新たに診断された神経膠芽腫においてベバシズマブの有益性は認められなかった（Abstract＃1）

RTOG 0825:新たに診断された神経膠芽腫に対する標準的な化学療法にベバシズマブを併用しても延命効果は認められなかった

RTOG 0825: No survival benefit to adding bevacizumab to standard chemoradiation for newly diagnosed glioblastoma

神経膠芽腫患者における第III相試験の結果、ベバシズマブはファーストライン治療として使用されるべきではないことが示唆された。ベバシズマブとテモゾロミド併用で治療された患者はテモゾロミド単独で治療された患者よりも副作用が多く、全生存期間は改善しなかった。この多施設臨床試験において、新たに診断された神経膠芽腫患者637人が化学放射線療法（テモゾロミドと放射線療法）にプラセボを追加する群または化学放射線療法にベバシズマブを追加する群に無作為に割り付けられた。全ての患者が化学放射線療法を開始する前に手術を施行された。全生存期間中央値は、両群間で統計的な差はなかった（プラセボ群16.1か月対ベバシズマブ群15.7か月）。無増悪生存期間中央値はプラセボ群と比較しベバシズマブ群で長かった（10.7か月対7.3か月）が、この差はこのスタディで規定された事前設定レベルには達しなかった。分子マーカー（MGMTメチル化状況および9つの遺伝子発現様式）に基づくサブグループ解析の結果、ベバシズマブを用いることにより生存期間が延長するサブグループは認められなかった。第49回American Society of Clinical Oncology年次集会プレナリーセッションで発表されたこの結果から、ベバシズマブはこれらの神経膠芽腫患者に対するファーストライン治療の一部としては使用すべきでないことが示唆された。

Full Text

A randomized phase III study finds no overall survival improvement from the addition of bevacizumab to standard first-line chemoradiation for glioblastoma. Patients who received bevacizumab also experienced more side effects compared to those treated with chemoradiation alone. The findings suggest that it should not be a part of first-line therapy for these patients with glioblastoma.

This study was presented during the plenary session of the 49th Annual Meeting of the American Society of Clinical Oncology.

Glioblastoma is the most common and most aggressive form of primary brain tumor. Bevacizumab, an antibody that blocks the growth of tumor blood vessels, is currently used for patients with recurrent glioblastoma. Despite a lack of clear evidence, bevacizumab has been used off-label as first-line therapy in certain patients, in hopes of increasing the benefit to the patient.

"Unless we can identify a group of patients that clearly benefits from early use of bevacizumab, it appears that it should not be used in the first-line setting," said Mark R. Gilbert, M.D., a professor of neuro-oncology at the University of Texas M.D. Anderson Cancer Center in Houston, Texas. "Bevacizumab remains an important part of our armory against glioblastoma, but in most situations it should be reserved as a salvage regimen."

In this multi-institutional clinical trial, 637 patients with newly diagnosed glioblastoma were randomly assigned to treatment with chemoradiation (temozolomide and radiation) plus placebo or chemoradiation plus bevacizumab. All patients had undergone surgery before starting chemoradiation. Patients were allowed to cross over to the placebo group or continue bevacizumab at the time of progression.

The median overall survival was not statistically different between the two groups (16.1 months with placebo vs. 15.7 months with bevacizumab). The median progression-free survival was longer in the bevacizumab group relative to the placebo group (10.7 months vs. 7.3 months), but the difference did not reach the pre-set level of significance prescribed for this study. A subgroup analysis based on molecular markers (MGMT methylation status and a nine-gene expression signature) found no subgroup with improved survival using bevacizumab.

Overall, there were more side effects in the bevacizumab group, particularly low platelet counts, blood clots and high blood pressure. However, Dr. Gilbert said that toxicity differences alone would not have precluded the decision to use bevacizumab had the trial found a survival benefit.

"Bevacizumab received FDA approval for recurrent glioblastoma based on dramatic radiographic activity in several phase II trials. Now, two separate multinational randomized phase III trials demonstrate that bevacizumab modestly increases progression-free survival but not overall survival for newly diagnosed patients. Although bevacizumab will clearly continue to have an important role in the treatment of patients with glioblastoma, the timing of its use, the specific subpopulation of patients that benefit the most, and the biological and clinical consequences of chronic VEGF inhibition on glioma and normal cells within the central nervous system need to be clarified," said Howard Fine, M.D., ASCO spokesperson and CNS tumors expert.

Researchers also assessed patients' quality of life, symptom burden and neurocognitive function, which also favored the group of patients who received chemoradiation alone; the findings from those analyses were presented in separate oral presentations at ASCO's 2013 Annual Meeting. This study component revealed that patients in the bevacizumab arm had a greater increase of symptom burden and more decline of neurocognitive function over time compared to patients in the placebo arm. Molecular profiles of tumor samples collected on this study, as well as imaging scans, are being examined to determine if there is any group of patients that could still benefit from bevacizumab in the first-line setting.

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