ADDING CHEMOTHERAPY TO RADIATION THERAPY IMPROVES SURVIVAL IN PATIENTS WITH GBM

Glioblastoma multiforme (GBM) is a fast-growing primary brain cancer that is difficult to treat. The standard treatment for GBM is surgery followed by radiation therapy. However, patients diagnosed with GBM usually have a poor prognosis (chance of recovery). Results of a recent, large, multi-institutional phase III clinical trial show that treating patients with radiation and chemotherapy improves both progression-free survival and overall survival in GBM.

“This trial shows, for the first time, that chemotherapy is effective in treating this disease,” said lead author Roger Stupp, MD, of the University Hospital Multi-disciplinary Oncology Center in Lausanne, Switzerland. “What is also impressive is that we saw the same result even though patients were treated in over 80 institutions throughout Europe, Canada, and Australia.”

In this study, more than 500 patients with GBM were randomized into two groups. One group received standard radiation therapy, and the other group received temozolomide (TMZ [Temodar]) during and after radiation therapy. TMZ is a chemotherapy drug that has shown some promise in treating recurrent brain cancer.

After two years of follow-up, the median survival time and progression-free survival was 15 months for the patients treated with both radiation and TMZ, and 12 months for the patients who received only radiation. The percentage of patients who survived for two years or more jumped from 10% in the radiation only group to 27% in the radiation plus TMZ group. Overall, this new treatment appeared safe and well tolerated.

Dr. Stupp cautioned that although this study will probably establish a new treatment standard, most people with GBM cannot be cured. “Patients are still not cured of their disease, so we need to do more research and clinical trials,” he said. (Abstract #0002)

WHAT THIS MEANS FOR PATIENTS

This new treatment is not a cure for GBM, but it can extend patients’ lives in a meaningful way. Many doctors have not suggested clinical trials for these patients before because of how fast these tumors grow and spread. Because of these positive results, more doctors may consider enrolling patients in clinical trials, which helps improve the treatment options overall for people with GBM.
Dear Friends,

This year ASCO celebrates 40 years of quality cancer care. Since the founding of the Society in 1964, improving the treatment, prevention, care, and quality of life for each person with cancer has been at the heart of ASCO’s mission. ASCO has enhanced its commitment in recent years by formally expanding its mission to serve not only the informational needs of its members, but also those of its members’ patients.

To support this commitment, ASCO publishes Cancer Advances, a series of consumer information resources designed to help inform people of the latest advances in cancer research. Cancer Advances: News from the 2004 ASCO Annual Meeting is designed to provide people living with cancer and their families with the latest information about cancer research, prevention, care, and treatment as presented each year at ASCO’s Annual Meeting. The information contained in this issue was presented at the 40th Annual Meeting of the American Society of Clinical Oncology held in New Orleans, Louisiana, from June 5 to 8, 2004. The theme of the meeting was 40 Years of Quality Cancer Care, reflecting the Society’s commitment to excellence in the care and treatment of people with cancer over the past 40 years.

These latest advances will improve the care and treatment of people living with cancer. I hope you find this newsletter helpful in understanding the recent developments that were reported at the 2004 ASCO Annual Meeting. For more information about cancer, please visit ASCO’s People Living With Cancer website (www.plwc.org).

Sincerely,

Margaret Tempero, MD
ASCO President

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**BRAIN CANCER**

**Chemotherapy Can Delay Brain Tumor Progression; Genetic Differences in Brain Tumors Linked to Survival**

Anaplastic oligodendrogliomas (AOs) and anaplastic oligoastrocytomas (AOAs) are rare but fast-growing tumors that develop in the brain. The standard treatment is surgery followed by radiation. Doctors also know that these tumors respond to a chemotherapy regimen called PCV (procarbazine, lomustine, and vincristine). This study was done to find out whether giving PCV before radiation treatment improved survival in people with AOs and AOAs.

The results showed that overall survival was not different between the patients who received chemotherapy before radiation (4.5 years) and those who received only radiation (4.5 years). However, the cancer took longer to progress in the patients who received both chemotherapy and radiation (2.6 years) compared with the patients who only received radiation (1.9 years). The combination treatment, though, was more toxic than radiation alone.

Doctors also collected tissue samples from the tumors, knowing that in the past, oligodendrogliomas with a certain genetic characteristic responded better to treatment than tumors without it. Interestingly, the patients with oligodendrogliomas that had this genetic feature lived longer, regardless of the treatment they received.

“Oligodendrogliomas with this genetic signature have a better natural history and response to treatment. Oncologists can learn to use this information to choose the most...”
appropriate treatment for these patients,” said J. Gregory Cairncross, MD, lead author and Professor of Clinical Neuroscience and Oncology at the University of Calgary in Canada.

While longer follow-up is needed to learn whether there are any longer-term differences in treatment, this study suggests that, in the future, doctors will be able to use genetic markers to assess the prognosis (chance of recovery) of patients with oligodendrogliomas. (Abstract #1500)

WHAT THIS MEANS FOR PATIENTS

These findings show that treating patients with both radiation and chemotherapy keeps the cancer from progressing longer than treatment with radiation alone. However, this new treatment also had more serious side effects and did not improve overall survival. This doesn’t mean that chemotherapy is not a good treatment option for this type of brain cancer. More research is needed to determine if other drugs may work better and cause fewer side effects, or whether chemotherapy would be more effective if it is given at the same time as radiation therapy. The second part of the study found a correlation between the genetic profile of a brain tumor and patient survival, which may someday help doctors plan individualized treatment.

New Tumor Marker Affects Prognosis in Glioma

Researchers have discovered a correlation between a tumor protein called epidermal growth factor receptor (EGFR) vIII (‘variant three’) and the prognosis (chance of recovery) of grade 3 and 4 primary brain tumors called gliomas. Primary brain tumors begin in the brain. A grade 4 tumor, also called glioblastoma, is the fastest-growing brain tumor. Grade 3 tumors are moderately aggressive, but may grow as fast as grade 4 tumors in some patients.

In this study, doctors studied 63 tumor samples from patients with grade 3 tumors. They found that patients whose tumor samples had the vIII protein lived an average of 7.2 months, whereas the patients whose tumors did not have vIII lived an average of 33 months.

Jan Buckner, MD, lead author and Professor of Oncology at the Mayo Clinic College of Medicine in Rochester, Minn, explained that this information could be used to identify which grade 3 gliomas might grow as quickly as grade 4 gliomas. “vIII expression is characteristic of glioblastoma multiforme, the most aggressive primary brain tumor. It is reasonable to treat patients with grade 3 gliomas and vIII expression as glioblastoma patients.” These results confirm previous findings that genetic markers of glioblastoma in grade 3 tumors are associated with a poor prognosis.

“Eventually, vIII expression may be important in selecting patients for clinical trial participation and for therapies that target individual molecular profiles,” said Dr. Buckner. (Abstract #1508)

WHAT THIS MEANS FOR PATIENTS

This study suggests that the presence of a tumor marker called vIII in grade 3 gliomas indicates a fast-growing tumor that should be treated like a grade 4 tumor. Previously, doctors determined prognosis and treatment by looking at how the tumor cells appeared under the microscope. Now, doctors may be able to use both the tumor grade and the tumor marker to help them better treat people with grade 3 gliomas.
Two new studies demonstrate that docetaxel (Taxotere) extends survival and relieves pain in men with prostate cancer that does not respond to hormone therapy. This type of cancer is called hormone-refractory, or androgen-independent, prostate cancer. Hormone therapy is a primary treatment for prostate cancer, but often loses its effectiveness over time.

The results of the first study showed a 20% survival advantage with a new chemotherapy regimen of docetaxel and estramustine (Estracyte) when compared with the current standard therapy of mitoxantrone (Novantrone) and prednisone in a randomized, phase III trial of more than 700 men. In addition, the new combination increased the time it took for the disease to progress: six months for the men who received docetaxel/estramustine, and three months for the men who received mitoxantrone/prednisone. For late-stage prostate cancer, an increase of three months’ survival time is considered significant.

“The findings show that docetaxel can effectively treat hormone-refractory prostate cancer. Docetaxel-based therapy is now a treatment to build upon,” said Daniel Petrylak, MD, lead author of the trial and Associate Professor of Medicine at Columbia University College of Physicians & Surgeons, Director of Genitourinary Oncology Program at New York Presbyterian Hospital in New York City. (Abstract #0003)

A second study of 1,006 men with hormone-refractory prostate cancer showed that docetaxel plus prednisone given every three weeks improved overall survival, reduced prostate-specific antigen (PSA) levels, and improved pain symptoms. In addition, this treatment had relatively few side effects, the most common one being neutropenia (a low number of white blood cells).

In this study, researchers compared three drug regimens: two different doses of docetaxel (once a week vs. once every three weeks) plus prednisone, or mitoxantrone plus prednisone (given every three weeks). At a median follow-up time of 20.7 months:

- Survival was significantly longer for men who received docetaxel once every three weeks (18.9 months) compared with those who received docetaxel weekly (17.4 months) or mitoxantrone plus prednisone every three weeks (16.5 months).
- In men who received docetaxel every three weeks, 45% had a reduction in their PSA levels, compared with 48% of the men who received docetaxel weekly, and 32% of the men who received mitoxantrone plus prednisone every three weeks.
- Men who received docetaxel every three weeks experienced greater pain relief (33%) compared with those who received weekly docetaxel (31%) or mitoxantrone plus prednisone every three weeks (22%).

“This is the first evidence of a survival advantage with chemotherapy in phase III trials in patients with hormone-refractory prostate cancer,” said Mario Eisenberger, MD, lead author of this study and R. Dale Hughes Professor of Oncology and Urology at Johns Hopkins School of Medicine in Baltimore, Md. “We have a real chance to finally develop a treatment approach that is not based primarily on hormonal therapy and make a real long-term impact on this disease.” (Abstract #0004)
Hormone Therapy For Non-Metastatic Prostate Cancer Increases Risk of Bone Fractures

A new study suggests that men taking a specific type of hormone therapy, called gonadotropin-releasing hormone (GnRH) agonists, for prostate cancer are at an increased risk of bone fractures. This risk increases the longer the treatment continues. GnRH agonists work by limiting production of the hormone testosterone. This type of hormone therapy is also called androgen deprivation therapy (androgens are male sex hormones).

“These results highlight the importance of osteoporotic fractures as an adverse effect of androgen deprivation therapy for prostate cancer,” said lead study author Matthew R. Smith, MD, PhD, of Massachusetts General Hospital Cancer Center and Assistant Professor of Medicine at Harvard Medical School in Boston.

In this study, investigators analyzed the Medicare claims of more than 3800 men with non-metastatic prostate cancer who received GnRH agonists and compared them with the claims from more than 7700 men who did not receive these drugs. They found that men who received GnRH agonist treatment were 40% more likely to suffer a fracture than the men who did not receive this treatment. In addition, men who were on this hormone therapy for more than three years had a higher risk of fracture than those who took the drugs for one year or less.

“We were surprised by the strength and consistency of the association between GnRH agonist treatment and fractures,” said Dr. Smith. “For men who require androgen-deprivation therapy, screening for osteoporosis and interventions to prevent fractures should become standard care.”

WHAT THIS MEANS FOR PATIENTS

Men with prostate cancer who already receive androgen deprivation therapy should talk to their doctor about osteoporosis screening and ways to prevent fractures. For example, bisphosphonates have been shown to increase bone mineral density in men receiving GnRH treatment for prostate cancer. Men who are considering hormone therapy are encouraged to talk to their doctor about the risks and benefits of this therapy.

New Drug Shows Promise in Treating Imatinib-Resistant GIST

A new drug called SU11248 shrinks or slows the progression of cancer in patients with gastrointestinal stromal tumor (GIST) whose tumors have stopped responding to the standard treatment of imatinib (Gleevec).

GIST is a rare cancer of the stomach or intestinal tract that is treatable with imatinib. However, imatinib eventually stops working in about half of all patients, and the cancer progresses.

“We’re not replacing imatinib as initial therapy for GIST, but we need to develop better therapies and make their effects last longer,” said lead author George D. Demetri, MD, Director of Sarcoma and Bone Oncology at the Dana-Farber Cancer Institute and Associate Professor of Medicine at Harvard Medical School in Boston, Mass.

In this small study, 48 patients with imatinib-resistant GIST were given SU11248 (taken as a pill once a day). Tumors in 26 patients (54%) either responded to this treatment or did not progress.
Three new studies suggest that adding rituximab (Rituxan), a monoclonal antibody therapy, to chemotherapy is an effective treatment for several types of non-Hodgkin lymphoma (NHL).

Monoclonal antibodies are laboratory-made substances that recognize and attach to specific proteins (called antigens) on the outside of lymphocytes (white blood cells). Rituximab binds to an antigen on lymphoma cells called CD20. Researchers think that this action helps the body’s immune system destroy the cancer cells.

In the first study, researchers found that two years of maintenance therapy with rituximab increases the time it takes for the cancer to progress after chemotherapy in patients with advanced indolent lymphoma. Indolent lymphoma is a slow-growing cancer that initially responds well to therapy, but eventually recurs in most patients. Maintenance therapy is given after chemotherapy to “maintain” a tumor’s response to that drug and keep the cancer from returning.

“We had hoped to see an improvement in time to progression, and the effect was even more robust than we hoped,” said Howard Hochster, MD, lead author of the study and Professor of Medicine at New York University School of Medicine. In fact, the results were so good, the study was stopped early so that all patients could receive rituximab.

In this phase III clinical trial, 149 patients with stage III or IV follicular and small lymphocytic lymphoma received chemotherapy, and 154 patients received chemotherapy followed by rituximab treatment. The chemotherapy regimen used in this trial was CVP (cyclophosphamide, vincristine, and prednisone).

After two years, cancer did not progress in 74% of the patients who received rituximab, compared with 42% of the patients who received only chemotherapy. After four years, cancer did not progress in 58% of the patients who received rituximab, compared with 34% of the patients in the other group. These differences did not appear to be related to tumor cell type (histology), the presence of cancer left behind after chemotherapy (residual disease), or the amount of cancer in the patient’s body (tumor burden).

“We hope this will eventually translate into improved survival in this disease. No treatment to date has shown survival improvement in indolent lymphoma,” said Dr. Hochster.

Hochster estimated that another five years of follow-up might be necessary to know whether this therapy increases overall survival. (Abstract #6502)

Maintenance therapy is given after chemotherapy to “maintain” a tumor’s response to that drug and keep the cancer from returning.

In another trial, researchers found that adding rituximab to chemotherapy improves survival in younger patients with low-risk diffuse large B-cell lymphoma (DLBCL). DLBCL is the most common type of non-Hodgkin lymphoma. The usual treatment for DLBCL is chemotherapy based on a chemotherapy regimen called CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone). Rituximab added to chemotherapy has already been shown to be an effective treatment in patients over age 60, so this trial was designed to learn if rituximab would have a similar benefit in younger patients with DLBCL.

More than 700 patients aged 18 to 60 with low-risk DLBCL who had not yet been treated were randomized into two groups: half received CHOP-like chemotherapy and the other half received CHOP-like chemotherapy and rituximab. These results were observed at 15 months:

- More patients who received chemotherapy plus rituximab continued to respond to their treatment (84%), compared with those who...
received only chemotherapy (63%).

- Eighty-five percent (85%) of the patients who received both chemotherapy and rituximab experienced a complete remission (CR), compared with 66% of the patients who received only chemotherapy.

- Of the patients treated with chemotherapy and rituximab, cancer in 6.3% of the patients progressed, compared with cancer in 17.7% of the patients treated with chemotherapy alone.

- Overall survival was 98.5% in the patients who received chemotherapy plus rituximab, and 92% in those who received chemotherapy alone.

Because these younger, low-risk patients start with a relatively good prognosis (chance of recovery), the investigators were surprised that they were able to improve the results in these patients. “The combination of a CHOP-like chemotherapy with rituximab has achieved the best results reported ever for young patients with low-risk aggressive lymphoma,” said the study’s lead author Michael Pfleundschuh, MD, Director of Medical Oncology at Saarland University Medical School in Homburg, Germany. If doctors continue to see positive results in the next several years, Dr. Pfleundschuh speculates that lymphoma in this set of younger patients could be considered curable. (Abstract #6500)

In the third study involving lymphoma, investigators found that adding rituximab to chemotherapy can slow the progression of mantle cell lymphoma (MCL). This subtype of non-Hodgkin lymphoma is most common in people over the age of 60 and does not often respond to treatment.

This study included 122 patients with newly diagnosed MCL. Sixty patients received CHOP and 62 patients received CHOP plus rituximab.

- Thirty-four percent (34%) of the patients who received CHOP plus rituximab experienced a complete remission (CR) compared with only 7% of the patients who received CHOP.

- Ninety-four percent (94%) of the patients who received CHOP plus rituximab experienced either a CR or a partial remission (PR) compared with 75% of the people who received CHOP alone.

- The time until the treatment stopped being effective was 22 months for the patients taking CHOP plus rituximab compared with 14 months for the patients receiving CHOP alone.

- There was no significant difference in treatment-associated side effects.

“Combining immunotherapy and chemotherapy may represent the new gold standard for treating MCL,” said one of the study’s lead authors, Martin Dreyling, MD, of the University of Munich in Germany. “Whereas rituximab alone has limited activity against MCL, combining it with chemotherapy improves treatment effectiveness considerably without any clinically significant increase in toxicity.” (Abstract #6501)

**WHAT THIS MEANS FOR PATIENTS**

These studies show that adding the monoclonal antibody therapy rituximab to current therapies is effective in treating patients of various ages, subtypes, and stages of non-Hodgkin lymphoma (NHL). The first study shows that rituximab is an effective maintenance therapy for people with indolent NHL. The second study shows that adding rituximab to chemotherapy improves survival in young, low-risk people with DLBCL. Finally, the third study demonstrates that adding rituximab to chemotherapy slows the progression of cancer in people with MCL. In each case, doctors will continue to study the long-term treatment response and side effects of rituximab.
Drug Shows Activity in Advanced BAC

Bronchioalveolar cell carcinoma (BAC) is a rare type of non-small cell lung cancer (NSCLC) that is most common in younger, non-smoking women. The number of people diagnosed with BAC increases each year. In the largest prospective trial to date of 138 patients with advanced BAC, researchers found that a drug called gefitinib (Iressa) produced a positive response, especially in patients who had not received any prior treatment.

Gefitinib works by shutting down a protein called the epidermal growth factor receptor (EGFR), which is why it is called an EGFR inhibitor.

The results showed that cancer in 19% of the previously untreated patients responded to gefitinib, with 6% of patients experiencing a complete response, which is when all signs of cancer disappear. In patients who had already been treated with other drugs, the cancer showed a 9% response rate to gefitinib, but there were no complete responses. The median survival rate was 12 months for the previously untreated patients and 13 months for those patients who had been previously treated with other chemotherapy.

“This trial demonstrates clear, long-lasting activity for gefitinib in a minority of patients with BAC,” said lead author Howard West, MD, of the Swedish Cancer Institute in Seattle, Wash. He suggested that gefitinib could become a new standard of care for patients with BAC.

Researchers also found that certain groups of patients responded differently to gefitinib. For example, women on gefitinib lived a median of 19 months, compared with an average of 8 months in men. Patients who developed a rash from gefitinib treatment lived longer (13 months) than those without a rash (5 months). Ongoing analysis of the data also suggests that patients who had never smoked live longer on gefitinib than former or current smokers. Similar results have been seen previously in other EGFR inhibitors.

Dr. West thought these results were interesting, but explained that more research needed to be done to understand why different groups of patients respond differently to the same treatment.

(W WHAT THIS MEANS FOR PATIENTS

These results add to existing data showing that gefitinib and drugs that target the EGFR pathway are effective in treating people with BAC. For reasons not yet understood, women, nonsmokers, and patients who develop a rash survive longer on this therapy.

U.S. and Japanese Patients With NSCLC Respond Differently to Chemotherapy

A new study shows that paclitaxel (Taxol) is more effective but also more toxic in Japanese patients with advanced stage non-small cell lung cancer (NSCLC) than in U.S. patients. Non-small cell lung cancer is the most common type of lung cancer.

To address differences in study results from country to country, doctors from the Japanese Four Arm Cooperative Study (FACS) and the Southwest Oncology Group (SWOG) in the United States designed separate, parallel phase III trials for the treatment of NSCLC. One group of patients in each trial received the same treatment—a combination of paclitaxel and carboplatin. Because the dose of paclitaxel the patients received was based on previous phase I studies, the Japanese patients received 200 mg/m² and the American patients received 225 mg/m².

The study found that the characteristics of the patients (such as age, ratio of men to women, stage, and type of cancer) enrolled in Japan were statistically identical to those of the patients enrolled in the United States. But, the response to treatment was different. After one year of treatment, 51% of the Japanese patients were living, compared with 37% of the American patients. The Japanese patients were also 2.5
times more likely to experience severe neutropenia (low white blood cell count) and almost five times more likely to experience neutropenia accompanied by a fever than U.S. patients.

“Results of a cancer clinical trial performed in one part of the world may not necessarily hold true for populations in another region,” said lead author David Gandara, MD, Director of Clinical Research at the University of California, Davis Cancer Center and Professor of Medicine at the University of California, Davis School of Medicine. “Compared to the relatively homogeneous population in Japan, the United States is very diverse. When we examine studies, we have to take these population-related differences into consideration.”

Dr. Gandara and his fellow researchers think that genetic differences in the way people’s bodies break down drugs may explain these results, and that this effect may be why the response to cancer treatments varies in different parts of the world. (Abstract #7007)

WHAT THIS MEANS FOR PATIENTS

The study demonstrates that people from different countries can have different responses to treatment, such as chemotherapy, than patients in the United States. This result may help doctors interpret clinical trial results from countries outside the United States.

Chemotherapy After Surgery Improves Survival in Patients with Early Lung Cancer

A new study shows that giving chemotherapy after surgery (adjuvant chemotherapy) results in a significant survival advantage in people with stage IB non-small cell lung cancer (NSCLC).

Stage IB NSCLC describes a small to medium-sized tumor that has not spread to the lymph nodes. This type of lung cancer is currently treated with surgery. The purpose of this study was to learn whether chemotherapy after surgery helped people with stage IB NSCLC live longer, because the results of previous studies have been conflicting.

In this study, researchers randomly assigned 344 patients with stage IB NSCLC to receive paclitaxel (Taxol) and carboplatin (Paraplatin) after surgery or surgery alone. After four years, 71% of the patients who received chemotherapy were living, compared with 51% of the patients who only had the surgery. This means that adjuvant chemotherapy lowered the risk of death by 38%. In fact, the results were so clear that the trial was stopped early so that all patients could receive adjuvant chemotherapy. “These figures will hopefully translate into an improvement in the cure rate in early stage lung cancer,” said lead investigator Gary Strauss, MD, MPH, of Rhode Island Hospital and Brown Medical School in Providence. He hopes that these results are convincing enough to change how patients with high-risk, early stage lung cancer are treated. (Abstract #7019)

WHAT THIS MEANS FOR PATIENTS

This study shows that adjuvant chemotherapy (chemotherapy after surgery) improves survival in a specific group of people with early stage NSCLC. More research is needed to know whether adjuvant chemotherapy could help people with operable, stage II cancers.
CANCER GENETICS

Patients’ Quality of Life May be Linked to Genetic Structure

A new study found an association between the quality of life of patients with metastatic colorectal cancer and variations in a set of genes called folate genes. The results of this study suggest that doctors may be able to identify and provide relief to those patients who are more at risk of certain side effects associated with cancer.

“Patients diagnosed with cancer are affected by their condition in different ways. These results suggest that a patient’s genetic structure may play a role in determining the quality of life after a diagnosis of cancer,” said Jeff Sloan, PhD, of the Mayo Clinic in Rochester, Minn.

In this study, 494 patients with metastatic colon cancer provided DNA samples and completed a quality of life questionnaire before they received chemotherapy. By collecting this information before treatment, the researchers could explore the relationship between genetic profile and quality of life without the influence of side effects from the treatment.

The researchers then analyzed three folate genes called DPYD, MTHFR, and TYMS, which are known to be associated with a person’s health. One interesting result is that patients with two variant forms of the DPYD gene experienced less fatigue than patients with the regular form of the gene.

“We want cancer patients to have the best quality of life possible,” said Dr. Sloan. “If we can identify cancer patients who have a genetic predisposition to fatigue, stress, or other quality of life deficits, we can intervene early to help them deal with these issues.”

Dr. Sloan and his colleagues will continue to investigate genes that may affect quality of life, with the goal of developing clinical interventions to improve the quality of cancer patients’ lives. For example, patients who are likely to experience fatigue could be offered sleep therapy, counseling, or exercise. (Abstract #0005)

WHAT THIS MEANS FOR PATIENTS

This is the first study to find a relationship between patients’ quality of life and their genes that is not dependent on the treatment they receive. In the future, doctors hope that they can analyze a patient’s genes to anticipate which patients will benefit the most from quality of life interventions.

Genetic Variation Is Associated With Treatment-Related Side Effects

A new study finds an increased risk of severe digestive side effects in patients with a specific genetic variation who were treated with radiation and platinum-based chemotherapy for non-small cell lung cancer (NSCLC).

In this study, doctors treated 147 patients with radiation and either cisplatin (Platinol) or carboplatin (Paraplatin) and recorded the gastrointestinal (GI) side effects, such as nausea, vomiting, and inflammation or irritation of the esophagus (esophagitis). They also analyzed each patient’s ERCC1 gene.

The investigators found that 30% of the patients who experienced more intense side effects had a variation in the ERCC1 gene. In comparison, only 14% of patients without this genetic variation experienced serious side effects.

“Our study raises interesting questions that will need to be validated in prospective trials before the results can be used in patient care,” said lead investigator Rebecca Suk, Continued on page 13

WHAT THIS MEANS FOR PATIENTS

Doctors are starting to understand why people have different reactions or responses to cancer treatment, and one of these reasons appears to be genetic. Once more of these studies are done in larger groups of people, doctors may someday be able to select treatment plans according to a patient’s genes. This individual approach to cancer treatment, though, is still many years away.
First Time Drugs Show Promise in Treating Metastatic Renal Cell Carcinoma

Renal cell carcinoma (RCC) is the most common kind of kidney cancer. Unfortunately, most cases are not diagnosed until the cancer has spread to other parts of the body (metastasized), which means that patients with metastatic RCC usually have limited treatment options. Two new studies demonstrate that metastatic RCC responds to new drugs that target multiple, specific pathways in cancer cells.

In the first study, John Hainsworth, MD, Director of Clinical Research at the Sarah Cannon Cancer Center in Nashville, Tenn, and colleagues gave 62 patients with RCC a combination of bevacizumab (Avastin) and erlotinib (Tarceva). Of the first 40 patients who were treated, cancer in 25% of the patients showed a partial response at eight weeks, and the cancer progressed in only 12% of the patients. In addition, the cancer did not get worse for six months in 71% of patients. Usually, doctors only see a 5% response to treatment with the standard therapy—either interleukin-2 or interferon.

Dr. Hainsworth cautioned that these results are still preliminary. "If these results are verified in larger trials, this treatment may emerge as the first well-tolerated regimen for people with renal cancer."

These drugs are specifically designed to act on proteins important to the cancer process. Researchers think that erlotinib blocks an enzyme called the epidermal growth factor receptor tyrosine kinase, which regulates cancer cell growth. Bevacizumab is a monoclonal antibody that blocks the activity of a protein called vascular endothelial growth factor, which helps the tumor form new blood vessels in a process called angiogenesis.

Interestingly, these two drugs block different pathways in the cancer cell, and may lead to a new approach in using targeted therapy. "Combining these targeted agents is the future of cancer treatment," said Dr. Hainsworth. The U.S. Food and Drug Administration recently approved bevacizumab, but erlotinib is still an experimental drug and is only available through clinical trials at this time. (Abstract #4502)

In the second study, 63 patients with metastatic RCC received a new chemotherapy pill called SU011248. The cancer showed a partial response in nearly a quarter of the patients. Six months after treatment, the cancer was still not growing in 14 of those patients. At this point in the study, the new drug appears safe and well tolerated, although patients experienced mild to moderate fatigue and gastrointestinal problems.

"During the past 15 years, I have conducted many studies for renal cancer, but none of them showed this degree of activity as a single agent," said Robert J. Motzer, MD, the study’s lead author and Attending Physician at Memorial Sloan-Kettering Cancer Center in New York City. "SU011248 clearly shows activity, is relatively well tolerated, and it’s a pill that patients can take at home."

Researchers think that SU011248 blocks several different targets in cancer cells, including those necessary for cancer cell growth and new blood vessel formation (angiogenesis). SU011248 still needs to be tested in phase III clinical trials to confirm these findings.

"This is a very exciting drug for possible use in the treatment of renal cancer,” added Dr. Motzer. “The disease has been considered ‘the unbeatable cancer,’ with resistance to all forms of chemotherapy and only a small proportion of patients responding to immunotherapies for a limited time." (Abstract # 4500)
A study of more than 5,000 postmenopausal women with osteoporosis shows that raloxifene (Evista), a drug used to treat bone loss, also lowers a woman’s risk of estrogen receptor (ER) positive invasive breast cancer. These findings mark eight years of follow-up without any new safety concerns.

Raloxifene is a type of drug called a SERM (selective estrogen receptor modulator), which means it acts like a natural estrogen in some ways. It is currently used for the prevention and treatment of osteoporosis. Osteoporosis is a condition marked by a decrease in bone size and strength. Postmenopausal women are at greater risk of developing this condition because their bodies stop producing the estrogen hormone, which helps protect against bone loss.

The CORE (Continuing Outcomes Relevant to Evista) trial is a follow-up to the MORE (Multiple Outcomes Of Raloxifene) trial. In the MORE trial, doctors compared raloxifene with no treatment (a placebo) over a four-year period in a large group of women. They found that the incidence of invasive breast cancer was reduced by 72% in women receiving raloxifene.

In the CORE trial, researchers continued to follow the women who were part of the MORE trial for four more years to learn whether raloxifene continues to lower the incidence of breast cancer in postmenopausal women. The CORE trial results showed that women who received raloxifene reduced their risk of invasive breast cancer by 59% during years four through eight. The magnitude of the risk reduction during the second four-year period was similar to that seen during the first four years. When the results of the CORE trial are combined with the results of the MORE trial, women taking raloxifene reduced their incidence of ER-positive invasive breast cancer by 66% over the eight-year period.

“These data add to the existing body of information that SERMs are an approach by which breast cancer incidence can be reduced,” said Silvana Martino, DO, of the Cancer Institute Medical Group and John Wayne Cancer Institute in Santa Monica, Calif, and lead author of this study. (Abstract #1000) ■
A new study from the University of Michigan and CHS National Cancer Control Center in Israel suggests that statins may be protective against colorectal cancer.

Statins are a group of widely-prescribed drugs that lower cholesterol. Previous studies have associated statin use with a reduction of colorectal cancer risk. Colorectal cancer is the second leading cause of cancer death in both men and women in the United States, second only to lung cancer.

In this case-control study, researchers compared the use of statins in 1,608 Israeli patients who were diagnosed with colon cancer and 1,734 Israelis who did not develop colorectal cancer. The researchers confirmed the use of statins from prescription records.

They found that people who took statins were 51% less likely to develop colorectal cancer than those who did not report taking statins. This protective effect was still significant even after researchers adjusted for other known risk factors of colorectal cancer.

“While the study’s results provide a compelling rationale for more research, it is too early to recommend that patients take statins to reduce their risk of colorectal cancer,” said Stephen Gruber, MD, PhD, senior investigator of the study, of the University of Michigan in Ann Arbor.

Other types of cholesterol-lowering drugs, such as fibrates, did not appear to protect against colon cancer. “We found that the protective effect of lipid lowering agents was restricted to statins,” said Dr. Gruber.

(Abstract #0001)

WHAT THIS MEANS FOR PATIENTS

At this time, statins are not approved for reducing the risk of colorectal cancer. People should not take statins to reduce their risk of colorectal cancer. The results of this study will likely lead to randomized, controlled clinical trials that test whether statins can be used to prevent or treat cancer.

ASCO PATIENT GUIDES

New ASCO Patient Guide Available

Hormone Therapy for Advanced Prostate Cancer describes the clinical recommendations for the management of men with metastatic, recurrent, or progressive (advanced) prostate cancer.

This patient guide addresses topics such as

- What is advanced prostate cancer
- The role of hormones and hormone therapy in advanced prostate cancer
- When to begin hormone therapy
- The role of nonsteroidal anti-androgen treatment
- The use of combined androgen blockade treatment
- What to ask your doctor about hormone therapy
- Where to find the original ASCO guideline

To order, please call 1-888-651-3038 or access it online at ASCO’s People Living With Cancer website (www.plwc.org).

CANCER GENETICS (Continued)

Continued from page 10

MD, of Harvard University in Boston, Mass. “However, as we learn more about how genetic differences affect treatment outcomes for lung cancer, we hope to one day be able to select treatment based on individuals’ genetic profiles.”

Chemotherapy and radiation cause DNA damage in both healthy and cancerous tissues. In patients with a functional ERCCI gene, the damage is repaired in the healthy tissue. The researchers hypothesized that in the patients with an alteration in the ERCCI gene, the damage cannot be repaired, and as a result, these patients experience more severe side effects.

(Abstract #2014)
Stage I seminoma is an early stage, slow-growing type of testicular cancer. The standard treatment is usually removal of the cancerous testicle (orchiectomy), followed by adjuvant radiation therapy. However, patients who receive radiation therapy also tend to have a higher risk of developing a second cancer in another organ 10 to 20 years later.

Results of a new European study show that one course of chemotherapy treatment with carboplatin (Paraplatin) is as effective as radiation therapy, and is associated with a lower risk of a second cancer in the near term. In men who are at risk of developing cancer in the remaining testicle, this research suggests that the use of chemotherapy may allow doctors to preserve the remaining testicle.

Doctors randomly assigned 904 patients with stage I seminoma to receive radiation after surgery, and 543 patients to receive a single dose of carboplatin after surgery. After two years of follow-up, the researchers found that cancer did not return in 98.1% of patients who received carboplatin treatment, compared with 97.2% of the patients who received radiation treatment. These numbers were also similar after three years of follow-up. To date, one man who received carboplatin has developed a tumor in the remaining testicle, compared with seven men who received radiation therapy.

“Though needing longer follow-up and larger numbers to be sure, this surprising finding is the first hint that ultimately research may make it possible for testis conservation to be as routine as breast conservation,” said lead author R. Timothy Oliver, MD, Sir Maxwell Professor in Oncology at Barts and The London Queen Mary’s School of Medicine in Great Britain.

Another advantage is that patients only need one chemotherapy treatment instead of three weeks of radiation therapy, which is more convenient for the patient and results in a shorter recovery time. Because these patients have only been followed for two or three years, researchers do not yet know the long-term effects of this therapy.

“This large, randomized trial establishes after 20 years of research and uncertainty that one shot carboplatin in the short term is as safe as radiation, is less toxic, and might open the way to using chemotherapy for testis conservation,” said Dr. Oliver. (Abstract #4517)

WHAT THIS MEANS FOR PATIENTS

Although testicular cancer is curable, men may experience second cancers or other long-term effects from radiation therapy. Because many men who develop testicular cancer are young, the possibility of long-term side effects is a significant issue. These data may introduce adjuvant chemotherapy as the new standard treatment for stage I seminoma, but the long-term risks of this treatment are not known at this time. Adjuvant chemotherapy also appears to be safer and more convenient for patients than adjuvant radiation therapy. The study did not evaluate this treatment in men with testicular nonseminomas.
Results of a phase III clinical trial show that bortezomib (Velcade) improves patient survival and slows the progression of multiple myeloma that has come back after initial treatment (relapsed).

Bortezomib also appears to cause fewer side effects in patients than a current standard treatment, dexamethasone.

In this study, doctors compared bortezomib to dexamethasone in 669 people with relapsed multiple myeloma. At the interim analysis, bortezomib delayed cancer progression by 5.7 months, compared with 3.6 months for dexamethasone.

Survival also appeared to be better in the patients taking bortezomib, with fewer deaths in this group. The results were so significant that the study investigators stopped the trial early so all patients could receive bortezomib.

In addition, the patients who received bortezomib experienced fewer serious infections (6.7%) than the patients who received dexamethasone (10.6%).

“These results confirm the activity in patients with relapsed multiple myeloma,” said lead author Paul Richardson, MD, of the Dana-Farber Cancer Institute in Boston, Mass. “Compared to dexamethasone, bortezomib had superior time to progression and less toxicity.”

Doctors will continue to monitor the safety and effectiveness of bortezomib in these patients. (Abstract #6511)

New Drug Delays Cancer Progression in Patients With Relapsed Multiple Myeloma

WHAT THIS MEANS FOR PATIENTS

While these results are preliminary, they support the findings of an earlier phase II trial of bortezomib in patients with multiple myeloma, which prompted the U.S. Food and Drug Administration to approve bortezomib for the treatment of multiple myeloma in 2003. Because of this study, bortezomib may become a standard treatment option for relapsed multiple myeloma and may be studied as a therapy for patients with earlier stage multiple myeloma.

Continued from page 5

GASTROINTESTINAL STROMAL TUMOR (Continued)

Continued from page 5

for six months or more. Tumors in six of the patients (13%) showed a partial response. The researchers also analyzed genes from the tumor samples and found that certain mutations, or changes, in a gene called KIT were associated with responses to SU11248. These studies are important because they may help researchers understand how new drug works.

Researchers think that SU11248 blocks several enzymes, called kinases, which are believed to be involved in cancer cell growth. “There is evidence that SU11248 shuts down several switches in cancer cells, while imatinib only shuts down a few,” said Dr. Demetri. “It may be possible that several switches need to be shut off in order for a patient to derive the most clinical benefit.”

Although GIST is a rare cancer, the pathways involved in the development and spread of this cancer are similar to those in other cancers. “Studies of SU11248 in GIST give us the foothold in the door of cancer,” said Dr. Demetri. He believes that knowing how this drug works could be helpful in understanding some of the more common cancers. (Abstract #3001)

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