



# Platinum Study Newsletter

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## SPECIAL POINTS OF INTEREST:

- *Update on Study Progress*
- *The Platinum Study Website link*
- *Summaries of two Platinum Study Publications*

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### Stay connected!

**If you have moved or changed your contact information, please notify your clinic or study staff.**

## A Platinum Study Update

The Platinum Study has now enrolled over 1,800 men throughout the U.S., Canada, and the U.K. We continue to analyze data provided by you, the study participant, and present scientifically important information at national and international levels.

Presenting this research at high profile, widely-attended conferences is a key way to ensure that our findings are widely disseminated to clinicians and scientists.

This newsletter concentrates on some of these findings that teach the medical community how they can help you. We had one abstract selected for a platform presentation at the American Society of Clinical Oncology (ASCO) Cancer Survivorship Symposium held January 27-28, 2017 in San Diego, CA. Additionally, three abstracts, with one designated as a platform presentation and late-breaking abstract, were presented at the ASCO Annual Meeting

(the top international scientific conference for cancer clinicians and researchers) held June 2-6, 2017 in Chicago, IL. And most recently, two abstracts were presented at the American Society of Human Genetics (ASHG) annual meeting held October 17-21, 2017 in Orlando, FL. In this edition, we share two summaries from the six publications resulting from this research to date. To read more, please visit The Platinum Study website at the address in the box below. As always, all data are presented in aggregate; no personal identifiers are used.

We sincerely thank you for participating in this study and we assure you we are actively analyzing the collected biologic samples and data to gain knowledge we believe will improve health outcomes for future patients.



## The Platinum Study Website

Please visit the Platinum Study website to sign up for the electronic version of future editions, view previous editions, and to stay up to date on study issues and news.

**<http://cancer.iu.edu/platinum>**

***We welcome your questions and ideas!*** Please let your study site know if you have suggestions for the website or future newsletters.

## Multi-Institutional Assessment of Adverse Health Outcomes Among North American Testicular Cancer Survivors After Modern Cisplatin-Based Chemotherapy

Chunkit Fung, Howard D. Sesso, Annalynn M. Williams, Sarah L. Kerns, Patrick Monahan, Mohammad Abu Zaid, Darren R. Feldman, Robert J. Hamilton, David J. Vaughn, Clair J. Beard, Christian K. Kollmannsberger, Ryan Cook, Sandra Althouse, Shirin Ardeshtir-Rouhani-Fard, Steve E. Lipshultz, Lawrence H. Einhorn, Sophie D. Fossa, Lois B. Travis, and for the Platinum Study Group.  
*Journal of Clinical Oncology* 2017; 35:1211-1222.

**Background:** It is common for testicular cancer patients to be treated with chemotherapy that contains platinum. Platinum-containing chemotherapy has been extremely successful and is the reason why the majority of patients survive testicular cancer. Unfortunately platinum-containing chemotherapy may also be associated with various short-term and long-term health effects. Many of these health effects are unknown, but due to the growing number of testicular cancer survivors, we have new opportunities to study these side effects and thus obtain the knowledge base to eventually set up guidelines for optimal follow-up care and for the prevention and treatment of adverse health outcomes.

**What we did:** Our research team established The Platinum Study, which is the largest study of testicular cancer survivors to date, and the only such investigation in the United States and Canada. Most of the cancer survivors who participated in the study received common forms of chemotherapy: 1) four cycles of etoposide and cisplatin (EPx4), 2) three cycles of bleomycin, etoposide, and cisplatin (BEPx3), or 3) four cycles of bleomycin, etoposide, and cisplatin (BEPx4). Cancer survivors were given a physical exam, answered questions about their health, and were asked permission to use information from their medical chart. Survivors were asked to identify if they had symptoms of adverse health outcomes, such as problems with hearing (called ototoxicity), nerve damage in arms/legs or hands/feet (called peripheral neuropathy), white or cold hands/fingers or toes/feet when it is cold (called Raynaud phenomenon), cardiovascular disease or risk factors (like obesity), thyroid disease, problems with balance, low testosterone, or kidney disease.

**What we found:** Participants in The Platinum Study were around 37 years old at the time of evaluation, and it had been about 4 years since most of them had completed chemotherapy. The research team found that 1 in 3 testicular cancer survivors reported three or more adverse health effects, while only 1 in 5 survivors reported none. Those who received BEPx3 were more likely to have Raynaud phenomenon than survivors who received EPx4. Those given EPx4 were more likely to have peripheral neuropathy than survivors who received BEPx3. Further, 1 in 6 testicular cancer survivors had both ototoxicity and peripheral neuropathy. In general, testicular cancer survivors had higher fasting total cholesterol and LDL cholesterol than did men in the general U.S. population. In addition, the research team found that survivors were likely to have more adverse health effects if they were older at time of study participation, currently smoking, had achieved lower educational level, or were not married. The research team also studied similar information in a separate series of men who had never had cancer and who were considered to represent all types of men across the United States. The research team then compared the health of the cancer survivors to the health of men who had never had cancer. Encouragingly, survivors who engaged in vigorous physical activity reported lower adverse health outcomes. **These observations indicate that pursuing a healthy lifestyle (for example, not smoking, being physically active, and maintaining an optimal weight) are especially beneficial to testicular cancer survivors. Survivors should also ask their health care providers to check their cholesterol levels.**

The full published version of this article can be accessed from our website at:

<http://cancer.iu.edu/platinum>.

## Comprehensive Audiometric Analysis of Hearing Impairment and Tinnitus After Cisplatin-Based Chemotherapy in Survivors of Adult-Onset Cancer

Robert D. Frisina, Heather E. Wheeler, Sophie D. Fossa, Sarah L. Kerns, Chunkit Fung, Howard D. Sesso, Patrick O. Monahan, Darren R. Feldman, Robert Hamilton, David J. Vaughn, Clair J. Beard, Amy Budnick, Eileen M. Johnson, Shirin Ardeshtir-Rouhani-Fard, Lawrence H. Einhorn, Steven E. Lipshultz, M. Eileen Dolan, and Lois B. Travis.

*Journal of Clinical Oncology* 2016; 34:2712-2720 (with Editorial).

**Background:** By the year 2024, the number of cancer survivors is expected to reach 19 million in the US. Cisplatin is a widely-used chemotherapeutic drug with known side effects that include hearing loss and the development of permanent tinnitus. Even though these are known side effects, there are limited scientific studies about the relationship between cisplatin dose and damaging effects on hearing function. Additionally, there are no follow-up hearing assessment guidelines for survivors of adult-onset cancer.

**What we did:** To help fill these gaps, through The Platinum Study, we conducted the largest and most comprehensive study of hearing impairment due to treatment with cisplatin. We performed thorough hearing evaluations in 488 men who had been diagnosed with adult-onset germ cell tumors and had been treated with standard cisplatin-based chemotherapy regimens. Patients participated in a hearing test, known as an audiogram, and also completed questionnaires about hearing loss-related symptoms like tinnitus as well as lifestyle habits, other conditions, and medication use. We compared our results in this group to a reference population of men.

**What we found:** It had been at least 1 year, since patients completed chemotherapy. Only 1 in 5 (20%) patients had a normal hearing test result during the audiogram. The remainder had hearing loss that was considered mild (25%), moderate (16%), moderately severe (21%), or severe (18%). Only 1.2% of survivors required hearing aids. As might be expected, the process of aging is also associated with hearing loss, but even when we removed the effect of age, we found that higher doses of cisplatin were linked to greater amounts of hearing loss across a range of frequencies (4, 6, 8, 10, and 12 Hz). Patients who received more than 300 mg/m<sup>2</sup> of cisplatin were more likely to have greater hearing loss at any one frequency. Patients with tinnitus (40%) were also likely to have reduced hearing at each frequency. High blood pressure, but not smoking status, was also associated with hearing loss. Cisplatin therapy did not worsen noise-induced hearing loss. **These results stress the importance of working with health care providers for annual questioning with regard to hearing status, and then making an appointment with a hearing specialist when necessary.**

The full published version of this article can be accessed from our website at:

<http://cancer.iu.edu/platinum>.

**PLEASE REMEMBER...**

**Schedule your Hearing Test**

**IT'S NOT TOO LATE!**

The information provided by this test is extremely important for helping us to advance this research and understand the types of hearing loss that may be associated with cisplatin-based chemotherapy.

If you haven't completed your hearing test, please contact your study site to schedule this important study exam.

*The visit should only take 15 to 20 minutes using state-of-the-art audiometry, helping us learn more than ever before about hearing after cisplatin-based chemotherapy in you, the survivor.*

Abstracts & Posters: *Selected highlights of your data in action...*

## 2017 American Society of Clinical Oncology Cancer Survivorship Symposium

### Metabolic Syndrome after Platinum-based Chemotherapy: A Multicenter Study of North American Testicular Cancer Survivors.

Testicular cancer is the most common cancer in young men, and there are growing numbers of survivors worldwide. Results of the analysis (featured in a platform presentation) showed that overall symptoms of the "metabolic syndrome" (a set of risk factors for cardiovascular disease) occurred in about 1 in 5 survivors, similar to a control population. However, survivors were in general more likely to have selected metabolic changes. Read more about our research results at <http://cancer.iu.edu/platinum>

Photo of Dr. Abu Zaid courtesy of © Todd Buchanan/ASCO 2017

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

### Adverse Health Outcomes in Relationship to Serum Testosterone Levels after Platinum-Based Chemotherapy: A Multi-Center Study of North American Testicular Cancer Survivors.

Results of the analysis made national headlines and were presented to ASCO in June. Serum testosterone levels were low in 38% of survivors, who were also more likely to take medications for high cholesterol, high blood pressure, or diabetes. "Our findings underscore the need to screen testicular cancer survivors for hypogonadism and treat those who have symptoms," said Dr. Mohammad Abu Zaid, lead investigator. Read more about our research results at <http://cancer.iu.edu/platinum>

## 2017 Meeting of the American Society of Human Genetics (ASHG)

### A Genome-wide Association Study of Cisplatin-induced Tinnitus in Adult Cancer Survivors. Lead Investigator: Brandon Mapes, MS

About 40% of participants in the Platinum Study indicate that they experience tinnitus. In this scientific abstract, we described a number of factors associated with this symptom, including larger total doses of cisplatin, increasing age, and noise exposure. We are currently working with other scientific investigators on a joint analysis of risk factors for tinnitus in both Platinum Study participants and survivors of other types of cancer who also received cisplatin. Read more about our research results at <http://cancer.iu.edu/platinum>

**Please visit <http://cancer.iu.edu/platinum> to read more about the above research results**

## What is Tinnitus?

Do you experience ringing in your ears? This might be tinnitus. Tinnitus can also include hissing, whistling, buzzing, and clicking noises. A relatively common condition, it affects almost 15% of the public to some extent. After cisplatin-based chemotherapy, you may be at an increased risk of developing tinnitus. Although there is no known cure, there are resources to help. The American Tinnitus Association, a national nonprofit organization, provides support, including examples of typical tinnitus sounds and information about the condition and how to manage it. One of our goals in the Platinum Study is to reduce the burden of side effects, such as tinnitus, to improve cancer survivors' health-related quality of life. Since cisplatin is used to successfully treat many types of cancer worldwide, our results will be applicable to substantial numbers of individuals.

Sources: American Tinnitus Association - <https://www.ata.org/>

Mayo Clinic - <https://www.mayoclinic.org/diseases-conditions/tinnitus/symptoms-causes/syc-20350156>

