

*Embargoed until 1:45 p.m. ET, Sunday, September 22, 2013*

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## **Study shows cisplatin combined with high-dose brachytherapy for advanced cervical cancer may be more beneficial**

Atlanta, September 22, 2013 — Adding the chemotherapy drug cisplatin to a treatment plan of radiation therapy (RT) and high-dose-rate brachytherapy (HDRB) for stage IIIB cervical cancer is beneficial, according to research presented today at the American Society for Radiation Oncology's (ASTRO's) 55<sup>th</sup> Annual Meeting. The study also indicated that the combined treatments produced acceptable levels of toxicity.

The randomized, controlled trial studied a total of 147 women in Brazil with stage IIIB squamous cell cervical cancer. A stage IIIB classification indicates that the cancer has spread to the pelvic wall and/or the tumor has become large enough to affect kidney function. Each patient received external beam radiation of 45 Gy to the pelvic region in 25 fractions; 14.4 Gy boost to the compromised parametrium (the connective tissue and fat adjacent to the uterus); and HDRB in the amount of four weekly fractions of 7 Gy prescribed to point A (the crossing of the uterine artery and the ureter).

Seventy-five patients received only RT and HDRB treatment—the RT group, and 72 patients received RT and HDRB plus weekly intravenous doses of 40 mg/m<sup>2</sup> of cisplatin during the pelvic

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radiotherapy sessions—the CHRT group. [Note: Some chemotherapy doses were determined based on body surface area (BSA), which doctors calculate using a patient’s height and weight. BSA is expressed in meters squared ( $m^2$ )]. The research was conducted from 2003 through 2010, with follow-up lasting until January 2013.

Kaplan-Meier survival curves were performed comparing the five-year, disease-free survival (DFS) and the overall survival (OS) of the RT and CHRT groups. Differences in survival were assessed utilizing the log-rank test. Patients in the CHRT group had significantly better DFS (Hazard Ratio (HR)=0.52, 95 percent Confidence Interval (CI) 0.28 to 0.98;  $p=0.04$ ) and had a better OS, but without statistical significance (HR=0.67, 95 percent CI 0.37 to 1.183;  $p=0.16$ ).

Toxicity levels, measured utilizing the Cooperative Group Common Toxicity Criteria of the Radiation Therapy Oncology Group, in the CHRT group were similar to those in the RT group, with grades 1 and 2 acute toxicity at 37.5 percent for CHRT group, and 28 percent for RT group ( $p=0.29$ ). Late toxicity grades 3 and 4 were 9.7 percent for the CHRT and 3 percent for the RT group ( $p=0.29$ ).

“In testing a new approach of chemotherapy with traditional external beam radiation therapy and high-dose-rate brachytherapy, we were extremely cautious about possible toxicity for the patients,” said Antonio Zuliani, MD, lead author of the study and a radiation oncologist at Campinas State University in Campinas, Brazil. “We were pleased by an increase in local control and the very low toxicity rates. We believe that these results demonstrate that this combined treatment protocol is safe to offer to patients and provides some beneficial improvements—in disease-free survival and toxicity levels.”

The abstract, “Efficacy of Concomitant Cisplatin Plus Radiotherapy and High Dose Rate Brachytherapy versus Radiotherapy Alone for Stage IIIB Epidermoid Cervical Cancer: A Ten-Year Randomized Controlled Trial,” will be presented in detail during a scientific session at ASTRO’s 55th Annual Meeting at 1:45 p.m. Eastern time on September 22, 2013. To speak with Dr. Zuliani, contact Michelle Kirkwood on September 22—25, 2013, in the ASTRO Press Office at the Georgia World Congress Center in Atlanta at 404-222-5303 or 404-222-5304, or email [michellek@astro.org](mailto:michellek@astro.org)

ASTRO's 55<sup>th</sup> Annual Meeting, held in Atlanta, September 22-25, 2013, is the premier scientific meeting in radiation oncology and brings together more than 11,000 attendees including oncologists from all disciplines, medical physicists, dosimetrists, radiation therapists, radiation oncology nurses and nurse practitioners, biologists, physician assistants, practice administrators, industry representatives and other health care professionals from around the world. The theme of the 2013 meeting is "Patients: Hope • Guide • Heal" and focuses on patient-centered care and the importance of the physician's role in improving patient-reported outcomes and the quality and safety of patient care. The four-day scientific meeting includes presentation of four plenary papers, 363 oral presentations, 1,460 posters and 144 digital posters in 70 educational sessions and scientific panels for 19 disease sites/tracks. Keynote and featured speakers include: William B. Munier, director of the Center for Quality Improvement and Patient Safety at the Agency for Healthcare Research and Quality; Darrell G. Kirch, MD, president and CEO of the Association of American Medical Colleges; James Cosgrove, PhD, director of the U.S. Government Accountability Office; Otis W. Brawley, MD, chief medical officer of the American Cancer Society; and Peter Friedl, MD, PhD, of St. Radboud University Nijmegen Medical Centre at the University of Nijmegen and MD Anderson Cancer Center.

## ABOUT ASTRO

*ASTRO is the premier radiation oncology society in the world, with more than 10,000 members who are physicians, nurses, biologists, physicists, radiation therapists, dosimetrists and other health care professionals that specialize in treating patients with radiation therapies. As the leading organization in radiation oncology, the Society is dedicated to improving patient care through professional education and training, support for clinical practice and health policy standards, advancement of science and research, and advocacy. ASTRO publishes two medical journals, International Journal of Radiation Oncology • Biology • Physics ([www.redjournal.org](http://www.redjournal.org)) and Practical Radiation Oncology ([www.practicalradonc.org](http://www.practicalradonc.org)); developed and maintains an extensive patient website, [www.ranswers.org](http://www.ranswers.org); and created the Radiation Oncology Institute ([www.roinstitute.org](http://www.roinstitute.org)), a non-profit foundation to support research and education efforts around the world that*

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*enhance and confirm the critical role of radiation therapy in improving cancer treatment. To learn more about ASTRO, visit [www.astro.org](http://www.astro.org).*

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**2013 American Society for Radiation Oncology (ASTRO) 55<sup>th</sup> Annual Meeting**  
**News Briefing, Tuesday, September 24, 2013, 8:15 a.m. Eastern time**

Scientific Session: Sunday, September 22, 2013, 1:45 – 3:15 p.m. ET, Georgia World Congress Center

**8 Efficacy of Concomitant Cisplatin Plus Radiotherapy and High Dose Rate Brachytherapy versus Radiotherapy Alone for Stage IIIB Epidermoid Cervical Cancer: A Ten-Year Randomized Controlled Trial**

A. C. Zuliani, L. O. Sarian, S. C. Esteves, G. A. Souza, M. O. Cunha, J. C. Teixeira, L. C. Teixeira, *Campinas State University, Campinas, Brazil*

**Purpose/Objective(s):** The best evidence for disease-free (DFS) and overall survival (OS) of women with stage IIIB cervical cancer undergoing chemoradiotherapy versus radiotherapy comes from a meta-analysis of 18 trials (CCCMAC, 2010). The benefit decreased from 10% for stages IB-IIA to 3% for stage III-IVA, and the confidence intervals of the hazard ratios were not significant. To better investigate the matter this study was conducted.

**Materials/Methods:** This is a randomized, controlled clinical trial comparing the disease-free (DFS) and overall survival (OS) of women with stage IIIB squamous cervical cancer receiving either cisplatin plus radiotherapy (CHRT) or radiotherapy alone (RT). All patients received external-beam radiation (45 Gy) to the pelvic region in 25 fractions, 14.4 Gy boost to compromised parametria and high dose rate brachytherapy (HDRB), four weekly fractions of 7Gy prescribed to point A. The CHRT group had concomitant weekly cisplatin (40mg/m<sup>2</sup>) during the pelvic teletherapy. Accrual lasted from September 2003 through July 2010. Follow-up lasted through January 2013, 147 patients were included (72 patients in CHRT group and 75 in the RT group) with a mean follow-up of 54.9 months (interquartile range = 55.4 months). Multivariate Cox Proportional hazards models were used to calculate the hazard ratios for OS and DFS. Univariate Kaplan-Meier survival curves were performed, comparing the 5-year DFS and OS. Differences in survival were assessed with the log-rank test. This research was approved and monitored by the institution's research ethics committee.

**Results:** Women with Karnofsky <90 had a significantly worse DFS (RR=2.52, 95%CI 1.23 to 4.78; p=0.01). The same was true for women with bilateral wall invasion (RR=2.93, 95%CI 1.21 to 7.13; p=0.02), and baseline Hb <10mg/dL (RR=2.22, 95%CI 1.01 to 4.93; p=0.04). Women allocated to the CHRT group had significantly better DFS (RR=0.52, 95%CI 0.28 to 0.98; p=0.04). OS was also negatively associated with Karnofsky <90 (RR=2.75, 95%CI 1.29 to 5.87; p<0.01), and baseline Hb <10mg/dL (RR=2.82, 95%CI 1.27 to 6.29; p=0.01). Patients in the CHRT group had a better OS, but without statistical significance (RR=0.67, 95%CI 0.37 to 1.183; p=0.16). Grades 1 and 2 acute toxicity was 37.5% for CHRT group, and 28% for RT group (p=0.29). Late toxicity grades 3 and 4 were 9.7% for the CHT and 3% for the RT groups (p=0.29).

**Conclusions:** This is the only randomized controlled trial comparing radiotherapy plus HDRB with chemoradiotherapy for stage IIIB squamous cell carcinoma of the cervix. This study suggests a small, but statistically significant benefit with the addition of cisplatin, with acceptable toxicity.

**Author Disclosure Block:** A.C. Zuliani: None. L.O. Sarian: None. S.C. Esteves: None. G.A. Souza: None. M.O. Cunha: None. J.C. Teixeira: None. L.C. Teixeira: None.