Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

The role of targeted therapies in the management of progressive glioblastoma: a systematic review and evidence-based clinical practice guideline.

Bibliographic Source(s)

Olson JJ, Nayak L, Ormond DR, Wen PY, Kalkanis SN, Ryken TC, AANS/CNS Joint Guidelines Committee. The role of targeted therapies in the management of progressive glioblastoma: a systematic review and evidence-based clinical practice guideline. J Neurooncol. 2014 Jul;118(3):557-99. [157 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The rating schemes used for the strength of the evidence (Class I-III) and the levels of recommendations (Level 1-3) are defined at the end of the "Major Recommendations" field.

Recommendation

Level III

Treatment with bevacizumab is recommended as it provides improved disease control compared to historical controls as measured by best imaging response and progression free survival at 6 months.

Given that there are a large number of therapies are available for progressive glioblastoma that may be applied under selected circumstances dependent on patient characteristics and treating physician judgment, it is strongly recommended that patients with progressive glioblastoma be enrolled in properly designed clinical investigations to provide convincing evidence of therapeutic value.

Definition:

Evidence Classification for Therapeutic Studies

Class I: Evidence provided by one or more well-designed randomized controlled clinical trials, including overview (meta-analyses) of such trials

Class II: Evidence provided by well-designed observational studies with concurrent controls (e.g., case control and cohort studies)

Class III: Evidence provided by expert opinion, case series, case reports and studies with historical controls

Evidence Classification for Diagnostic Studies

Class I: Evidence provided by one or more well-designed clinical studies of a diverse population using a "gold standard" reference test in a blinded evaluation appropriate for the diagnostic applications and enabling the assessment of sensitivity, specificity, positive and negative predictive values, and where applicable, likelihood ratios

Class II: Evidence provided by one or more clinical studies of a restricted population using a "gold standard" reference test in a blinded evaluation of diagnostic accuracy and enabling assessment of sensitivity, specificity, positive and negative predictive values, and where applicable, likelihood ratios

Class III: Evidence provided by expert opinion, studies that do not meet the criteria for the delineation of sensitivity, specificity, positive and negative predictive values, and where applicable, likelihood ratios

Levels of Recommendation

Level 1: Generally accepted principles for patient management, which reflect a high degree of clinical certainty (usually this requires Class I evidence which directly addresses the clinical questions or overwhelming Class II evidence when circumstances preclude randomized clinical trials)

Level 2: Recommendations for patient management which reflect clinical certainty (usually this requires Class II evidence or a strong consensus of Class III evidence)

Level 3: Other strategies for patient management for which the clinical utility is uncertain (inconclusive or conflicting evidence or opinion)

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Progressive glioblastoma

Guideline Category

Management

Treatment

Clinical Specialty

Neurology

Oncology

Intended Users

Advanced Practice Nurses

Hospitals

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To provide a cataloging, review, and systematic evaluation of progressive glioblastoma treatments to allow the practicing physician to determine their role in patient management
- To provide the latest up-to-date evidence-based recommendations for the management of patients with progressive glioblastoma centering on questions related to commonly encountered clinical scenarios

Target Population

Adult patients with progressive glioblastoma

Interventions and Practices Considered

1. Bevacizumab
2. Enrollment in properly designed clinical investigations

Note: See the original guideline document for detailed information concerning other interventions that were considered but not recommended.

Major Outcomes Considered

- Improvement in average life expectancy
- Time of disease progression
- Improved disease control
- Quality of life
- Survival
- Mortality

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The following electronic databases were searched from January 1990 through June 2012: MEDLINE and EMBASE. A broad search strategy using a combination of subheadings and text words was employed. In brief, a search was executed for progressive glioblastoma treatment with targeted therapies. Specifically that included progressive, recurrent, or relapsing glioma or glioblastoma and combined with targeted therapy and molecular agents and then quality of life, survival and mortality. The search strategy is documented in the companion document (see the "Availability of Companion Documents" field). Reference lists of included studies were also reviewed.

Literature Eligibility Criteria

- Published in English

- Adult patients (age ≥18) with progressive glioblastoma were included in the study and the data on their outcomes could be separated from other histologies
- Fully published (i.e., not in abstract form) peer reviewed primary studies involving targeted therapy used alone or in combinations
- Number of study participants with progressive glioblastoma ≥5
- For studies with mixed histologic populations, baseline pretreatment and outcome information on study participants is provided for patients with progressive glioblastoma separate from other histologies
- For studies with consideration of more than one treatment regimen, baseline pretreatment and outcome information on study participants is provided in a manner that can be separated by treatment

Number of Source Documents

The search resulted in 232 publications being identified as having potential relevance. Importantly the search for cytotoxic chemotherapy related publications identified a number of manuscripts also dealing with targeted therapies and resulted in additions to this group. A total of 1,673 publications were identified by the search method and underwent title and abstract screening. Of those, 299 were deemed better information regarding this guideline.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Evidence Classification for Therapeutic Studies

Class I: Evidence provided by one or more well-designed randomized controlled clinical trials, including overview (meta-analyses) of such trials

Class II: Evidence provided by well-designed observational studies with concurrent controls (e.g., case control and cohort studies)

Class III: Evidence provided by expert opinion, case series, case reports and studies with historical controls

Evidence Classification for Diagnostic Studies

Class I: Evidence provided by one or more well-designed clinical studies of a diverse population using a "gold standard" reference test in a blinded evaluation appropriate for the diagnostic applications and enabling the assessment of sensitivity, specificity, positive and negative predictive values, and where applicable, likelihood ratios

Class II: Evidence provided by one or more clinical studies of a restricted population using a "gold standard" reference test in a blinded evaluation of diagnostic accuracy and enabling assessment of sensitivity, specificity, positive and negative predictive values, and where applicable, likelihood ratios

Class III: Evidence provided by expert opinion, studies that do not meet the criteria for the delineation of sensitivity, specificity, positive and negative predictive values, and where applicable, likelihood ratios

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Studies which met the eligibility criteria had their data extracted by one reviewer and the extracted information was checked by a second reviewer. Evidence and summary tables, reporting the extracted study information and evidence classification, were generated for all of the included studies for each of the questions. The literature in the evidence tables was expanded upon in the scientific foundation of each section so as to emphasize important points supporting its classification and contribution to recommendations.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Writing groups were created from the entire clinical guideline panel based on expertise to address each of the disciplines and areas of therapy chosen to be part of this set of clinical guidelines. Each group was involved with literature selection, creation and editing of the evidence/summary tables for their specific discipline. Using this information, the writing groups then drafted the clinical practice guideline for their respective discipline. The draft guidelines were then circulated to the entire clinical guideline panel for feedback, discussion, and ultimately approval.

Both the evidence classification and the strength of the recommendations were graded according to the American Association of Neurological Surgeons (AANS)/Congress of Neurological Surgeons (CNS) (see the "Rating Scheme for the Strength of the Evidence" and "Rating Scheme for the Strength of the Recommendations" fields). The class of evidence assigned to each study was based on study design (i.e., class I, II, or III). The strength of the recommendations made (i.e., level 1, 2, or 3) was directly linked to the evidence classification and took into account aspects of study quality and whether or not the plan was accomplished, not just study design. Specifically, the level of a recommendation made could be decreased, based on consensus input, if there were methodological concerns regarding the studies that provided evidence for that particular recommendation.

See Figure 1 in the methodology document (see the "Availability of Companion Documents" field) for an outline of the key steps in the process of developing these clinical practice guidelines.

Rating Scheme for the Strength of the Recommendations

Levels of Recommendation

Level 1: Generally accepted principles for patient management, which reflect a high degree of clinical certainty (usually this requires Class I evidence which directly addresses the clinical questions or overwhelming Class II evidence when circumstances preclude randomized clinical trials)

Level 2: Recommendations for patient management which reflect clinical certainty (usually this requires Class II evidence or a strong consensus of Class III evidence)

Level 3: Other strategies for patient management for which the clinical utility is uncertain (inconclusive or conflicting evidence or opinion)

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The completed evidence-based clinical practice guidelines on the diagnosis and management of progressive glioblastoma were presented to the Joint Guidelines Committee (JGC) of the American Association of Neurological Surgeons (AANS)/Congress of Neurological Surgeons (CNS) for approval. The reviewers for the JGC were vetted by the Journal of Neuro-Oncology for suitability and expertise to serve as reviewers for the purposes of publication in that journal also. As part of their evaluation process, the JGC reviewers could provide input on the content of the clinical practice guidelines.

Development of this set of evidence-based clinical practice guidelines was editorially independent from the funding agencies. The funding agencies (CNS Executive Committee, and AANS/CNS Joint Tumor Section Executive Committee) review of these guideline papers, following JGC

assessment and recommendations for endorsement but prior to submission for publication, was limited to whether or not to endorse or reject this body of work.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate treatment of patients with progressive glioblastoma with bevacizumab to improve survival outcomes

Potential Harms

The use of bevacizumab alone is not without toxicities as the authors of one study report the most common grade 3 or greater toxicities for the use of this agent alone include hypertension (8.3%) and convulsions (6.0%).

Qualifying Statements

Qualifying Statements

The information in these guidelines reflects the current state of knowledge at the time of completion. The presentations are designed to provide an accurate review of the subject matter covered. These guidelines are disseminated with the understanding that the recommendations by the authors and consultants who have collaborated in their development are not meant to replace the individualized care and treatment advice from a patient's physician(s). If medical advice or assistance is required, the services of a physician should be sought. The proposals contained in these guidelines may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in these guidelines must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Olson JJ, Nayak L, Ormond DR, Wen PY, Kalkanis SN, Ryken TC, AANS/CNS Joint Guidelines Committee. The role of targeted therapies in the management of progressive glioblastoma: a systematic review and evidence-based clinical practice guideline. J Neurooncol. 2014 Jul;118(3):557-99. [157 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2014 Jul

Guideline Developer(s)

American Association of Neurological Surgeons - Medical Specialty Society

Congress of Neurological Surgeons - Professional Association

Source(s) of Funding

These guidelines were funded exclusively by the CNS and Tumor Section of the American Association of Neurological Surgeons and the Congress of Neurological Surgeons (CNS) whom received no funding from outside commercial sources to support the development of this document unless otherwise stated in this section.

Guideline Committee

Guideline Panel

Composition of Group That Authored the Guideline

Authors: Jeffrey J. Olson, MD, Department of Pathology and Laboratory Medicine, Emory University School of Medicine, Atlanta, GA; Lakshmi Nayak, MD, Dana-Farber Cancer Institute, Boston, MA, Department of Neurology Brigham and Women's Cancer Center, Boston, MA; David Ryan Ormond, MD, Department of Neurological Surgery, Emory University School of Medicine, Atlanta, GA; Patrick Y. Wen, MD, Dana-Farber Cancer Institute, Boston, MA, Department of Neurology, Brigham and Women's Cancer Center, Boston, MA; Steven N. Kalkanis, MD, Department of Neurosurgery, Henry Ford Health System, Detroit, MI; Timothy Charles Ryken, MD, MS, FACS, Department of Neurosurgery, Iowa Spine and Brain Institute, Iowa City, IA

Financial Disclosures/Conflicts of Interest

Task Force Members report potential conflicts of interest (COI) prior to beginning work on the guideline and at the time of publication. COI

disclosures are reviewed by the Task Force Chair and taken into consideration when determining writing assignments. Resolution of potential COIs included Task Force members being assigned to chapters that did not involve or in any way relate to the potential COIs disclosed.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available to subscribers from the Journal of Neuro-Oncology Web site .

Availability of Companion Documents

The following is available:

- Olson JJ, Ryken TC. Kalkanis SN. Introduction, rationale, and methodology. J Neurooncol. 2014 Jul;118(3): 429–434. Electronic copies: Available to subscribers from the Journal of Neuro-Oncology Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on September 3, 2014.

Copyright Statement

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions.

Disclaimer

NGC Disclaimer

The National Guideline Clearinghouseâ„¢ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion-criteria.aspx.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.