切除不能進行・再発大腸がんにおいて原発巣部位が予後を予測する（Abstract 3504）

原発巣部位が左側の大腸がんは右側の大腸がんよりも生存期間を延長させる

Cancer originating on the left side of colon associated with longer survival versus the right side

大規模臨床試験の後ろ向き解析の結果、大腸内の原発巣部位は生存期間を予測し、切除不能進行・再発大腸がん患者に対する最良の治療選択に役立つ可能性があることが示された。このデータは、原発巣が左側大腸（下行結腸、S状結腸、および直腸）の患者は右側大腸（盲腸および上行結腸）の患者に比べ、生存期間が有意に長いことを示している。このスタディ結果は、2016年American Society of Clinical Oncology年次集会で発表される。

Full Text

A retrospective analysis of data from a large clinical trial finds that the location of the primary tumor within the colon predicts survival and may help inform optimal treatment selection for patients with metastatic colorectal cancer. The study will be presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago.

The data show that patients whose primary tumors originate on the left side of the colon (the descending colon, sigmoid colon, and rectum) survive significantly longer than those whose tumors originate on the right side (the cecum and ascending colon).

"While previous studies had suggested that tumor location may impact clinical colorectal cancer outcomes, the effect we observed in this analysis appears to be far greater than we expected," said lead study author Alan P. Venook, MD, Professor of Medicine at the University of California, San Francisco. "These findings will likely change the way we approach colorectal cancer treatment and research, even as we seek to more deeply understand the biology driving the difference in outcomes between right- and left-sided cancers."

Researchers retrospectively evaluated data from the Phase III CALGB/SWOG 80405 clinical trial, a federally funded clinical trial designed to compare bevacizumab and cetuximab in combination with chemotherapy as initial therapy for metastatic colorectal cancer.

For the primary analysis, researchers identified data from 293 patients with right-sided primary tumors and 732 patients with left-sided primary tumors. This analysis included only patients without a mutated KRAS gene, which is a known biomarker of response to certain colorectal cancer therapies (cetuximab is approved only for treating KRAS wild-type tumors).

In this patient population, those with left-sided tumors had longer median overall survival (33.3 months), compared to those with right-side tumors (19.4 months). Among patients who received cetuximab, patients with left-sided tumors lived 36 months, while those with right-sided tumors lived 16.7 months. Similar trends were observed among patients receiving another treatment, bevacizumab: overall survival was 31.4 months and 24.2 months for patients with left- and right-sided tumors, respectively.

While the original trial found no significant advantage in overall or progression-free survival in patients treated with bevacizumab or cetuximab, this analysis suggests that the relative effectiveness of cetuximab and bevacizumab may differ depending on primary tumor location. Researchers are in the process of examining the molecular biology that presumably underlies these findings.

Among patients with right-sided tumors, treatment with bevacizumab was associated with longer survival than that of cetuximab (24.2 months vs. 16.7 months). Conversely, among patients with left-side tumors, treatment with cetuximab was associated with longer overall survival than bevacizumab (36 months vs. 31.4 months).

Because the CALGB/SWOG trial was initiated before KRAS mutation status was known to be an important factor in use of cetuximab, there was a smaller population of patients who had KRAS mutations (an additional 213). In this separate analysis, researchers found that those with left-sided tumors also lived longer compared to patients with right-sided tumors (median overall survival: 30.3 months vs. 23.1 months).

"This is the largest study to date of tumor location in colorectal cancer, and it strongly suggests that this unexpected factor could answer some long-standing questions about why certain patients do better than others," said ASCO President Julie M. Vose, MD, MBA, FASCO, ASCO President. "It is also an important reminder, in this exciting era of precision medicine, that genomics is not the only source of insight into how cancers should be studied and treated."

This study received funding and support from BMS, Genentech, and Imclone in collaboration with the National Cancer Institute.

ASCO2016特集

進行期メラノーマにおいてPD-1阻害薬は生存期間を改善する（Abstract 9503）

KEYNOTE：進行期メラノーマ患者に対するPD-1阻害薬pembrolizumabは生存期間の改善をもたらす

KEYNOTE : PD-1 inhibitor pembrolizumab provides long-term survival benefit for patients with advanced melanoma

新規に診断され治療歴を有する進行期メラノーマ患者を対象とした第1b相トライアル（KEYNOTE-001）の長期追跡の結果、pembrolizumab開始3年後40%の患者が生存しており、36か月後の全生存率はイピリムマブ投与を過去に受けた者と受けていない者とで同等であった。注目すべきは、今回のスタディ対象患者の15%が、免疫関連効果判定基準に基づく完全寛解を得たことである。これらの患者のうち、89%が寛解を維持している。イピリムマブが生存期間を延長する初めての薬剤として承認された2011年までは、進行期メラノーマ患者の全生存期間中央値は1年未満であった。このスタディ結果は、2016年American Society of Clinical Oncology年次集会で発表される。

Full Text

Long-term follow-up from a phase 1b trial (KEYNOTE-001) in newly diagnosed and previously treated patients with advanced melanoma, showed that 40% of patients were alive three years after starting pembrolizumab, with similar 36-month overall survival rates in both groups. The study will be presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago.

Under accelerated review in the United States, pembrolizumab was initially approved in September 2014 for the treatment of advanced melanoma, based on data from KEYNOTE-001. Additional clinical studies (KEYNOTE-002 and KEYNOTE-006) have also shown a survival benefit with pembrolizumab in patients with advanced melanoma when compared with chemotherapy or ipilimumab.

Notably, 15% of patients in this study experienced complete remissions according to immune-related response criteria; of these patients, 89% remain in remission. Before 2011, when ipilimumab was approved as the first drug to extend survival, patients with advanced melanoma had a median overall survival of less than one year.

"Advanced melanoma is still a very challenging cancer, which is why it is so remarkable that such a large proportion of patients see a long-term survival benefit from this therapy," said lead study author Caroline Robert, MD, PhD, Head of the Dermatology Unit at the Institut Gustave-Roussy in Paris, France. "The results of this study further demonstrate the potential for long-term benefit with pembrolizumab."

The phase I study included 655 patients diagnosed with advanced melanoma. Seventy-five percent of patients had previously received other treatments, including ipilimumab. Study participants received pembrolizumab at 2 or 10 mg/kg every three weeks, or 10 mg/kg every two weeks. During the trial, 2 mg/kg every three weeks was determined to be the optimal dose. Patients remained on treatment until disease progression, intolerable toxicity or investigator decision.
The three-year overall survival rate for patients treated with pembrolizumab was 40%, and the median overall survival was 24.4 months.

Survival rates differed slightly, however, based on prior melanoma therapy. Among patients who had not received any prior treatment, survival was slightly higher, at 45%. Three-year survival rates were the same among patients who had previously received ipilimumab and those who had not (41% in both groups). The average time on pembrolizumab was 11.3 months. A total of 61 (9%) patients stopped pembrolizumab after a complete response was achieved, and 97% remained in remission at time of analysis. For patients who remained in remission after stopping pembrolizumab, the median time they remained in remission after stopping pembrolizumab was 10 months and ongoing. According to the researchers, while it is difficult to make any definitive conclusions based on this single-arm, early phase trial, these encouraging survival data suggest that patients can benefit from pembrolizumab regardless of whether they received previous treatments.

Overall, pembrolizumab was well tolerated, with safety and tolerability consistent with that observed in other large-scale clinical trials. The most common adverse events related to pembrolizumab were fatigue (40%), itchiness (28%) and rash (23%) and only 8% of patients stopped the treatment because of side effects related to pembrolizumab.

"New therapies that block the PD-1 are extending survival for many patients, and for some may offer the prospect of living longer than ever after a diagnosis with advanced melanoma. In a matter of a few years, these therapies have truly transformed the outlook for patients with melanoma and many other hard-to-treat cancers," said Don S. Dizon, MD, FACP, ASCO spokesperson. This study received funding and support from Merck, Kenilworth, NJ, USA.

ASCO2016特集

多発性骨髄腫に対する幹細胞移植は依然として望ましい治療法である（Abstract 8000）

新規薬剤時代においてもなお、多発性骨髄腫に対する自家幹細胞移植は重要である

Autologous stem cell transplant remains important for multiple myeloma even in novel agent era

2016年American Society of Clinical Oncology年次集会で発表された第III相試験の早期結果から、自家幹細胞移植（ASCT）を実施された65歳未満の多発性骨髄腫患者は、新規薬剤を用いた化学療法のみ実施された患者に比べ、無増悪生存期間の長いことが示された。無増悪生存期間中央値にはまだ到達しなかったが、ASCTを実施された患者は、ボルテゾミブ-メルファラン-プレドニゾン治療のみで移植を受けなかった患者に比べ、進行が緩徐であった。疾患が未進行の患者では、ASCT群患者は移植を受けなかった患者に比べ、将来のいずれの時点においても進行リスクが24%低かった。

Full Text

Early findings from a phase III clinical trial showed that patients with multiple myeloma who received an autologous stem cell transplant (ASCT) survived longer without disease progression than those who received only chemotherapy using novel agents. This is the largest study reported to date aimed at comparing ASCT with a bortezomib-based regimen alone in patients younger than 65. The study was presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago.

ASCT is an intensive procedure in which a patient's blood-forming stem cells are harvested from the blood and stored. After treatment with high-dose chemotherapy, the stem cells are given back to the patient.

The proteasome inhibitor bortezomib has been incorporated into the standard treatments for patients with newly diagnosed multiple myeloma, whether or not they are able to undergo ASCT. For patients younger than 65, however, the continued need for ASCT has been debated in the era of novel agents, such as bortezomib (patients older than 65 are often unable to undergo ASCT).

"Our findings show that autologous stem cell transplant should remain the preferred treatment for patients with multiple myeloma age 65 and under," said lead study author Michele Cavo, MD, Head of the Seràgnoli Institute of Hematology at the University of Bologna. "While transplant-free treatment with novel agents remains an intriguing prospect, the reality is that stem cell transplant remains a powerful and proven approach, and with novel agents playing a supporting role, it is more effective than ever."

The randomized phase III study included 1,266 patients who were newly diagnosed with multiple myeloma. Following induction therapy with bortezomib-cyclophosphamide-dexamethasone, patients were randomly assigned to receive either bortezomib-melphalan-prednisone (VMP), or high-dose melphalan followed by single ASCT. (In treatment centers with a standard policy of performing double ASCTs, patients were randomly assigned to either VMP or single ASCT or double ASCT.)

In the second stage of the study, patients in both groups were randomly assigned to consolidation therapy with bortezomib-lenalidomide-dexamethasone or no consolidation therapy. All patients received maintenance therapy with lenalidomide until disease progression or intolerable toxicity. A planned interim analysis was performed in January 2016.

At the time of the analysis, median follow-up after the first treatment randomization was two years (23.9 months). While median progression-free survival was not yet reached, the data showed that patients who received stem cell transplants progressed more slowly than those who received VMP therapy without transplant. Among patients who had not yet experienced disease progression, those in the ASCT arm had a 24% lower risk of progressing at any future time point compared to those not receiving transplant.

The benefit of transplant was confirmed in a further multivariate analysis and was even greater among certain patients at high risk of early progression. Patients with advanced disease (according to International Staging System III) randomized to the ASCT arm had a 48% lower chance of progressing at the next analysis compared to those not receiving transplant; among patients with certain high-risk genetic factors, ASCT was associated with a 28% lower chance of future progression compared to VMP therapy without transplant. In comparison with patients who did not have a transplant, those receiving ASCT were also more likely to achieve a high quality response (at least 90% tumor cell mass reduction) to treatment (74% vs. 84%, respectively), which is an important indicator of longer survival.

Interim analysis of data related to the second randomization to consolidation therapy or no consolidation therapy is not yet complete. The study is ongoing, and future analyses will assess overall survival, toxicity and quality of life as well as other measures.

"Even in an age of novel therapies, proven approaches can retain their value. This study demonstrated that combining the best of both worlds – initial therapy with a novel agent followed by stem cell transplant – resulted in the best patient outcomes," said ASCO President Julie M. Vose, MD, MBA, FASCO, ASCO President.

This study received funding from the Haemato Oncology Foundation for Adults in the Netherlands (HOVON).

ASCO2016特集

早期臨床試験であっても個別化治療は治療成績を改善する(Abstract 11520)

第I相試験において適切な治療が患者の予後を改善する

Precision medicine yields better outcomes for patients in phase I clinical trials

13,000人超の患者を組み入れた346の第I相臨床試験のメタ解析の結果、腫瘍の分子学的特性に基づいた治療を選択された患者は、有意に予後が良好であることが示された。適切な治療を用いた群では腫瘍縮小率が30.6%であり、適切な治療を用いてない群では4.9%であった。無増悪生存期間においても、適切な治療群で長かった(期間中央値5.7か月対2.95か月)。筆者らは、第I相試験の患者選択においても腫瘍バイオマーカーはますます用いられるべきである、と述べている。このスタディ結果は、2016年American Society of Clinical Oncology年次集会で発表された。

Full Text

A meta-analysis of 346 phase I clinical trials involving more than 13,000 patients found that patients whose treatment was selected based on the molecular characteristics of their tumor had significantly better outcomes. The study was presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago.

"Our study suggests that, with a precision medicine approach, we can use a patient's individual tumor biomarkers to determine whether they are likely to benefit from a particular therapy, even when that therapy is at the earliest stage of clinical development," said lead study author Maria Schwaederle, PharmD, of the Center for Personalized Cancer Therapy, University of California-San Diego School of Medicine. "This strategy often results in good outcomes for patients, and I hope it will encourage and reassure doctors and patients considering enrollment in precision medicine-based phase I trials."

Previous meta-analyses of phase II and phase III trials by the same researchers observed similarly improved outcomes with precision medicine approaches.

According to the authors, this is the first study to show that such benefits are apparent even at the first stage of clinical development. It suggests that tumor biomarkers should be increasingly used to select patients for phase I clinical trials.
The study examined efficacy and safety data from 346 phase I trials published between 2011 and 2013. The analysis included 58 treatment arms that employed precision medicine – defined as using biomarkers to select patients for treatment – and 293 that did not (all but one of these precision medicine trials evaluated a targeted agent: the trial evaluated the chemotherapy drug topotecan, which is believed to inhibit hypoxia-inducible factor 1-alpha (HIF-1 alpha), and patients in that trial were tested for this marker).

The researchers found that in treatment arms employing precision medicine, tumor shrinkage rates were 30.6%, compared to 4.9% in those that did not. Patients in precision medicine arms also had a longer progression-free survival compared to other arms (median 5.7 months vs. 2.95 months).

Results were similar in a sub-analysis that included 57 trials of targeted therapies – drugs that target specific genes or proteins found in cancer cells. In this group, treatment arms using biomarkers to assign patients to treatments had tumor shrinkage rates of 31.1%, compared to 5.1% for those that did not. Additionally, researchers found that matching patients to therapy based on genomic (DNA) biomarkers resulted in higher tumor shrinkage rates (42%) compared to protein biomarkers (22.4%).

In this analysis, the high tumor shrinkage rates and prolonged time to disease progression observed with precision medicine approaches suggest that phase I studies, which have traditionally focused on safety, can also provide important insights into efficacy and the patients likely to benefit most. Incorporating survival endpoints into phase I trials may help accelerate development of important new therapies, the authors suggested.

"Precision medicine is not the future of cancer care, it is the present. This study reinforces that the more we personalize treatment to the patient and the tumor, the better the outcomes – even in the earliest phases of research," said Don S. Dizon, MD, FACP, ASCO spokesperson. "This is the same approach ASCO's TAPUR trial is using, and we anticipate it will also bring new insights that lead to better therapies for patients in need."

This study received funding and support from the Joan and Irwin Jacobs Philanthropic Fund.

ASCO2016特集

新規レジメンは多発性骨髄腫の進行を緩徐にする（Abstract LBA4）

Daratumumabベースの3剤併用療法は多発性骨髄腫の進行を緩徐にする

Three-drug daratumumab-based regimen slows progression of multiple myeloma

ランダム化第III相試験の結果、標準的な2剤併用療法（ボルテゾミブおよびデキサメタゾン）にdaratumumabを上乗せすることにより、再発または難治性多発性骨髄腫の予後が著明に改善した、と2016年American Society of Clinical Oncology年次集会で発表された。Dratumumabとの併用療法により、病勢進行リスクは70%減少し、最良部分奏効率は29%から59%、完全奏効率は9%から19%に倍増した。Daratumumabはがん細胞の表面に存在するCD-38と呼ばれる蛋白質を標的とする。この結果から、3剤併用療法は再発／難治性多発性骨髄腫の新たな治療選択肢に位置付けられるであろう。

Full Text

Initial findings from a pivotal phase III trial showed that daratumumab added to a standard two-drug regimen (bortezomib and dexamethasone) markedly improved outcomes for patients with recurrent or refractory multiple myeloma.

The daratumumab combination reduced the risk of cancer progression by 70%, and doubled both very good partial response rates from 29% to 59% and complete response rates from 9% to 19%. Daratumumab, the first monoclonal antibody approved for multiple myeloma, targets a protein on the surface of cancer cells called CD-38.

These data were presented in ASCO's Plenary Session, which features four abstracts deemed to have the greatest potential to impact patient care, out of the more than 5,000 abstracts featured as part of the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting.

"We've suspected for a long time that CD-38 is the major treatment target for multiple myeloma, but these results are unprecedented in this cancer," said lead study author Antonio Palumbo, MD, a chief of the Myeloma Unit at the Department of Oncology, University of Torino in Torino, Italy. "It's clear now that we'll be moving to a three-drug regimen with daratumumab as the standard of care."

This first randomized clinical trial of daratumumab included nearly 500 patients with relapsed or refractory multiple myeloma. Patients received eight cycles of either regimen, followed by daratumumab maintenance therapy for patients in the daratumumab group.

"Daratumumab is a fast-acting drug — in many cases tumors shrank in just a month. As a result of shrinkage and slower tumor growth, patients had less pain and a better quality of life," said Dr. Palumbo.

He noted that daratumumab did not substantially worsen the most common side effects of the standard regimen. Patients in the daratumumab group experienced slightly higher rates of hematologic toxicity, infections, and peripheral neuropathy.

Longer patient follow up is needed to determine the impact of this daratumumab combination on patient survival. A clinical trial that combines daratumumab with another standard therapy for recurrent multiple myeloma is underway. Additional clinical trials are testing various daratumumab-based regimens for patients with newly diagnosed multiple myeloma.

Daratumumab is one of the first drugs with the ability to directly kill myeloma cells and at the same time stimulate the immune system response to attack the tumor. The direct effect explains rapid tumor shrinkage, whereas the immune effect sustains prolonged responses to the treatment.

"Here, we've seen what can happen for patients when we select the treatment based on a common target in multiple myeloma," said ASCO President Julie M. Vose, MD, MBA, FASCO. "The new treatment regimen appears to rapidly slow cancer growth in many patients. This study affirms the efficacy of daratumamab that was seen in earlier, smaller clinical trials in this setting."

Multiple myeloma is an uncommon cancer. In 2012, 114,250 were diagnosed worldwide. This study received funding from Janssen Research & Development.

ASCO2016特集

卵巣がん進行の緩徐化（Abstract LBA5503）

経静脈投与に腹腔内化学療法を追加することにより卵巣がんの進行が緩徐になる

Adding intraperitoneal chemotherapy to intravenous therapy slows progression of ovarian cancer

手術が成功し、経静脈投与（IV）化学療法に加え腹腔内（IP）化学療法を施行された一部の進行卵巣がん女性においては、IV化学療法のみの施行に比べ効果が高いようである。手術前に最初に化学療法を施行された女性においては、IPおよびIV化学療法を施行された患者の23.3%が9か月後に進行したのに対し、IV化学療法のみの患者におけるその割合は42.2%であった。このスタディ結果は2016年American Society of Clinical Oncology年次集会で発表された。

Full Text

For some women with advanced ovarian cancer that was successfully treated surgically, delivering chemotherapy intraperitoneal (IP) as well as intravenously (IV) appears more effective than IV chemotherapy alone. For women who were initially treated with chemotherapy prior to surgery (e.g., neoadjuvant therapy), the initial results from a randomized phase II trial show that 23.3% of women who received IP and IV chemotherapy had disease progression at nine months, vs. 42.2% of those who received IV chemotherapy alone.

The study was presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting.

According to the authors, the proportion of women with ovarian cancer who receive neoadjuvant chemotherapy prior to surgery is growing. Women who undergo optimal debulking surgery following this approach may now be candidates for IP/IV combination chemotherapy.

IP chemotherapy allows the delivery of higher doses of chemotherapy to the tumor, while sparing other parts of the body from side effects. Several prior randomized clinical trials showed that IP chemotherapy improved outcomes for certain women with ovarian cancer. However, this is the first randomized study to explore the benefit of IP chemotherapy among women who had received neoadjuvant chemotherapy.

"At this early time frame, we already see that women are doing better with IP chemotherapy, without a significant difference in toxicity," said lead study author Helen Mackay, MD, Divisional Head of Medical Oncology and Hematology at the Sunnybrook Odette Cancer Centre in Toronto, Canada. "However, women should consider the side effects of IP and IV chemotherapy, as well as recovery from cancer surgery, when discussing this option with their doctors."

This randomized phase II trial compared the efficacy and side effects of two combination chemotherapy regimens in patients with stage IIB – IV epithelial ovarian cancer. The majority (82%) of women had stage IIIC disease.

In this study, 275 women received neoadjuvant platinum – based chemotherapy, followed by surgery to remove their ovarian cancer. Following debulking surgery, 200 were randomly assigned to treatment with IV chemotherapy or an IV/IP regimen.

At nine months, 42.2% of women who received IV chemotherapy had disease worsening compared to 23.3% of those treated with IP/IV chemotherapy. The median progression– free survival was similar between the two groups – 11.3 months with IV chemotherapy and 12.5 months with the IV/IP regimen. The median overall survival was longer with IV/IP therapy than with IV therapy alone (59.3 months vs. 38.1 months), but the difference was not statistically significant.

"Although this randomized phase II trial was not statistically powered to evaluate survival, our results offer information on how to incorporate IP chemotherapy when women receive neoadjuvant chemotherapy followed by debulking surgery," said Dr. Mackay. "The findings also offer supportive and additional information to the previous published adjuvant randomized trials that showed an improvement in overall survival when IP chemotherapy was given following initial optimal debulking surgery."

The rate of severe side effects was slightly lower among women who receive IP/IV chemotherapy (16% vs. 23%), but this difference was not statistically significant.

Prior research has suggested that some molecular subtypes of ovarian cancer are more sensitive to chemotherapy than others. The researchers plan to assess tissue samples collected during this study to see if certain biologic characteristics were associated with improved outcomes with IP vs. IV chemotherapy. "If we can identify the long term survivors, we hope this will help us better predict who truly benefits from this approach," said Dr. Mackay.

"Intraperitoneal chemotherapy is an effective yet underused treatment for women with newly diagnosed ovarian cancer that has been successfully removed surgically. These data now suggest that IP treatment may have a role in the postoperative setting for women who initially were treated with intravenous chemotherapy," said Don Dizon, MD, FACP, ASCO Expert in ovarian cancer. "Furthermore, this study provides reassurance for patients and providers that the carboplatin-based IP regimen is both effective and well tolerated with maintenance of quality of life. That said, we need to further define those who derive the greatest benefit from this approach and to identify better options for all women with ovarian cancer."

In 2012, 239,000 women were diagnosed with ovarian cancer worldwide. Due to lack of screening and specific symptoms, most women already have late-stage disease at the time of their diagnosis.

The study received funding support from the Canadian Cancer Society Research Institute (CCSRI), Cancer Research, UK (CR UK) and NIH/NCI (US).

ASCO2016特集

化学放射線療法は高齢の神経膠芽腫患者の生存期間を延長する(Abstract LBA2)

高齢の神経膠芽腫患者はテモゾロミドを用いた化学放射線療法により生存期間が延長する

Elderly patients with glioblastoma live longer with chemoradiation using temozolomide

2016年American Society of Clinical Oncology年次集会で発表されたランダム化第III相試験の結果、短期放射線療法中にテモゾロミド化学療法を併用、その後月1回維持療法として追加することにより、高齢神経膠芽腫患者の生存期間が延長し、死亡リスクは33%低下することが示された。テモゾロミドの有益性は、40%の患者において認められたMGMTプロモーターメチレーションと呼ばれる腫瘍マーカーを有する患者において、特に顕著であった。副作用はテモゾロミド投与患者においてやや多かったが、全体的なQOLは放射線療法単独群と比べ同等であった。

Full Text

A Canadian-led randomized phase III trial found that adding temozolomide chemotherapy during short-course radiation therapy, followed by monthly maintenance doses of temozolomide, significantly improved survival of elderly patients with glioblastoma, reducing the risk of death by 33%.

These data were presented in ASCO's Plenary Session, which features four abstracts deemed to have the greatest potential to impact patient care, out of the more than 5,000 abstracts featured as part of the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting.

This is the first study to test the combination of temozolomide and radiation therapy in older adults, who account for half of all patients with this disease. While side effects were slightly greater among patients receiving temozolomide, overall quality of life was similar in both patient groups.

"Although glioblastoma disproportionately affects older patients, there are no clear guidelines for treating these patients, and practice varies globally," said lead study co- author James R. Perry, MD, FRCPC, The Crolla Family Endowed Chair in Brain Tumour Research at the Odette Cancer and Sunnybrook Health Sciences Centres in Toronto, Canada. "This study provides the first evidence from a randomized clinical trial that chemotherapy in combination with a shorter radiation schedule significantly extends survival without a detriment to quality of life."

This international phase III trial was led by the Canadian Cancer Trials Group (CCTG) with collaboration from the European Organization for the Research and Treatment of Cancer (EORTC) and the Trans-Tasmin Radiation Oncology Group (TROG).

Investigators enrolled 562 patients 65 years and older who were newly diagnosed with glioblastoma. The median patient age was 73 years and two-thirds were older than 70 years. The patients were randomly assigned to either short-course radiation therapy (40Gy in 15 fractions over 3 weeks) with concurrent and adjuvant temozolomide or radiation therapy alone.

Chemoradiation extended the median overall survival from 7.6 months with radiation therapy alone to 9.3 months. In addition, tumor growth was slower in the temozolomide group, with median progression-free survival of 5.3 months vs. 3.9 months.

"Although the difference in median survival seems modest, temozolomide significantly increased the chances of surviving two or three years. For an individual patient, that can mean being able to be part of another family holiday or celebration," said Dr. Perry. The 1-year and 2-year survival rates were 37.8% and 10.4% with radiation plus temozolomide versus 22.2% and 2.8% with radiation therapy alone.

The benefit of temozolomide was greater among 165 patients with MGMT promoter methylation, a genetic abnormality linked to better response to chemotherapy and longer survival in this disease. In this subset of patients, the median overall survival was 13.5 months with temozolomide and 7.7 months with radiation therapy alone. Patients who received temozolomide had a 47% lower risk of death than those who received radiation therapy alone.

Quality-of-life analyses using standardized questionnaires EORTC QLQ-C30 and BN20 showed no differences in physical, cognitive, emotional, and social functioning between the two groups. However, patients who received temozolomide had more nausea, vomiting, and constipation than those who received radiation therapy alone.

Glioblastoma is the most common primary brain tumor in adults and among the top five causes of death due to cancer. Glioblastoma occurs primarily in older people; the average age at diagnosis is 64 years.

"Glioblastoma is frequently diagnosed in older individuals, and these are important data showing that our best therapies can work and be tolerable for elderly patients," said Brian Alexander, MD, MPH, ASCO Expert in brain cancers. "It's good to have an option to offer patients that we know can have a positive impact, though still physicians and their patients need to weigh the benefits of this approach carefully."

This study received funding from the Canadian Cancer Society Research Institute and by an unrestricted grant from Schering-Plough/Merck Inc.

ASCO2016特集

新たな抗体は小細胞肺がんにおける有効性を示した(Abstract LBA8505)

新規の抗体薬物複合体は再発小細胞肺がんにおいて有望であるとの早期結果が示された

Novel antibody drug conjugate shows early promise in recurrent small cell lung cancer

ヒト初回投与臨床試験の早期結果から、抗体薬物複合体(ADC)rovalpituzumab tesirine (Rova-T) の再発小細胞肺がん(SCLC)に対する有効性が期待できることが示された。新規の抗DLL3抗体と強力な抗がん剤を組み合わせたこの治療により、腫瘍内DLL3レベルの高い患者の89%において腫瘍増殖を抑制し、39%において腫瘍を縮小した。この結果から、DLL3は初のSCLC予測バイオマーカーとなる可能性が示唆された。このスタディ結果は2016年American Society of Clinical Oncology年次集会で発表された。

Full Text

Early findings from a first-in-human clinical trial showed that antibody drug conjugate (ADC) rovalpituzumab tesirine (Rova-T) shows promising efficacy against recurrent small cell lung cancer (SCLC). The treatment, which combines a novel anti- DLL3 antibody with a powerful anticancer agent, halted tumor growth in 89% of patients with high levels of DLL3 in the tumor and shrank tumors in 39%.

The study was presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting.

"We've seen too few successes in recent years for small cell lung cancer, which makes these early signs of efficacy all the more encouraging," said lead study author Charles M. Rudin, MD, PhD, a medical oncologist and chief of Thoracic Oncology Service at Memorial Sloan Kettering Cancer Center in New York. "Although these results are preliminary, rovalpituzumab tesirine seems to be the first targeted therapy to show efficacy in small cell lung cancer, and we may have identified DLL3 as the first predictive biomarker in this disease."

The ADC rovalpituzumab tesirine comprises an anti-DLL3 antibody and a cancer-killing agent, pyrrolobenzodiazepine dimer, which damages DNA. The antibody component of the ADC serves to deliver the anticancer agent to the tumor and into cancer cells.

Approximately two thirds of patients with SCLC have high level DLL3 on the surface of cancer cells, and the protein is essentially absent from healthy adult tissues. DLL3 is known to regulate cancer stem cell biology in SCLC. Rovalpituzumab tesirine is the first agent to target DLL3.

The Phase I study enrolled 74 patients with SCLC that worsened despite at least one prior systemic therapy. About two-thirds of patients had extensive-stage disease at diagnosis, and the other third had limited-stage disease. When tissue samples were available, the researchers assessed levels of DLL3 protein in the tumor tissue.

Eleven out of 60 (18%) evaluable patients experienced tumor shrinkage, and 41 (68%) achieved clinical benefit (having at least stable disease). Nearly all the patients who responded to the treatment had elevated levels of DLL3 in their tumor.

Among the 26 patients with the highest levels of DLL3 in the tumor, 10 (39%) responded to the ADC, and had a median overall survival of 5.8 months and a 1-year survival of 32%. Within this group of patients, the 12 patients who were receiving the ADC as third- line therapy responded particularly well, with 50% having tumor shrinkage (confirmed objective response).

The most common severe treatment-related toxicities included serosal effusion (fluid build-up around the heart or lungs), low platelet counts, and skin reactions. These adverse effects appeared generally to be manageable with medications, or resolved without specific interventions.

The findings of this early-stage trial will need to be confirmed in larger clinical trials. A single-arm phase II pivotal trial in patients with DLL3-positive SCLC that has worsened despite at least two prior therapies was launched earlier this year. Other upcoming trials will evaluate rovalpituzumab tesirine in first line SCLC and other DLL3-expressing neuroendocrine cancers.

Antibody-drug conjugates (ADCs) are large molecules in which anticancer drugs are attached to an antibody. The antibody targets a protein that is abundant on the surface of cancer cells, but is preferably rarely found on healthy cells.

When the antibody attaches to the target protein on a cancer cell, the cancer cell internalizes the ADC. Inside the cancer cell, the cancer drug is released from the antibody where it exerts its cancer-killing effect. Through such targeted delivery of cancer drugs to cancer cells, collateral damage to healthy tissues is minimized. In fact, the cancer drug in the rovalpituzumab tesirine ADC is so potent that it cannot be given by itself, but it is safe when given in the context of an ADC.

There are only two ADCs currently approved in the United States for the treatment of patients with cancer. However, dozens of different ADCs are being tested in clinical trials.

SCLC accounts for 10% to 15% of lung cancers. This type of lung cancer is very difficult to treat and most patients survive only a year or less after diagnosis. The standard initial therapy for SCLC is chemotherapy with etoposide and platinum-drug.

"This is another example of a new wave of highly targeted treatments, which deliver anticancer drugs even more precisely to where they are needed," said Gregory Masters, MD, FACP, FASCO, ASCO Expert in lung cancer. "These results mark a good, early sign of success against a cancer for which we urgently need better therapy options."

This study received funding from Stemcentrx, Inc.

ASCO2016特集

膀胱がん免疫療法による生存に関する有益性が認められた(Abstract LBA4500)

進行膀胱がん患者は抗PD-L1免疫療法の恩恵を受ける

Patients with advanced bladder cancer benefit from Anti-PDL-L1 immunotherapy

2016年American Society of Clinical Oncology年次集会で発表された非ランダム化第II相臨床試験の結果、抗PD-L1免疫療法薬atezolizumabは、新規に進行膀胱がんと診断され、シスプラチンベースの化学療法に不適な患者において有効であることが示された。Atezolizumabは約4分の1の患者の腫瘍を縮小し、14.8か月の生存期間中央値をもたらした。一般的に、カルボプラチンベースの化学療法を行った場合、この状況における患者の生存期間は9～10か月である。現在この状況における患者の治療選択肢は限られており、多くの患者が選択するのは支持療法だけである。

Full Text

Anti-PD-L1 immunotherapy atezolizumab is effective in patients with previously untreated advanced bladder cancer and not eligible for the standard treatment with cisplatin. According to a non-randomized phase II trial, atezolizumab shrank tumors in about a quarter of patients and yielded a median survival of 14.8 months. Typically, patients in this setting have a survival of nine to 10 months with carboplatin-based regimens.

The study was presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting.

"Up to half of patients with advanced bladder cancer are too frail to receive the only known survival-prolonging treatment, cisplatin. There is really no standard treatment for such patients," said lead study author Arjun Vasant Balar, MD, an assistant professor of medicine at the New York University Langone Medical Center and Director of Genitourinary Medical Oncology at the NYU Perlmutter Cancer Center in New York, NY. "We are encouraged to see that atezolizumab immunotherapy may help address this major unmet need."

The trial, called IMvigor210, is a single-arm phase II study of atezolizumab in patients with locally advanced or metastatic bladder cancer. All patients had urothelial cancer.

The study included two groups of patients: those receiving atezolizumab as a second-line therapy and those receiving atezolizumab as an upfront treatment. The researchers have previously reported results from the second-line therapy group. Based on those results, the FDA granted accelerated approval for atezolizumab after treatment with a platinum- based regimen.

With a median follow-up of 14.4 months, 28 out of 119 (24%) patients responded to the treatment. The longest duration of response thus far is greater than 18 months, and 21 of 28 (75%) responses were ongoing at the time of data analysis. The median overall survival was 14.8 months.

Overall, atezolizumab was well-tolerated, with only 10-15% of patients experiencing severe adverse effects. The most common toxicities were hypothyroidism, liver function abnormalities, rash, and diarrhea. "The majority of our patients had few or no side effects from atezolizumab and only 6% of patients discontinued treatment because of toxicity.
This is in stark contrast to the approximate 20% rate of treatment discontinuation from toxicity observed with carboplatin-based chemotherapy regimens. Immunotherapy appears to be much easier to tolerate than chemotherapy, and this is especially important for elderly patients," said Dr. Balar.

Atezolizumab is an antibody targeting PD-L1, a component of the PD-1/PD-L1 immune checkpoint. When atezolizumab attaches to PD-L1 on the surface of tumor cells, it prevents it from interacting with PD-1 receptors on immune cells and thus unleashes the immune system to attack the tumor.

IMvigor210 is the first trial to test the efficacy of atezolizumab as the initial treatment in patients with advanced bladder cancer. These data are encouraging, and the researchers are planning a randomized phase III trial of atezolizumab as an upfront treatment for advanced bladder cancer.

A randomized clinical trial of atezolizumab as an adjuvant treatment for early-stage bladder cancer is also underway. Meanwhile, there are several ongoing clinical trials exploring other immune checkpoint inhibitors, including nivolumab, durvalumab, and pembrolizumab, in localized and advanced bladder cancer.

Bladder cancer is the fifth most common cancer in adults. Approximately 450,000 patients were diagnosed worldwide in 2012. Bladder cancer is largely a disease of the elderly; the average age at diagnosis is 70 years. This cancer is also closely linked to smoking, with 80% of patients being former smokers.

The standard upfront treatment for advanced bladder cancer is cisplatin-based chemotherapy. Patients receiving this therapy have a median survival of 12-15 months. However, for 30-50% of patients with advanced bladder cancer, cisplatin chemotherapy is not considered a safe option due to their advanced age, kidney function, and/or ongoing

medical conditions. Such patients may receive carboplatin-based chemotherapy, which provides a median survival of 9-10 months.

"This and other immunotherapies have brought new momentum to bladder cancer treatment, which until recently had seen practically no treatment advances in more than a decade," said Charles Ryan, MD, ASCO Expert in bladder cancer. "The fact that this treatment appears safe for elderly patients, who too often have few good options, is all the more encouraging."

This study received funding from Genentech, a member of the Roche Group.

ASCO2016特集

血液検査は組織生検に対する非侵襲的な代替法である（Abstract LBA11501）

リキッドバイオプシーは進行固形がんの治療方針決定に役立つ可能性がある

Liquid biopsy may help guide treatment decisions for advanced solid tumors

進行がん患者15,000人超のリキッドバイオプシーの解析の結果、循環腫瘍DNAにおけるゲノム変異は、対応する腫瘍組織において認められるものとほぼ一致していることが示された。これらの結果から、患者の血液内に流出した腫瘍DNAの解析は、組織生検がジェノタイプ判定には不十分、または安全に施行できない場合、非常に有益で低侵襲の代替法となり得ることが示唆された。さらにこの検査は、臨床上の方針決定に重要となり得る、経時的に進展するがんの変化をモニターする機会となる。このスタディ結果は2016年American Society of Clinical Oncology年次集会で発表された。

Full Text

A large-scale genomic analysis finds that patterns of genetic changes detected in blood samples (liquid biopsy) closely mirror those identified in traditional tumor biopsy. With blood samples from more than 15,000 patients and 50 different tumor types, this is one of the largest cancer genomics studies ever conducted.

The study was presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting.

"These findings suggest that analysis of shed tumor DNA in patient blood, also known as a liquid biopsy, can be a highly informative, minimally-invasive alternative when a tissue biopsy is insufficient for genotyping or cannot be obtained safely," said study presenter Philip Mack, PhD, Professor and Director of Molecular Pharmacology at the University of California Davis Comprehensive Cancer Center. "Moreover, this test, known as Guardant360, provides an unparalleled opportunity to monitor changes in the cancer as it evolves over time, which can be critical when patients and physicians are discussing treatment options for continued tumor control."

Currently, doctors largely rely on tumor biopsies to assess whether tumors have certain genetic mutations that can be targeted by available cancer drugs. Tumor biopsy involves a surgical procedure, however, and patients are not always healthy enough to undergo it, and frequent repeated tests are not always feasible.

Tumor cells also shed small pieces of their genetic material or DNA into the bloodstream. This so-called circulating tumor DNA (ctDNA) can be collected from the blood and analyzed in the lab to help inform treatment decisions for individual patients, similar to tumor biopsy. According to the authors, this is the largest study to use ctDNA analysis to select the appropriate targeted treatments for individual patients.

This study included 15,191 patients with advanced lung cancer (37%), breast cancer (14%), colorectal cancer (10%), and other cancers (39%). Each patient provided one or more blood samples for analysis of ctDNA.

This study assessed the accuracy of liquid biopsies, as compared to tumor samples, in two ways. First, it compared the patterns of genomic changes in ctDNA to those found in 398 patients with available results of genetic testing of the tumor tissue. When ctDNA was positive for key abnormalities in *EGFR*, *BRAF*, *KRAS*, *ALK*, *RET*, and *ROS1* that drive tumor growth, the same mutations were reported in tissue 94-100% of the time. Most ctDNA alterations were found at very low levels. Half occurred at a frequency below 0.4% of the total DNA in circulation. The accuracy of the liquid biopsy assay remained high even at these low levels.

The authors also assessed consistency in the frequencies of specific changes in ctDNA against previously published data from genomic analyses of tumor tissue, including data from The Cancer Genome Atlas. The findings suggest that liquid biopsy provides an accurate snapshot of the genomic landscape of the tumor.

Across multiple cancer genes and different classes of alterations correlations typically ranged from 0.92-0.99. However, one general exception was found in which ctDNA findings were often not seen in tumor biopsies: detection of new genomic alterations associated with resistance to targeted cancer drugs, such as the EGFR T790M resistance mutations in patients on *EGFR* inhibitor therapy. The authors hypothesize that these alterations were absent in the tissue-based population data because those patients had yet to receive treatment.

Based on the genetic changes the blood test revealed, the researchers provided the study participants' physicians with lists of possible treatment options, including FDA-approved drugs and/or clinical trials. Overall, ctDNA testing revealed a possible treatment option for nearly two-thirds of patients tested (63.6%), which included FDA-approved drugs as well as eligibility for clinical trials.

Clinical utility was evident among lung cancer patients. In 362 lung cancer cases, tissue was insufficient for testing or partially tested in 63%. Among these cases, the ctDNA test identified key genetic mutations at frequencies consistent with their prevalence in the published literature, providing these patients with their only source of an actionable target.

A liquid biopsy can be used periodically to monitor disease progression, response to therapy, and development of treatment resistance. If a repeat test suggests that the cancer is getting worse or becoming resistant to treatment, doctors may be able to adjust the patient's treatment plan.

Periodic liquid biopsy, which requires a simple blood draw, may be preferable to repeat tissue biopsy in terms of patient safety and convenience. In addition, because genetic changes in ctDNA often occur before signs of tumor growth are apparent on a scan, liquid biopsy can help doctors adjust treatment sooner.
Liquid biopsy has another important advantage over tissue biopsy. The genetic changes that drive tumor growth often differ in different parts of the tumor. Because tissue biopsy removes only small pieces of the tumor, key mutations can be missed, depending on what area of the tumor is sampled. Analysis of ctDNA provides information on all the different genetic changes that may be present in the tumor.

Although ctDNA mutations were detected in 83% of the blood samples in this study, not all patients had sufficient ctDNA for the test. For example, the researchers found that the ability to detect ctDNA is lower for patients with glioblastoma, presumably because the blood-brain barrier makes it more difficult for ctDNA from a brain tumor to enter the circulation.

They are addressing this by increasing the sensitivity of the assay to detect mutations at extremely low levels of ctDNA, which will not only make the test more sensitive for all solid cancer types in advanced stages, but also in applying this technology to cancers in earlier stages.

"The fact that genomic mutations vary not only patient to patient but also change over time has been a constant challenge in cancer treatment, especially in the precision medicine era," said Sumanta Kumar Pal, MD, ASCO expert in developmental therapeutics. "Having a good, reliable option beyond a tumor biopsy could have a major impact on our ability to select the right therapy for the right patient."

ASCO2016特集

小児神経芽腫の有望な治療法（Abstract LBA3）

タンデム自家移植はハイリスク神経芽腫患者の予後を改善する

Double stem-cell transplant improves outcomes for children with high-risk neuroblastoma

2016年American Society of Clinical Oncology年次集会で取り上げられたランダム化第III相試験の結果、タンデム自家移植を用いた集中的治療が、ハイリスクの小児神経芽腫患者の予後を改善することが示された。このトライアルでは、新規にハイリスク神経芽腫と診断された小児（年齢中央値3.1歳）を組み入れた。患者の大多数（88%）がstage 4であり、38.2%はMYCN遺伝子増幅と呼ばれるハイリスクの遺伝子異常を有していた。3年後、タンデム移植を施行された患者の無再発率は61.4%であったのに対し、シングル移植を施行された患者では48.4%であった。副作用は、タンデム移植とシングル移植で同等であった。

Full Text

Historically, less than 50% of children with high-risk neuroblastoma live five or more years after diagnosis. A National Cancer Institute (NCI) funded phase III trial performed by the Children's Oncology Group found that adding a second autologous stem-cell transplant (ASCT) to standard therapy improves outcomes for these patients.

At 3 years, 61.4% of patients who received a double transplant were alive and cancer-free, compared to 48.4% of those who received a single transplant. Side effects were similar between single and double transplant.

These data were presented in ASCO's Plenary Session, which features 4 abstracts deemed to have the greatest potential to impact patient care, out of the more than 5,000 abstracts featured as part of the 2016 American Society of Clinical Oncology Annual Meeting.

"This finding will change the way we treat children with high-risk neuroblastoma in North America, which still claims many young lives and is in urgent need of better treatments," said lead study author Julie R. Park, MD, an attending physician at Seattle Children's Hospital and professor in pediatrics at the University of Washington School of Medicine in Seattle, Washington. "However, the regimen we use for high-risk neuroblastoma is also the most aggressive and toxic regimen we give to children with cancer. For that reason, future research needs to focus on both exploring possible late effects of current therapy and developing newer less toxic therapies."

The trial enrolled children newly diagnosed with high-risk neuroblastoma (median age 3.1 years). The majority of patients (88%) had Stage 4 disease and 38.2% had a tumor high-risk genetic abnormality called MYCN amplification.

All patients received 6 cycles of a multi-agent induction chemotherapy regimen including an initial 2 cycles of high-dose cyclophosphamide/topotecan followed by collection of stem cells from the blood to be used for subsequent transplantation. At completion of the induction therapy, patients were randomly assigned to receive a single ASCT with carboplatin-etoposide-melphalan (CEM) chemotherapy or a double (tandem) ASCT with thiotepa–cyclophosphamide prior to the first ASCT followed by a modified CEM chemotherapy prior to second ASCT. In the tandem ASCT group, patients received the two transplants in the span of 6 to 8 weeks.

In the single ASCT group, 129 out of 179 patients were subsequently enrolled onto a trial delivering anti-GD2 (dinutuximab) plus cytokine immunotherapy after single transplant consolidation therapy. A similar proportion of patients, 121 out of 176, received this immunotherapy following a tandem transplant consolidation therapy.

The primary endpoint of the study was 3-year event-free survival (EFS) or the percentage of patients who have not had an "event" at three years after randomization. An "event" was defined as worsening or recurrence of cancer, diagnosis of a second cancer, or death from any cause.

Among all patients on the study, the 3-year EFS from enrollment was 51% and 3-year overall survival (OS) was 68.3%. Among patients randomized, the 3-year EFS rate from time of randomization was significantly higher following tandem transplant (61.4%) compared to single transplant (48.4%). The 3-year overall survival rate was slightly higher in the tandem transplant group than the single transplant group (74% vs. 69.1%), but the difference was not statistically significant.

"We know that most neuroblastoma recurrences occur within two to three years from diagnosis and that patients who had not had a recurrence at three years have a better chance of long-term survival. The study was not designed to observe a difference in overall survival, as this would take many years and can not be adequately controlled for additional therapies received after an initial disease recurrence," said Dr. Park. The researchers will continue following patients on this study for 10 years.

Outcomes were generally better among patients who enrolled onto the immunotherapy trial that included anti-GD2 antibody plus cytokines after the transplant. Among those patients, the 3-year EFS rate was significantly higher for those who had been assigned to tandem transplant (73.2%) compared to those assigned to single transplant (55.5%). The 3-year overall survival rate was significantly higher with a tandem transplant than with a single transplant (85.6% vs. 75.8%).

The rates of severe toxicities were similar between treatment groups. Fewer treatment-related deaths occurred among patients who received a tandem transplant than among those who received a single transplant (2 vs. 8).

"So much of the story of progress against childhood cancers has been learning to use potent therapies better. This is yet another example of how commitment to clinical research delivers potentially lifesaving results," said Stephen P. Hunger, MD, ASCO expert in pediatric cancers. "Still, this is a more aggressive approach and these children will need to be closely followed throughout their lives for long-term side effects."

The study received funding from the National Institutes of Health and was performed through the Children's Oncology Group consortium.

ASCO2016特集

乳がんに対するホルモン療法の延長は良好な結果をもたらす（Abstract LBA1 and LBA506）

10年間のホルモン療法はQOLを低下させることなく乳がんの再発を減少させる

Ten years of hormone therapy reduces breast cancer recurrence without compromising quality of life

第III相臨床試験の結果、ER陽性乳がん患者において、アロマターゼ阻害薬（AI）による術後補助療法を5年から10年に延長することで、その後のがん再発が3分の1減少することが示された。追跡期間中央値6.3年の時点で、副次的評価項目である全生存期間に差はなかった。対側乳がん年間罹患率は、レトロゾール群においてプラセボ群よりも低く（0.21% vs. 0.49%）、乳がん予防効果が示された。患者の全体的なQOLは、2群間で同等であった。このスタディは、2016年American Society of Clinical Oncology年次集会プレナリーセッションで取り上げられた。

Full Text

A randomized phase III clinical trial, MA.17R found that postmenopausal women with early breast cancer benefit from extending aromatase inhibitor (AI) therapy with letrozole from 5 to 10 years. Following five years of an AI and any duration of prior tamoxifen, women who received letrozole for five additional years had a 34% lower risk of recurrence than those who received placebo. The trial was led by the Canadian Cancer Trials Group with participation from the National Clinical Trials Network.

These results were discussed in ASCO's Plenary Session, which features four abstracts deemed to have the greatest potential to impact patient care, out of the more than 5,000 abstracts featured as part of the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting.

"Women with early-stage hormone-receptor positive breast cancer face an indefinite risk of relapse," said lead study author Paul Goss, MD, FRCP, PhD, director of Breast Cancer Research at Massachusetts General Hospital in Boston, Massachusetts and Professor of Medicine at Harvard Medical School. "The study provides direction for many patients and their doctors, confirming that prolonging aromatase inhibitor therapy can further reduce the risk of breast cancer recurrences. Longer AI therapy also showed a substantial breast cancer preventative effect in the opposite, healthy breast."

Overall survival was not significantly different in MA.17R between the two groups but Dr. Goss notes that because of the slow chronic relapsing nature of hormone-receptor positive breast cancer, overall survival has proved difficult to demonstrate in clinical trials. Because of this, most endocrine therapies for breast cancer have gained regulatory approval based solely on improvement of disease-free survival.

Patient overall quality of life was comparable between the two groups. Small differences in physical role functioning in favor of placebo was observed but these were not considered clinically significant. "A large proportion of women with early breast cancer are long-term survivors. As hormone therapy is given over a long period of time, measuring how women feel is very important," said Julie Lemieux, MD, lead author of the analysis of patient-reported outcomes from MA.17R, and a researcher at the Centre hospitalier universitaire de Québec in Canada.

The trial enrolled 1,918 postmenopausal women who had received five years of any one of three AI therapies either as initial treatment or after any duration of prior tamoxifen. Although patients were allowed to enroll up to two years after completing previous AI therapy, about 90% began receiving letrozole or placebo within six months of completing prior therapy.

Patient-reported quality of life was measured using the standard SF-36 questionnaire, which covers various areas of physical health and mental health, and a menopause-specific questionnaire, MENQOL. Of the 1,918 study participants, 1,428 were eligible to complete initial quality of life assessments. These were repeated at 12, 24, 36, 48 and 60 months, with more than 85% of women completing the questionnaires at follow-up.

Impact on Risk of Recurrence and New Breast Cancer (LBA1 - Plenary): Women in the extended letrozole group had a 34% lower risk of breast cancer recurrence. The annual incidence of contralateral breast cancer was lower in the letrozole group than in the placebo group (0.21% vs. 0.49%), indicating a breast cancer prevention effect. At five years of follow-up, 95% of women receiving letrozole and 91% of those receiving placebo were breast cancer free. The five-year overall survival was 93% for women receiving placebo and 94% for those receiving letrozole (not statistically significant).

This study received funding from the Canadian Cancer Society Research Institute, the National Institutes of Health and Novartis.

Quality of Life Findings (LBA506): Overall, there were no significant differences in either overall quality of life or menopause-specific quality of life between women who took letrozole for five years and those who received placebo. Small differences in physical role functioning were detected in favor of placebo but these were less than that considered clinically meaningful.

This study received funding from the Janssen Research & Development.

In 2012, there were more than six million women around the world who survived at least five years after breast cancer diagnosis; the vast majority of these women have estrogen receptor-positive breast cancer, and may wish to consider these findings.

"These data are important to the millions of women around the world with ER positive breast cancer, and suggest that longer durations of widely-available therapy reduce the risk of cancer recurrence, and prevent second cancers from arising," said Harold J. Burstein, MD, FASCO, ASCO expert in breast cancer. "Ten years of any therapy is a long time. Fortunately, most women tolerate extended treatment reasonably well, with few side effects. Now, women can talk with their clinical team and make informed decisions to extend adjuvant endocrine therapy, or not."

ASCO2016特集

膵がんに対する術後補助化学療法（Abstract LBA4006）

カペシタビンを用いた併用化学療法は膵がん術後の生存期間を延長させる

Chemotherapy combination with capecitabine extends survival after pancreatic cancer surgery

2016年American Society of Clinical Oncology年次集会で発表されたランダム化第III相試験の結果、ゲムシタビンによる化学療法にカペシタビンを上乗せすることにより、膵がんの術後予後が改善することが示された。この2剤併用療法は、毒性を大幅に増加させることなく、推定5年生存率を16.3%から28.8%に上昇させた。全生存期間中央値は、併用療法群で28.0か月であったのに対し、ゲムシタビン単独群では25.5か月であった。生存期間中央値の差はわずかに見えるかもしれないが、このがんにとって長期生存期間の改善は大幅な改善である、と筆者らは指摘している。

Full Text

A European phase III trial, one of the largest ever conducted in pancreatic cancer, showed that adding the oral drug capecitabine chemotherapy to gemcitabine prolongs survival without increased toxicity. Adjuvant gemcitabine chemotherapy is currently the standard of care worldwide after surgical removal of pancreatic cancer.

The study was presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting.

"Unfortunately, most patients are not candidates for surgery when they are diagnosed with pancreatic cancer," said lead study author John P. Neoptolemos, MA, MB, BChir, MD, FMedSci, the chair of surgery in the Department Molecular and Clinical Cancer Medicine at the University of Liverpool in Liverpool, United Kingdom. "These findings are significant because they show that those patients who can undergo surgery have a fighting chance of surviving this cancer with the combination of two commonly used chemotherapies."

With 732 patients, the European Study Group for Pancreatic Cancer (ESPAC) 4 trial is the second-largest clinical trial ever conducted in patients with pancreatic cancer who had undergone surgery. Within 12 weeks of surgery, patients with early-stage pancreatic ductal adenocarcinoma were randomly assigned to receive either gemcitabine alone or gemcitabine with capecitabine for 24 weeks.

The median overall survival was 28.0 months with the combination regimen vs. 25.5 months with gemcitabine alone. The estimated 5-year survival rates were 28.8% vs. 16.3% in the two groups. "The difference in median survival may seem modest, but the improvement in long-term survival is substantial for this cancer," said Dr. Neoptolemos. "We've gone from a five-year survival rate of 8% with surgery alone to nearly 30% with adjuvant therapy."

According to the authors, the patient characteristics were representative of a real---world pancreatic cancer population. A large proportion of patients had unfavorable prognostic factors, such as locally advanced or aggressive disease, large tumor size, or incomplete removal of the tumor.

The survival advantage with the combination regimen was similar irrespective of such factors. Patients who had been smokers but stopped smoking after their diagnosis had better outcomes than those who continued smoking.

Overall, there were no major differences in the types and severity of side effects between the two groups. Severe diarrhea was slightly more common with the combination regimen (14 vs. 5 patients), as was fatigue (16 vs. 14 patients). Quality of life was also comparable between the two groups.

The safety of this new gemcitabine-capecitabine chemotherapy regimen opens the opportunity to add other treatments to this combination, which might further improve outcomes for patients. Future research efforts will focus on developing tests to predict which patients would benefit most from a particular adjuvant therapy.

In 2012, 338,000 people were diagnosed with pancreatic cancer worldwide.

"Pancreatic cancer remains one of the most hard-to-treat cancers. It is a major win to find that adding a generic chemotherapy not only improves survival for these patients, but does so with little effect on patients' quality of life," said Smitha Krishnamurthi, MD, ASCO Expert in pancreatic cancer.

This study received funding from Cancer Research UK.

ASCO2016特集

希少脳腫瘍治療を変化させる可能性（Abstract LBA2000）

術後補助化学療法は1p/19q co-deletionのない退形成性神経膠腫患者の予後を改善する

Adjuvant chemotherapy improves outcomes for patients with anaplastic glioma without 1p/19q co-deletion

2016年American Society of Clinical Oncology年次集会で発表された第III相試験の早期結果から、標準的放射線療法にテモゾロミドによる術後補助化学療法を上乗せすることにより、1p/19q co-deletionのない退形成性神経膠腫患者の生存期間が延長することが示唆された。推定5年生存率は、放射線療法と術後補助化学療法の併用群で56%であったのに対し、テモゾロミドによる術後補助化学療法の非併用群では44%であった。増悪までの期間中央値は、テモゾロミド併用群で2倍以上であった（42.8か月対19か月）。これらの結果は、この希少脳腫瘍患者の治療選択肢を拡大し治療法を変化させるはずである、と筆者らは述べている。

Full Text

Patients with anaplastic glioma without 1p/19q co-deletion benefit from adjuvant chemotherapy, according to early results from a European phase III trial. The estimated five-year survival rates were 56% with radiation therapy and adjuvant temozolomide versus 44% without adjuvant temozolomide. Addition of adjuvant temozolomide also delayed disease progression by more than two years.

The study was presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting.

"Until this study, doctors had no evidence to support the use of adjuvant temozolomide in patients with grade III anaplastic glioma," said lead study author Martin J. van den Bent, MD, a professor of neuro-oncology at Erasmus MC Cancer Center in Rotterdam, The Netherlands. "These findings should expand treatment choices and change the way we treat patients with this rare form of brain cancer."

Co-deletion of chromosome arms 1p and 19q occurs in a specific type of brain cancer. Patients who have this genetic abnormality tend to respond better to chemotherapy and live longer. The Concurrent and Adjuvant Temozolomide Chemotherapy in Non---1p/19q Deleted Anaplastic Glioma (CATNON) trial was limited to patients who lack 1p/19q co-deletion (a separate trial focuses on patients who have this marker).

Researchers randomly assigned 748 patients to four different treatment groups:

- ●Radiation therapy alone
- ●Temozolomide during radiation therapy
- ●Temozolomide during and after radiation therapy
- ●Temozolomide after radiation therapy (adjuvant temozolomide)

The study was conducted by the European Organisation for Research and Treatment of Cancer (EORTC) and enrolled patients in 118 institutions in Europe, North America, and Australia.

Patients who received temozolomide after radiation therapy with or without concurrent temozolomide had slower disease progression than those treated without adjuvant therapy. The median time to disease progression was more than double in the adjuvant temozolomide group (42.8 months vs. 19 months).

The median overall survival has not been reached in patients treated with adjuvant temozolomide. Long-term survival estimates also support the use of adjuvant temozolamide; 56% of patients were alive at five years with adjuvant temozolomide compared to 44% with radiation therapy alone or with temozolomide given during radiation therapy. The results of the temozolomide treatment given only during radiation therapy are not yet available and final data from this study are expected in 2020.

Temozolomide is an oral drug and is generally well tolerated by patients. The most common toxicities in the temozolomide study arms were mainly hematologic (e.g., low platelets and white blood cells), with severe toxicity in 5-10% of patients.

Future research will focus on identifying patients who are most likely to benefit from adjuvant temozolomide. The researchers plan to assess or re-examine additional genetic abnormalities known to affect prognosis in this cancer: MGMT promotor methylation and IDH mutation.

"As physicians, our goal is to make every treatment matter, which includes recommending only treatments that our patients need – no more and no less. This study offers a good answer to a long-standing question, showing that adding temozolomide following radiation or concurrent chemoradiation offers clear benefits. For decades, anaplastic glioma has proven not only hard to treat, but also hard to study because it is so rare, making this finding even more important," said Brian Alexander, MD, MPH, ASCO Expert in brain cancers.

Anaplastic gliomas are uncommon, accounting for about 2% of primary brain cancers and highly aggressive tumors. They often occur in young adults – the median age at diagnosis is 35 to 50 years. Grade III anaplastic gliomas can grow quickly and progress to glioblastoma within a few years of diagnosis.

This study received funding from an unrestricted grant from Schering Plough/MSD, by the EORTC Cancer Research Fund, by Cancer Research UK, by NRG grants U10CA180868 (NRG Oncology Operations) and U10CA180822 (NRG Oncology SDMC); and by Cancer Australia. Temozolomide was made available for this study by Schering Plough/MSD.

ASCO2016特集

Claudin18.2 –胃がんの新たな標的（Abstract LBA4001）

このクラスで初めての抗体が進行胃がん患者の生存期間を改善する

First-in-class antibody improves survival for patients with advanced gastric cancer

2016年American Society of Clinical Oncology年次集会で発表されたランダム化第II相試験の結果、新たな免疫療法IMAB362が進行胃がん患者の生存期間を大幅に延長させることが示された。IMAB362は、全ての胃がんの約70%において存在する、細胞表面のclaudin18.2を標的とした初めての抗体である。化学療法単独に比べ、IMAB362は増悪までの期間中央値を4.8か月から7.9か月に、全生存期間中央値を8.4か月から13.2か月に延長した。Claudin18.2レベルが最も高い患者における生存期間中央値は、IMAB362を用いた場合16.7か月であり、化学療法単独では9か月であった。

Full Text

Findings from a European phase II study showed that the novel, first-in-class antibody IMAB362 can significantly extend median survival when added to standard chemotherapy (13.2 months vs. 8.4 months) for patients with advanced gastric cancer. This therapy targets a protein called claudin18.2, and patients in the study with the highest levels of claudin18.2 had an even longer median overall survival (16.7 months).

The study was presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting.

"As claudin18.2 is abundant in gastric tumors, we estimate that half of all patients with advanced gastric cancer may be candidates for this new treatment," said lead study author Salah-Eddin Al-Batran, MD, a medical oncologist and director at the Institute of Clinical Cancer Research, Nordwest Hospital in Frankfurt am Main, Germany. "In addition, this unique target is not present in any healthy tissues except the lining of the stomach, thereby minimizing treatment side effects."

Besides gastric cancer, claudin18.2 is found in a variety of other tumors, including pancreatic, lung, esophageal, and ovarian. Claudin18.2 belongs to a family of proteins that make tight junctions, which control the flow of molecules between cells in a layer. In tumors, however, tight junctions become disrupted and claudin proteins lose their primary role.

IMAB362 is the first antibody to target claudin18.2. When the antibodies attach to claudin18.2 on the surface of cancer cells, various types of cellular and soluble immune effectors respond by killing the cancer cells that are coated with antibodies. These processes are known as antibody‐dependent cell‐mediated cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC).

Gastric cancer is the fifth most common cancer in the world, with nearly one million new patients diagnosed with this disease in 2012. The first-line treatment for advanced or recurrent gastric cancer is chemotherapy. The addition of trastuzumab to chemotherapy provides some benefit to the group of patients with HER2-positive tumors, but only 15% all gastric cancers are HER2-positive.

The study included 161 patients with advanced or recurrent gastric or gastroesophageal junction cancer with a specific minimal level of claudin18.2 in the tumor (assessed from analysis of tumor biopsy specimen with a validated CE-marked diagnostic assay). The patients had not received prior therapy for metastatic cancer and were not eligible to receive HER2 therapy trastuzumab. The patients were randomly assigned to receive standard chemotherapy (epirubicin, oxaliplatin, and capecitabine) alone or with IMAB362.

Compared to chemotherapy alone, IMAB362 extended the median time to disease progression from 4.8 to 7.9 months and the median overall survival from 8.4 to 13.2 months. Among the patients with the highest levels of claudin18.2, the median overall survival was 16.7 months with IMAB362 and 9 months with chemotherapy alone.

According to the authors, the treatment was well tolerated. Vomiting (34.5% of patients with grade 1/2 and 3.6% with grade 3/4 in control arm vs. 55.8% of patients with grade 1/2 and in 10.4% with grade 3/4 in IMAB362 arm) and low blood counts or neutropenia (21.4 % of patients with grade 1/2 and 21.4 % with grade 3/4 in control arm vs. 23.4% of patients with grade 1/2 and in 32.5% with grade 3/4 in IMAB362 arm) were slightly more common in the IMAB362 group. The rates of severe adverse effects were not increased with IMAB362 compared to chemotherapy alone.

"It's exciting to see immunotherapy improving survival in gastric cancer. Claudin18.2 is commonly expressed in multiple cancers, and this treatment may apply to half of all patients with gastric cancer," said Smitha Krishnamurthi, MD, ASCO Expert in gastric cancer.

A phase III study is planned for launch in early 2017. The researchers are also planning a phase II study of IMAB362 in patients with pancreatic cancer.

This study received funding from Ganymed Pharmaceuticals AG.

ASCO2016特集

モバイルフレンドリーなウェブアプリケーションが肺がんの生存期間を延長する（Abstract LBA9006）

ウェブを介したフォローアップアプリケーションは進行肺がん治療後の生存期間を改善した

Web-mediated follow-up application improved survival following treatment for advanced lung cancer

第III相試験の結果、受診日間の症状を自己報告するウェブアプリケーションにより、標準的なフォローアップに比べ、1年生存率が26%上昇したことが示された。初回化学療法、放射線療法、または手術終了後、stage III/IV肺がん患者133人が、ウェブを介したフォローアップまたは標準的なフォローアップの群にランダムに割り付けられた。全生存期間中央値は、このアプリケーションを用いた患者では19か月であったのに対し、標準的なフォローアップ患者では12か月であった。患者のQOLもまた、このアプリケーションを用いた患者の方が優れていた。このスタディ結果は2016年American Society of Clinical Oncology年次集会で発表された。

Full Text

A Web-mediated follow-up application (Moovcare™) improves advanced lung cancer survival, according to a French multicenter randomized phase III study. Researchers analyzed the association and evolution of self-reported clinical symptoms over time. The median overall survival of patients who used the application was 19 months, compared to 12 months for those who received standard follow-up care. Patient quality of life was also better among patients who used the application.

The study was presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting.

"Through personalized follow-up using this convenient and simple online application, we can detect complications and signs of relapse and offer appropriate care earlier," said lead study author Dr. Fabrice Denis, MD, PhD, a researcher at the Institut Inter-regional de Cancérologie Jean Bernard in Le Mans, France. "This approach introduces a new era of follow-up in which patients can give and receive continuous feedback between visits to their oncologist."

After completing initial chemotherapy, radiation therapy, or surgery, 133 patients with stage III/IV lung cancer were randomly assigned to Web-mediated follow-up or standard follow-up. The standard follow-up included doctor visits and CT scans every 3-6 months (or more often at the researcher's discretion).

Patients in the Web-application group had the same schedule of planned doctor visits but three times fewer scheduled scans. They used the Web application to self-assess symptoms weekly. Caregivers could also enter data on behalf of the patients. The application analyzed 12 symptoms and reported results to the oncologist. An algorithm assessed specific changes in symptoms and triggered email alerts for the doctor, who would then confirm the need of anticipated exams/visits to adapt cancer treatment, including supportive care options.

At one year, 75% of patients were still alive in the Web-application group, compared to 49% in the standard follow-up group. The study was stopped at planned interim analysis because of good results.

Relapse rates were similar in both groups: 51% and 49% in the standard and Web-application groups, respectively. The general well being of patient (performance status) at the time of relapse was good in the Web-application group, so the majority (74%) of those patients were able to receive the full recommended treatment for the recurrence. In contrast, only one-third of patients in the standard follow-up group were well enough to receive optimal treatment for cancer recurrence.

Overall quality of life assessed using standard quality-of-life questionnaires FACT-L, FACT G, and TOI, was better in the Web-application group. Web-application follow-up also reduced by 50% the average number of imaging tests per patient per year.

The findings are consistent with the results of two other studies using tele-health follow-up. However, according to the authors, this is the first randomized trial showing a major improvement in survival with Web-mediated follow-up versus standard follow-up. It is also the first time that an algorithm for early detection of a symptomatic relapse or complication was used to trigger early supportive care or treatment.

In addition, review of patient-reported symptoms did not add burden to the doctors: on average, it took oncologists only 15 minutes per week to follow 60 patient and automated decreased the frequency of patient phone calls to the office.

Lung cancer is the most common cancer worldwide. In 2012, there were 1.8 million new lung cancer diagnoses worldwide and an estimated 1.59 million deaths due to lung cancer. Despite advances in surgery, chemotherapy, radiotherapy, targeted therapy, and immunotherapy, lung cancer remains a devastating disease. According to the authors, almost all (80-90%) lung cancer relapses are symptomatic.

This study received funding from the Institut de Cancérologie de l'Ouest / Sephira Inc. and Sivan Innovation, the maker of the Moovcare application.

ASCO2016特集

個別化医療によりがんの治療選択肢が広がる可能性がある（Abstract LBA11511）

個別化医療により進行がん患者の治療選択肢が広がる可能性がある

Precision medicine approach may expand therapeutic options for patients with advanced cancers

腫瘍内分子異常を有する患者と対応する分子標的治療とを適合させた、第II相試験の有望な早期結果が報告された。12の異なる型の進行がんを有する患者129人中29人において、FDAが承認した適応以外の薬剤が奏効した。特定の分子変異を有する4つの腫瘍タイプにおいて、有望な奏効性が認められたことから、これらの腫瘍を有する他の参加者にも薬剤の使用が拡大されている。有効性が最も確実視されたのは、HER2異常を有する患者であった。このスタディ結果は2016年American Society of Clinical Oncology年次集会で発表された。

Full Text

Researchers reported encouraging early results from a phase II trial that matches patients with molecular abnormalities in the tumor to corresponding targeted treatments. Twenty-nine of 129 patients with 12 different types of advanced cancers responded to drugs outside of U.S. FDA-approved indications. The promising responses seen in four tumor types with specific molecular alterations has already led to expansion of these tumor cohorts to additional participants.

The study was presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting.

"With genomic testing of tumors becoming increasingly available, studies such as ours will help more patients benefit from precision medicine approaches," said lead study author John D. Hainsworth, MD, senior investigator at Sarah Cannon Research Institute in Nashville, TN. "Although it is still early to draw conclusions, our findings suggest that, for example, HER2-targeted therapy could be expanded beyond the current indications of HER2-positive breast and gastric cancers. Our study gives strong early signals for activity of HER2-targeted therapy in HER2-amplified colorectal cancers (those with extra copies of *HER2* gene), and possibly other HER2-positive cancers."

MyPathway is an ongoing non-randomized, open-label trial that evaluates four treatment regimens in patients with advanced cancer for whom no beneficial treatment is available. This is a nationwide study with 39 currently participating sites.

To be eligible for the study, patients must have had previous molecular studies of the cancer showing abnormalities in the HER2, BRAF, Hedgehog or EGFR pathways. Patients were then matched with drugs targeting those abnormalities. Patients received a combination of trastuzumab and pertuzumab if they had HER2 abnormalities (amplification, overexpression, or mutation); vemurafenib for BRAF mutations; vismodegib for Hedgehog pathway mutations; and erlotinib for EGFR mutations. Only tumor types outside of current indications for these treatments were eligible.

Among the first 129 patients enrolled in the study, 82 had alterations in HER2, 33 in BRAF, 8 in Hedgehog and 6 in EGFR. All patients had an advanced solid tumor and had received a mean of three prior therapies. A total of 29 patients with 12 different types of cancer responded to targeted treatment. Fourteen responders have progressed after a median of 6 months of treatment (range 3-14 months); 15 responses are ongoing at 3+ to 11+ months.

The most promising efficacy was seen among patients with HER2 abnormalities – 7 of 20 patients with colorectal cancer, 3 of 8 with bladder cancer, and 3 of 6 with biliary cancer experienced objective responses (tumor shrinkage of 30% or more). Based on these results, recruitment to each of these groups has been expanded.
The group of patients with lung cancer and BRAF mutations will also be expanded. Among the first 15 patients in that group, 3 had objective responses and 2 had stable disease lasting for at least 4 months.

"This study speaks to the incredible potential of precision medicine to help us identify new treatments, but it also underscores the need to explore this genomic-based testing and treatment approach in a learning environment, like a clinical trial," said Sumanta Kumar Pal, MD, ASCO expert in developmental therapeutics. "It's likely there are factors that we are not yet aware of that explain why certain patients benefit from targeted therapies while others don't, even when their tumors have the same abnormality. We need to find these answers so we can match more patients to potentially beneficial treatments and spare patients from treatment that is unlikely to improve or prolong their lives."

The study is designed to accrue up to 500 patients. Groups that show low benefit will be stopped early, while groups that demonstrated efficacy will be expanded. The researchers also plan to incorporate emerging new regimens targeting these pathways. For example, cobemetinib, a MEK inhibitor, will soon be added to vemurafenib for patients with BRAF mutations. Incorporation of new agents targeting additional molecular abnormalities is also planned in the future.

The study received funding from Genentech, Inc.

ASCO2016特集

膠芽腫においては切除範囲が生存率に関連する（Abstract e13500）

膠芽腫の切除範囲が生存率と増悪に関連する

Extent of resection in glioblastoma associated with likelihood of survival and disease progression

膠芽腫患者においては切除範囲が生存率と増悪に関連する、と*JAMA Oncology*オンライン版に掲載され、併せて一部が2016 Annual Meeting of the American Society of Clinical Oncologyで抄録として公開された。研究者らは37のスタディ（患者計41,117人）のメタ解析において、全摘出（GTR）と部分摘出（STR）、または生検を全生存率および無増悪生存期間について比較した。その結果、GTRはSTRに比べ1年生存率を61%上昇させ、2年生存率を19%上昇させる可能性がある、と報告された。

Full Text

The extent of resection in patients with glioblastoma, an aggressive and often fatal brain tumor, was associated with the likelihood of survival and disease progression, according to a new study published online by *JAMA Oncology* and published in part as an abstract in conjunction with the 2016 Annual Meeting of the American Society of Clinical Oncology.

Glioblastoma multiforme (GBM) is the most common malignant brain tumor in adults. The optimal combination of medical, surgical and radiation therapy has not been defined. The surgical component can range from minimally invasive biopsy to a craniotomy with the goal of gross total resection (GTR). But not every patient receives an aggressive resection. The anatomy of the brain and concern about injury to important surrounding structures with resulting impairment mean the goal of GTR can be difficult to attain.

Michael Glantz, M.D., of the Penn State Milton S. Hershey Medical Center, Hershey, Penn., and coauthors compared GTR with subtotal resection (STR) or biopsy with overall and progression-free survival in a meta-analysis of 37 studies (41,117 patients).

The study reports a lower relative risk of death at one and two years. The authors suggest GTR may increase the likelihood of 1-year survival compared with STR by about 61 percent and may increase the likelihood of two-year survival by about 19 percent. The one-year risk for mortality for STR compared with biopsy was reduced and the risk for mortality was less for any resection compared with biopsy at years one and two, according to the results.

Overall, a reduction in mortality was associated with an increasing extent of resection. GTR also was associated with decreased disease progression over one year.

The authors note the results should be interpreted in the context of important caveats, including that GTR and STR groups differed on a number of factors and that the extent of tumor resection was defined by authors in studies, often imprecisely.

"Although the available studies are retrospective and mostly carry a high risk for bias and confounding, an overwhelming consistency of the evidence (including three class 2 studies) supports the superiority of GTR over STR and biopsy. … Therefore, when clinically feasible, the body of literature favors GTR in all patients with newly diagnosed GBM," the authors conclude.

ASCO2016特集