

Phase II Study of Concurrent Chemoradiotherapy Using Nedaplatin for Locally Advanced Uterine Cervical Carcinoma (KGROG0501): Final Results

YUZURU NIIBE^{1,2}, TAKASHI ONDA³, KEITARO MATSUO⁴, YUSUKE INOUE⁵ and KAZUSHIGE HAYAKAWA²

¹Department of Radiology, Toho University Omori Medical Center, Tokyo, Japan;
²Departments of ²Radiology and Radiation Oncology, ³Obstetrics and Gynecology, and
⁵Diagnostic Radiology, Kitasato University School of Medicine, Sagamihara, Japan;
⁴Division of Molecular Medicine, Aichi Cancer Center Research Institute, Nagoya, Japan

Abstract. *Aim:* This phase II study using nedaplatin evaluated the effectiveness and safety of concurrent chemoradiotherapy for locally advanced uterine cervical carcinoma. *Patients and Methods:* Patients met the following eligibility criteria: International Federation of Gynecology and Obstetrics (FIGO) stage Ib, IIa, IIb with bulky tumor (≥ 40 mm) or pelvic lymph node swelling (≥ 10 mm), in FIGO stage IIIa, IIIb or IVa. Treatment adopted external radiation therapy combined with intracavitary brachytherapy using weekly nedaplatin at 30 mg/m² totaling five cycles. The primary endpoint was 3-year overall survival. *Results:* From June 2005 to May 2010, 45 eligible patients with uterine cervical carcinoma were registered. Histopathology was squamous cell carcinoma in 36 and adenocarcinoma in nine. The median follow-up period was 39 months. The 3-year overall survival rate was 73.0% (95% confidence interval=56.2-84.2%). No severe acute or late toxicities occurred. *Conclusion:* This phase II study showed external radiation therapy combined with intracavitary brachytherapy using weekly nedaplatin to be effective and safe.

Concurrent chemoradiotherapy (CCRT) has been the standard treatment in the USA for locally advanced uterine cervical carcinoma (LAUCC) since the GOG120 randomized controlled trial (RCT) demonstrated the superiority of CCRT over radiotherapy alone in 1999 (1). Several randomized

RCTs worldwide demonstrated the same findings (2-4). Regimes of concurrent chemotherapy in GOG120 and other countries used a weekly dose of 40 mg/m² of intravenous cisplatin for 6 weeks. The radiation therapy dose was the cumulative linear quadratic equivalent dose (EDQ2) of 73-86 Gy at point A.

In Japan, the JGOG1066 study using the world standard cisplatin regimen was the first to demonstrate feasibility and effectiveness of CCRT for LAUCC in a Japanese population, although in 2012, 13 years after the GOG120 study (5). Thus, the standard care for LAUCC using CCRT of global standard regimen using cisplatin has been established in Japan. However, the use of a weekly dose of 40 mg/m² of intravenous cisplatin for 6 weeks has several problems. Firstly, the use of intravenous cisplatin requires hydration to lower renal toxicity. Secondly, there was no evidence for the need for 40 mg/m² and six cycles of cisplatin in the Japanese population, a lower dose and fewer cycles of platinum drugs may achieve the same results.

Thus, this phase II study using nedaplatin, a platinum drug with less renal toxicity, evaluated the effectiveness and safety of CCRT for LAUCC using a weekly dose of 30 mg/m² of intravenous nedaplatin for 5 weeks without hydration. The dose of nedaplatin of this phase II study was based on a phase I study (6). Furthermore, this study compared the findings of histopathology, lymph node (LN) status and the maximum tumor diameter (MTD).

Patients and Methods

Study design and purpose. Kitasato University Ethics Committee approved this study protocol (04-17). At the time of the start of this phase II study, prospective study registration was not required. Thus, this phase II study was not registered before initiation, although the protocol summary was published in 2007 (7). Finally, the study was registered in University Hospital Medical Information Network – Clinical Trial Registry (UMIN-CTR) (UMIN0000

Correspondence to: Associate Professor Yuzuru Niibe, MD, Ph.D., Department of Radiology, Toho University Omori Medical Center, 6-11-1, Omori-Nishi, Ota-ku, Tokyo 143-8541, Japan. Tel: +81 337624151, Fax: +81 337685386, e-mail: yniibe-toho@umin.org

Key Words: Phase II study, chemoradiotherapy, locally advanced uterine cervical carcinoma, nedaplatin, squamous cell carcinoma, adenocarcinoma.

25688). We briefly describe here the study purpose, eligibility criteria, exclusion criteria and endpoints.

The aim of this phase II study was to evaluate the efficacy and safety of chemoradiotherapy using a weekly dose of intravenous nedaplatin at 30 mg/m² for 5 weeks for LAUCC in a Japanese population in prospective study.

This study was designed and performed by Kitasato Gynecologic Radiation Oncology Group (KGROG), with study code KGROG0501.

Eligibility criteria. Study eligibility criteria were as follows: i) Pathologically-proven squamous cell carcinoma (SCC) and adenocarcinoma or adenosquamous cell carcinoma (AC); ii) clinical International Federation of Gynecology and Obstetrics (FIGO) stage Ib, IIa, IIb with bulky tumor [≥40 mm as assessed by pelvic magnetic resonance imaging (MRI)] or pelvic lymph node swelling [≥10 mm assessed by pelvic computed tomography (CT)] or clinical FIGO stage IIIa, IIIb or IVa (8); iv) age 20-75 years; v) Eastern Cooperative Oncology Group Performance Status 0-2; vi) no prior radiation therapy for the abdomen and pelvis; vii) adequate bone marrow, kidney and liver function (white blood cell count ≥2,500 mm³, neutrophils ≥1,000 mm³, hemoglobin ≥8.0 g/dl, platelet count ≥75,000 mm³, creatinine ≤2.0 mg/dl, 24-h creatinine clearance ≥60 ml/min, glutamine oxaloacetic transaminase and glutamine pyruvic transaminase ≤2 times the upper limit of normal value at our institution, total bilirubin <2 times (the upper limit of normal at our institution); and viii) written informed consent.

Exclusion criteria. Exclusion criteria were as follows: i) Other active cancer except carcinoma *in situ* or controlled for more than 2 years; ii) long-term and continuous steroid use; iii) serious complications (heart disease within 3 months, chronic heart failure, neurovascular disease within 3 months, uncontrolled disease); iv) para-aortic lymph node swelling (≥10 mm) by abdominal CT; and v) judged to be ineligible for this protocol by the attending physicians.

Endpoints. The primary endpoint was 3-year overall survival (OS) and the secondary endpoints were initial tumor response, 2-year OS, 2- and 3-year progression-free survival (PFS), 3-year locoregional control (LRC), pattern of failure (initial site), acute adverse events (based on the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0) (9), protocol completion rate and late adverse events (based on The Radiation Therapy Oncology Group/ European Organization for Research and Treatment of Cancer late radiation morbidity scoring schema (10).

Accompanying investigations were performed as follows; histopathology, pelvic lymph node status and maximum tumor diameter (MTD).

Sample size. The sample size was calculated as 45 (alpha=0.05, two-sided and beta=0.1, non-compliance 10%) to detect an effect size on 3-year OS as 40% expected with the threshold value as 20%.

Treatment methods. Radiation therapy: External beam radiation therapy combined with intracavitary high-dose rate brachytherapy was adopted in this study. Firstly, external beam radiation therapy covering the entire pelvis started using a fraction size 1.8 to 2 Gy, five times per week and two to four fields, totaling 30-32 Gy. After that, radiation therapy to the entire pelvis using a fraction size 2 Gy,

Table I. Patient characteristics.

Characteristic	Value	
Median age (range), years	55 (31-73)	
FIGO stage, n (%)		
Ib	3	6.7%
IIa	1	2.2%
IIb	12	26.7%
IIIa	0	0%
IIIb	28	62.2%
IVa	1	2.2%
Histopathology, n (%)		
Squamous cell carcinoma	36	80.0%
Adenosquamous cell carcinoma	0	0%
Adenocarcinoma	9	20.0%
Maximum tumor diameter (mm), n (%)		
<40	6	13.3%
40-<50	10	22.2%
50-<60	6	13.3%
60-<70	11	24.4%
70-<80	3	6.7%
80≤	9	20.0%

FIGO: International Federation of Gynecology and Obstetrics.

anterio-posterior- and posterior-anterior field with central shielding was performed totaling 50 to 52 Gy. Concomitantly, intracavitary high-dose rate brachytherapy was performed using a fraction size 5 to 6 Gy to point A, once a week four to six times (in the case of 6-Gy fraction size, maximum set at 4). Total dose to point A was 20 to 30 Gy.

Chemotherapy: A weekly dose of 30 mg/m² of intravenous nedaplatin for 5 weeks for LAUCC was performed. Chemotherapy was performed without hydration in the setting of concurrent use of radiation therapy. Nedaplatin was infused intravenously in 500 ml saline for 3 h and 5-hydroxytryptamine receptor antagonist drugs were used to avoid nausea. When grade 4 hematological toxicity or non-hematological grade 3 or greater toxicity occurred, chemotherapy was paused and withheld for one week. At the restart of chemotherapy, use of 100% or 80% of dose reduction of nedaplatin was judged by attending gynecologic oncological physicians.

Follow-up. The first consultation was 2 weeks after the treatment and blood tests were performed at the same time. One and 3 months after treatment, blood tests, pelvic MRI and abdominal and pelvic CT were performed, and the tumor response evaluated according to Response Evaluation Criteria in Solid Tumor (RECIST) (11). Response rate was evaluated using pelvic MRI at the time of one month or 3 months after the treatment. For the first year, blood tests pelvic MRI and abdominal and pelvic CT were performed every 3 months. After 1-year follow-up, blood tests, pelvic MRI and abdominal and pelvic CT were performed every 6 months for a total follow-up of 3 years.

Statistical analysis. OS, PFS and LRC curves were constructed by Kaplan–Meier method with outcomes compared using the log-rank test. Statistical significance was set at *p*<0.05. Statistical software

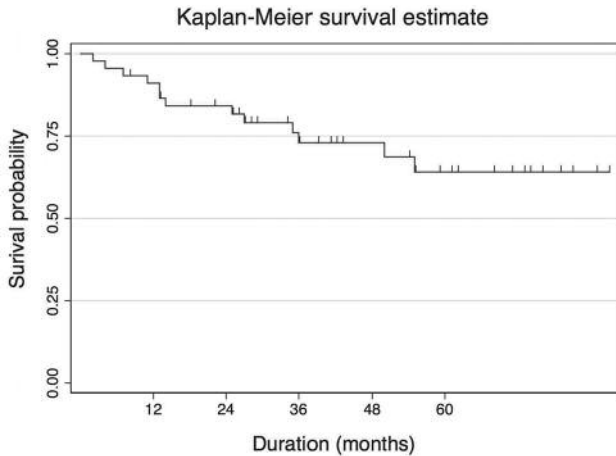


Figure 1. Kaplan–Meier curve for overall survival (OS) of all registered patients. The median follow-up was 39 months (range=2-87 months). The 3-year OS was 73.0% (95% confidence interval=56.2-84.2%).

used in this study was STATA ver 13 (StataCorp LLC, College Station TX, USA). All statistical analyses were performed by K.M. independently of clinical sections of this study group.

Ethics. This phase II study was reviewed and approved by Kitasato University School of Medicine Ethics Committee (04-17).

Results

Patient registration. From June 2005 to May 2010, 45 eligible patients with LAUCC were registered. Patient characteristics are listed in Table I.

Protocol completion rate. Forty-four out of the 45 registered patients completed the protocol treatment (completion rate: 97.8%). All registered patients completed radiation therapy. One patient stopped chemotherapy after the first cycle because of grade 4 hematological morbidity and this patient refused to continue further chemotherapy.

Follow-up period. The median follow-up overall (45 patients) was 39 months (range=2-87 months).

Radiation therapy. All patients registered in this study were treated with radiation therapy. External beam radiation therapy covering the entire pelvis started using a fraction size 1.8 Gy, five times per week adopted 2 fields in 12 patients and 4 fields in 33 patients adopted to a total of 30.6 Gy (all registered patients). Radiation therapy to the entire pelvis was given using a fraction size of 2 Gy with central shielding (Japanese standard method) to 50.6 Gy (all registered patients). Concomitantly, intracavitary high-dose rate brachytherapy was performed using a fraction

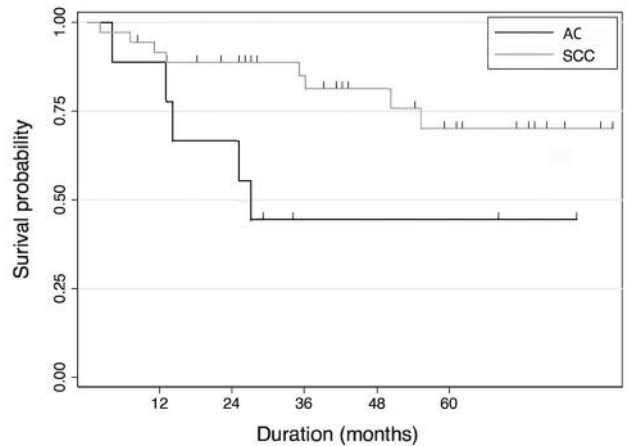


Figure 2. Kaplan–Meier curve for overall survival (OS) stratified by histopathology. The 3-year OS was 81.3% (95% confidence interval=62.7-91.3%) in patients with squamous cell carcinoma (SCC) ($n=36$) was 44.4% (95% confidence interval=13.6-71.9%) in patients with adenocarcinoma (AC) ($n=9$). This difference was statistically significant ($p=0.0291$).

size 6 Gy to point A, once a week totaling four times to a total dose of 24 Gy.

Initial tumor response. Initial tumor response was evaluated according to RECIST. Thirty-six patients achieved complete response. Eight patients achieved partial response. No patient had stable or progressive disease at initial tumor response. However, one patient died suddenly before evaluation of initial tumor response. Autopsy of this patient was refused by their family although autopsy whole-body imaging was performed under consent. This patient's death was not related to LAUCC or treatment-related. Thus, this patient's initial tumor response was recorded as not evaluable.

Survival. The 3-year OS of the whole patient group was 73.0% [95% confidence interval (CI)=56.2-84.2%] (Figure 1).

Stratified by clinical stage according to FIGO, the 3-year OS of those with stage Ib, IIa IIb IIIb and IVa disease was 100% ($n=3$), 100% ($n=1$), 91.7% (95% CI=53.90-98.78%; $n=12$), 64.8% (95% CI=42.65-80.12%; $n=28$) and 0% ($n=1$), respectively.

Stratified by histopathology, the 3-year OS of those with SCC was significantly higher (81.3%, 95% CI=62.7-91.3%; $n=36$) than that of patients with AC (44.4%, 95% CI=13.6-71.9%; $n=9$) ($p=0.029$; Figure 2).

Stratified by pelvic LN status, the 3-year OS of patients without positive LNs was 75.7% (95% CI=55.6-87.6%; $n=33$) but did not differ significantly from those with LN-positive LAUCC (76.2%, 95% CI=33.2-93.5%; $n=12$) ($p=0.95$).

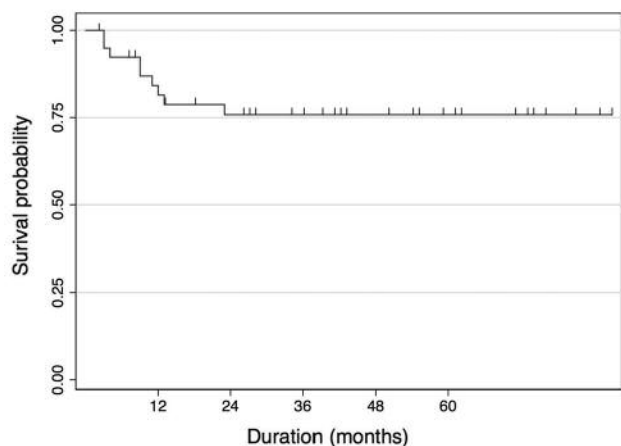


Figure 3. Kaplan–Meier curve for progression-free survival (PFS) of all registered patients. The 2-year PFS was 71.9% (95% confidence interval=54.9-83.4%) and 3-year PFS was 68.6% (95% confidence interval=51.2-80.4%).

MTD did not significantly affect the 3-year OS of patients ($p=0.19$), although OS had a tendency to be worse as MTD grew [MTD <50 mm: 92.9% (95% CI=59.1-99.0%; $n=15$), 50 mm to <70 mm: 67.3% (95% CI=38.3-84.9%; $n=18$), ≥ 70 mm: 63.5% (95% CI=23.8-86.6%; $n=12$)].

The 2- and 3-year PFS of patients overall was 71.9% (95% CI=54.9-83.4%) and 68.6% (95% CI=51.2-80.4%), respectively (Figure 3).

Locoregional control. The 2- and 3-year LRC rates were 75.8% (95% CI=58.6-86.6%) and 73.0% (95% CI=56.2-84.2%), respectively.

Stratified by histopathology, the 3-year LRC of patients with SCC was significantly ($p<0.01$) better at 86.4% (95% CI=67.7-94.7%; $n=36$) compared to patients with AC (28.6%, 95% CI=4.1-61.2%; $n=9$).

Pattern of failure. Ten patients experienced relapse of disease of the uterus, two patients at pelvic lymph nodes, and 10 patients from disease of extrapelvic region (including concomitant failure in the uterus and extrapelvic region).

Acute toxicity. Grade 1 hematological toxicity occurred in 10 patients, grade 2 in 13 patients, grade 3 in 15 patients and grade 4 in seven. There was no non-hematological toxicities of grade 3 or greater (Table II).

Late toxicity. Grade 3 and or greater late toxicities occurred in three patients, all three patients experienced toxicity of of small and large intestine (Table III).

Table II. Acute hematological toxicity experienced by study patients according to the CTCAE ver 3.0 (9).

Toxicity	Grade, no. of patients				
	0	1	2	3	4
WBC	6	7	12	15	5
Neutrophils	16	6	9	8	6
Hgb	0	20	13	11	1
Plt	8	19	10	8	0

WBC: White blood cell; Hgb: hemoglobin; Plt: platelets.

Table III. Late toxicity experienced by study patients according to the Radiation Therapy Oncology Group/European Organization for Research and Treatment Cancer (10).

Toxicity	Grade, no. of patients			
	0-1	2	3	4
Small intestine and colon	34	7	3	0
Rectum	43	2	0	0
Bladder	45	0	0	0

Discussion

The 3-year OS of patients overall was 73.0% (95% CI=56.2-84.2%). The expected 3-year OS of this study was 40% based on the Japanese standard of a nation-wide survey performed by Japan Society of Obstetrics and Gynecology (12), which was the cut-off line for effectiveness for a single arm phase II study. Thus, the present study was effective enough, because the lower limit of the 3-year OS of 95% CI was 56.2%. This is better than the expected 3-year OS. Furthermore, the 2- and 3-year LRC rates were 75.8% (95% CI=58.6-86.6%) and 73.0% (95% CI=56.2-84.2%), which were also acceptable results.

As for acute and late toxicity, there was no severe toxicities in this study. From the 3-year LRC, this study indicates that a lower dose of platinum drug (30 mg/m²) and fewer cycles (once a week totaling five cycles) of weekly chemotherapy than those of standard CCRT for LAUCC was effective.

Furthermore, compared to the JGOG1066 study using six cycles/6 weeks of 40 mg/m² cisplatin with hydration, this study using five cycles of 30 mg/m² nedaplatin without hydration, having more bulky tumor of LAUCC than JGOG1066. The percentage of patients with MTD ≥ 80 mm in our study was 20%, while that of JGOG1066 was only

Table IV. Comparison of this study (KGROG0501) and JGOG1066 (5)

Study	2-Year PFS (95% CI)	2-Year LRC (95% CI)	AC (%)	MTD \geq 80 mm (%)
JGOG1066, CCRT using cisplatin	66.0% (54.0-76.0%)	73.0% (61.0-82.0%)	7	10
Present study (KGROG0501)	71.9% (54.9-83.4%)	75.8% (58.6-86.6%)	20	20

PFS: Progression-free survival, LRC: locoregional control, AC: adenocarcinoma MTD: maximum tumor diameter, JGOG: Japanese Gynecologic Oncology Group, KGROG: Kitasato Gynecologic Radiation Oncology Group, CCRT: concurrent chemoradiotherapy.

10%, and our study included more patients with AC (20%) compared with JGOG1066 (10%) (Table IV). JGOG1066 reported that patients with bulky tumor LAUCC had a worse prognosis than those with non-bulky LAUCC (5). JGOG1066 also reported that the 2-year PFS of patients with MTD \geq 70 mm was 39% compared with 77% for those with MTD <50 mm ($p=0.036$). This prospective trial's accompanying study demonstrated a tendency for patients with larger MTD to have a worse prognosis than those with smaller MTD. Moreover, this study showed 3-year OS of patients with SCC to be almost twice that of patients with AC (81.3% *vs.* 44.4%; $p=0.0029$). This indicates that patients registered in our study might have been at somewhat high risk than those in JGOG1066.

Remarkably, this study demonstrated a 2-year PFS of 71.9% (95% CI=54.9-83.4%) compared with 66% (95% CI=54-76%; $n=71$) for JGOG1066, which used the international standard regimen. There was no statistically significant difference between the two prospective phase II studies for LAUCC. However, considering our study consisted of patients with somewhat worse prognoses, our regimen not requiring hydration might be better than JGOG1066 requiring hydration, greater dose per cycle and more total cycles. Of course, this study was not a phase III trial and did not compare these two regimens (KGROG0501 *versus* JGOG1066) by means of randomization.

Other phase II studies of CCRT for LAUCC using nedaplatin were reported (8, 9). However, these two reports included only SCC of LAUCC. Thus, comparison with this study requires caution because our study included patients with AC, a group with more unfavorable prognosis.

Yokoyama *et al.* reported that 45 patients were enrolled in their phase II CCRT study using 30 mg/mm² nedaplatin per week totaling six cycles (13). The completion rate of their study was 88.9% (40 out of 45 patients completed the study). However, the completion rate of our study was 97.8% (44 out of 45 patients). Their 3-year OS was 78.0% (95% CI=56-90.0%), excluding the five patients not completing the protocol schedule. On the other hand, that of our study was 73.0% (95% CI=56.2-84.2%), including one patient who did

not complete therapy and 20% of patients with AC. These results suggest that using weekly nedaplatin at 30 mg/mm² for five rather than six cycles is an appropriate regimen of CCRT for LAUCC. Furthermore, Yuan *et al.* reported that in their phase II CCRT study using weekly nedaplatin at 30 mg/mm² totaling six cycles (30 patients) (14), the completion rate was 80%. This also supported the superiority of our recommended schedule.

As for the limitations of this study, the number of patients registered was adequate to evaluate the 3-year OS. However, there was not an adequate number of registered patients to evaluate histopathology, MTD and LN status. This study was not a phase III study comparing the KGROG0501 regimen with that of JGOG1066 and therefore definitive conclusions on this issue cannot be drawn.

In conclusion, the CCRT regimen used here in KGROG0501 is a promising treatment method with comparable outcomes to the international standard regimen in a Japanese population, JGOG1066. The prognosis of patients with AC appears to be worse than that of patients with SCC from this study.

Conflicts of Interest

Dr. Niibe reports Grants from Shionogi &CO., Ltd. during part of the conduct of the study.

Acknowledgements

This study was partly supported by the Japan Society Promotion of Science, KAKENHI Grant number JP 18790909.

References

- Rose PG, Bundy BN, Watkins EB, Thigpen JT, DeppeG, Maiman MA, Clarke-Pearson DL and Insalaco S: Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. *N Engl J Med* 340: 1144-1153, 1999.
- Lanciano R, Calkins A, Bundy BN, Parham G, Lucci JA 3rd, Moore DH, Monk BJ and O'Connor DM: Randomized comparison of weekly cisplatin or protracted venous infusion of fluorouracil in combination with pelvic radiation in advanced cervix cancer: a Gynecologic Oncology Group study. *J Clin Oncol* 23: 8289-8295, 2005.

- 3 Thomas G, Ali S, Hoebbers FJ, Darcy KM, Rodgers WH, Patel M, Abulafla O, Lucci JA 3rd and Begg AC: Phase III trial to evaluate the efficacy maintaining hemoglobin levels above 12.0 g/dL with erythropoietin *vs.* above 10.0 d/dL without erythropoietin in anemic patients receiving concurrent radiation and cisplatin for cervical cancer. *Gynecol Oncol* 108: 317-325, 2008.
- 4 Duenas-Gonzalez A and Zarba JJ, Patel F, Alcedo JC, Beslija S, Casanova L and Pattaranutaporn P: Hameed S, Blair JM, Barraclough H and Orland M: Phase III, open label, randomized study comparing concurrent gemcitabine plus cisplatin and radiation *versus* concurrent cisplatin and radiation in patients with stage IIIB to IVA carcinoma of the cervix. *J Clin Oncol* 29: 1678-1685, 2011.
- 5 Toita T, Kitagawa R, Hamano T, Umayahara K, Hirashima Y, Aoki Y, Oguchi M, Mikami M, Takizawa K and Cervical Cancer (Vulva Cancer) Committee of Japanese Gynecologic Oncology Group: Phase II study of concurrent chemoradiotherapy with high-dose-rate intracavitary brachytherapy in patients with locally advanced uterine cervical cancer: Efficacy and toxicity of a low cumulative radiation dose schedule. *Gynecol Oncol* 126: 211-216, 2012.
- 6 Idei T, Sakamoto H, Nakajima Y, Hiraiwa Y, Takami N, Chishima F, Ohtani K, Nagaishi M, Yamamoto T, Kawamori J, Himi K and Tanaka Y: Concurrent weekly nedaplatin-based radiotherapy for high risk, recurrent and advanced cervical cancer. *Gan To Kagaku Ryoho* 30: 505-509, 2003.
- 7 Niibe Y, Hayakawa K, Tsunoda S, Kanai T, Imai M, Arai M, Arai T, Kawaguchi M, Jobo T, Hamada Y, Yago K, Unno N and Kitasato Gynecologic Radiation Oncology Group: Phase II study do radiation therapy combined with weekly nedaplatin in locally advanced uterine cervical carcinoma: Kitasato Gynecologic Radiation Oncology Group (KGROG0501). *Jpn J Clin Oncol* 37: 70-72, 2007.
- 8 International Federation of Gynecology and Obstetrics. <https://www.figo.org/> (accessed in October 14, 2017).
- 9 Common Terminology Criteria for Adverse Events v3.0 (CTCAE). https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/ctcae3.pdf. (accessed in October 14, 2017).
- 10 RTOG/EORTC Late Radiation Morbidity Scoring Schema. <https://www.rtog.org/ResearchAssociates/AdverseEventReportin g/RTOGEORTCLateRadiationMorbidityScoringSchema.aspx>. (accessed in October 14, 2017).
- 11 Response Evaluation Criteria in Solid Tumors (RECIST). <https://www.cibmtr.org/DataManagement/TrainingReference/Manuals/DataManagement/Documents/appendix-n.pdf>.
- 12 Japan Society of Obstetrics and Gynecology. <http://www.jsog.or.jp/english/index.html>.
- 13 Yokoyama Y, Takano T, Nakahara K, Shoji T, Sato H, Yamada H, Yaegashi N, Okamura K, Kurachi H, Sugiyama T, Tanaka T, Sato A, Tase T and Mizutani H: A phase II multicenter trials of concurrent chemoradiotherapy with weekly nedaplatin in advanced uterine cervical carcinoma: Tohoku Gynecologic Cancer Unit Study. *Oncol Rep* 19: 1551-1552, 2008.
- 14 Yuan G, Wu L, Huang M, Li N and An J: A phase II study of concurrent chmo-radiotherapy with weekly nedaplatin in advanced squamous cell carcinoma of the uterine cervix. *Radiat Oncol* 9: 55, 2014.

Received September 17, 2017

Revised October 15, 2017

Accepted October 23, 2017