# ナッツの摂取が大腸がん再発リスクを低下させる (Abstract 3517)

## ナッツ類を食べる人は大腸がん再発リスクが半減する

## Chance of colon cancer recurrence nearly cut in half in people who eat tree nuts

ステージIII大腸がん患者826人を対象とした観察研究の結果、1週間のナッツ摂取量が2オンス(約57g)以上であった者は、ナッツを摂取しない者に比べ、がん再発率が42%低く、死亡リスクが57%低かった。ピーナッツまたはピーナッツバターを摂取した者においては、がんの再発または死亡の有意な減少はなく、筆者らはこの有益性は木の実(アーモンド、クルミ、ヘーゼルナッツ、カシューナッツ、およびペカンナッツなど)に限られると結論付けた。これらの結果は、2017年American Society of Clinical Oncology年次集会のポスターセッションで発表された。

## Full Text

An observational study of 826 patients with stage III colon cancer showed that those who consumed two ounces or more of nuts per week had a 42% lower chance of cancer recurrence and 57% lower chance of death than those who did not eat nuts.

A secondary analysis revealed the benefit of nut consumption was limited to tree nuts. Tree nuts include almonds, walnuts, hazelnuts, cashews, and pecans, among others. These findings will be presented at the upcoming 2017 ASCO Annual Meeting.

"Numerous studies in the fields of heart disease and diabetes have shown the benefits of nut consumption, and we felt that it was important to determine if these benefits could also apply to colorectal cancer patients," said lead study author Temidayo Fadelu, MD, a clinical fellow in medicine at Dana Farber Cancer Institute. "Patients with advanced disease who benefit from chemotherapy frequently ask what else they can do to reduce their chances of recurrence or death, and our study is an important contribution to the idea that modifying diet and physical activity can be beneficial."

There was no associated reduction in cancer recurrence and death among patients who consumed peanuts or peanut butter. According to the authors, the reason may be that, being legumes, peanuts have a different metabolic composition than tree nuts.

Patients with stage III colon cancer have up to a 70% chance of surviving three years after treatment, which typically includes surgery and/or chemotherapy. While numerous prior studies have looked at diet as a potential cancer prevention tool, this is one of the first in colon cancer to look at the role of nut consumption and its influence on recurrence and mortality, according to the authors.

The researchers analyzed a questionnaire from a CALGB clinical trial of patients with stage III colon cancer that began in 1999. The questionnaire, which was given after completion of chemotherapy, asked about dietary intake, including whether or not patients ate nuts and what types of nuts they consumed.

Researchers were particularly interested in nut consumption because it has been linked to lower incidence of obesity, type 2 diabetes, and reduction in insulin resistance. These health conditions represent a state of excess energy and are each associated with a higher risk of recurrence and death from colon cancer.

The authors analyzed the associations between overall nut consumption, and just tree nut consumption, and the risk of cancer recurrence and death. Patients who consumed two or more ounces of all types of nuts per week (19% of all patients in the study) had a 42% lower chance of cancer recurrence and 57% lower chance of death than those patients who did not eat nuts after completion of their cancer treatment. The benefit of eating nuts was consistent across known factors that can influence cancer recurrence, including patient age, body mass index, gender, and common genomic changes in the tumor.

When looking at just tree nut consumption, the chance of recurrence was 46% lower and the chance of death was 53% lower for those that ate at least two ounces per week, than for those who did not. Given that there was no significant reduction in cancer recurrence or death for those that ate peanuts or peanut butter, the authors conclude that in this study, the benefit is likely limited to tree nuts. More research is needed to understand the lack of association with peanuts.

"Basic healthy eating can often be overlooked during cancer treatment. This study shows that something as simple as eating tree nuts may make a difference in a patient's long-term survival," said ASCO President Daniel F. Hayes, MD, FACP, FASCO. "Nut consumption and a healthy diet are generally factors that clinicians and patients should perhaps pay attention to as they design the approach to treatment for colorectal cancer."

"We need to look at the potential positive impact of nut consumption on survival at other stages of colon cancer, particularly stage IV. Ultimately, we need to understand how nuts confer this protective effect, as well as possibly conduct a randomized, controlled clinical trial where diet recommendations are given at the start of the study to prove that tree nuts can reduce recurrence and death after treatment for colon cancer," said Dr. Fadelu.

"It should be emphasized that the authors are not suggesting that eating nuts should be considered a substitute for standard chemotherapy and other treatments for colon cancer, which have dramatically improved survival," said Dr. Hayes. "Rather, patients with colon cancer should be optimistic, and they should eat a healthy diet, including tree nuts, which may not only keep them healthier, but may also further decrease the chances of the cancer coming back."

This study was funded by the National Cancer Institute, of the National Institutes of Health, and Pfizer.

## ASCO2017特集

# 胆管がん患者の生存期間延長(Abstract 4006)

## BILCAP：経口抗がん剤が胆管がん患者の生存期間を1年以上延長する

## BILCAP: Oral chemotherapy extends survival by more than a year in biliary tract cancer

胆管がん患者447人を対象とした第III相ランダム化比較試験の結果、術後にカペシタビンを投与することにより、手術単独の場合と比較し、生存期間中央値が15か月延長することが示された、と2017年American Society of Clinical Oncology年次集会で発表された。がん再発までの期間中央値は、カペシタビン投与群で25か月であり、コントロール群では18か月であった。最も顕著な副作用は、カペシタビンによく見られる手足の発疹であった。これらの所見は、本疾患に新たな標準治療の基盤を提供する可能性がある。

## Full Text

A phase III randomized clinical trial of 447 patients with biliary tract cancers (BTCs) showed that giving capecitabine after surgery extends survival by a median of 15 months compared to surgery alone. The finding could provide the basis for a new standard of care in the disease.

This trial, called BILCAP, is one of the first randomized studies of adequate size to look at the use of adjuvant therapy in this rare and hard-to-treat cancer. The study is being presented at the 2017 ASCO Annual Meeting in Chicago.

"Biliary tract cancer is a disease of decidedly unmet need as until recently there has been little research on treating the disease," said lead study author John N. Primrose, MD, Professor of Surgery at the University of Southampton, United Kingdom. "Our trial is the first to enroll a sufficient number of patients to show that chemotherapy after surgery can have a significant improvement in survival, with modest side effects."

Patients with BTCs face considerable odds in that only about 20% of such cancers can be surgically removed, and for those that have a successful surgery, fewer than 10% survive five years.

At the time the trial was designed in the U.K. there was no standard of care for adjuvant therapy in BTC. Capecitabine was chosen out of several commonly used systemic therapies because it could be given as a tablet and had shown efficacy in pancreatic cancer, a disease with similarly poor outcomes. Subsequent to the start of the trial, two chemotherapy agents in combination, gemcitabine and cisplatin, have evolved to be the current standards of care in the setting of advanced BTC on the basis of results from other studies done in the U.K.

In the trial, 447 patients were randomly assigned to either treatment with capecitabine for 6 months or observation for recurrence of cancer. More than 80% of the patients were followed for at least three years with regular clinical exams, CT imaging, and a variety of blood tests that could be useful later in determining biomarkers for tumors.

While patients in the observation group lived a median of 36 months after surgery, those who received capecitabine lived a median of 51 months. Capecitabine was associated with a 20% lower chance of death than observation, but the difference was not statistically significant for the overall population of 447 patients in this study, which includes patients that stopped capecitabine early. However, in the subgroup of 430 patients that received treatment per study protocol, capecitabine was associated with a 25% lower chance of death than observation, and this difference was statistically significant.

The median time to cancer recurrence was 25 months for patients who received capecitabine and 18 months for patients in the control group. The most notable side effect related to treatment was a rash on the hands and feet, which is common with capecitabine. There were no deaths due to the use of capecitabine.

"One of the major benefits of our trial is the fact that we now have a tumor tissue collection associated with very robust clinical data which will be used for genomic exploration," said Dr. Primrose. "Since we started planning this trial at the start of this century, a number of new agents have become available, including several that treat cancer based on its genetic profile. This is where our tumor tissue repository will play an important role."

"This study helps resolve long-standing questions about adjuvant treatment for biliary tract cancer, for which there has been no standard of care," said ASCO President Daniel F. Hayes, MD, FACP, FASCO. "This oral chemotherapy is widely available and can offer patients the chance to live more than a year longer.

Dr. Primrose emphasized, however, that new approaches are urgently needed to develop and recruit patients for clinical trials in biliary cancer, as this trial's ten-year timeline is much too long to conduct a trial in a rapidly evolving era of treatments and approaches. International cooperation is desperately needed, he noted.

The authors are currently working on a subgroup analysis as there are four distinct types of BTC – three of which involve the liver and its ducts and one of which involves the gallbladder. This analysis may help define more precisely which patients could benefit the most from adjuvant chemotherapy.

This study received funding from Cancer Research UK.

## ASCO2017特集

# 分子標的治療は肺がんの再発を遅延させる (Abstract 8500)

## ADJUVANT：ゲフィチニブは非小細胞肺がんの再発予防において術後補助化学療法よりも有効である

## ADJUVANT: Gefitinib more effective than adjuvant chemotherapy in preventing recurrence of non-small cell lung cancer

分子標的治療薬ゲフィチニブは、標準治療である化学療法よりも術後再発予防においてより有効なようである。第III相臨床試験において、ゲフィチニブを投与された上皮成長因子受容体（*EGFR*）陽性、ステージII-IIIA非小細胞肺がん（NSCLC）の患者は、通常の化学療法を受けた患者に比べ、無再発期間が約10か月長かった。再発までの期間中央値は、ゲフィチニブ群で28.7か月であり、化学療法群で18か月であった。試験期間中に76人が死亡した（全登録患者の34.2%）；41人はゲフィチニブ群、35人は化学療法群であった。このスタディ結果は2017年American Society of Clinical Oncology年次集会で発表された。

## Full Text

The targeted therapy gefitinib appears more effective in preventing recurrence after lung cancer surgery than the standard of care, chemotherapy. In a phase III clinical trial, patients with epidermal growth factor receptor (*EGFR*)-positive, stage II-IIIA non-small cell lung cancer (NSCLC) who received gefitinib went about 10 months longer without recurrence than patients who received chemotherapy. The study is being presented at the 2017 ASCO Annual Meeting.

"Adjuvant gefitinib may ultimately be considered as an important option for stage II-IIIA lung cancer patients with an active *EGFR* mutation, and we may consider routine *EGFR* testing in this earlier stage of lung cancer," said lead study author Yi-Long Wu, MD, a director of the Guangdong Lung Cancer Institute, Guangdong General Hospital, Guangzhou, China. "We intend to follow these patients until we can fully measure overall survival as opposed to disease-free survival, which just measures disease recurrence."

Due to high chance of recurrence, the five-year survival for patients with stage II-IIIA NSCLC is only 40%. About 25% of all patients who are diagnosed with NSCLC are eligible to have surgery to remove the tumors with the hope of a cure. Among that group, about 30% or 140,000 people worldwide have an *EGFR* mutation in the tumor and may benefit from adjuvant treatment with *EGFR*-targeted therapy to reduce the chance of recurrence.

Following surgery, 222 patients who had confirmed activating *EGFR* mutations in the tumor were randomly assigned to receive gefitinib or chemotherapy (vinorelbine plus cisplatin). Patients received gefitinib daily for 24 months or the standard therapy regimen every three weeks for four cycles. According to the authors, chemotherapy was given for a shorter period of time because it is usually not tolerated well for longer periods of time. All patients were followed for disease relapse for about three years.

"Two recent targeted therapy trials of adjuvant therapy did not show benefit in NSCLC, in part because they included stages I, II, and III of the disease in their design," said Dr. Wu. "The earlier trials only looked to see if patients showed overexpression, or over-activity, of *EGFR*, but not mutations in *EGFR*. Our trial recruited patients who had been confirmed to have activating *EGFR* mutations so we believe these reasons account for why other trials showed no benefit of a targeted therapy while ours did."

Gefitinib blocks the signaling through the *EGFR* and is only effective in cancers with mutated and overactive *EGFR*.

The median time to recurrence was 28.7 months for patients who received gefitinib and 18 months for those who received chemotherapy. There were 76 patient deaths (34.2% of all enrollees) during the trial period; 41 occurred in the gefitinib group and 35 in the chemotherapy group.

Far fewer patients experienced severe side effects with gefitinib (12%) than with chemotherapy (48%). The most common serious side effect in the gefitinib group was elevated liver enzymes, whereas patients in the chemotherapy group had more severe quality of life concerns, including vomiting, nausea, low blood counts, and anemia.

As the researchers have a tissue repository from the surgically removed lung tumors, they plan to perform a comprehensive biomarker analysis looking for other potential biomarkers for gefitinib response or resistance, in addition to *EGFR*. Dr. Wu stated that a fuller analysis of treatment outcomes is also planned.

"This study identifies a subset of patients with lung cancer who can benefit from a targeted treatment that causes far fewer side effects than chemotherapy," said ASCO President-Elect Bruce E. Johnson, MD, FASCO. "It's also clear evidence that we can use precision medicine not only in patients with advanced cancer, but also in those with earlier stage disease."

ADJUVANT (NCT01405079) is the first randomized trial to compare gefitinib (G) with vinorelbine+cisplatin (VP) in completely resected pathological stage II-IIIA (N1-N2) NSCLC with *EGFR*-activating mutation.

This study received funding from Chinese Thoracic Oncology Group (CTONG) and AstraZeneca China.

## ASCO2017特集

# 結腸がん治療後の健康的なライフスタイルは生存率を改善する(Abstract 10006)

## 結腸がん患者の治療後の食事や行動で経過に差が出る

What patients with colon cancer eat, drink, and do after treatment makes a difference

ステージIII結腸がん患者992人を対象としたスタディの結果、術後補助化学療法中および療法後は健康的なライフスタイルであったと報告した患者は、あまり健康的でないライフスタイルであった患者に比べ経過が良好であることが示された、と2017年American Society of Clinical Oncology年次集会で発表された。健康的なライフスタイルスコアが最も高い患者は、スコアが最も低い患者に比べ、死亡リスクが42%低く、再発率も低い傾向にあった。飲酒をスコアに含めると、ライフスタイルスコアが最も高い患者群は、スコアが最も低い患者群に比べ、死亡率が51%低く、再発率も36%低かった。

## Full Text

A study of 992 patients with stage III colon cancer found that those who reported a healthy lifestyle during and following adjuvant treatment had a 42% lower chance of death and a trend for lower chance of cancer recurrence than those who had less healthy lifestyles. The study is being presented at the 2017 ASCO Annual Meeting.

"Colorectal cancer survivors need survivorship care, including guidance on what they can do to lower their risk of recurrence," said lead study author Erin Van Blarigan, ScD, Assistant Professor of Epidemiology and Biostatistics, University of California San Francisco. "In response to patient interest and need, the American Cancer Society (ACS) published 'Nutrition and Physical Activity Guidelines for Cancer Survivors' in 2012, but it is not known if following the guidelines after cancer diagnosis is associated with improved outcomes."

This study found that colon cancer patients whose lifestyle matched the ACS guidelines had longer disease-free survival and overall survival.

The patients were part of a clinical trial that enrolled from 1999 to 2001 and looked at the effect of two types of adjuvant chemotherapy for colon cancer on cancer recurrence and death. Lifestyle was assessed twice as part of the trial using validated surveys. Patients were assigned a score from 0-6 that measured the degree to which their lifestyle matched the ACS guidelines for cancer survivors. A score of zero indicated no healthy behaviors while a score of six indicated that the patients observed all of the healthy behaviors. Specifically, researchers assessed individuals based on recommendations for:

- Maintaining a healthy body weight
- Engaging in regular physical activity
- Eating a diet rich in whole grains, vegetables, and fruits and low in red meat and processed meat

Alcohol use was also included in the assessment as it is included ACS Guidelines for Cancer Prevention. Each of the healthy behaviors was equally weighted, but assessing dietary components was a bit more complex as the researchers had to score red and processed meat, whole grains, and vegetables and fruits individually and then build an overall dietary score.

Over a median follow-up of 7 years, the 91 survivors who had the highest healthy lifestyle scores (5-6 points) had a 42% lower risk of death and a trend for reduced chance of recurrence than the 262 survivors with the lowest lifestyle scores (0-1 points). When drinking alcohol was included in the score, the 162 survivors with the highest lifestyle score (6-8 points) had a 51% lower chance of death and a 36% lower chance of cancer recurrence than the 187 survivors who had the lowest healthy lifestyle scores (0-2 points).

The associations were not driven by any particular lifestyle factor; body weight, regular physical activity, and a healthy diet were all important. The researchers note that many cancer survivors have ongoing health problems, such as diabetes or heart disease, and a healthy lifestyle can help improve overall health. They further emphasize that their study's novel findings indicate that a healthy lifestyle may improve colon cancer-specific outcomes as well.

"It should be emphasized that the authors are not suggesting that a healthy life-style alone should be considered a substitute for standard chemotherapy and other treatments for colon cancer, which have dramatically improved survival. Rather, patients with colon cancer should be optimistic, and they should eat a healthy diet and exercise regularly, which may not only keep them healthier, but may also further decrease the chances of the cancer coming back," said Dr. Hayes.

"Our research team is conducting clinical trials to evaluate the feasibility and acceptability of digital health lifestyle interventions, such as Fitbit for colorectal cancer patients," said Dr. Van Blarigan. "If our interventions are acceptable and useful to patients, we will test their impact on risk of cancer recurrence and mortality in future studies."

"This study clearly shows that in addition to good, standard cancer treatment, which has reduced mortality due to colorectal cancer substantially, what patients eat, drink, and do afterward can make a difference," said ASCO President Daniel F. Hayes, MD, FACP, FASCO. "Patients often ask what else they can do in addition to chemotherapy to prevent their cancer from coming back, and the good news is that we have some information to point them to from a fairly large dataset."

This study received funding from the National Cancer Institute, of the National Institutes of Health.

## ASCO2017特集

# ワクチン使用による経口HPV感染の軽減 (Abstract 6004)

## HPVワクチン接種は経口HPV感染を減少させるが、十分に活用されていない

## HPV vaccination may reduce oral HPV infections but is still under-utilized

HPVワクチン接種の経口HPV感染に及ぼす影響を調査した初めての大規模試験の1つで、このワクチンの高度な予防効果の可能性が示された。米国における若年成人を対象としたこのスタディの結果、ワクチン接種を1回以上受けたと報告した者はワクチン接種を受けなかった者に比べ、高リスクのHPV感染有病率が88%低かった。研究者らは、HPVワクチン接種率は、特に男性においては依然として低く、それがこのワクチンの集団レベルの有益性を限定している、と述べている。このスタディ結果は2017年American Society of Clinical Oncology年次集会で発表された。

## Full Text

In one of the first large studies to explore the possible impact of HPV vaccination on oral HPV infections, researchers found it may confer a high degree of protection. The study of young adults in the United States showed that the prevalence of high-risk HPV infection was 88% lower among those who reported getting at least one vaccine dose than among those who were not vaccinated.

Researchers reported that HPV vaccination rates remain low, especially among males, which limits population-level benefits of the vaccine. The study is being presented at the 2017 ASCO Annual Meeting in Chicago.

"Rates of HPV-caused oral cancers continue to rise every year in the U.S., particularly among men. And yet, no clinical trial has evaluated the potential use of the HPV vaccine for the prevention of oral HPV infections that could lead to cancer," said senior study author Maura L. Gillison, MD, PhD, who conducted the research at Ohio State University but is now a professor of medicine at the University of Texas MD Anderson Cancer Center. "Given the absence of gold-standard, clinical trial data, we investigated whether HPV vaccine has had an impact on oral HPV infections among young adults in America," said Dr. Gillison.

The authors based their study of oral HPV infections by assessing data from part of the National Health and Nutrition Examination Survey (NHANES) of Americans from 2009 through 2016. The NHANES is designed to assess the health and wellness of the U.S. population.

In this analysis, the researchers focused on 2,627 young adults ages 18 through 33 during the period 2011-2014, comparing those who had received one or more doses of an HPV vaccine to those who had not. For the purposes of this study, the researchers evaluated the prevalence of the four HPV types (16, 18, 6 and 11) included in HPV vaccines prior to 2016 (the time at which a newer vaccine that protects against five additional HPV strains was introduced). HPV infection was detected from oral rinse samples that were collected by mobile health facilities supported by NHANES. The laboratory tests for HPV infection were developed and performed in Dr. Gillison's lab.

The researchers found that from 2011 through 2014 fewer than 1 in 5 (18.3%) young adults reported receiving at least one dose of the HPV vaccine before age 26. The vaccination rate was much lower among men than women (6.9% vs. 29.2%) at this time.

Prevalence of oral HPV infections covered by the vaccine was lower among vaccinated vs. unvaccinated young adults (0.11% vs. 1.61%) corresponding to an 88% reduction in prevalence for vaccinated youth. In contrast, the prevalence of oral infection with 33 HPV types not covered by the vaccine was about the same between vaccinated and non-vaccinated groups (4% for those vaccinated vs. 4.7% for the unvaccinated; difference not statistically significant).

Due to low uptake of the HPV vaccine in the U.S. thus far as reported by NHANES, the researchers estimate that the impact of HPV vaccination on the prevalence of vaccine-covered, oral HPV infections in the general population was modest, reducing prevalence by 17% overall; and by 25% in women and by about 7% in men between 2011 and 2014.

"While we were encouraged that there was a notable impact of the vaccine on oral HPV infections among vaccinated individuals, that benefit was modest overall and lower than we would hope in men due to low vaccine uptake," stated Dr. Gillison.

Dr. Gillison emphasized that HPV vaccination is currently indicated for the prevention of cervical, vulvar, vaginal, and anal cancers in women and anal cancers in men. Whether the vaccines could eventually reduce the rising incidence of oral cancers related to oral HPV infection is thus far unknown.

"The HPV vaccine is one of the most important advances in cancer prevention in the last several decades. Parents who choose to have their children vaccinated against HPV should realize that the vaccine may provide additional benefits, such as prevention of oral HPV infections linked to oral cancers," she concluded.

"The HPV vaccine has the potential to be one of the most significant cancer prevention tools ever developed, and it's already reducing the world's burden of cervical cancers," said ASCO President-elect Bruce E. Johnson, MD, FASCO. "The hope is that vaccination will also curb rising rates of HPV-related oral and genital cancers, which are hard to treat. This study confirms that the HPV vaccine can prevent oral HPV infections, but we know it only works if it's used."

This study received funding from The National Institute of Dental and Craniofacial Research, of the National Institutes of Health.

## ASCO2017特集

# 結腸がんに対する補助療法の改善 (Abstract LBA1)

## 結腸がん術後補助化学療法に対する個別化治療のためのリスクに基づく新たな標準治療が世界的研究により定められた

## Global study sets new risk-based standard to personalize chemotherapy for colon cancer after surgery

リンパ節転移陽性結腸がん（ステージIII）に対する術後補助化学療法は、一部の患者では長期にわたる標準コースの半分しか必要でない可能性がある、と2017年American Society of Clinical Oncology年次集会で発表された。北米、ヨーロッパ、およびアジアにおける6つの臨床試験の解析において、比較的再発リスクの低い患者では3か月間の化学療法は6か月間の化学療法と同様に有効であった。3か月の治療レジメンはまた、副作用、特に神経障害が少なかった。筆者らは、再発リスクの低い60%の患者にとって3か月の化学療法は新たな標準治療となるであろう、と示唆している。

## Full Text

After surgery for lymph-node positive colon cancer (stage III), some patients may only need half of the long-standing standard course of chemotherapy. In an analysis of six clinical trials with over 12,800 patients, three months of chemotherapy was nearly as effective as six months in patients with relatively lower recurrence risk and caused fewer side effects, particularly nerve damage.

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 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

Chemotherapy lowers the chance of cancer recurrence after colon cancer surgery. Since 2004, the standard adjuvant treatment has been a combination of chemotherapies (FOLFOX or CAPOX), given over a period of six months.
The goal of this study, which pooled data from 6 studies conducted in North America, Europe, and Asia, was to determine if three months of chemotherapy was as effective as 6 months. While the primary endpoint was not proven statistically, a shorter, 3-month course of chemotherapy was associated with a less than 1% lower chance of being colon cancer free at three years compared to the standard 6-month course (74.6% vs. 75.5%). In patients considered at low risk of cancer recurrence (60% of patients in the study), the difference was even smaller (83.1% in patients receiving a 3-month course vs. 83.3% in patients receiving a 6-month course).

"Our findings could apply to about 400,000 colon cancer patients worldwide every year. For 60% of these patients, who have lower risk for cancer recurrence, three months of chemotherapy will likely become the new standard of care," said senior study author Axel Grothey, MD, an oncologist at the Mayo Clinic Cancer Center in Rochester, Minnesota. "Patients with higher risk colon cancer, however, should discuss these results with their doctor to see if a shorter course of therapy would be right for them, taking into account their preference, age, and ability to tolerate chemotherapy."

A key side effect of one of the chemotherapies in the regimen – oxaliplatin – is nerve damage, which can result in permanent numbness, tingling, and pain. The longer a patient receives oxaliplatin, the greater the chance for severe and long-lasting nerve damage. Nerve damage (numbness/tingling of the hands and feet) was substantially less common in patients receiving a 3-month course of chemotherapy vs. a 6-month month course (15% vs. 45% with FOLFOX and 17% vs. 48% with CAPOX).

"Many side effects of chemotherapy, such as hair loss, go away over time, but nerve damage is a side effect some patients have to deal with for the rest of their lives," said Dr. Grothey.

This study is a prospective, pre-planned analysis of pooled data from six concurrent, phase III clinical trials conducted in 12 countries. It was established more than 10 years ago as so-called IDEA collaboration (International Duration Evaluation of Adjuvant therapy). A steering committee oversaw the study design, and an independent statistical center reviewed the results from all six clinical trials (findings from three of which are being presented at the ASCO Annual Meeting). The study received public funding only.

"We needed this large number of patients to answer the study question, but at the time this study began in 2007 it was not possible to run one study of that size anywhere in the world," said Dr. Grothey. "With more than 12,834 patients, this is the largest collaboration of its kind in oncology."

Patients were followed for a median time of 39 months. For all patients combined, the rate of disease-free survival at three years was slightly lower with three months of chemotherapy than with six months of chemotherapy (74.6% vs. 75.5%). The type of chemotherapy regimen selected affected the difference in 3-year disease-free survival between the 3-month and 6-month treatment duration (75.9% vs. 74.8% with CAPOX and 73.6% vs 76.0% with FOLFOX), although the difference was relatively small in both cases.

In the subset of patients with lower risk colon cancer (defined as cancer spread to 1-3 lymph nodes and not completely through the bowel wall), the disease-free survival rate at three years was almost identical for those who received 3 (83.1%) and 6 months of chemotherapy (83.3%).

The rate of clinically meaningful (grade 2 or greater) nerve damage differed depending on the type of chemotherapy regimen received, but was consistently higher for people who received 6 months versus 3 months of chemotherapy (45% vs. 15% with FOLFOX and 48% vs. 17% with CAPOX).

"Aside from nerve damage, longer chemotherapy also means more diarrhea and fatigue, more doctor appointments, blood draws, and time away from work and social interactions," said Dr. Grothey.

"This is extremely important work that will affect the lives of many of my patients hopefully tomorrow, and will allow us to provide a more personalized approach to our patients with colon cancer. Although addressing the question, 'can we give less treatment?' is of major importance to patients and their doctors, it is rare to see this type of study. Given that these questions are unlikely to be of interest to the pharmaceutical industry, federal support for these trials is critical," said Dr. Baxter.

"In this case, less is more. We're now able to spare many patients with colon cancer unnecessary side effects of an additional three months of chemotherapy without compromising results. This study is an excellent example of how existing treatments can be refined to work even better for patients," said ASCO Expert Nancy Baxter, MD.

This study was funded by grants from the Medical Research Council, National Institute for Health Research, National Cancer Institute, Italian Agency for Drugs (AIFA), Japanese Foundation for Multidisciplinary Treatment of Cancer, French Ministry of Health, and French National Cancer Institute (Inca).

## ASCO2017特集

# 症状を自己報告するウェブベースのシステムは患者の生存期間延長に役立つ(Abstract LBA2)

## ウェブベースの症状報告システムは苦痛を軽減する行動につながり、予後を改善する

## Web-based symptom reporting system leads to actions that alleviate suffering and improve outcomes

766人の患者を対象としたランダム化臨床試験の結果、簡便な介入ー患者がリアルタイムで症状を報告することができ、医師への警告のきっかけとなるウェブベースのツールーは、生存期間延長などの大きな恩恵をもたらし得ることが示された。この試験では、外来化学療法を施行されている進行固形がん（泌尿生殖器、婦人科、乳腺及び肺）の患者766人を組み入れた。化学療法中の症状をこのツールを使用して定期的に報告した患者は、この方法を使用しなかった患者に比べ、生存期間中央値が5か月長かった。彼らはまた、より長期の化学療法に耐えることができた。この結果は、2017年American Society of Clinical Oncology年次集会Plenary Sessionで発表された。

## Full Text

A randomized clinical trial of 766 patients shows that a simple intervention - a web-based tool that enables patients to report their symptoms in real time, triggering alerts to clinicians - can have major benefits, including longer survival. Patients with metastatic cancer who used the tool to regularly report symptoms while receiving chemotherapy lived a median of 5 months longer than those who did not use the tool.

These findings 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 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

"Patients receiving chemotherapy often have severe symptoms, but doctors and nurses are unaware of these symptoms up to half of the time," said lead study author Ethan M. Basch, MD, MSc, FASCO, Professor of Medicine at the Lineberger Comprehensive Cancer Center of the University of North Carolina, who was practicing at Memorial Sloan Kettering Cancer Center in New York when the study was conducted. "We show that using a web-based symptom reporting system that alerts the care team about problems leads to actions that alleviate suffering and improve patient outcomes."

An earlier report from the same study showed that use of the tool was associated with better quality of life, and fewer visits to the emergency room and hospitalizations. Compared to patients who received usual care, patients who used web-based symptom monitoring were also able to tolerate chemotherapy longer.

"The improvement in survival we saw may seem modest, but it is greater than the effect of many targeted cancer drugs for metastatic cancer," said Dr. Basch.

The study enrolled 766 patients with advanced solid tumors (genitourinary, gynecologic, breast, and lung) who were receiving outpatient chemotherapy. The patients were randomly assigned to report their symptoms via tablet computers (intervention group) or to a group whose symptoms were monitored and documented by clinicians, as is usual care in clinical practice. In the usual care group, patients discussed symptoms during visits with oncologists. They were also encouraged to telephone the office between visits if any concerning symptoms arose.

On a weekly basis, patients in the intervention group reported on 12 common symptoms experienced during chemotherapy, including appetite loss, difficulty breathing, fatigue, hot flashes, nausea, and pain, and graded them on a 5-point scale. The web-based tool, Symptom Tracking and Reporting or STAR, was developed for research purposes and is not commercially available. Patients could report the symptoms remotely from home or at the doctor's office during oncology or chemotherapy visits, using tablet computers or computer kiosks. Doctors received symptom reports during visits, and nurses received email alerts when patients reported severe or worsening symptoms.

All patients in the intervention group, including those with little prior experience using the Internet, were willing and able to regularly report their symptoms via the web throughout chemotherapy. Nurses took immediate clinical actions more than three-quarters of the time when patients reported severe or worsening symptoms. Compared to patients who received usual care, patients who used the web tool to self-report symptoms had a longer median overall survival (31.2 months vs. 26 months).

"Online technologies have transformed communications in practically every aspect of our lives, and now we're seeing they're also allowing patients to take an active role in their care and get immediate access to their care provider," said ASCO Expert Harold J. Burstein, MD, PhD, FASCO. "It's impressive that something as simple as this not only improves quality of life, but in this case, helps patients live longer. I think we'll soon see more cancer centers and practices adopting this model."

These findings are being confirmed in a larger clinical trial, which uses an updated, more user-friendly online tool that works on both personal computers and mobile devices. The study is being conducted in community practices across the United States.

"Symptom management is a central part of what oncology care teams do," said Dr. Basch. He noted that this study supports broader use of online tools in routine practice to enable patients to communicate symptoms to the care team in real time.

This study was funded by the Conquer Cancer Foundation of the American Society of Clinical Oncology (ASCO).

## ASCO2017特集

# OlaparibはBRCA関連転移性乳がんの増殖を遅延させる(Abstract LBA4)

## スタディの結果、PARP阻害剤が乳がん治療において重要な役割を果たす可能性があることが示唆された

## Study findings suggest PARP inhibitors could play an important role in breast cancer treatment

約300人の女性を対象とした第III相臨床試験の結果により、PARP阻害剤がBRCA関連乳がんの新たなタイプの治療として導入される可能性がある。Olaparibを投与された患者の約60%において腫瘍が縮小したのに対し、化学療法を施行された患者におけるその割合は29%であった。追跡期間中央値14か月の時点で、がん再発率はolaparib投与群で化学療法群より42%低かった。がん進行までの期間中央値はolaparib投与群で7か月であり、化学療法群で4.2か月であった。このスタディ結果は、2017年American Society of Clinical Oncology年次集会Plenary Sessionで取り上げられた。

## Full Text

Findings from a phase III clinical trial of about 300 women may introduce PARP inhibitors as a new type of treatment for breast cancer. Compared to standard chemotherapy, the oral targeted medicine olaparib reduced the chance of progression of advanced, BRCA-related breast cancer by 42%, delaying progression by about 3 months.

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 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

"This is the first demonstration of improved outcomes with a PARP inhibitor compared to standard treatment in women with BRCA mutation-associated breast cancer," said lead study author Mark E. Robson, MD, Clinic Director of the Clinical Genetics Service and medical oncologist at Memorial Sloan Kettering Cancer Center in New York. "It is especially encouraging to see that olaparib was effective against triple negative breast cancers that arise in women with inherited, germline *BRCA* mutations. This type of breast cancer is particularly difficult to treat and often affects younger women."

Up to 3% of all breast cancers occur in people with inherited changes in genes BRCA1 and BRCA2. These changes lower the cell's ability to repair damaged DNA. Olaparib blocks other key players in the cell's DNA repair machinery, PARP1 and PARP2. Because of their underlying defect in DNA repair, cancer cells with *BRCA* mutations are particularly vulnerable to treatments that target PARP.

"This study is proof of the principle that breast cancers with defects in a specific DNA damage repair pathway are sensitive to a targeted therapy designed to exploit that defect," said Dr. Robson.

The study enrolled patients with inherited BRCA mutations who had metastatic breast cancer that was either hormone receptor-positive or triple negative (estrogen receptor-negative, progesterone-receptor negative, and HER2-negative). Women with HER2-positive breast cancer were not included in this study because there are already very effective targeted treatments for this group. All patients had up to two prior rounds of chemotherapy for metastatic breast cancer, and those with hormone receptor-positive cancer had received hormonal therapy.

The researchers randomly assigned 302 patients to receive olaparib tablets or standard chemotherapy (either capecitabine, vinorelbine, or eribulin) until the cancer worsened or the patient developed severe side effects.

Tumors shrank in about 60% of patients who received olaparib, compared with 29% of those who received chemotherapy. At a median follow-up of about 14 months, patients who received olaparib had a 42% lower chance of cancer progression than those who received chemotherapy. The median time to progression was 7 months with olaparib and 4.2 months with chemotherapy.

After progression, the researchers kept track of patients to see how long it would be before the cancer worsened again. The time to second progression was also longer in patients receiving olaparib, indicating that the cancers did not return in a more aggressive way once olaparib stopped working. The study is insufficiently mature to permit a determination if the benefits provided by olaparib translate into prolongation of overall survival at this time.

The most common side effects in the olaparib group were nausea and anemia, whereas low white blood cell counts, anemia, fatigue, and rash on hands and feet were most common in the chemotherapy group. Severe side effects were less common with olaparib, occurring in 37% of patients compared to 50% of those treated with chemotherapy. Only 5% of patients needed to stop olaparib due to side effects. Health-related quality of life was significantly better in the olaparib group.

"Olaparib will probably be best used early in the course of metastatic breast cancer. It helps preserve patient quality of life, offers the chance to postpone the need for IV chemotherapy, and avoids side effects like hair loss and low white blood cell counts," said Dr. Robson.

"These long-awaited findings show that this new class of treatment can deliver better results for women with BRCA-positive breast cancer," said ASCO President Daniel F. Hayes, MD, FACP, FASCO. "What's remarkable is that we are now able to not only tailor breast cancer treatment based on the genetic changes in the tumor, but also on the inherited factors driving its development."

Given the relatively small size of the study, it is difficult to tell which subset of patients would benefit the most from olaparib.

This is the first of four ongoing phase III clinical trials of PARP inhibitors in breast cancer to report findings. More research is needed to determine how well olaparib works in cancers that worsen despite platinum-based chemotherapy, a standard regimen not included in this study, and whether platinum-based chemotherapy would be useful after cancers worsen despite olaparib.

This study was funded by AstraZeneca.

## ASCO2017特集

# 多発性骨髄腫に対する新たなタイプの免疫療法 (Abstract LBA3001)

## CAR T細胞療法は多発性骨髄腫を長期寛解に持ち込む

## CAR T-cell therapy sends multiple myeloma into lasting remission

2017年American Society of Clinical Oncology年次集会で発表された早期臨床試験において、多発性骨髄腫患者35人中33人（94%）が新たなタイプの免疫療法－B細胞成熟蛋白BCMAを標的としたキメラ抗原受容体（CAR）T細胞－を受けることにより臨床的寛解を得た。治療効果を示す最初の徴候はCAR T細胞の初回注射から10日と、早期に出現した。CAR-T細胞療法は、各患者に対し個別に作成される。患者自身のT細胞が収集され、ラボで遺伝子の再構成が行われ、患者に注射し戻される。多くの患者は、軽度の副作用を発現するのみである。

## Full Text

In an early clinical trial, 33 out of 35 (94%) patients had clinical remission of multiple myeloma upon receiving a new type of immunotherapy - chimeric antigen receptor (CAR) T cells targeting B-cell maturation protein or BCMA. Most patients had only mild side effects.

The study was presented in at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

"Although recent advances in chemotherapy have prolonged life expectancy in multiple myeloma, this cancer remains incurable," said study author Wanhong Zhao, MD, PhD, an associate director of hematology at The Second Affiliated Hospital of Xi'an Jiatong University in Xi'an, China. "It appears that with this novel immunotherapy there may be a chance for cure in multiple myeloma, but we will need to follow patients much longer to confirm that."

CAR T-cell therapy is custom-made for each patient. The patient's own T cells are collected, genetically reprogrammed in a lab, and injected back into the patient. The reprogramming involves inserting an artificially designed gene into the T-cell genome, which helps the genetically reprogrammed cells find and destroy cancer cells throughout the body.

Over the past few years, CAR T-cell therapy targeting a B-cell biomarker called CD19 proved very effective in initial trials for acute lymphoblastic leukemia (ALL) and some types of lymphoma, but until now, there has been little success with CAR T-cell therapies targeting other biomarkers in other types of cancer. This is one of the first clinical trials of CAR T cells targeting BCMA, which was discovered to play a role in progression of multiple myeloma in 2004.

The authors report results from the first 35 patients with relapsed or refractory multiple myeloma enrolled in this ongoing phase I clinical trial in China. First signs of treatment efficacy appeared as early as 10 days after initial injection of CAR T cells (patients received three split doses of cells over a week). Overall, the objective response rate was 100% and 33 (94%) patients had an evident clinical remission of myeloma (complete response or very good partial response) within two months of receiving CAR T cells.

To date, 19 patients have been followed for more than four months, a pre-set time for full efficacy assessment by the International Myeloma Working Group (IMWG) consensus. Of the 19 patients, 14 have reached stringent complete response (sCR) criteria, one patient has reached partial response, and four patients have achieved very good partial remission (VgPR) criteria in efficacy.

There has been only a single case of disease progression from VgPR; an extramedullary lesion of the VgPR patient reappeared three months after disappearing on CT scans. There has not been a single case of relapse among patients who reached sCR criteria. The five patients who have been followed for over a year (12-14 months) all remain in sCR status and are free of minimal residual disease as well.

Cytokine release syndrome or CRS, a common and potentially dangerous side effect of CAR T-cell therapy, occurred in 85% of patients, but it was only transient. In the majority of patients symptoms were mild and manageable. CRS is associated with symptoms such as fever, low blood pressure, difficulty breathing, and problems with multiple organs. Only two patients on this study experienced severe CRS (grade 3) but recovered upon receiving tocilizumab (an inflammation-reducing treatment commonly used to manage CRS in clinical trials of CAR T-cell therapy). No patients experienced neurologic side effects, another common and serious complication from CAR T-cell therapy.

"While it's still early, these data are a strong sign that CAR T-cell therapy can send multiple myeloma into remission," said ASCO Expert Michael S. Sabel, MD, FACS. "It's rare to see such high response rates, especially for a hard-to-treat cancer. This serves as proof that immunotherapy and precision medicine research pays off. We hope that future research builds on this success in multiple myeloma and other cancers."

The researchers plan to enroll a total of 100 patients in this clinical trial, at four participating hospitals in China. "In early 2018 we also plan to launch a similar clinical trial in the United States. Looking ahead, we would also like to explore whether BCMA CAR T-cell therapy benefits patients who are newly diagnosed with multiple myeloma," said Dr. Zhao.

This study was funded by Legend Biotech Co.

## ASCO2017特集

# EGFR遺伝子変異陽性肺がんの新たな治療の可能性(Abstract LBA8507)

## 第2世代EGFR阻害薬はEGFR遺伝子変異陽性非小細胞肺がん患者の生存期間を改善する

Second-generation EGFR inhibitor improves survival in EGFR positive non-small cell lung cancer

第III相臨床試験の結果は、上皮成長因子受容体（EGFR）遺伝子変異陽性非小細胞肺がんと新規に診断された患者に対し、新たな治療の可能性を指し示している。研究者らはアジアおよびヨーロッパの患者452人を、dacomitinibまたはゲフィチニブを投与する群にランダムに割り付けた。Dacomitinib投与群はゲフェチニブ投与群に比べ、がん進行または死亡の確率が41%低かった。無増悪生存期間はdacomitinib投与群で14.7か月であり、ゲフィチニブ投与群では9.2か月であった。しかし、副作用はdacomitinib投与群でより重篤であった。このスタディ結果は2017年American Society of Clinical Oncology年次集会で発表された。

## Full Text

Findings from a phase III clinical trial point to a potential new treatment for patients newly diagnosed with advanced, epidermal growth factor receptor (*EGFR*)-positive non-small cell lung cancer (NSCLC). Compared to the EGFR inhibitor gefitinib, one of the standard targeted medicines for this disease, second-generation EGFR inhibitor dacomitinib delayed cancer growth by a median of 5.5 months more.

The study was presented at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

Each year, about 140,000 people worldwide are diagnosed with EGFR-positive NSCLC. EGFR-positive cancers have genetic changes that lead to an overactive EGFR protein, which fuels the growth of cancer cells. EGFR tyrosine kinase inhibitors (TKI) are the standard treatment for people with newly diagnosed EGFR-positive NSCLC. This study is the first phase III head-to-head comparison of two EGFR TKIs.

"We changed the treatment paradigm for EGFR-positive lung cancer a few years ago when targeted therapy replaced chemotherapy," said lead study author Tony Mok, MD, a professor and chair of the Department of Clinical Oncology at the Chinese University of Hong Kong in Hong Kong, China. "This study shows that dacomitinib may be an even more effective treatment for these patients. However, patients should be aware of the need to deal with potential side effects when making treatment decisions."

Due to its chemical properties, dacomitinib blocks EGFR more effectively than first-generation inhibitors, such as gefinitib and erlotinib, and this explains its ability to keep tumor growth in check longer. On the other hand, this also leads to stronger suppression of the normal EGFRs in healthy tissues, causing more side effects such as skin rash, acne, and diarrhea.

In this phase III clinical trial, researchers randomly assigned 452 patients newly diagnosed with IIIB or IV, EGFR-positive NSCLC to receive dacomitinib or gefitinib. The patients were enrolled in Asia and Europe.

Patients who received dacomitinib had a 41% lower chance of cancer progression or death than those who received gefitinib. The progression-free survival was 14.7 months with dacomitinib, compared to 9.2 months with gefitinib. Longer follow up is needed to assess the median overall survival.

The most common severe (grade 3) side effects of dacomitinib were acne (in 14% of patients) and diarrhea (in 8% of patients). The dose of daconitinib was lowered in about 60% of patients due to side effects. Liver enzyme abnormalities were the most common severe (grade 3) side effect of gefitinib (in 8% of patients).

"It's been nearly 15 years since EGFR-targeted therapies were introduced, helping extend survival for thousands of patients in the time since. The second generation of these therapies is more effective, but can also cause greater side effects, so patients and their doctors will need to weigh the risks and benefits," said ASCO Expert John Heymach, MD, PhD.

"Dacomitinib is a more potent, second-generation EGFR inhibitor that shares the issue of increased side effects in the skin and gastrointestinal tract, like afatinib. In spite of this, the activity seen in this study should allow for consideration of this effective therapy in this patient population," said Dr. Mok. Another second-generation EGFR inhibitor, afatinib, is already FDA approved as an initial treatment for EGFR-positive NSCLC. Dacomitinib is not yet approved for any indication.

Pfizer and SFJ Pharmaceuticals Group have a collaborative development agreement to conduct ARCHER 1050 across multiple sites.

## ASCO2017特集

# アレクチニブは肺がんの無増悪生存期間を改善する(Abstract LBA9008)

## 新たなALK阻害剤は現在の標準治療よりも肺がんの増殖を1年以上長く停止させる

## New ALK inhibitor halts lung cancer growth more than a year longer than current standard of care

2017年American Society of Clinical Oncology年次集会で発表された第III相臨床試験の結果は、ALK融合遺伝子陽性非小細胞肺がん患者に対し、より有効な初回治療を指し示した。現在の標準治療であるクリゾチニブに比べ、新たなALK阻害剤アレクチニブは、がん増殖を期間中央値で15か月長く停止させ（無増悪生存期間中央値はアレクチニブで25.7か月、クリゾチニブで10.4か月）、重篤な副作用は少なかった。さらに、12か月後の脳転移率はアレクチニブ治療群の方がはるかに低かった（9% vs. 41%）。

## Full Text

Findings from a phase III clinical trial point to a more effective initial treatment for patients with ALK-positive non-small cell lung cancer (NSCLC). Compared to crizotinib, the current standard of care, the newer ALK inhibitor alectinib halted cancer growth for a median of 15 months longer and caused fewer severe side effects.

The study was featured at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

"This is the first global study to compare alectinib with crizotinib in ALK-positive lung cancer and establishes alectinib as the new standard of care for initial treatment in this setting," said lead study author Alice T. Shaw, MD, PhD, Director of Thoracic Oncology at Massachusetts General Hospital Cancer Center in Boston, MA. "Alectinib was especially beneficial in controlling and preventing brain metastases, which can have a major impact on patients' quality of life."

About 5% of NSCLCs are ALK-positive, meaning they have a genetic rearrangement where the *ALK* gene is fused with another gene.

Crizotinib is the first medicine to specifically target ALK. Although the majority of patients initially benefit from crizotinib, the cancer typically starts growing again within a year. Alectinib is a more potent, next-generation inhibitor of ALK. It was initially approved in 2015 for use in patients with advanced NSCLC that worsens despite crizotinib.

In this open label clinical trial (ALEX), researchers randomly assigned 303 patients with stage IIIB or IV, ALK-positive NSCLC to receive alectinib or crizotinib. The patients had not received prior systemic therapy for advanced NSCLC.

Alectinib reduced the risk of cancer progression or death by 53% compared with crizotinib. Based on independent review, alectinib extended the median time to progression by about 15 months (median progression-free survival was 25.7 months with alectinib and 10.4 months with crizotinib).

"Nobody imagined it would be possible to delay advanced lung cancer progression by this much. Most targeted therapies for lung cancer are associated with a median progression-free survival of roughly 12 months," said Dr. Shaw.

While both treatments cross the blood-brain barrier, alectinib was more effective in preventing brain metastases than crizotinib, because it can better penetrate into the brain. At 12 months, the incidence of brain metastases was much lower with alectinib than with crizotinib (9% vs. 41%).

Overall, severe side effects were less common with alectinib than with crizotinib, occurring in 41% vs. 50% of patients. The most common side effects of alectinib were fatigue, constipation, muscle aches, and swelling, whereas crizotinib caused gastrointestinal problems and liver enzyme abnormalities.

"The fact that this second-generation targeted treatment halted advanced lung cancer growth for more than two years while preventing brain metastases is a remarkable result in this difficult disease," said ASCO Expert John Heymach, MD, PhD. "Thanks to this advance, we are on the road to helping these patients live longer and better."

The researchers will continue to follow patients on this study to see if those treated with alectinib live longer than those treated with crizotinib. Meanwhile, several ongoing clinical trials are comparing other next-generation ALK inhibitors to crizotinib in the first-line setting.

This study was funded by F. Hoffmann-La Roche.

## ASCO2017特集

# 浸潤性乳がんのリスクを低下させる (Abstract LBA500)

## PERTAIN：第2のHER2阻害薬を上乗せすることで、一部の女性において浸潤性乳がんのリスクが低下する可能性がある

## PERTAIN: Adding a second HER2 blocker may lower risk of invasive breast cancer for some women

HER2陽性乳がん患者4,805人を対象とした第III相PERTAIN臨床試験の結果、術後の標準治療トラスツズマブに第2の抗HER2薬ペルツズマブを上乗せすることで、そのベネフィットはわずかではあるが、有効である可能性が示唆された、と2017年American Society of Clinical Oncology年次集会で発表された。トラスツズマブにペルツズマブを上乗せすることで、トラスツズマブ単独に比べ、3年後の浸潤性乳がんへの進展が19%低下した。追跡期間中央値約4年の時点で、浸潤性乳がんに進展した患者はペルツズマブ群の171人（7.1%）に対し、プラセボ群では210人（8.7%）であった。

## Full Text

A phase III clinical trial of 4,805 women with HER2-positive breast cancer suggests adding a second HER2 targeted medicine, pertuzumab, to standard of care trastuzumab after surgery may help, although the benefit is modest.

The study, known as PERTAIN, was featured at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

At an early follow up of three years, 93.2% of women who received trastuzumab alone had not developed invasive disease compared with 94.1% of those who received pertuzumab and trastuzumab, a difference of 1%. While the prognosis for patients who receive standard of care trastuzumab is already favorable, patients in the study who received pertuzumab and trastuzumab had a 19% lower chance of developing invasive breast cancer than those who received trastuzumab alone.

Invasive breast cancer begins in the milk ducts or glands and spreads into surrounding tissue. From there it can spread to nearby lymph nodes and beyond. Invasive breast cancer is therefore much more difficult to treat than non-invasive cancer.

"Women with HER2-positive breast cancer used to have a worse prognosis than those with HER2-negative cancer, but the advent of HER2-targeted therapy changed the outlook for these women," said lead study author Gunter von Minckwitz, MD, PhD, President of the German Breast Group in Neu-Isenburg, Germany. "Our early findings suggest that we may be able to further improve outcomes for some women by adding a second HER2-targeted treatment, without increasing risk for serious side effects."

While trastuzumab targets only HER2, pertuzumab blocks HER2 and HER3. Using both antibodies establishes a more complete blockade of cancer cell growth signals and may lower the chance of treatment resistance. The authors estimate that about 8% of all patients diagnosed with breast cancer have early, HER2-positive disease and may benefit from this adjuvant therapy.

Following mastectomy or lumpectomy, nearly 5,000 patients with HER2-positive, early breast cancer were randomly assigned to receive standard adjuvant chemotherapy for 18 weeks plus one year of either trastuzumab and placebo or trastuzumab and pertuzumab. The study did not include patients with very small tumors (less than 1 cm across), as those patients could be treated with only chemotherapy (without the need for a HER2 blocker).

Overall, 63% of patients had node-positive disease, and 36% had hormone receptor-negative disease. There were similar proportions of patients with either disease characteristic in the two treatment groups.

The addition of pertuzumab to trastuzumab lowered the chance of developing invasive breast cancer by 19% compared to trastuzumab alone. At a median follow up of almost 4 years, 171 (7.1%) patients in the pertuzumab group had developed invasive breast cancer, compared to 210 (8.7%) patients in the placebo group.

At 3 years, an estimated 94.1% of patients in the pertuzumab group were free of invasive breast cancer, compared to 93.2% of patients in the placebo group. The benefit from pertuzumab appeared slightly greater among patients with node-positive disease – the three-year invasive disease-free survival rate was 92% with pertuzumab vs. 90.2% with placebo. In contrast, in the patients with node-negative cancer, invasive disease-free survival rate was not influenced by pertuzumab at this early point of analysis.

"These are very early results, but given that the absolute benefit from adding pertuzumab was modest, we should consider using it primarily in women with the highest risk – those with node-positive and hormone receptor-negative breast cancer," said Dr. von Minckwitz.

The rates of serious side effects were low and similar in both groups – heart failure or heart-related death occurred in 0.7% of patients in the pertuzumab group and in 0.3% of patients in the placebo group. Severe diarrhea was more common with pertuzumab, occurring in 9.8% of patients, compared to 3.7% of those who received placebo.

"The introduction and success of HER2 targeted treatment was a turning point in breast cancer care," said ASCO Expert Harold J. Burstein, MD, PhD, FASCO. "It's promising that some women in this study benefited more from treatment with two HER2-targeted therapies rather than one, but it's clear this approach may not be advantageous for women with a lower risk for recurrence."

The researchers will continue following patients to explore potential long-term benefits of pertuzumab. Meanwhile, they are exploring tumor samples collected in this study for biomarkers that may help predict which patients benefit from the addition of pertuzumab.

"We also need more research to determine the optimal duration of adjuvant therapy. It is possible that patients may not need a full year of treatment after surgery; six months may be enough," said Dr. von Minckwitz.

This study was funded by Hoffmann-La Roche Ltd.

## ASCO2017特集

# 新規診断転移性前立腺がんにおける予後の改善 (Abstract LBA3)

## LATITUDE：アビラテロンは転移性前立腺がんの増殖を18か月遅延させ、生存期間を延長する

## LATITUDE: Abiraterone delays metastatic prostate cancer growth by 18 months and extends survival

高リスク、転移性前立腺がんと新規診断された患者に対し、アビラテロンとプレドニゾンを標準ホルモン療法に併用することで死亡リスクを38%低下させる、と2017年American Society of Clinical Oncology年次集会で取り上げられた。アンドロゲン遮断療法の施行歴のない男性1,200人を対象とした多国間共同第III相臨床試験LATITUDEにおいて、アビラテロンは増悪までの期間中央値を14.8か月から33か月に、2倍以上増加させた。全生存期間中央値はアビラテロン群では未到達、プラセボ群では34.7か月であった。

Full Text

Adding abiraterone acetate plus prednisone to standard hormonal therapy for men newly diagnosed with high-risk, metastatic prostate cancer lowers the chance of death by 38%. In a phase III clinical trial of 1,200 men, abiraterone also more than doubled the median time until the cancer worsened, from 14.8 months to 33 months.
The study was featured at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

"There is a large unmet need to improve treatment for men with newly diagnosed metastatic cancer, who die of the disease within less than five years on average," said lead study author Karim Fizazi MD, PhD, head of the Department of Cancer Medicine at Gustave Roussy, University Paris-Sud in Villejuif, France. "The benefit from early use of abiraterone we saw in this study is at least comparable to the benefit from docetaxel chemotherapy, which was observed in prior clinical trials, but abiraterone is much easier to tolerate, with many patients reporting no side effects at all."

Prostate cancer growth is fueled by testosterone. Androgen deprivation therapy, or ADT, is active against prostate cancer by preventing testicles from making testosterone. Despite ADT, the adrenal glands and prostate cancer cells continue making small amounts of androgens. Abiraterone stops production of testosterone throughout the body by blocking an enzyme that converts other hormones to testosterone.

LATITUDE is a multinational, randomized placebo-controlled phase III clinical trial of men with newly diagnosed, high-risk metastatic prostate cancer who had not previously received ADT. All patients had at least two of three risk factors: Gleason score of 8 or more, 3 or more bone metastases, or 3 or more visceral metastases.

The patients were randomly assigned to receive ADT plus abiraterone and prednisone or ADT plus placebo. Corticosteroid prednisone is routinely given with abiraterone to manage certain side effects of abiraterone, such as low potassium or high blood pressure.

At a median follow up of 30.4 months, men who received abiraterone had a 38% lower risk of death than those who received placebo. The median overall survival had not yet been reached in the abiraterone group and was 34.7 months in the placebo group. Abiraterone was also associated with a 53% lower risk of the cancer worsening than the placebo and resulted in cancer growth being delayed by a median of 18.2 months.

Several severe side effects were more common with abiraterone acetate and prednisone than placebo: high blood pressure (in 20% vs. 10% of men), low potassium level (10.4% vs 1.3%), and liver enzyme abnormalities (in 5.5% vs. 1.3% of men).

"We need to be cautious when using abiraterone in men who have an increased risk for heart problems, such as those with diabetes," said Dr. Fizazi.

"For men who are diagnosed with advanced prostate cancer, treatment has evolved into more effective approaches, first with chemotherapy and now with abiraterone," said Sumanta Kumar Pal, MD, ASCO Expert. "This is good news because using abiraterone could help many people live longer with fairly few additional side effects."

"We had been treating metastatic prostate cancer the same way for 70 years until docetaxel chemotherapy was shown to improve survival in 2015, and now in 2017 we show abiraterone is also helping patients live longer," said Dr. Fizazi. "The next step is to see if adding abiraterone on top of docetaxel offers further benefit," a study which is currently ongoing in Europe.

This study was funded by Janssen Research and Development.

## ASCO2017特集

# Larotrectinibは多様な腫瘍タイプに効果的である (Abstract LBA2501)

## 新薬は小児および成人のがん種を問わず、持続的な有効性を示す

## New drug shows durable efficacy across diverse pediatric and adult cancers

分子標的、経口、がんの発生部位に関係なく変異の型に基づく、初めての療法ー患者の年齢やがんの種類にかかわらず有効な薬剤ーが開発されたようである。Larotrectinibは、がん細胞内のTRK遺伝子が他の遺伝子と融合する際の遺伝子異常による産物であるトロポミオシン受容体キナーゼ(TRK)融合蛋白質の、選択的阻害薬である。17の異なる型の進行がんを有する成人および小児を対象とした臨床試験において、larotrectinibによる治療は76%の患者で奏効を認めた。Larotrectinibに対する奏効は持続的であり、79%が治療開始後12か月の時点で持続していた。このスタディ結果は2017年American Society of Clinical Oncology年次集会で取り上げられた。

## Full Text

Scientists may have developed the first targeted, oral, tumor-type agnostic therapy – a cancer medicine that works comparably well across many kinds of cancer, regardless of patient age. In clinical trials of adults and children with 17 different types of advanced cancer, larotrectinib treatment resulted in responses in 76% of patients. Response to larotrectinib has been durable, with 79% of responses ongoing 12 months after starting treatment.

The study was featured at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

Larotrectinib is a selective inhibitor of tropomyosin receptor kinase (TRK) fusion proteins, which are a product of a genetic abnormality when a *TRK* gene in a cancer cell fuses with one of many other genes. It is estimated that this abnormality occurs in about 0.5% – 1% of many common cancers, but in greater than 90% of certain rare cancers, such as salivary gland cancer, a form of juvenile breast cancer, and infantile fibrosarcoma.

"*TRK* usions are rare, but occur in many different cancer types. In fact, at this point it is hard to find a cancer type where *TRK* fusions have not been reported," said lead study author David Hyman, MD, Chief of Early Drug Development at Memorial Sloan Kettering Cancer Center in New York. "These findings embody the original promise of precision oncology: treating a patient based on the type of mutation, regardless of where the cancer originated. We believe that the dramatic response of tumors with *TRK* fusions to larotrectinib supports widespread genetic testing in patients with advanced cancer to see if they have this abnormality."

Researchers analyzed data from 55 patients with *TRK* fusions enrolled in three ongoing phase I and phase II clinical trials. All patients (12 children and 43 adults) had locally advanced or metastatic cancer, including colon, lung, pancreatic, thyroid, salivary, and gastrointestinal cancers, as well as melanoma and sarcoma.

"This dataset, subject to independent central radiology review, will be submitted to FDA for larotrectinib's regulatory approval. If approved, larotrectinib could become the first therapy of any kind to be developed and approved simultaneously in adults and children, and the first targeted therapy to be indicated for a molecular definition of cancer that spans all traditionally-defined types of tumors," said Dr. Hyman.

In the first 50 patients with 17 different cancer types who have been on the study long enough to have at least two scans, 38 (76%) of these patients had a response. Of those, three patients with pediatric sarcomas previously not amenable to surgery went on to receive potentially curable surgery after larotrectinib shrank the tumors.

The median duration of treatment response has not yet been reached, as the majority of patients are still responding to treatment. At 12 months into treatment, 79% of responding patients remain progression free. To date, the longest duration of treatment response has been 25 months and is ongoing.

The most common side effects were fatigue and mild dizziness, which was expected as the normal TRK protein has a role in controlling balance. No patients needed to stop treatment due to side effects.

"Because larotrectinib was designed to target only TRK, it has been very well tolerated and does not cause many of the side effects associated with chemotherapy and multi-targeted therapy," said Dr. Hyman.

"Though the study is small and early, it demonstrates compelling evidence that may pave the way for a new class of drugs for rare tumors that could inform the future of precision medicine," said Sumanta Kumar Pal, MD, ASCO Expert.

*TRK* fusions were first discovered in colon cancer in 1982, but only recent technological advances, particularly next-generation sequencing (NGS), have enabled systematic detection of this abnormality. To date, scientists have found more than 50 different partner genes that fuse with one of three *TRK* genes (NTRK 1, 2, and 3).

*TRK* fusions arise early in cancer development and remain present as tumors grow and spread. The abnormal TRK fusion proteins are constantly "turned on," sending cancer cells signals to keep growing and dividing. "*TRK* fusions are like an ignition switch for cancer," said Dr. Hyman.

Although there are other experimental treatments that block TRK along with other proteins, larotrectinib is the first to selectively block TRK. This characteristic improves potency of the drug, while lowering side effects.

The researchers have identified what they believe to be the primary means by which tumors may grow resistant to larotrectinib, and they are studying another TRK-targeted therapy, LOXO-195, for the treatment of patients with cancer that regrows after initially responding to larotrectinib.

This study was funded by Loxo Oncology, Inc.

## ASCO2017特集

# 短期および長期の放射線治療は患者の可動性を維持するのに役立つ(Abstract LBA10004)

## 転移性脊髄圧迫症状の治療には単回照射で十分である

## Single radiation treatment sufficient to treat metastatic spinal cord compression symptoms

転移性がん患者において一般的に認められる脊髄圧迫は、QOL損失の主要な原因である。放射線治療は疼痛やその他の症状を緩和するのに広く用いられているが、標準的な推奨スケジュールはなく、方法も様々である。2017年American Society of Clinical Oncology年次集会で取り上げられた第III相臨床試験の結果、単回照射療法がまる1週間の放射線療法と同様に有効であることが示された。8週後に、単回照射を受けた患者の69.5%、および5回照射を受けた患者の73.3%は同様の歩行状態を有し、短期および長期の放射線療法のいずれもが患者の可動性を維持するのに役立つことが示された。

### Full Text

A common complication in people with metastatic cancer, spinal cord compression is a major detriment to quality of life. Radiation treatment is widely used to relieve pain and other symptoms, but there is no standard recommended schedule, and approaches currently vary. Findings from a phase III clinical trial show that a single radiation treatment is as effective as a full week of radiation.

The study was featured at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

"Our findings establish single-dose radiotherapy as the standard of care for metastatic spinal canal compression, at least for patients with a short life expectancy," said lead study author Peter Hoskin, MD, FCRP, FRCR, an oncologist at the Mount Vernon Cancer Centre in Middlesex, United Kingdom. "For patients, this means fewer hospital visits and more time with family."

Many patients with advanced solid tumors develop bone metastases, and up to 10% of all patients with cancer will have metastatic spinal cord compression.

The study enrolled 688 patients with metastatic prostate (44%), lung (18%), breast (11%), and gastrointestinal cancers (11%). The median age was 70 years, and 73% were male. The researchers randomly assigned patients to receive external beam spinal canal radiation therapy either as a single dose of 8 Gy or as 20 Gy split in five doses over five days.

The primary endpoint of the study was ambulatory status, measured on a four-point scale:

Grade 1: Able to walk normally
Grade 2: Able to walk with walking aid (such as cane or walker)
Grade 3: Has difficulty walking even with walking aids
Grade 4: Dependent on wheelchair

At study entry, 66% of patients had ambulatory status 1 to 2.

At eight weeks, 69.5% of patients who received single-dose radiation therapy and 73.3% of those who received five doses had ambulatory status 1 to 2, showing that both shorter- and longer-course radiation treatments helped patients stay mobile. The median overall survival was similar in the two groups – 12.4 weeks with single dose vs. 13.7 weeks with five doses (the difference was not statistically significant). The proportion of patients with severe side effects was similar in the two groups (20.6% vs. 20.4%), but mild side effects were less common in the single-dose group (51% vs. 56.9%).

Prof. Hoskin emphasized that early recognition and prompt treatment of spinal cord compression symptoms are critical to achieve best results with radiation therapy.

"Longer radiation may be more effective for preventing regrowth of metastases in the spine than single-dose radiation. Therefore, a longer course of radiation may still be better for patients with a longer life expectancy, but we need more research to confirm this," said Prof. Hoskin.

"Spinal cord compression is a debilitating condition that many patients with advanced cancer experience. Until now, patients often had to spend multiple days traveling back and forth to undergo radiation treatments. This study means that without compromising care, we can help patients have more time to focus on the things they enjoy instead of on the cancer," said Joshua A. Jones, MD, MA, ASCO Expert.

Patients with metastatic breast cancer were under-represented in this clinical trial, as were younger patients. For certain patients with spinal cord compression, surgery instead of or in addition to radiation therapy may be recommended.

This study was funded by Cancer Research UK.

## ASCO2017特集

# 胸膜中皮腫に対する初めての免疫療法の兆しが見える(Abstract LBA8507)

## MAPS-2：早期研究の結果、免疫療法は悪性胸膜中皮腫を有効に治療する可能性があることが示唆された

## MAPS-2: Early research suggests immunotherapy may effectively treat malignant pleural mesothelioma

フランスにおいて現在進行中のMAPS-2と呼ばれる第II相臨床試験の早期結果から、免疫療法が再発後悪性胸膜中皮腫の増殖を遅延させる可能性があることが示された。12週後にがんが増悪しなかったのは、nivolumab投与群では44%であり、nivolumabとipilimumabの併用投与群では50%であった。平均追跡期間10.4か月後、無増悪生存期間中央値は、nivolumab単独群で4か月であり、nivolumabとipilimumab併用群で5.6か月であった。これらの結果は、この状況における免疫チェックポイント阻害薬の使用を支持するものである。このスタディ結果は2017年American Society of Clinical Oncology年次集会で取り上げられた。

## Full Text

Malignant pleural mesothelioma or MPM is a rare cancer, but its incidence has been rising. This cancer is usually associated with asbestos exposure, and patients have a median life expectancy of only 13-15 months. All patients relapse despite initial chemotherapy, more than 50% of them within six months after stopping treatment. There are currently no effective therapeutic options for patients with MPM.

Early findings from an ongoing phase II clinical trial in France, MAPS-2, show that immunotherapy may slow the growth of MPM after relapse. At 12 weeks, cancer had not worsened in 44% of patients who received nivolumab and in 50% of those who received nivolumab with ipilimumab.

The study was featured at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

"Our findings suggest that immunotherapy may provide new hope to patients with relapsed mesothelioma," said lead study author Arnaud Scherpereel, MD, PhD, head of the Pulmonary and Thoracic Oncology Department at the University Hospital (CHU) of Lille in Lille, France. "This randomized phase II trial may be enough to support the use of immune checkpoint inhibitors in this setting, but it is too early to conclude whether nivolumab alone or the combination of nivolumab and ipilimumab is better."

This multi-center clinical trial enrolled 125 patients with advanced MPM who had received up to two prior treatments, including standard platinum-based chemotherapy. The majority of patients (80%) were male, and the median age was 72 years. The patients were randomly assigned to treatment with nivolumab alone or nivolumab with ipilimumab until the cancer worsened; 70% of patients received at least 3 cycles of either treatment.

The authors report results from the first 108 patients treated on the study. The disease control rate or DCR, defined as the percentage of patients in which cancer either shrank or did not grow, was 44% among the patients who received nivolumab only and 50% among those who received nivolumab with ipilimumab (the 12-week DCR for all treatments previously tested in relapsed MPM was less than 30%). Tumors shrank in 17% of patients treated with nivolumab and 26% of those treated with nivolumab and ipilimumab.

After a mean follow-up of 10.4 months of the 125 patients, the median progression-free survival time was 4 months with nivolumab alone and 5.6 months with nivolumab and ipilimumab. The median overall survival was 10.4 months in the nivolumab group and had not reached in the nivolumab with ipilimumab group. Mature quality-of-life data are not yet available.

The side effects were rather mild overall with the most common being thyroid problems, colon inflammation, and skin rash. Severe side effects were more common in the nivolumab plus ipilimumab group (18% vs. 10%), in which three treatment-related deaths occurred.

With 125 patients, MAPS-2 is the largest clinical trial of immune checkpoint inhibitors in mesothelioma to date, according to the authors. Many ongoing clinical trials are exploring nivolumab and other immune checkpoint inhibitors as second- or third-line treatments for MPM. In addition, several larger clinical trials investigating immune checkpoint inhibitors as initial therapy for MPM are already under way.

"Mesothelioma cells build a protective tumor microenvironment to shield themselves against the immune system's attacks and even act against anti-tumor immune response," said Dr. Scherpereel. "Therefore, therapies that shift the tumor microenvironment from a state of immune suppression to one of immune activation may hold promise in MPM."

"We're seeing a second wave of immunotherapy with expansion of its use in more cancer types. This study shows that immunotherapy may represent an effective new treatment approach for mesothelioma, a disease for which we've long had too little to offer," said ASCO Expert Michael S. Sabel, MD, FACS. "These results will serve as a building block to improve the outlook for patients with this cancer."

Malignant pleural mesothelioma is a cancer that begins in the lining of the lungs. This cancer is associated with occupational exposure to asbestos, which causes chronic inflammation. It typically takes 30 to 40 years from asbestos exposure to development of MPM.

The peak of asbestos use was between the 1960s and the 1980s. Although use of asbestos has been banned in the United States and many European countries, asbestos is still being used and extracted in many developing countries. "For these reasons, we expect to continue to see growing incidence of mesothelioma in the coming decades," said Dr. Scherpereel.

This study was funded by Bristol-Myers Squibb.

## ASCO2017特集

# 心理的介入はがん患者の苦悩を緩和する (Abstract LBA10001)

## 短期間の心理的介入は、がん患者のうつ症状を軽減し心理的ウェルビーイングを改善する

## Brief psychological intervention reduces depression and improves psychological well-being in cancer patients

進行がん患者305人を対象としたランダム化臨床試験の結果、Managing Cancer And Living Meaningfully (CALM) と呼ばれる短期間の心理的介入が、患者や家族が進行がんの実際的な感情的損害を処理するのに役立つことが示唆された。3か月後、CALMを受けた患者の52%においてうつ症状が臨床的に重要な軽減を示したのに対し、通常のケアを受けた患者におけるその割合は33%であった。CALMを受けた患者はまた、3か月後および6か月後の心理的ウェルビーイングが改善しており、エンド・オブ・ライフへの準備がよりできていた。このスタディ結果は2017年American Society of Clinical Oncology年次集会で発表された。

## Full Text

Advanced cancer triggers enormous distress and brings challenges that can seem overwhelming. Yet, most cancer centers lack systematic approaches to help patients and families manage the practical and emotional toll of advanced cancer.

Findings from a randomized clinical trial of 305 patients with advanced cancer suggest that a brief psychological intervention, called Managing Cancer And Living Meaningfully (CALM), could help fill this need. At three months, 52% of patients who received CALM had a clinically important reduction in depressive symptoms, compared to 33% of patients who received usual care. Patients who received CALM also had improved psychological well-being at three and six months and were more prepared for the end of life.

The study was presented at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

"This brief talking therapy helps patients facing advanced cancer, and their loved ones, sustain what is meaningful in their life despite its limitations, and face the future," said lead study author Gary Rodin, MD, Head of the Department of Supportive Care at the Princess Margaret Cancer Centre in Toronto, Canada. Dr. Rodin developed CALM with colleagues Sarah Hales, MD, PhD, and Chris Lo, PhD, and notes that training is underway to help expand the approach to cancer centers worldwide.

"It provides time and space for reflection on the threats and challenges associated with advanced cancer, the experience of a secure base in the therapeutic relationship, and support for the regulation and modulation of emotions," said Dr. Rodin.

CALM is a psychological intervention developed specifically for patients with advanced cancer. It consists of three to six 45- to 60-minute sessions delivered over three to six months by trained health care professionals, such as social workers, psychiatrists, psychologists, palliative care doctors and nurses, and oncologists. Family members or partners are invited to attend the CALM sessions. The sessions focus on four broad domains:

- Symptom control, medical decision-making, and relationships with health care providers
- Changes in self-concept and personal relationships
- Spiritual well-being and the sense of meaning and purpose in life
- Future-oriented concerns, hope, and mortality

"CALM is distinct from other interventions in that it is meant to help patients live with advanced disease, rather than just prepare them for the end of life, and in that it is focused on both the practical and the more existential concerns faced by those with advanced cancer," stated Dr. Rodin.

In this study, 305 patients with advanced cancer were recruited at a comprehensive cancer center in a large urban area in Canada. The patients were randomly assigned to CALM therapy plus usual care or to usual care alone (control group).

Participants in the control group received routine oncology treatment and follow-up, as well as a clinic-based distress screening. About one-third of patients in the control group received some specialized psychosocial oncology care, but less than 10% received any structured or semi-structured psychotherapy.

Researchers measured depressive symptoms (using the Patient Health Questionnaire-9) and other outcomes at study entry (baseline), and at three (primary endpoint) and six months (trial endpoint).

Compared to patients in the usual care group, patients in the CALM intervention group reported less severe depressive symptoms at three months, and the difference between the two groups was even greater at six months. In terms of clinical impact, for participants with depressive symptoms of at least subthreshold severity (clinically significant and associated with impairment, but which do not meet full criteria for the diagnosis of a major depressive disorder) at study entry, a greater proportion of those receiving CALM than those receiving usual care had a clinically important reduction in severity of symptoms, both at three months (52% CALM vs. 33% usual care) and six months (64% CALM vs. 35% usual care).

CALM also helped prevent depression in 137 patients who did not have depressive symptoms at study entry. At three months, only 13% of such patients who received CALM developed depressive symptoms (of at least subthreshold severity) versus 30% of those who received usual care.

At both three and six months, the CALM group reported greater preparation for end of life, greater opportunity to talk about concerns about the future and to be less frightened, and a greater ability to express and manage feelings. At six months these effects were strengthened, and the CALM group also felt more able to understand their cancer experience, deal with changes in relationships as a result of cancer, explore ways of communicating with their health care team and family, and clarify their values and beliefs.

"A diagnosis of advanced cancer weighs heavily on patients and families, and this study gives a new approach that can ease this burden," said ASCO Expert, Don S. Dizon, MD, FACP. "As oncologists, our job isn't just to treat our patients' physical symptoms. It's also to connect them with other forms of support to help them cope and plan for the future."

The next steps for this research will include enhancing understanding of the therapeutic process of CALM, the optimal approaches to training clinicians in the intervention, the refinement of measurement tools that best capture the clinical outcomes, and the effectiveness of implementation in diverse clinical settings and geographic regions.

This study was funded by the Canadian Institutes of Health Research.

## ASCO2017特集

# 乳がん罹患後の妊娠は再発率を上昇させない（Abstract LBA10066）

## 妊娠を考えている乳がん患者にとって心強い情報

## Reassuring information for women with breast cancer who are contemplating pregnancy

1,200人の女性を対象としたレトロスペクティブ研究の結果から、妊娠を考えている乳がん既往者に安心が届けられた、と2017年American Society of Clinical Oncology年次集会で報告された。がんと診断されてからの追跡期間中央値10年ののち、無病生存期間は妊娠した女性と妊娠しなかった女性とで、エストロゲン受容体（ER）の発現状況に関係なく、差がなかった。二次解析の結果、妊娠し出産または中絶、乳がんの診断後2年未満に妊娠または2年超経過してから妊娠、母乳育児をしたか否かで、無病生存期間に差はなかった。

## Full Text

Findings from a retrospective study of 1,200 women provide reassurance to breast cancer survivors who are contemplating pregnancy. In the study, women who became pregnant after an early breast cancer diagnosis, including those with estrogen receptor (ER)-positive tumors, did not have a higher chance of cancer recurrence and death than those who did not become pregnant.

The study was featured in a presentation at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

Breast cancer is the most common cancer in women of reproductive age. Taking into account current trends toward delaying childbearing, breast cancer in young women may occur before the completion of reproductive plans. Although half of young women with newly diagnosed breast cancer report interest in having children, less than 10% become pregnant after treatment. In fact, of all cancer survivors, breast cancer survivors are the least likely to have a baby after diagnosis.

Doctors and patients have long been concerned that pregnancy could increase the chance of breast cancer recurrence, particularly for women with ER-positive disease. Because ER-positive breast cancer is fueled by estrogen, the fear is that hormone levels during pregnancy could coax any occult cancer cells – those that may remain in the body after treatment – to grow.

Another concern regarding pregnancy in women with ER-positive cancer is the need to interrupt adjuvant hormone therapy before trying to achieve a pregnancy. Such hormone therapy helps prevent cancer recurrence, and it is recommended that women receive it for at least 5 years and in some cases up to 10 years.

"Our findings confirm that pregnancy after breast cancer should not be discouraged, even for women with ER-positive cancer," said lead study author Matteo Lambertini, MD, a medical oncologist and ESMO fellow at the Institut Jules Bordet in Brussels, Belgium. "However, when deciding how long to wait before becoming pregnant, patients and doctors should consider each woman's personal risk for recurrence, particularly for women who need adjuvant hormone therapy."

With 1,207 patients, this is the largest study to investigate the safety of pregnancy after breast cancer and the only to address this question specifically in women with ER-positive breast cancer, according to the authors.

This study included women who were diagnosed with non-metastatic breast cancer before 2008, under the age of 50. The majority (57%) had ER-positive cancer, and more than 40% had poor prognostic factors, such as large tumor size and cancer spread to the axillary lymph nodes. Among the 1,207 patients included in the study, 333 of the women became pregnant, and 874 did not (as per the case-control study design, researchers matched each patient who became pregnant with three patients who had similar cancer characteristics but did not become pregnant).

The median time from diagnosis to conception was 2.4 years. Women with ER-positive breast cancer tended to achieve pregnancy later than those with ER-negative disease; 23% of patients with ER-positive disease had a pregnancy beyond 5 years from diagnosis as compared to 7% in those with ER-negative tumors.

After a median follow-up of about 10 years from cancer diagnosis, there was no difference in disease-free survival between women who became pregnant and those who did not, irrespective of ER status. Secondary analyses showed that there was no difference in disease-free survival compared to women who did not become pregnant, irrespective of whether women completed the pregnancy or had an abortion, became pregnant less than two years or more than two years from breast cancer diagnosis, and whether patients had breastfed.

Among survivors of ER-positive cancer, there was also no difference in overall survival between women who became pregnant and those who did not. Survivors of ER-negative breast cancer who became pregnant had a 42% lower chance of dying than those who did not become pregnant.

"It's possible that pregnancy could be a protective factor for patients with ER-negative breast cancer, through either immune system mechanisms or hormonal mechanisms, but we need more research into this," said Dr. Lambertini.

Although there was limited data on breastfeeding in this study (64 patients, with 25 women who reported having breastfed their newborn), the results suggest that breastfeeding is feasible, even after breast surgery.

"These data provide reassurance to breast cancer survivors that having a baby after a breast cancer diagnosis may not increase the chance of their cancer coming back. For many young women around the world who want to grow and expand their families, it's very comforting news," said Erica L. Mayer, MD, MPH, ASCO Expert.

Although large, this study had limited information on the use of assisted reproductive technologies (such as in vitro fertilization) in breast cancer survivors, and HER2 status was unknown for about 80% of the women. Further research is also needed to study the effect of pregnancy on health outcomes of women with BRCA mutations, a group that generally develops breast cancer at a younger age.
A large clinical trial (the POSITIVE study) is under way investigating the impact of interrupting adjuvant hormone therapy to allow for pregnancy in women with ER-positive breast cancer. This study will also provide further insight on the impact of reproductive technologies and breastfeeding.

This study was partly supported by grants from Les Amis de l'Institut Bordet and the European School of Oncology (ESO). The International Breast Cancer Study Group (IBCSG) study, which provided patient information for this study, was partially funded by the National Institutes of Health.

## ASCO2017特集

# 精巣腫瘍による性腺機能低下症は慢性的な健康問題と関連がある（Abstract LBA10012）

## PLATINUM：精巣腫瘍によるテストステロン低値は長期にわたる合併症と関連がある

## PLATINUM: Low testosterone levels after testicular cancer linked to long-term health complications

テストステロンが正常値の精巣腫瘍既往者に比べ、性腺機能低下症を有する精巣腫瘍既往者は広範囲に及ぶ慢性的な健康上の問題を有する可能性が高い、と2017年American Society of Clinical Oncology年次集会で発表された。Platinum Studyにおける精巣腫瘍既往者491人のうち、38%がテストステロン低値またはテストステロン補充療法中であった。テストステロン低値の精巣腫瘍既往者は、高コレステロール、高血圧、勃起不全、糖尿病、および不安や抑うつに対する薬剤を内服している割合が高かった（それぞれ20% vs. 6%、19% vs. 11%、20% vs. 12%、6% vs. 3%、15% vs. 10%）。

## Full Text

In a large study, 38% of 491 testicular cancer survivors had low testosterone levels, known as hypogonadism. Compared to survivors with normal testosterone levels, survivors with hypogonadism were more likely to have a range of chronic health problems, including high blood pressure, diabetes, erectile dysfunction, and anxiety or depression.

The study was presented at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

"Because testicular cancer occurs at a young age and is highly curable, many survivors may live upwards of five decades," said lead study author Mohammad Issam Abu Zaid, MBBS, an Assistant Professor of Medicine at the Indiana University School of Medicine in Indianapolis, Indiana. "Our findings underscore the need for clinicians to assess testicular cancer survivors for physical signs or symptoms of hypogonadism and to measure testosterone levels in those who do."

Low testosterone can be present at the time of a testicular cancer diagnosis, or it can develop as a side effect of surgery or chemotherapy. While it has been known that low testosterone occurs in a significant proportion of testicular cancer survivors, this is one of the first studies to examine its relationship with long-term health complications in North American patients.

This analysis comes from the first 491 patients enrolled in The Platinum Study, which aims to be the largest study of testicular cancer survivors worldwide, with over 1,600 survivors already enrolled and still actively recruiting. All patients received chemotherapy and were younger than 55 when they were diagnosed with cancer. The median age at clinical evaluation was 38 years.

The goal of the Platinum Study is to follow the lifelong health of men who received cisplatin chemotherapy for testicular cancer. Researchers collect health information through comprehensive questionnaires and blood samples, as well as basic measurements like blood pressure and a hearing test. The study also aims to identify genes that may raise the chance of developing long-term health problems, such as nerve damage and hearing loss.

Among the 491 survivors, 38% had a low testosterone level or were on testosterone replacement therapy. Being overweight or obese was associated with a higher chance of having low testosterone, as was older age. The researchers also found a genetic abnormality (in the sex hormone binding globulin gene) that appears to predispose some men to low testosterone, but this needs to be confirmed in larger studies. Survivors participating in vigorous physical activity appeared to have higher levels of testosterone.

Compared to survivors with normal testosterone, testicular cancer survivors with low testosterone were more likely to take medicine for:

- High cholesterol (20% vs. 6%)
- Hypertension (19% vs. 11%)
- Erectile dysfunction (20% vs. 12%)
- Diabetes (6% vs. 3%)
- Anxiety or depression (15% vs. 10%)

"Some of these health problems have been previously linked to low testosterone levels among men in the general population and in a few studies of testicular cancer survivors, but this study is one of the most comprehensive to date – we are looking at 15 different health conditions," said Dr. Abu Zaid.

"We can now cure 19 out of 20 cases of testicular cancer, but a significant number of testicular cancer survivors have low testosterone, and that can affect other aspects of their health. Based on this study and others, clinicians should ask testis cancer survivors whether they have symptoms of low testosterone and should watch for signs of associated health problems," said Timothy D. Gilligan, MD, MSc, ASCO Expert.

The researchers will continue to follow this group of survivors and expand the analysis to the entire cohort of 1,600 survivors enrolled on the study to date. They also plan to eventually enroll a group of survivors who were cured with surgery only, to parse out the effects of surgery vs. chemotherapy on the development of adverse health outcomes and further examine testosterone levels.

The study was funded by the National Cancer Institute, National Institutes of Health.

## ASCO2017特集

# 心理的介入はがん再発の恐怖を軽減する（Abstract LBS10000）

## 心理的介入はリラクゼーショントレーニングよりも、がん既往者の再発に対する恐怖を緩和する

## Psychological intervention relieves cancer survivors fear of recurrence better than relaxation training

すべてのがん患者の約50%および若年乳がん既往者の約70%が、中等度から重度の再発の恐怖を報告している。第II相ランダム化臨床試験において、研究者らは、再発の恐怖が重度であると報告したステージI-IIIの乳がん、大腸がん、または悪性黒色腫の既往者222人を、Conquer Fear 心理的介入またはリラクゼーショントレーニング（コントロール群）にランダムに割り付けた。その結果、Conquer Fear は介入直後、3か月後および6か月後の再発の恐怖を大幅に軽減した。全般性不安障害、がん特異的苦悩、およびQOLは心理的介入群がリラクゼーショントレーニングよりも優れていた。このスタディ結果は2017年American Society of Clinical Oncology年次集会で取り上げられた。

## Full Text

About 50% of all cancer survivors and 70% of young breast cancer survivors report moderate to high fear of recurrence. The fear can be so distressing that it negatively affects medical follow-up behavior, mood, relationships, work, goal setting, and quality of life. Yet, interventions to alleviate this fear are lacking.

In a phase II randomized clinical trial, a psychological intervention called Conquer Fear substantially lowered fear of recurrence immediately after the intervention, and three and six months later. General anxiety, cancer-specific distress, and quality of life were better in the psychological intervention group immediately after therapy.

The study was featured at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

"The reduction in fear of recurrence in the psychological intervention group was large enough to improve survivors' psychological and emotional wellbeing," said lead study author Jane Beith, MD, PhD, a Medical Oncologist at the University of Sydney in Australia, who developed the Conquer Fear intervention with colleagues, including psycho-oncologist Phyllis Butow, BA(Hons)Dip Ed, MClinPsych, MPH, PhD. "The majority of participants were young women with breast cancer, but we expect the intervention may be appropriate for other patients who have moderate to high fear of recurrence."

The Conquer Fear psychology intervention is based on a novel theoretical framework developed by the authors (the intervention was developed for research and is not yet used in clinical practice). Trained study therapists delivered the intervention in five 60- to 90-minute individual, face-to-face sessions over 10 weeks. Conquer Fear focuses on:

- Accepting the inherent uncertainty of whether the cancer would come back
- Teaching strategies to control worry
- Giving survivors more control over where they place their attention
- Helping them focus on what they want to get out of life
- Choosing a sensible level of cancer screening and sticking to it

Researchers randomly assigned 222 survivors of stage I-III breast cancer, colorectal cancer, or melanoma who reported high fear of recurrence to either the Conquer Fear intervention or relaxation training (control group). All survivors had completed cancer treatment two months to five years before enrolling in this study and were cancer free at the time.

Survivors in the control group received five 60-minute, individual, face-to-face relaxation sessions. The sessions were delivered over 10 weeks by trained study therapists and incorporated muscle relaxation, meditative relaxation, and visualization and quick relaxation techniques. Both groups received instructions for home-based practice.

To measure change in fear of cancer recurrence, researchers used total scores from a validated 42-item questionnaire called Fear of Cancer Recurrence Inventory or FCRI. The scores range from 0 to 168, with higher scores indicating worse fear of recurrence. Survivors completed the questionnaire at enrollment, immediately after the intervention, and three and six months later.

The average FCRI score at baseline was 82.7 in the intervention arm and 85.7 in the control arm. The primary outcome of the study, total fear-of-cancer-recurrence score, was reduced significantly more in the intervention group (by 18.1 points on average) than in the control group (by 7.6 points on average), immediately after the intervention. This represents a standardized effect size of 0.44, within the range considered clinically important.

FCRI scores continued to decrease over time, with significant difference between groups at 6 months, decreasing by 27.2 points on average in the intervention group and 17.8 points on average in the control group.

The researchers also explored other patient outcomes, including cancer-specific distress (how much someone is plagued with thoughts about cancer), general distress (anxiety, depression, and stress), and quality of life (covers independent living, physical pain, mental health, happiness, coping, relationships, and self-worth). The psychological intervention had a greater positive effect on these outcomes than relaxation training.

"The number of people surviving cancer is higher than ever before, but many survivors fear that the cancer will return even long after they have finished treatment. The hope is that the positive results of this fear-reducing intervention will pave the way for making it more widely available to patients," said Don S. Dizon, MD, FACP, ASCO Expert.

The authors note that while Conquer Fear is effective in a face-to-face format, it is a time- and resource-intensive intervention. Other formats, such as delivery via internet, in a group, or by phone, may be possible. A stepped care approach could also be considered, with only those with severe fear of recurrence receiving face-to-face intervention.

"In this study, the interventions were delivered by experienced psycho-oncologists. It is possible that community psychologists or other professionals who have basic training in cognitive therapy could deliver the interventions, given appropriate training and supervision," said Dr. Beith.

This study was funded by Cancer Australia, beyond blue and National Breast Cancer Foundation.

## ASCO2017特集