PARP阻害剤は難治性乳がん治療に有望である（Abstract #: CRA501 and P3）

PARP阻害剤と化学療法の組み合わせはtriple-negative乳がんの新たな治療選択肢となる可能性がある

PARP inhibitor plus chemotherapy may offer new treatment option for triple-negative breast cancer

新たなクラスの標的治療PARP阻害剤は難治性乳がん治療に対し有望であるとの二つのスタディの結果が第45回American Society of Clinical Oncology学会で発表された。PARPは”ポリ（ADPーリボース）ポリメラーゼ”の略称である。無作為化phase IIスタディの結果、治験薬PARP阻害剤BSI-201を従来の化学療法に加えて投与された転移性triple-negative乳がん患者は、通常の標準的な化学療法のみを受けた患者と比較し生存期間が有意に長く無増悪生存期間も長かったことが示された。BSI-201を投与された患者の約62%において臨床上の有益性が認められたのに対し、化学療法のみの群におけるその割合は21%であった。治療に対する全体の奏効率はBSI-201を含む併用療法群で標準的な化学療法のみの群よりも有意に高かった（それぞれ48%対16%）。BSI-201を投与された女性の生存期間中央値は9.2ヵ月であり無増悪生存期間中央値は6.9ヵ月であったのに対し、標準治療のみを受けた患者においてはそれぞれ5.7ヵ月と3.3ヵ月であった。さらに、小規模なphase II多国籍多施設スタディの結果、BRCA1またはBRCA2変異を有し前治療に抵抗性であった進行乳がんの女性の40%において、治験薬のPARP阻害剤olaparib投与後に腫瘍の縮小が認められた。

Full Text

Two new studies report results on the effect of a new class of targeted therapy called PARP inhibitors on traditionally difficult-to-treat breast cancers - so-called "triple negative" breast cancer and BRCA1-2 deficient breast cancers.

PARP is short for "poly (ADP-ribose) polymerase." Cancer cells use the PARP enzyme to repair DNA damage, including the damage inflicted by chemotherapy drugs. Researchers are examining whether drugs that inhibit the PARP enzyme will diminish this self-repair mechanism and make cancer cells more sensitive to treatment and promote cancer cell death.

A randomized Phase II study, featured in ASCO's plenary session, shows that women with metastatic triple-negative breast cancer who received the investigational PARP inhibitor BSI-201, in combination with conventional chemotherapy, lived significantly longer and experienced significantly better progression-free survival than women who received standard chemotherapy alone.

"The results of this study provide early evidence that BSI-201 is a promising treatment for women with triple-negative breast cancer, an aggressive form of the disease for which we need new, more effective therapies," said Joyce O'Shaughnessy, M.D., co-director of the Breast Cancer Research Program at Baylor- Charles A. Sammons Cancer Center in Dallas, Texas.

Triple-negative breast cancers are particularly hard to treat since they lack receptors for estrogen, progesterone and HER2, which are targeted by widely available and effective drugs.

In this study, clinical benefit rate (defined by complete and partial responses and stable disease of at least 6 months), response rate, progression-free survival, and overall survival were compared among 116 women with metastatic triple-negative breast cancer who were randomly assigned to receive a standard chemotherapy treatment (gemcitabine and carboplatin) plus BSI- 201, or standard treatment alone.

Approximately 62 percent of patients receiving BSI-201 showed clinical benefit, compared with 21 percent in the chemotherapy only group. The overall response rate to treatment with the drug combination containing BSI-201 was significantly greater (48 percent) than in the group receiving only standard chemotherapy (16 percent). Women who received BSI-201 had a median survival of 9.2 months and median progression-free survival of 6.9 months compared with 5.7 months and 3.3 months, respectively, in women who received standard treatment alone.

The incidence of side effects was similar between the two groups. BSI-201 itself was well-tolerated and did not contribute any new side effects nor add to the known side effects of gemcitabine and carboplatin.

A small, Phase II international multi-center study reports that more than a third of women with BRCA1 or BRCA2 mutations and advanced breast cancer that persisted despite prior treatment experienced tumor shrinkage after receiving the investigational PARP inhibitor olaparib.

"The findings of our study provide very promising evidence that the potent PARP inhibitor olaparib may be useful for treating BRCA-deficient breast cancers," said lead author Andrew Tutt, MB ChB, Ph.D., director of the Breakthrough Breast Cancer Research Unit at Kings College in London. "However, this drug is in a very early stage of development, and additional clinical trials are necessary to determine the best way to use olaparib in women with BRCA-deficient breast cancer. We are actively discussing the design of future PARP inhibitor studies for women with BRCA1 and BRCA2 mutations."

This study is the first to evaluate olaparib when used alone in women with BRCA-deficient breast cancer. A prior Phase II study showed that some women with BRCA-deficient ovarian cancers responded to olaparib. Tumors that arise in patients with BRCA mutations have a defect in their ability to repair DNA.

By adding olaparib, the tumor cells are deprived of another DNA repair mechanism. It is thought that this added inhibition of DNA repair with olaprib then leads to cancer cell death.

In this study, Dr. Tutt and his colleagues examined the response rate to olaparib (as evidenced by tumor shrinkage) in 54 women with breast cancer that was deficient in BRCA1 or BRCA2 and that persisted despite several rounds of standard chemotherapy. Forty percent of the patients responded to olaparib (experienced tumor shrinkage) at the higher of the two doses used in the study.

Olaparib was well tolerated, with the most common side effects being mild fatigue, nausea and vomiting.

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頻回な血液検査によるCA125の測定は不必要な可能性がある（Abstract #: P1）

血中CA125レベル上昇に基づき治療を行っても症状発現を待って治療を行うのと再発性卵巣がん患者の生存率は変わらない

Treatment based on rising CA125 blood levels does not improve survival for recurrent ovarian cancer compared to waiting for symptoms to arise

血中CA125レベル上昇のみを指標に卵巣がんの再発に対し治療を早期に開始しても、症状発現まで治療を遅延させた場合と比較し全生存期間は変わらないとのヨーロッパの研究者らの報告が第45回American Society of Clinical Oncology学会で発表された。研究者らは、初回化学療法後に寛解しCA125上昇後にセカンドラインの化学療法を開始した患者265人と、CA125上昇後症状（骨盤痛や腫脹）が発現してから治療を開始した患者264人を比較した。早期治療開始群は治療遅延群よりも治療開始が5ヵ月早かったにもかかわらず、全生存期間は両群間で同等であり、ファーストライン化学療法終了後41ヵ月であった（ハザード比1.01、95%、CI 0.82-1.25、p=0.91）。研究者らは、血清マーカーのみの上昇を基に早期治療を開始しても生存率の点では有益性はなく、したがって卵巣がん患者の経過観察におけるルーチンのCA125計測は有用でないと結論付けている。患者は症状発現後に治療を開始しても大丈夫である、と安心してよいようである。

Full Text

European researchers report that starting treatment early for an ovarian cancer relapse based on CA125 blood levels alone does not improve overall survival, compared with delaying treatment until symptoms arise.

"Women who've completed ovarian cancer treatment often worry about a relapse, and they undergo frequent blood tests for CA125 in the hope of catching it early," said lead author Gordon Rustin, M.D., professor of oncology at Mount Vernon Cancer Center in Hertfordshire, United Kingdom. The study was conducted by the MRC/NCRI and EORTC Gynae Cancer Intergroups. "We thought that delaying chemotherapy might make overall quality of life worse, due to the symptoms of ovarian cancer, but this was not seen in women on this trial. Since there is no benefit from early chemotherapy, patients may choose to avoid the inconvenience and anxiety associated with frequent retesting for CA125 levels as well as unnecessary early initiation of treatment for relapse."

CA125 is a marker of growth for several cancers, including ovarian cancer, and is measured by a blood test. Women who have undergone treatment for ovarian cancer may have their CA125 levels tested as often as every three months for several years after initial treatment.

In this study, investigators compared overall survival between 265 women with ovarian cancer in remission after initial chemotherapy who began second-line chemotherapy after experiencing a rise in CA125, and 264 women with rising CA125 whose treatment was delayed until symptoms of relapse appeared (such as pelvic pain or bloating).

Even though the early treatment group started second-line chemotherapy an average five months before the delayed treatment group, overall survival was the same between both groups: 41 months since completion of first-line chemotherapy.

The researchers added that this trial provides important information that will help women make informed choices about their follow-up and treatment. They can be reassured that treatment can safely be delayed until symptoms develop.

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胃がんのオーダーメイド標的治療（Abstract #: LBA4509）

HER-2陽性の胃がん患者においては標準治療にトラスツズマブを追加することにより生存率が改善する

Adding trastuzumab to standard treatment improves survival in patients with HER2-positive gastric cancer

胃がん患者に対するトラスツズマブの初めての無作為化国際多施設phase IIIスタディにおいて、標準治療に加えトラスツズマブを投与された患者は標準治療のみを受けた患者と比較し生存期間が有意に長かったと第45回American Society of Clinical Oncology学会で発表された。このスタディの対象となった患者3,807人中22.1%において腫瘍内HER-2増加が認められた。これらの患者のうち局所進行性、再発性、または転移性HER-2陽性胃がん患者594人が標準化学療法（5-フルオロウラシルまたはカペシタビンおよびシスプラチン）とトラスツズマブの併用、または標準化学療法のみを受ける群に無作為に割り付けられた。生存期間中央値はトラスツズマブ併用群で13.8ヵ月であったのに対し標準化学療法のみの群では11.1ヵ月であり、死亡リスクの26%軽減が認められた。治療に対する忍容性は概して良好であり、トラスツズマブ群において想定外の副作用は生じなかった。HER-2陽性乳がんに対し使用されていたトラスツズマブが他のがんに対しても有効であることが今回初めて明らかにされた。

Full Text

The first randomized, international and multicenter phase III study of trastuzumab in patients with gastric cancer has found that patients who received trastuzumab plus standard chemotherapy lived significantly longer than patients who received standard chemotherapy alone, with a 26 percent reduction in the risk of death. This is the first time trastuzumab - used to treat HER2-positive breast cancer - has been proven effective in another cancer.

"This is the first phase III study to report improved overall survival with a personalized, targeted treatment for gastric cancer," said Eric Van Cutsem, M.D., Ph.D., professor at the University Hospital Gasthuisberg in Leuven, Belgium, and lead author of the study. "These data indicate that trastuzumab has the potential to have a place in the treatment of a cancer other than breast cancer, and to become a common treatment for gastric cancer patients who are candidates for this drug."

Trastuzumab is a targeted cancer therapy that works by blocking the HER2 receptor. This receptor, which can fuel cancer growth, is present in high amounts in up to 25 percent of breast cancers. High amounts of HER2 have been found in a similar percentage of patients with gastric cancer.

Among 3,807 gastric cancer patients in the study, 22.1 percent had high amounts of HER2 in their tumors. Of these patients, 594 with locally advanced, recurrent or metastatic HER2-positive gastric cancer were randomized to receive either standard chemotherapy (5-fluorouracil or capecitabine and cisplatin) plus trastuzumab or standard chemotherapy alone.

Median overall survival was 13.8 months in the trastuzumab group versus 11.1 months in the standard chemotherapy group. The treatment was generally well tolerated, and there were no unexpected side effects in the trastuzumab group: the rate of symptomatic congestive heart failure was similar between the two groups. The incidence of decreased ventricular ejection fraction was generally low (5.9 percent in the trastuzumab group compared with 1.1 percent in the standard therapy group) and the mean ventricular ejection fraction remained above 60 percent throughout the study.

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患者の免疫機能を用いたB細胞性リンパ腫の標的治療（Abstract #: P2）

治療がんワクチンは濾胞性リンパ腫患者の無病生存期間を有意に延長させる

Therapeutic cancer vaccine significantly prolongs disease-free survival for follicular lymphoma

8年間の無作為化コントロールphase III臨床研究の結果、患者特異的治療ワクチンBiovaxIDは濾胞性非ホジキンリンパ腫の無病生存期間を有意に延長させることが示された。この治療は患者の免疫機能を用いて従来の化学療法に対する反応を増強させるものである。第45回American Society of Clinical Oncology学会で発表されたこのスタディにおいて、PACE（プレドニゾン、ドキソルビシン、シクロフォスファミドおよびエトポシド）化学療法により完全寛解となった濾胞性リンパ腫患者177人をBiovaxIDワクチン群（ワクチンとKLH/GM-CSF）またはコントロール群（KLH/GM-CSFのみ）に無作為に割り付けた。研究者らは化学療法に対する完全寛解を6ヵ月以上維持し、実薬ワクチン（76人）またはコントロール（41人）を投与された患者117人を解析した。経過観察期間中央値56.6ヵ月後（12.6～89.3ヵ月）、無病生存期間中央値はBiovaxID群で44.2ヵ月であったのに対しコントロール群では30.6ヵ月であり（p=0.045; HR=1.6）、47%延長した。筆者らは、このワクチンは患者の免疫系を動員し腫瘍性B細胞のみを探して破壊するユニークなものであり、この方法は他のB細胞性リンパ腫の治療にも応用できる可能性があると述べている。

Full Text

An eight-year randomized, controlled phase III clinical study has shown that a patient-specific therapeutic vaccine, BiovaxID, significantly prolongs disease-free survival in follicular non-Hodgkin's lymphoma.

The study, which is being featured in ASCO's plenary session, found that patients who received the vaccine experienced a median disease-free survival of approximately 44 months compared to approximately 30 months for those who received a control vaccine - an increase of 47 percent. BiovaxID is individually manufactured from a tissue biopsy obtained from a patient's own tumor. The vaccine targets an idiotype expressed by cancerous B cells in follicular lymphoma and spares normal, healthy B cells that do not express the tumor idiotype.

The final vaccine is administered as a subcutaneous injection along with granulocyte-monocyte colony stimulating factor (GM-CSF) and keyhole limpet hemocyanin (KLH), which together enhance the potency of the immune response induced by BiovaxID. A previous phase II study demonstrated that patients receiving the BiovaxID vaccine develop a highly specific immune response against tumor cells.

"With this vaccine, we've now moved into an era where we can safely use a patient's immune system to effectively fight follicular lymphoma and enhance the response to conventional chemotherapy," said Stephen J. Schuster, M.D., associate professor at the University of Pennsylvania School of Medicine and the study's lead author. "Because this vaccine uniquely recruits the patient's immune system to seek and destroy only tumor B cells, this approach may be applicable to the treatment of other B-cell lymphomas."

The study achieved its primary endpoint of prolonging disease-free survival in patients vaccinated with BiovaxID after achieving a complete response to chemotherapy. In the study, 177 patients with follicular lymphoma who had achieved a complete response to PACE (prednisone, doxorubicin, cyclophosphamide and etoposide) chemotherapy were randomized to the BiovaxID vaccine arm (vaccine plus KLH/GM-CSF) or to the control arm (KLH/GM-CSF alone). Investigators analyzed the cohort of 117 patients who, as per study protocol requirements, maintained a complete response to chemotherapy for at least six months and received active (76 patients) or control (41 patients) vaccine. After a median follow-up of 4.71 years (56.6 months, range: 12.6 - 89.3 months), the median disease-free survival in the BiovaxID arm was 44.2 months compared with 30.6 months in the control arm, which is a statistically significant difference.

BiovaxID demonstrated a favorable safety profile and was very well tolerated by patients. Further studies are planned to examine the role of BiovaxID in patients with other B-cell lymphomas and as maintenance therapy in patients with follicular lymphoma.

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メラノーマに対するがんワクチンにおいて有望な結果が得られた（Abstract #: CRA9011）

転移性メラノーマ患者においてワクチンは奏効率を改善し無増悪生存期間を延長する

Vaccine improves response rate and extends progression-free survival in patients with metastatic melanoma

Phase III多施設トライアルの予備的所見によると、転移性メラノーマ患者において、gp100:209-217(210M)ペプチドと呼ばれる新たながんワクチンを標準治療に追加することにより、奏効率が倍になり無増悪生存期間が延長し、有意な副作用は認められなかったと第45回American Society of Clinical Oncology学会で発表された。このワクチンは投与されると、T細胞を刺激し増加させ、細胞表面のgp100抗原を発見することによりメラノーマ細胞を探し出し攻撃する。このスタディにおいて、ワクチンおよびインターロイキン−2（IL-2）投与群に無作為化割り付けされた患者86人とIL-2のみの投与群に割り付けられた患者93人における奏効率、無増悪生存期間、および全生存期間を比較した。ワクチン群において2倍以上の患者が治療に反応し腫瘍が縮小した（22.1%対9.7%、p=0.0223）。無増悪生存期間はワクチン群においてIL-2のみの群よりも長かった（2.9ヵ月対1.6ヵ月、p=0.0101）。研究者らはまた、標準治療に加えワクチン治療を受けた患者は標準治療のみを受けた患者よりも5ヵ月長く生存し（17.6ヵ月対12.8ヵ月、p=0.0964）、全生存期間も延長する傾向が見られたことも報告した。

Full Text

Preliminary findings from a phase III, multicenter trial show that adding a novel cancer vaccine - called gp100:209-217(210M) peptide - to standard therapy doubles response rates and extends progression-free survival in patients with metastatic melanoma, without causing significant side effects.

"This study is one of the first to show positive, promising results for a cancer vaccine in melanoma" said lead author Douglas Schwartzentruber, M.D., medical director of the Center for Cancer Care at Goshen Health System in Indiana and clinical associate professor of surgery at Indiana University. "Metastatic melanoma is a very difficult disease to treat successfully and is very resistant to most therapies. These results will give patients and the oncology community hope that we are making some progress against this disease."

The vaccine is made from a peptide that is part of the gp100 protein - an antigen found on the surface of melanoma cells that acts as a marker for melanoma cells. When administered, the vaccine stimulates T cells to multiply and to seek and attack melanoma cells by locating this gp100 antigen. It was administered with interleukin-2 (IL-2), a standard therapy for advanced melanoma that boosts the immune response to the vaccine.

In this study, response rate, progression-free survival, and overall survival were compared between 86 patients who were randomly assigned to receive the vaccine plus IL-2, and 93 patients who received IL-2 alone. More than twice as many patients in the vaccine group responded to treatment with tumor shrinkage (22.1 percent versus 9.7 percent). Progression-free survival and overall survival were also longer in the vaccine group (2.9 months and 17.6 months, respectively) compared with the IL-2 only group (1.6 months and 12.8 months). Researchers reported a trend toward improved overall survival among patients who received it along with standard therapy, who lived nearly five months longer than those who received standard therapy alone. The vaccine was well tolerated; swelling and redness at the injection site were the only side effects. The investigators are continuing to follow the patients to see how long the vaccine remains effective and to assess its value in various patient subgroups

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肺がんの進行に重要な役割を果たす二つのパスウェイを標的とする新たな治療薬（Abstract #: CRA8003）

分子標的治療薬vandetanibは進行非小細胞肺がん患者の無増悪生存期間を改善する

Targeted therapy vandetanib improves progression-free survival in patients with advanced non-small cell lung cancer

国際トライアルの結果、ドセタキセルに分子標的治療治験薬vandetanibを加えることにより、ファーストライン治療後に進行した進行非小細胞肺がん（NSCLC）患者の無増悪生存期間が改善することが示されたと第45回American Society of Clinical Oncology学会で発表された。VandetanibはNSCLCにおいて役割を果たすことが知られている二つの受容体（上皮増殖因子受容体[EGFR]および血管内皮増殖因子[VEGF]）の両方を標的とした初めての薬剤である。このスタディでは、既に化学療法で治療された患者1,391人をドセタキセルとvandetanib、またはドセタキセルとプラセボを投与する群に無作為に割り付けた。経過観察期間中央値12.8ヵ月後にvandetanib群の患者はプラセボ群と比較し疾患進行のリスクが21%低下した（無増悪生存期間中央値はvandetanib群で17.3週間、プラセボ群で14週間、p=0.001）。全生存期間には統計学的有意差はなかったが、奏功率の有意な改善が認められた（17%対10%、p=0.001）。またvandetanib治療によりがん自体による症状も軽減し症状増悪のリスクも22%低下した（p=0.002）。

Full Text

The results of an international trial have shown that adding the experimental targeted therapy vandetanib to docetaxel improves progression-free survival in patients with advanced non-small cell lung cancer (NSCLC) whose disease has progressed after first-line treatment. This is the first phase III study to show that adding a targeted therapy to second-line chemotherapy with docetaxel results in a clinical benefit for patients with advanced NSCLC. It is also the first phase III trial of vandetanib for NSCLC, which is being evaluated for certain types of thyroid cancer as well.

Vandetanib is a pill that targets two receptors already known to play a role in NSCLC - epidermal growth factor receptor (EGFR) and vascular endothelial growth factor (VEGF). These receptors are targeted separately by other drugs, but vandetanib is the first drug to target both.

In this study 1,391 patients who had previously been treated with chemotherapy were randomized to receive the docetaxel and vandetanib, or docetaxel and placebo. After a median follow-up of 12.8 months, patients in the vandetanib group had a 21 percent reduction in the risk of disease progression compared with patients in the placebo group. The median progression-free survival time was 17.3 weeks in the vandetanib arm versus 14 weeks in the control arm.

While there was no statistical difference in overall survival, a significant improvement in objective response rate was observed. Vandetanib treatment was also associated with an improvement in symptoms related to the underlying cancer and a 22 percent reduction in the risk that symptoms would worsen. For example, it took longer for patients in the vandetanib group to report that their disease symptoms, such as cough, weight loss, and difficulty breathing, had worsened.

Some side effects were more common in the vandetanib arm, including diarrhea (42 percent versus 33 percent in the placebo group), rash (42 percent versus 24 percent), and low white blood cell counts (32 percent versus 27 percent). Other side effects (nausea, vomiting, and anemia) were more common in the control group. About 22 percent of patients in the study discontinued vandetanib due to side effects, which is relatively low for a second-line therapy in advanced lung cancer.

"Clearly in a disease as heterogeneous as lung cancer the need to target multiple pathways has become clear - hence, this agent targeting two key pathways critical for NSCLC growth and metastasis is novel and could play a key role," said Roy S. Herbst, M.D., Ph.D., chief of thoracic medical oncology at the University of Texas M.D. Anderson Cancer center and the study's lead author. "The fact that more patients had an improvement in the symptoms from their lung cancer suggests that the drug could be important for the future management of this disease."

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予防的治療により重度の薬剤性発疹の発現を減らすことができる（Abstract #: CRA4027）

予防的なクリームおよび抗生剤投与により大腸がん分子標的治療薬に一般的に見られる重度の発疹の発現を減少させることができる

Prophylactic creams and antibiotics reduce common, severe skin rash associated with targeted colon cancer drug

大腸がん患者にpanitumumabを投与する前に保湿剤、日焼け止め、ステロイド軟膏および経口抗生剤を処方することにより重度の発疹の発現が半数以上減少すると第45回American Society of Clinical Oncology学会で発表された。Panitumumabを投与された約90%の患者およびセツキシマブを投与された患者の最大75%に有意なざ瘡様発疹が出現する。この発疹は美容上問題となるだけでなく治療を遅延させるほどの重篤な皮膚感染症を引き起こしうる。このスタディでは、panitumumabベースの治療開始24時間前に6週間の予防的皮膚処置（保湿剤、日焼け止め、ステロイド軟膏およびドキシサイクリン）を試行する群に無作為に割り付けられた転移性大腸がん患者48人と、発疹が発現してから治療を開始する群に割り付けられた患者47人における皮膚毒性を比較した。予防的治療群患者においては29%に皮膚毒性が認められたのに対し、発疹が出現して治療を開始した群では62%に認められた。予防的治療群の患者はまた、外見上も身体的にも快適でありライフスタイルを大きく改善する必要もないことから、QOLの点でも良好であると報告している。

Full Text

Giving patients with colon cancer a combination regimen consisting of moisturizers, sunscreen, topical corticosteroids and oral antibiotics before they receive panitumumab reduces the incidence of a severe skin rash by more than half according to research presented at the 45th Annual Meeting of the American Society of Clinical Oncology. In addition, it has a significant impact on patients' quality of life, and decreases delays in receiving therapy, which could potentially impact cancer outcomes.

Panitumumab belongs to a class of drugs known as epidermal growth factor receptor (EGFR) inhibitors.

"The skin toxicity caused by EGFRs like panitumumab and cetuximab can be devastating for patients. It prevents many patients from agreeing to take these drugs and either delays or interrupts treatment for many others, reducing the effectiveness of therapy," explained Edith Mitchell, M.D., clinical professor of medicine and medical oncology at Thomas Jefferson University in Philadelphia and the study's lead author. "Prophylactic skin treatment is likely to become a new standard of care for patients receiving these drugs."

About 90 percent of patients receiving panitumumab and up to 75 percent of those who take cetuximab develop a significant acne-like rash that is not only cosmetically unattractive, but can lead to serious skin infections causing delays in treatment. The rash develops because these drugs target the epidermal growth factor receptor, which is found in very high amounts in the skin.

In this study, skin toxicity was compared between 48 patients with metastatic colorectal cancer who were randomly assigned to receive prophylactic skin treatment (moisturizers, sunscreen, topical steroids and the antibiotic doxycycline) for six weeks starting 24 hours before panitumumab-based therapy and 47 patients whose skin was not treated until after the rash developed.

Twenty-nine percent of those in the prophylactic group experienced skin toxicity versus 62 percent of those in the delayed treatment group. Patients who received the prophylactic skin treatment also reported better quality of life than those whose rash was not treated until after it developed because they felt better about their appearance and were more physically comfortable, with less impairment of their lifestyle.

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微小転移乳がんの治療（Abstract #: CRA596）

乳がん患者におけるセンチネルリンパ節微小転移は追加治療の必要性を強力に示唆する

Sentinel node micrometastases strongly indicate need for additional treatment in patients with breast cancer

オランダの研究グループは、センチネルリンパ節微小転移を有する早期乳がん患者は追加の腋窩リンパ節に対する追跡治療を受けなければ有意に高率に再発すると報告した。第45回American Society of Clinical Oncology学会で発表されたこのレトロスペクティブスタディでは、1997～2005年に早期乳がんの手術を施行されセンチネルリンパ節にマクロ転移の認められなかった患者2,700人を組み入れ、センチネルリンパ節内に腫瘍細胞を認めない、isolated tumor cell（ITC）を認める、微小転移（0.2mm～2.0mmの転移）を認める、の3群に分別された。全ての患者は、さらなる治療を受けない、残存する腋窩リンパ節切除、または腋窩リンパ節に対する放射線治療のいずれかを受けた。微小転移を有する患者における5年間の再発率は治療を受けなかった群において、手術または放射線治療を受けた群よりも4.5倍高かった。センチネルリンパ節内に腫瘍細胞を認めない、およびITCのみを認める群においては追加の腋窩リンパ節治療による再発率の有意な改善は認めなかった。

Full Text

A group of Dutch researchers has found that women with early-stage breast cancer who have micrometastases in the sentinel lymph node have a significantly higher rate of recurrence if they do not receive follow-up treatment on additional axillary lymph nodes. They also report that about one in ten doctors are not treating these very small metastases.

For patients with early-stage breast cancer, physicians examine the sentinel lymph node to determine the extent that cancer has spread and whether additional treatment is needed in the remaining axillary lymph nodes. Treatment generally involves a second operation to remove the axillary lymph nodes, but radiation therapy is also used. For macrometastases - metastases greater than 2.0 mm - evidence of the need for further treatment has been clear.

Evidence has been less certain, however, for patients with micrometastases - metastases between 0.2 mm and 2.0 mm, and for patients with isolated tumor cells (individual cells or tumor cell clusters smaller than 0.2 mm).

"We found that about 10 percent of doctors are not treating micrometastases. This is most likely due to concern about overtreatment and a lack of clear data on these very small metastases, but our study provides explicit evidence that foregoing treatment for micrometastases results in high cancer recurrence rates. We hope these findings will be a tipping point for doctors not currently treating women for this stage of cancer," said Vivianne Tjan-Heijnen, M.D., Ph.D., a professor of medical oncology at the Maastricht University Medical Center in the Netherlands and the study's lead author. "Additionally, our study suggests that radiation therapy is a good alternative to surgery, which could spare many women additional recovery, although more data to confirm these findings are warranted."

This retrospective study included about 2,700 women who underwent surgery for early-stage breast cancer between 1997 and 2005 and had a sentinel node biopsy that showed no evidence of macrometastases. Women were then divided into three groups: Those with no tumor cells in the sentinel node, those with isolated tumor cells, and those with micrometastases. All women either underwent no additional treatment, surgery to remove remaining axillary nodes, or radiation therapy to the axillary nodes.

For patients with micrometastases, the five-year recurrence rate in the axillary nodes was 4.5 times higher for patients who had no additional treatment than for patients who had either surgery or radiation. Additional axillary treatment did not significantly improve recurrence rates among women with either no tumor cells or only isolated tumor cells in the sentinel node.

Until further studies addressing the clinical relevance of isolated tumor cells or micrometastases in the SLN are complete, the Panel recommends routine ALND for patients with micrometastases (>0.2 <2 mm) found on SNB, regardless of the method of detection.

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一般的な抗うつ薬のタモキシフェンの有効性に関する影響
(Abstracts #: CRA508 and CRA509)

ホットフラッシュの治療に一般的に用いられる抗うつ薬が乳がん再発予防目的に使用されるタモキシフェンの有効性に影響するか否かに関するスタディの結果は一致していない

Studies report mixed findings on whether antidepressants commonly used to treat hot flashes impact effectiveness of tamoxifen for preventing breast cancer recurrence

第45回American Society of Clinical Oncology学会で発表された、2D6阻害薬がタモキシフェンの乳がん再発予防効果を低下させるか否かについての二つのレトロスペクティブスタディの結果は異なっていた。ホットフラッシュ治療にタモキシフェンと同時に用いられる最も一般的な2D6阻害薬は、抗うつ薬のfluoxetineおよびパロキセチンである。一つのスタディでは、米国の薬剤給付管理会社Medcoのデータベースで、乳がん治療を受けその後再発予防目的でタモキシフェンを投与された女性を調査した。タモキシフェンのみを内服した患者の2年間の再発率は7.5%であり、一方タモキシフェンと2D6阻害薬の両者を内服した女性（両薬剤の平均重複内服期間は255日）の再発率は13.9%であった。これらの結果から抗うつ薬SSRIがタモキシフェン療法の有効性を低下させる可能性が示唆された。他のスタディではオランダの3つのデータベースを解析し、早期乳がんの手術後にタモキシフェンを投与された女性1,962人を抽出した。タモキシフェンのみを内服した女性または2D6阻害薬内服期間が60日未満であった女性（1,812人）の再発率は14.6%であった。一方タモキシフェンを2D6阻害薬と同時に内服した期間が60日以上であった患者（150人）の再発率は13.3%であった。これらの相違を解決するにはさらなるリサーチが必要である。

Full Text

Hot flashes are a common side effect of tamoxifen treatment to prevent breast cancer recurrence, and are often managed with the antidepressant drugs fluoxetine and paroxetine. Two retrospective studies report mixed results on whether 2D6 inhibitors reduce the effectiveness of tamoxifen for preventing breast cancer recurrence. Additional research is needed to resolve these differences, though women may want to consider alternative antidepressants in the meantime.

In the body, tamoxifen is broken down to several active compounds; endoxifen is one of the most biologically active of these metabolites. Previous research has shown women who have a gene mutation that prevents them from making the 2D6 enzyme, which converts tamoxifen to endoxifen, do not get the same benefit from tamoxifen as women with a normal version of the gene. Other studies have suggested that drugs that inhibit the 2D6 enzyme reduce blood levels of endoxifen in women taking tamoxifen.

2D6 inhibitors include a variety of drugs, but the two most common are fluoxetine and paroxetine. These drugs, known as selective serotonin reuptake inhibitors (SSRIs), have often been prescribed to reduce hot flashes caused by tamoxifen. Similar drugs can be used to treat both hot flashes and depression that do not inhibit 2D6.

U.S. study finds women taking 2D6 inhibitors with tamoxifen have higher rates of breast cancer recurrence
This study, conducted by the U.S. pharmacy benefit management company Medco, examined women in Medco's database who were treated for breast cancer and then initiated and were adherent to tamoxifen therapy to prevent recurrence. The study identified 945 women who took tamoxifen alone and an additional 353 who were treated with both tamoxifen and a 2D6.

The researchers found that women taking tamoxifen alone had a recurrence rate of 7.5 percent over a two-year period, compared with a 13.9 percent recurrence rate for women taking tamoxifen and a 2D6 inhibitor. The average time of overlap when both drugs were taken was 255 days.

"These findings suggest that some drugs commonly prescribed to help reduce hot flashes associated with tamoxifen therapy may be decreasing the effectiveness of their anti-cancer treatment," said Robert Epstein, M.D., Chief Medical Officer at Medco and one of the study's authors. "If women are taking tamoxifen and need an SSRI to reduce their hot flashes, there are other SSRI drug options that don't inhibit 2D6 or result in the higher recurrence rates."

Dutch study finds 2D6 inhibitors have little effect on breast cancer recurrence rate
A study from Holland analyzed data from three national databases, and identified 1,962 women who were treated with tamoxifen following surgery for early-stage breast cancer. The researchers found that about 11 percent had taken a 2D6 inhibitor at some point while they were also taking tamoxifen.

After a median follow-up time of 4.1 years (for patients who are event-free at time of analysis), the researchers found that among women who took tamoxifen alone or took a 2D6 inhibitor for less than 60 days (1,812 women), 14.6 percent experienced a recurrence. Among patients who took tamoxifen at the same time as a 2D6 inhibitor for 60 days or more (150 women), 13.3 percent experienced a breast cancer recurrence.

"Based on our findings and previous studies, we don't have strong evidence that it's unsafe to use 2D6 inhibitors during tamoxifen therapy," said Vincent O. Dezentje, M.D., a trainee in oncology at Leiden University Medical Center and the study's first author. "But because the number of patients on both tamoxifen and 2D6 inhibitors was small in our study (and because of a possible confounding or modifying effect of CYP2D6 genotype), our findings will need to be confirmed in larger trials. Until a link between 2D6 inhibitors can be definitively confirmed, doctors and patients should be cautious about using these drugs together."

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乳房部分照射と従来の放射線療法の比較（Abstract #: CRA532）

早期乳がんに対する乳房部分照射は従来の全乳房照射と同程度に有効である可能性がある

Partial breast irradiation may be as effective as traditional whole-breast radiation therapy for early-stage cancer

第45回American Society of Clinical Oncology学会で発表された3つの臨床試験のメタ解析の結果、早期乳がんに対する乳房部分照射は全生存率および転移の減少において従来の全乳房照射と有効性が同等である可能性が示された。研究者らは、乳房部分照射と従来の全乳房照射を比較した3つの臨床試験の対象となった女性1,140人のデータを評価した。全生存率および転移は二群間で有意差がなかった。しかし、乳房部分照射を受けた女性は原発巣の乳がんと同側の乳がん再発率が2倍であり、近傍の腋窩リンパ節のがん発現率が3倍であった。これらの再発は全生存率には影響しなかった。研究者らは、他の現在進行中の臨床試験の結果が解析されるまでは乳房部分照射は試験的治療と考えておくべきであると警告している。

Full Text

A meta-analysis of data from three clinical trials shows that partial breast irradiation may offer the same benefits in terms of overall survival and reduction of metastases as conventional whole-breast radiation therapy for early-stage breast cancer. Investigators noted that several additional randomized studies are currently under way and no recommendations about this approach can be made until they are complete.

"Although more research is necessary, this study suggests that partial breast irradiation may be safe and feasible for women with early-stage breast cancer because it does not jeopardize patient survival or increase the risk of metastasis," explained lead author Antonis Valachis, M.D., associate breast cancer researcher at the Panhellenic Association for Continual Medical Research in Greece. "Partial breast irradiation reduces treatment time and radiation exposure to normal tissue, may improve cosmetic results, and is likely to enhance patients' ability to comply with therapy."

Conventional radiation therapy is commonly used to treat early-stage breast cancer after lumpectomy and it is typically given to the whole breast five days a week for six weeks. Partial breast irradiation, which was developed in the early 1990s, is targeted only to the breast tumor area. It may be given during surgery (either through radioactive seeds or through an inserted balloon catheter) with one application, or using targeted external three-dimensional conformal radiation therapy delivered over five to seven days after surgery is completed.

Dr. Valachis and his colleagues evaluated data on 1,140 women in three clinical trials comparing partial breast irradiation and traditional whole-breast radiation therapy. There were no significant differences in overall survival or the development of metastases between the two groups. However, women who received partial breast irradiation were twice as likely to experience cancer recurrence in the same breast as the primary tumor and three times more likely to develop cancer in the nearby axillary lymph nodes. These recurrences had no affect on overall survival, however.

The researchers cautioned that partial breast irradiation will continue to be considered investigational until the results of additional, ongoing clinical trials can be analyzed.

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アジュバント療法としてのベバシズマブは有益でない（Abstract #: LBA4）

標準アジュバント化学療法へのベバシズマブの追加は早期結腸がんの無病生存率を改善しない

Adding bevacizumab to standard adjuvant chemotherapy does not improve disease-free survival for early-stage colon cancer

Phase IIIトライアルの結果、標準アジュバント化学療法にベバシズマブを追加しても局所進行結腸がんの無病生存率を改善しないことが示された。このスタディは2,710人の患者を組み入れ、標準アジュバント化学療法を6ヵ月間受ける群またはベバシズマブと組み合わせたアジュバント化学療法を6ヵ月間施行した後にベバシズマブ投与を6ヵ月間行う群に無作為に割り付けた。対象者は全員ステージIIまたはIIIの結腸がん患者で、先に手術で腫瘍を除去された。経過観察期間中央値3年間の後、がんを有さず生存していたのはベバシズマブ群患者で77.4%であったのに対しコントロール群におけるその割合は75.5%であり、その差は統計学的に有意ではなかった。両群ともに想定外の副作用はなく、ベバシズマブによる毒性は忍容できるものであった。第45回American Society of Clinical Oncology学会で発表されたこのスタディは、アジュバント療法としてベバシズマブを使用した結果を報告した初めてのものである。

Full Text

The results of a randomized, phase III trial have found that adding bevacizumab to standard adjuvant chemotherapy did not improve disease-free survival in early-stage colon cancer.

This was the first study to report results on the use of bevacizumab as an adjuvant treatment. The antibody, which targets the vascular endothelial growth factor (VEGF) receptor, is currently approved in the United States for metastatic colorectal, breast, and lung cancers, and other trials are ongoing to evaluate it as an adjuvant treatment for a variety of solid tumors.

The current study enrolled 2,710 patients who were randomized to receive six months of standard adjuvant chemotherapy or six months of adjuvant chemotherapy combined with bevacizumab plus an additional six months of bevacizumab after the chemotherapy had ended. All patients in the study had stage II or stage III disease and first had surgery to remove their tumors. After a median follow-up of three years, the investigators found that 77.4 percent of patients in the experimental group (bevacizumab) were alive and free of disease, compared with 75.5 percent of patients in the control group, a difference that was not statistically significant. There were no unexpected side effects in either arm and the toxicities from bevacizumab were well tolerated.

"One interesting effect was that during the year that patients were receiving bevacizumab we saw a benefit in disease-free survival that subsequently diminished when follow-up was completed," said Norman Wolmark, M.D., chairman of the Department of Human Oncology at Allegheny General Hospital and the study's lead author. "Our overall conclusion is that bevacizumab was not effective as an adjuvant treatment for early-stage colon cancer, but the transient benefit we saw in patients who received bevacizumab illustrates that we have more to learn about how this reagent works, and we need to design more clinical trials to determine how it can be used most effectively."

The trial was conducted by the National Surgical Adjuvant Breast and Bowel Project (NSABP) group, chaired by Dr. Wolmark, and was funded by the National Cancer Institute.

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センチネルリンパ節生検は早期子宮頸がんに対する有効な方法である（Abstract #: CRA5506）

早期子宮頸がんに対するセンチネルリンパ節生検は現在の標準的な方法と比較し有効で侵襲の少ない方法である

Sentinel node biopsy is effective, less invasive option for early-stage cervical cancer compared with current standard

プロスペクティブな多施設スタディの結果、早期子宮頸がんの大多数の女性に対し、従来の侵襲の大きい骨盤内リンパ節郭清の代わりにセンチネルリンパ節（SN）生検が施行可能であることが示唆された、とフランスの研究者らが第45回American Society of Clinical Oncology学会で発表した。過去のスタディでは子宮頸がん患者においてがん細胞を有する確率の最も高い骨盤内リンパ節へのがんの拡がりを予測するのにSN生検を用いることができることが示された。今回のスタディでは研究者らは、骨盤内リンパ節を全て郭清された早期子宮頸がん患者128人の骨盤の非典型的部位のセンチネルリンパ節生検の結果を評価した。そしてセンチネルリンパ節のマクロ転移（>2mm）に加え微小転移がん（径0.2～2mm）およびisolated tumor cellを解析した。彼らは骨盤内リンパ節全郭清およびそれに関連した合併症は81.2%の患者において避けることができたことを示した。40%近くの患者において、SN生検のみで患者の疾患に関するさらなる重要な情報が得られたであろう；例えば、リンパ液排出がまれな経路を通じて骨盤腔または腹腔内のまれな部位へ流出しているのを示すのにSN生検はルーチンの方法よりも有用であった。

Full Text

Most women with early-stage cervical cancer can safely undergo sentinel node biopsy in lieu of the traditional, more invasive pelvic lymph node removal, which can lead to more significant side effects. Sentinel node biopsy was also as effective for detecting cancer spread to atypical areas of the pelvis.

A prospective multicenter study conducted by researchers in France suggests that the majority of women with early-stage cervical cancer can safely undergo sentinel node (SN) biopsy - a technique in which only one to three lymph nodes are removed to determine whether cancer has spread - in lieu of the traditional, more invasive pelvic lymph node removal. This study showed that SN biopsy was just as useful as full pelvic lymph node removal for identifying even small amounts of cancer cells that spread to lymph nodes in atypical areas of the pelvis.

"Sentinel node biopsy is a good option for women with cervical cancer because it enables us to remove fewer lymph nodes to get information about cancer spread, and could decrease the risk of complications from surgery, such as lymphedema," said Fabrice Lecuru, M.D., Ph.D., professor at George Pompidou European Hospital in Paris, and the study's lead author. "Previous studies have shown that sentinel node biopsy can be used to assess cancer spread in usual areas of the pelvis, but our findings add to this growing body of research by showing that this approach is also effective for identifying cancer spread in less common areas of the pelvis and the abdomen. This approach may become a new standard of care for early-stage cervical cancer."

Ten to 15 percent of patients with early-stage cervical cancer experience recurrence. Some are due to lymph nodes that were missed during surgery or because of undetected cancer spread to other lymph nodes. During standard surgery, several pelvic lymph nodes are removed and examined for the presence of cancer cells. During SN biopsy, however, a blue dye and radioactive substance that can be traced with imaging techniques are used to locate the first lymph node (the sentinel node) where cancer cells would travel after leaving the cervix. If this node is free of cancer cells, no other lymph nodes should be removed. Since the removal of lymph nodes may impair lymphatic drainage and cause lymphedema, doctors have been assessing SN biopsy to see if it can be used to gauge cervical cancer spread.

Prior studies have shown that SN biopsy can be used in cervical cancer patients to predict cancer spread to lymph nodes in the pelvis most likely to contain cancer cells. But in this study, Dr. Lecuru and his colleagues also evaluated the biopsy of sentinel nodes in atypical areas of the pelvis in 128 women with early-stage cervical cancer who also had full pelvic lymph node removal for comparison. They then analyzed sentinel nodes for micrometastastic cancer (0.2 to 2 mm in size) and isolated tumor cells as well as areas of cancer greater than 2 mm (macrometastases).

After analyzing these nodes, researchers demonstrated that full pelvic lymph node removal and its associated complications could have been avoided in 81.2 percent of women. Researchers also found that in nearly 40 percent of women, SN biopsy alone would have provided additional, important information about patients' disease; for example, SN biopsy was more useful than routine techniques for showing that lymphatic drainage occurred via unusual pathways to less commonly explored areas of the pelvis or of the abdomen, and for detecting micrometastases or isolated tumor cells.

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小児がんの既往者はPTSDのリスクが高い（Abstract #: CRA10002）

小児がん既往者の外傷後ストレス障害のリスクは低いが、他者と比較し高い

Childhood cancer survivors have low, but increased risk of post-traumatic stress disorder

第45回American Society of Clinical Oncology学会で発表された小児がん既往者のスタディ（Childhood Cancer Survivor Study）の報告によると、小児がんの既往のある成人における外傷後ストレス障害（PTSD）発症率は、健康な彼らの兄弟姉妹よりも4倍以上高いとのことである。しかし、それでも小児がん既往者におけるPTSD発現率は依然として低かった（9%）。この解析では、小児がんの既往のある成人6,542人と彼らの兄弟姉妹368人におけるPTSD症状、臨床上の苦痛、および機能障害を比較した。既往者の9%および兄弟姉妹の2%がPTSDを有していた。4歳未満でがんと診断され頭部に放射線照射を受けた者はPTSDのリスクが高かった。PTSDは、四肢切断、放射線療法、または複数の治療などの集中治療を受けた者において多く認められた。他のがんの既往者と比較し、神経芽細胞腫やWilms'腫瘍の既往者においてはPTSDの発症は少なかった。またPTSDは、未婚者、大学教育を受けていない者、年収＄20,000未満の者、失業者により多く認められた。これらの因子は医師らがPTSDのリスクの高い小児がん既往者を見極めるのに役立つ可能性がある。

Full Text

A new report from the Childhood Cancer Survivor Study shows that the incidence of post-traumatic stress disorder (PTSD) among adult survivors of pediatric cancers was more than four times greater than that of their healthy siblings. However, the incidence of PTSD among survivors remained low overall-at 9 percent.

"The good news is that more than 90 percent of survivors of childhood cancer don't have PTSD, even though they went through a very difficult experience," said lead author Margaret Stuber, M.D., Jane and Marc Nathanson Professor of Psychiatry at the University of California, Los Angeles David Geffen School of Medicine. "However, some do have longstanding functional difficulties that require attention. Assessment for PTSD should therefore be considered part of the long-term health screening for childhood cancer survivors."

The Childhood Cancer Survivor Study is a comprehensive long-term follow-up study funded by the National Cancer Institute. In this analysis, PTSD symptoms, clinical distress, and functional impairment were compared between 6,542 adult childhood cancer survivors and 368 of their siblings. Nine percent of survivors and 2 percent of their siblings were found to have PTSD. Survivors who had been diagnosed before the age of four, and treated with radiation to the head, were at increased risk of PTSD.

Other factors also influenced PTSD incidence, including diagnosis and type of treatment. PTSD was more common among those who had been treated with intensive therapies, such as amputation, radiation, or multiple modalities. Compared to survivors of other cancers, PTSD was less common among survivors of neuroblastoma, which usually occurs in very young children, and Wilms' tumor, the therapy for which usually involves only surgery.

Dr. Stuber and her colleagues also found that PTSD was more common among unmarried individuals, survivors with less than a college education, individuals earning less than $20,000 per year, or who were unemployed, although the specific relationship between these factors and PTSD was unclear. She concluded, however, that these factors may help clinicians identify childhood cancer survivors who are at high risk of PTSD.

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エルロチニブは肺がん患者の生存率を改善することが明らかになった（Abstract #: LBA8002）

ATLAS：ベバシズマブ維持療法にエルロチニブを追加することにより進行非小細胞肺がん患者の予後が改善する

ATLAS: Adding erlotinib to bevacizumab maintenance therapy in patients with advanced non-small cell lung cancer improves outcomes

化学療法とベバシズマブによる初回治療後に、ベバシズマブによる維持療法にエルロチニブを追加することによりベバシズマブ単独投与と比較し、非小細胞肺がん患者の進行が遅延したとの研究結果が、ある国際研究チームにより第45回American Society of Clinical Oncology学会で発表された。この二重盲検phase IIIトライアルは768人の患者をベバシズマブとエルロチニブまたはベバシズマブとプラセボを投与する群に無作為に割り付けた。患者は全員がファーストライン治療として4クールの化学療法とベバシズマブ投与を受けていた。進行の認められなかった患者に対してはその後ベバシズマブを継続し、プラセボかエルロチニブを投与する群に無作為に割り付けた。このスタディはこのトライアルの二回目に計画されたデータの中間解析を報告したものであり、有意な有効性の改善がエルロチニブ群において認められた。エルロチニブ群の患者はがん進行のリスクが29%低かった。無増悪生存期間中央値はエルロチニブとベバシズマブ併用群で4.8ヵ月であり、ベバシズマブープラセボ投与群では3.7ヵ月であった。両群ともに想定外の副作用は認められなかった。これらの結果を基にトライアルは予定より早く中止された。

Full Text

An international team of researchers has shown that adding erlotinib to bevacizumab maintenance therapy after initial treatment with chemotherapy and bevacizumab in patients with advanced non- small cell lung cancer delays disease progression better than bevacizumab alone.

"There is ongoing interest among medical oncologists about the potential role of maintenance therapy for patients with advanced non-small cell lung cancer," said Vincent A. Miller, M.D., Associate attending Physician on the Thoracic Oncology Service at Memorial Sloan-Kettering Cancer Center and lead author of the study, known as ATLAS. "Bevacizumab is a core component of the treatment of advanced non-small cell lung cancer (NSCLC), and we've shown here we can delay progression with the addition of a targeted agent, erlotinib. Critical future work will try to determine which patients will get the greatest benefit from this combination, based in large part on the identification of genetic biomarkers."

Maintenance therapy, a relatively new concept in NSCLC, refers to the continuation of one or more agents of a chemotherapy regimen but not the whole regimen to delay progression of disease and potentially improve survival after patients have received several months of stronger standard chemotherapy, which can carry significant side effects. This is the first study to show that adding erlotinib to maintenance therapy with bevacizumab delays disease progression in patients who have already received bevacizumab as part of their initial chemotherapy. Both bevacizumab and erlotinib have fewer side effects than traditional cytotoxic chemotherapy.

Previous research has shown that bevacizumab along with chemotherapy improved progression-free and overall survival among patients with advanced, metastatic, or recurrent non-squamous NSCLC when compared to chemotherapy alone. In that study, bevacizumab was continued after chemotherapy until disease progression. The purpose of the current study was to determine if progression could be further delayed by the addition of erlotinib.

In this randomized, double-blind, phase III trial, 768 patients were randomized to receive bevacizumab plus erlotinib or bevacizumab plus placebo. All patients had already received four cycles of chemotherapy and bevacizumab as first-line therapy. Patients who had not progressed then continued bevacizumab and were blinded and randomized to receive placebo or erlotinib.

This study reports the results of the trials second planned interim analysis of the data, which identified a statistically significant improvement in efficacy, favoring the erlotinib group; the trial was stopped early based on these findings. Patients in the erlotinib group experienced a 29 percent reduced risk of disease progression. Median progression-free survival was 4.8 months for patients in the erlotinib plus bevacizumab group, compared with 3.7 months for patients in the bevacizumab-placebo group. There were no unexpected side effects in either arm.

ASCO2009特集

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[News Flash 15] MSH2蛋白は化学療法の有効性を予測する

MSH2蛋白は化学療法の有効性を予測する（Abstract #: CRA7502）

ILAT：MSH2 DNA修復蛋白の少ない非小細胞肺がん患者は化学療法の有効性が高い

ILAT: Patients with non-small cell lung cancer lacking MSH2 DNA repair protein fare better with chemotherapy

国際アジュバント肺トライアル（International Adjuvant Lung Trial ：IALT）の解析の結果、腫瘍のMSH2蛋白レベルは外科的に除去された非小細胞肺がん（NSCLC）患者のシスプラチンベースの化学療法に対する長期の有効性を予測することが報告された、と第45回American Society of Clinical Oncology学会で発表された。腫瘍がMSH2を有する（”MSH2陽性”）NSCLC患者257人と腫瘍がMSH2を有さないあるいは腫瘍のMSH2レベルの低い（”MSH2陰性”）患者416人の全生存率を比較した。MSH2陰性の患者においては、シスプラチンを投与された患者の生存期間中央値は58ヵ月であったのに対し化学療法を受けなかった患者のそれは42ヵ月であった。MSH2陽性患者では、化学療法を施行された患者の全生存期間中央値は49ヵ月であったのに対し化学療法を受けなかった患者のそれは58ヵ月であった。次にこのスタディで明らかとなったことは、MSH2の的中率が、ERCCと呼ばれる過去に同定されたもうひとつのDNA修復関連蛋白のそれと同等であったことである。腫瘍内の両蛋白レベルの低い患者のうちシスプラチン治療を施行された者は化学療法を施行されなかった者と比較し生存期間が21ヵ月長かった（55ヵ月対34ヵ月、p=0.01）。研究者らは、シスプラチンベースの化学療法から得られる長期の有益性を予測するにはERCC1にMSH2レベルを組み合わせてもよいであろうと結論付けている。

Full Text

An analysis from the International Adjuvant Lung Trial (IALT) reports that tumor levels of the MSH2 protein predict long-term response to cisplatin-based chemotherapy among patients with surgically removed non-small cell lung cancer (NSCLC).

MSH2 is a protein that cancer cells use to repair DNA damaged by cisplatin. Researchers found that patients with no or low levels of the MSH2 protein respond better to treatment than patients with high levels.

A secondary finding of this study was that the predictive value of MSH2 was equal to that of a second, previously identified protein associated with DNA repair, called ERCC1. And when tumor levels of both ERCC1 and MSH2 are taken into account, researchers report they can further identify patients most likely to benefit from cisplatin-based chemotherapy.

"We have identified new and easily performed assays that can be used to predict response to chemotherapy in patients with non-small cell lung cancer by measuring tumor levels of two key proteins - ERCC1 and MSH2," said Pierre Fouret, M.D., Ph.D., professor at Institut Gustave Roussy (Villejuif, France) and Universite Pierre et Marie Curie (Paris, France) and the study's lead author. "This development is a step toward more personalized treatment for patients whose lung cancers have been surgically removed."

Cisplatin is commonly used as a postoperative treatment for NSCLC, but not all patients benefit. In this study, overall survival was compared between 257 patients with NSCLC whose tumors contained MSH2 ("MSH2-positive") and 416 whose tumors contained no MSH2 or low levels of this protein ("MSH2- negative"). Patients were then grouped by whether or not they underwent cisplatin-based adjuvant chemotherapy.

Adjuvant cisplatin-based chemotherapy increased overall survival among MSH2-negative patients, but did not benefit MSH2-positive patients. For MSH2-negative patients, median overall survival was 58 months for those who received cisplatin versus 42 months for those who did not receive chemotherapy. Among MSH2-positive patients, median overall survival was 49 months for those who received chemotherapy versus 58 months among those who did not.

Investigators also found that the predictive value of MSH2 and ERCC1 together was greater than either one alone. Patients with low tumor levels of both proteins who were treated with cisplatin-based chemotherapy lived 21 months longer than those who did not receive chemotherapy (55 months versus 34 months). The investigators concluded that MSH2 status may be combined with ERCC1 to predict long-term benefit from cisplatin-based chemotherapy.

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