider TTFields therapy for glioblastoma (category 2B)

[a] For patients aged ≤70 y with a poor PS (KPS <60), adjuvant treatment consists of hypofractionated brain RT (preferred) ± concurrent or adjuvant temozolomide, or temozolomide, or palliative/best supportive care; follow-up consists of brain MRI 2-6 wk after RT, then every 2-4 mo for 3 y, and then every 3-6 mo indefinitely. [b] For patients aged >70 y with a poor PS (KPS <60), adjuvant treatment consists of hypofractionated brain RT, or temozolomide, or palliative/best supportive care; follow-up consists of brain MRI 2-6 wk after RT, then every 2-4 mo for 3 y, and then every 3-6 mo indefinitely.
KPS: Karnofsky Performance Score; MGMT: O6-methylguanine-DNA methyltransferase; NCCN: National Comprehensive Cancer Network; PS: performance score; RT: radiotherapy; TTFields: tumor treating fields.

1. NCCN Clinical Practice Guidelines in Oncology. Central Nervous System Cancers. Version 3.2019. https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed October 25, 2019.

Access the activity, "Brainstorming Personalized Care Strategies in Glioblastoma: Rethinking and Refining Therapeutic Algorithms With Tumor Treating Fields and Novel Systemic Approaches," at **PeerView.com/19GBM.**

PRACTICE AID

Patient Resources From the American Brain Tumor Association: Questions to Ask When Diagnosed With a Brain Tumor[1]

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Some people—and some doctors—are reluctant to talk about serious and painful issues. However, an open, communicative relationship between patients and doctors will lead to the best outcome. You may need to advocate for yourself to get the answers you need.

Questions About Your Brain Tumor

- What can you tell me about my brain tumor?
- How do you expect my brain tumor to progress?
- What is my prognosis?
- How likely is recurrence?

Questions to Ask Yourself

- Does my healthcare team seem interested in my questions?
- Does my healthcare team spend enough time with me and address my concerns?
- Do I feel comfortable with the doctor's recommendations?
- Is the doctor open to me seeking a second opinion?

Questions About Your Lifestyle

- Do I have to change my diet?
- Do I have to make any lifestyle changes?

How to Get Support

- Where can I get more information about my diagnosis?
- What support services are available to me and my family/caregiver?
- How do I talk to my employer about my diagnosis?
- How do I talk to my family and friends about my diagnosis?

Questions About Diagnostic Testing

- Does the center/hospital offer genotyping?
- When is the optimal time to have genotyping?
- If your center doesn't provide genotyping, where do you refer patients who desire this testing?

Questions About Treatment Options

- What treatment options are available?
- Can treatment wait?
- How long do I have to make decisions about my course of treatment?
- Are there alternative treatment options?
- How do you determine if the treatment is effective?
- What are common treatment side effects?
- Can I work and/or resume activities, including driving, while in treatment?

General Questions for Your Healthcare Team

- How many patients who have brain tumors with my tumor type do you treat each year?
- What other specialists will be a part of my healthcare team (eg, neuro-oncologist, neurosurgeon, radiation oncologist, nurse, social worker, nutritionist, physical therapist)?
- What does each specialist do?
- How will each of these specialists communicate with you about my treatment?
- If I am hospitalized, will you be my doctor?

Questions to Ask Prior to Surgery

- Where is the tumor located, and what is its size?
- What are the risks of removing the tumor? In other words, will surgery affect my memory? My ability to think? My physical movement? My speech?
- How can I ensure enough of the tumor is removed, so that I have the option to have genotyping?
- If the tumor is inoperable, what treatments do you recommend?
- What happens after surgery?

Questions About Clinical Trials

- What clinical trials are available, and when would I be eligible to participate?
- Where can I find information about clinical trials?
- What are the possible risks and benefits of participating in a clinical trial?
- How will the clinical trial doctors coordinate with you while I participate in a clinical study?

Additional Resources From the American Brain Tumor Association (ABTA)

- The ABTA is here for you every step of the way; healthcare staff is available through the CareLine to answer any questions you may have and offer additional resources, often available locally
- Contact the ABTA toll free at (800) 886-ABTA (2282) or email ABTAcares@abta.org
- You can access additional resources on the ABTA's website, www.abta.org, including on-demand webinars on a variety of topics affecting patients with brain tumors and their caregivers

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Seek a Second Opinion

Do not be afraid to get a second opinion before starting treatment. In fact, a second opinion is quite normal for complex medical conditions, and many doctors welcome it. A second opinion from a brain tumor specialist can offer an alternative perspective about your diagnosis and treatment. Some insurance plans do require a second opinion, while others may only cover a second opinion if the patient or doctor requests it.

Before you get a second opinion, here are a few tips

Gather Your Medical Records

A new doctor will need to evaluate your medical records, so gather all of your medical records from the time of diagnosis. They include all imaging tests, pathology slides, blood work, operative and consultation reports, office visit records, and any other testing that may have been done. You can request these records from your doctor's office or from the hospital's medical records department. There may be a charge for obtaining copies.

Get a Referral to a Brain Tumor Specialist

Ask your doctor or a trusted source for a referral to a brain tumor specialist. When surgery or long-term treatment is involved, most doctors welcome a colleague's opinion and can help by providing a recommendation.

Check for Insurance Coverage

Check with your insurance company. If you are seeking a second opinion with a doctor outside of your network, ask about the costs and advocate for yourself to get the treatment and care that will be best for you.

Choose the Doctor With the Best Assessment

Go with the best assessment. It's possible that the treatment plan from the doctors will be different. To weigh your options, ask yourself about the potential benefits of each treatment plan. Talk about your concerns with the doctors. In some cases, a third opinion is warranted.

If your doctor is unable to recommend a brain tumor specialist for a second opinion, call the ABTA at 800-886-ABTA (2282) or visit www.abta.org to help locate a brain tumor treatment center.

1. American Brain Tumor Association. Brain Tumors: A Handbook for the Newly Diagnosed. https://2knaef3o0jpz4ff42k23tr6l-wpengine.netdna-ssl.com/wp-content/uploads/2018/03/newly-diagnosed.pdf. Accessed October 28, 2019.

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Selected Ongoing Clinical Trials for Glioblastoma Actively Recruiting Patients[1]

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Clinical Trials for Patients With Newly Diagnosed Glioblastoma

2-THE-TOP (NCT03405792)

- **Treatment:** TTFields + temozolomide + pembrolizumab vs TTFields + temozolomide alone
- **Primary endpoint:** PFS
- **Estimated enrollment:** 29 patients

NCT02343549

- **Treatment:** TTFields + bevacizumab + temozolomide
- **Primary endpoint:** survival at 12 months
- **Estimated enrollment:** 46 patients

NCT02717962 (Group 2)

- **Treatment:** VAL-083
- **Primary endpoint:** OS
- **Estimated enrollment:** 107 patients

INSIGhT (NCT02977780)

- **Treatment:** temozolomide vs abemaciclib + temozolomide vs CC-115 vs neratinib + temozolomide
- **Primary endpoint:** OS
- **Estimated enrollment:** 280 patients

NCT04105374

- **Treatment:** surgery + RT + temozolomide vs Toca 511 + Toca FC + RT + temozolomide
- **Primary endpoints:** PFS and OS
- **Estimated enrollment:** 900 patients

NCT03345095

- **Treatment:** RT + temozolomide + marizomib followed by adjuvant temozolomide + marizomib vs RT + temozolomide + adjuvant temozolomide
- **Primary endpoint:** OS
- **Estimated enrollment:** 750 patients

Clinical Trials for Patients With Recurrent Glioblastoma

NAVIGATE (NCT02576431)

- **Treatment:** larotrectinib
- **Primary endpoint:** ORR by IRC
- **Estimated enrollment:** 320 patients

NCT04051606

- **Treatment:** regorafenib
- **Primary endpoint:** mOS
- **Estimated enrollment:** 22 patients

NCT01894061

- **Treatment:** TTFields + bevacizumab
- **Primary endpoint:** PFS
- **Estimated enrollment:** 40 patients

NCT02626364 (Group 1)

- **Treatment:** VAL-083
- **Primary endpoint:** OS
- **Estimated enrollment:** 107 patients

NCT02626364

- **Treatment:** crenolanib
- **Primary endpoint:** PFS at 6 months
- **Estimated enrollment:** 33 patients

The MATCH Screening Trial (NCT02465060)

- **Treatment:** targeted therapy directed by genetic testing
- **Primary endpoint:** ORR
- **Estimated enrollment:** 6,452 patients

CSCRGBM (NCT03632135)

- **Treatment:** chemoID-guided treatment vs investigator's choice
- **Primary endpoint:** OS
- **Estimated enrollment:** 300 patients

NCT02323880

- **Treatment:** selinexor
- **Primary endpoints:** maximum tolerated dose, toxicity, and PK
- **Estimated enrollment:** 81 patients

NCT03430791

- **Treatment:** nivolumab + TTFields vs nivolumab + ipilimumab + TTFields
- **Primary endpoint:** ORR
- **Estimated enrollment:** 60 patients

WIZARD 201G (NCT03149003)

- **Treatment:** DSP-7888 dosing emulsion + bevacizumab vs bevacizumab alone
- **Primary endpoints:** safety, tolerability, and OS
- **Estimated enrollment:** 200 patients

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GBM AGILE (NCT03970447) | Phase 3[1-3]

Why Is GBM AGILE Not an RCT Trial?

- In RCTs, patients are randomly assigned either to receive the experimental therapy or a control (SOC or placebo); researchers compare health outcomes between the two over time to determine whether the new therapy was effective
- Some major drawbacks of traditional RCTs are that they are lengthy, expensive, and limited to evaluating one new therapy at a time

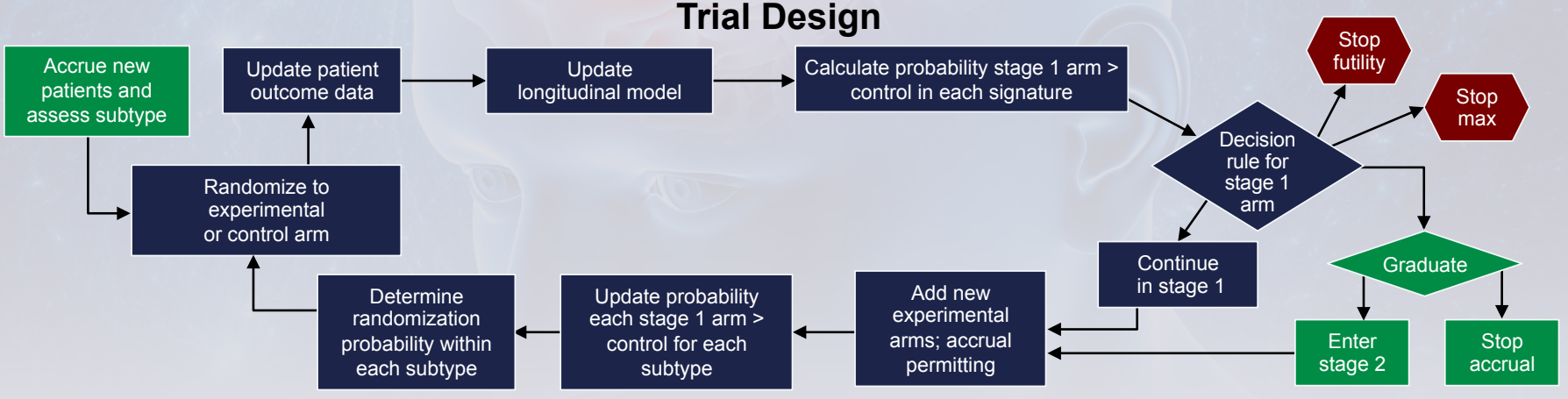
Who Is Eligible for GBM AGILE?

- Enrollment is open to patients with newly diagnosed and recurrent glioblastoma in order to evaluate which therapies work best for each type and biomarker subtypes
- GBM AGILE will take place across multiple clinical sites (eg, academic research centers, hospitals, cancer institutions) throughout the United States, Canada, Australia, and elsewhere
- Estimated enrollment is 550 patients

How Are Treatments Selected and Biomarkers/Targets Identified?

- Therapies and associated biomarkers will be added during the course of the trial; identification of robust data supporting the treatments and biomarkers is paramount
- Potential experimental arms and associated enrichment biomarkers can be identified by investigators within the trial or proposed by outside investigators; they will then be prioritized and reviewed by the various GBM AGILE committees prior to inclusion
  - As of November 2019, regorafenib is the first experimental drug in this trial

Trial Design



IRC: independent radiology committee; mOS: median overall survival; ORR: overall response rate; PK: pharmacokinetics; RT: radiotherapy; SOC: standard of care; TTFields: tumor treating fields.

1. https://clinicaltrials.gov. Accessed October 28, 2019. 2. https://www.gcaresearch.org/gbm-agile/. Accessed October 28, 2019. 3. Alexander BM et al. *Clin Cancer Res*. 2018;24:737-743.

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