Postoperative Survival and Ambulatory Outcome in Metastatic Spinal Tumors: Prognostic Factor Analysis

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Objective: The purposes of this study are to estimate postoperative survival and ambulatory outcome and to identify prognostic factors thereafter of metastatic spinal tumors in a single institute.

Methods: We reviewed the medical records of 182 patients who underwent surgery for a metastatic spinal tumor from January 1987 to January 2009 retrospectively. Twelve potential prognostic factors (age, gender, primary tumor, extent and location of spinal metastases, interval between primary tumor diagnosis and metastatic spinal cord compression, preoperative treatment, surgical approach and extent, preoperative Eastern Cooperative Oncology Group (ECOG) performance status, Nurick score, Tokuhashi and Tomita score) were investigated.

Results: The median survival of the entire patients was 8 months. Of the 182 patients, 80 (44%) died within 6 months after surgery, 113 (62%) died within 1 year after surgery, 138 (76%) died within 2 years after surgery. Postoperatively 47 (26%) patients had improvement in ambulatory function, 126 (69%) had no change, and 9 (5%) had deterioration. On multivariate analysis, better ambulatory outcome was associated with being ambulatory before surgery \(p=0.026\) and lower preoperative ECOG score \(p=0.016\). Survival rate was affected by preoperative ECOG performance status \(p<0.001\) and Tomita score \(p<0.001\).

Conclusion: Survival after metastatic spinal tumor surgery was dependent on preoperative ECOG performance status and Tomita score. The ambulatory functional outcomes after surgery were dependent on preoperative ambulatory status and preoperative ECOG performance status. Thus, prompt decompressive surgery may be warranted to improve patient’s survival and gait, before general condition and ambulatory function of patient become worse.

Key Words: Prognosis · Spinal metastasis · Surgery · Survival · Ambulatory outcome.

INTRODUCTION

Metastatic spinal cord compression (MSCC) is a relatively common complication of cancer, occurring in 5-14% of all cancer patients\(^1\). The life expectancy of most MSCC patients is quite short, with reported median survival ranging between 2 and 6 months\(^2\). In long-term survivors, local control of MSCC becomes important. Thus, the expected survival affects the selection of the treatment modality for the individual patient.

There have been extensive studies that looked at several factors that might affect the prognosis, including histological diagnosis of the primary tumor, tumor node metastases classification, staging, disease-free interval, results of hematologic examinations, presence or absence of visceral metastases, functional status (walking, medical comorbidities, and extent of disease), and clinical symptoms.

The management of spinal column metastatic disease includes surgery, radiotherapy, surgery plus adjuvant radiotherapy, but the optimal management is controversial. First-line therapy is corticosteroids, and radiotherapy is the mainstay of treatment for most patients; however, a recent randomized trial has shown that the combination of radical surgery and radiation is superior to radiation only\(^3\). The primary goals of treatment are to relieve pain and preserve or restore function when managing patients affected by spinal metastasis.

The aim of this study is to analyze the prognostic significance of various clinical variables on the survival and postoperative ambulatory function.

MATERIALS AND METHODS

Between January 1, 1987, and January 1, 2008, 182 patients...
with metastatic spine tumors underwent 190 operations at our hospital. Eight patients underwent reoperation due to local recurrence. There were 111 male and 71 female patients with a median age of 56 years (range, 17-80 years). We obtained the survival data of patients from the Korean Ministry of Public Administration and Security. Twelve potential prognostic factors were investigated. The factors considered were age, gender, type of primary tumor, location of spinal metastases, interval between diagnosis of primary tumor and MSCC, preoperative treatment, surgical approach and extent, preoperative Eastern Cooperative Oncology Group (ECOG) performance status (1-restricted in physically, 2-capable of all self care, 3-only limited self care, 4-completely disabled), Nurick score (1-no difficulty in walking, 2-slight difficulty in walking, 3-difficulty in walking, 4-able to walk with help, 5-Chair bound or bedridden), Tokuhashi and Tomita score (metastatic spinal tumor grading system).

Table 1 shows the primary tumor sites of metastatic spinal tumor patients. Most patients had primary liver cancer (21%) or lung cancer (19%). Other primary tumors are also noted (renal cell carcinoma, breast cancer, multiple myeloma, and so on).

Other patient characteristics are summarized in Table 1 and 2. The commonest vertebral sites affected were thoracic spinal level (51%). A total of 128 patients underwent operation via posterior approach. Of these, 120 patients (66%) received preoperative therapies including radiotherapy, chemotherapy or both modalities. Sixty-two patients (34%) had no preoperative treatment. One-hundred-fifty-one patients (79%) required postoperative adjuvant therapies (radiotherapy, chemotherapy, and so on). Thirty-one patients (21%) had no postoperative adjuvant therapy due to patients' general condition and demand of patients and their family.

For the statistical analysis, SPSS 12.0 software was used. Univariate and multivariate analyses were done. In univari-
ate analysis, survival rates were calculated according to the Kaplan-Meier method. The difference between the Kaplan-Meier curves was assessed in a univariate manner with the log-rank test. The significant prognostic factors determined by univariate analysis \((p<0.20)\) then were subjected to multivariate analysis with the Cox’s proportional hazards model.

Potential prognostic factors were included for possible associations with ambulatory function by means of univariate and multivariate analysis, which was performed with logistic regression and the backward stepwise (likelihood ratio) method. To settle multicollinearity between Tomita and Tokuhashi score, backward stepwise elimination method was used.

**RESULTS**

**Survival**

The median survival of the entire patient population was 8 months (95% confidence interval 6-10). Of the 182 patients, 80 (44%) died within 6 months after surgery, 113 (62%) died within 1 year after surgery, 138 (76%) died within 2 years after surgery (Fig. 1).

In univariate analysis, survival was significantly associated with gender, type of primary tumor, preoperative ECOG performance status, preoperative Nurick score, Tomita and Tokuhashi score (Table 1). The Kaplan-Meier statistics was used to estimate survival for each of the four ECOG and five Nurick scores (Fig. 2, 3).

In Table 1, survival according to the type of primary tumor showed statistically significant difference. The longest median survival period was 21 months in patients with prostate tumor metastasis, followed by 17 months with breast tumor metastasis. The shortest median survival period was 4 months on patients with lung cancer metastasis. Median survival of ECOG score 1 was 43 months, however that of score 4 was 2 months. Median survival of Nurick score 1 was 23 months, while that of score 5 was 5 months. Median survival of Tokuhashi score 2 was 1 months, that of score 14 was 104 months. In Tomita score, median survival of score 2 was 65 months, but score 10 was 5 months. Female (12 months) survived longer than male (6 months) (Table 1).

Other prognostic factors (age, tumor location, diagnostic interval, preoperative adjuvant treatment, extent of operation, surgery approach) were included for possible associations with ambulatory function by means of univariate and multivariate analysis, which was performed with logistic regression and the backward stepwise (likelihood ratio) method. To settle multicollinearity between Tomita and Tokuhashi score, backward stepwise elimination method was used.
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The surgical approach) are shown in Table 2. The \( p \)-values of their prognostic factors were over 0.05.

The significant prognostic factors determined by univariate analysis then were subjected to multivariate analysis. \( p \)-values of the factors under 0.20 were included in multivariate analysis. Survival was significantly affected by ECOG performance status and Tomita score before surgery (Table 3).

Functional outcome

The change of postoperative ECOG score at discharge and postoperative ambulatory function are shown in Table 4. In 35% of patients, ECOG score was improved at discharge. But 5% patients were aggravated. Ambulatory status before and after surgery were also evaluated. Postoperatively 47 (26%) patients had improvement in ambulatory function, 126 (69%) had no change, and 9 (5%) had deterioration (Table 4). At the endpoint clinical examination 103 patients had unassisted gait, 43 patients were able to walk with assistance, 20 patients could move their legs but were without gait function, and 16 patients were totally paralyzed. In Table 5, preoperative and postoperative ambulatory function evaluation using the Nurick score was shown at a glance.

The significant prognostic factors on postoperative ambulatory function were investigated. The univariate and multi-

\[ p \]-values were obtained from the multivariate analysis performed with the ordered-logit model. *Statistically significant value. ECOG: Eastern Cooperative Oncology Group, CI: confidence interval

Table 3. Multivariate analysis of potential prognostic factor for survival rate (cox regression model)

| Variables                        | Relative hazard (95% CI) | \( p \) value |
|----------------------------------|--------------------------|-------------|
| Gender                           |                          |             |
| 1 male                           | 1.0                      | 0.359       |
| 2 female                         | 0.846 (0.592-1.209)      |             |
| Group of primary tumor           |                          |             |
| 1 very rapid growth              | 1.0                      | 0.152       |
| 2 rapid growth                   | 1.833 (0.899-3.735)      |             |
| 3 moderate growth                | 1.412 (0.690-2.892)      |             |
| 4 slow growth                    | 0.990 (0.483-2.029)      |             |
| 5 very slow growth               | 1.430 (0.694-2.944)      |             |
| Preoperative ECOG status         |                          |             |
| 1 restricted in physically       | 1.0                      | <0.001*     |
| 2 capable of all self care       | 3.206 (1.647-6.244)      |             |
| 3 only limited self care         | 2.035 (0.969-4.273)      |             |
| 4 completely disabled            | 4.984 (1.955-12.707)     |             |
| Preoperative Nurick score        |                          |             |
| 1 no difficulty in walking       | 1.0                      | 0.823       |
| 2 slight difficulty in walking   | 1.338 (0.636-2.821)      |             |
| 3 difficulty in walking          | 1.643 (0.679-3.974)      |             |
| 4 able to walk with help         | 1.649 (0.665-4.088)      |             |
| 5 chair bound or bedridden       | 1.677 (0.638-4.408)      |             |
| Operative extent                 |                          |             |
| 1 no removal                     | 1.0                      | 0.119       |
| 2 only biopsy                    | 2.255 (0.876-5.809)      |             |
| 3 partial removal                | 0.798 (0.161-3.944)      |             |
| 4 subtotal removal               | 3.225 (1.598-6.509)      |             |
| 5 total removal                  | 1.596 (0.977-2.605)      |             |
| Operative approach               |                          |             |
| 1 anterior                       | 1.0                      | 0.747       |
| 2 posterior                      | 1.219 (0.584-2.546)      |             |
| 3 combine                        | 1.037 (0.524-2.053)      |             |
| Tokuhashi score group            |                          |             |
| 1 score 2-8                      | 1.0                      | 0.132       |
| 2 score 9-11                     | 0.358 (0.130-0.982)      |             |
| 3 score 12-15                    | 0.455 (0.194-1.069)      |             |
| Tomita score group               |                          |             |
| 1 score 2-3                      | 1.0                      | <0.001*     |
| 2 score 4-5                      | 2.103 (0.883-5.008)      |             |
| 3 score 6-7                      | 3.164 (1.242-8.061)      |             |
| 4 score 8-10                     | 7.842 (2.862-21.485)     |             |

Fig. 2. The Kaplan-Meier estimates of survival for each of the four ECOG scores. ECOG: Eastern Cooperative Oncology Group.

Fig. 3. The Kaplan-Meier estimates of survival for each of the five Nurick scores.
variate analysis were performed with logistic regression. For logistic regression, we divided the type of primary tumor into 5 groups (1 : lung, stomach, 2 : liver, gallbladder, unidentified, 3 : others, 4 : kidney, uterus, 5 : breast, prostate, thyroid). The primary site of cancer was graded from 1 to 5 based on the association between the site of the primary lesion and the mean survival period previously observed in patients. Tokuhashi and Tomita score were divided into three and four groups in their prognosis and treatment strategy. In univariate analysis, preoperative ECOG performance scale, preoperative ambulatory status and Tokuhashi score group were significant prognostic factors. Moreover, group of primary tumor and surgical approach were included for multivariate regression analysis.

Among the various clinical variables, 2 factors were significantly associated with postoperative ambulatory status. The factors were preoperative ECOG performance score and preoperative ambulatory status. The likelihood odds ratio that patients could walk after surgery for patients who were ambulatory before surgery compared with patients who were not able to walk when surgery started was 5.603. The odds ratio that low preoperative ECOG score compared with high preoperative ECOG score was 9.843 (Table 7).

**DISCUSSION**

With recent advances in surgical techniques and instrumentation, direct decompressive surgery has become the standard treatment for MSCC caused by solid primary tumors because of its increased efficacy over conventional radiotherapy in preserving neurological function. Moreover, early surgical decompression before irreversible neural injury occurs may reduce damage to the spinal cord and nerve roots, allowing better recovery of neurological function.

In this study of 182 patients with MSCC, 47 (26%) patients had improvement in motor function postoperatively, 126 (69%) had no change, and 9 (5%) had deterioration. After multivariate analysis, preoperative ambulatory ability and ECOG performance status were associated with postoperative gait function. Moreover, preoperative ECOG performance status and Tomita score might have influenced on survival rate.

The life expectancy of most MSCC patients is in general relatively short, depending on the type of primary tumor and visceral metastasis, bone metastasis. However, Tokuhashi score has six prognostic factors. Additionally, performance status, number of metastases in the vertebral body and Frankel grade are included. In our study, both scoring systems are significant prognostic predictors on postoperative survival, but they are not significant on postoperative ambulatory function. On multivariate analysis, only Tomita scoring system was a statistically significant predictor of postoperative survival. We speculated that there might be some confounding bias with other variables in Tokuhashi scoring system, such as performance status, number of metastases in the vertebral body and Frankel grade. Therefore, there could have been significant influence on patient's survival on univariate analysis.

There are various scoring systems for the preoperative evaluation of the prognosis of metastatic spinal tumors. Tomita and Tokuhashi score are most widely used. Tomita score has three prognostic factors. These are primary tumor, visceral metastasis, bone metastasis. However, Tokuhashi score has six prognostic factors. Among the various clinical variables, 2 factors were significantly associated with postoperative ambulatory status. The factors were preoperative ECOG performance score and preoperative ambulatory status. The likelihood odds ratio that patients could walk after surgery for patients who were ambulatory before surgery compared with patients who were not able to walk when surgery started was 5.603. The odds ratio that low preoperative ECOG score compared with high preoperative ECOG score was 9.843 (Table 7).

**Table 4. Postoperative ECOG score change and ambulatory rate**

| ECOG status change at discharge | Number of patients (%) |
|-------------------------------|------------------------|
| Improved                      | 66 (35)                |
| Stationary                    | 94 (49)                |
| Aggravated                    | 9 (5)                  |
| Hopeless discharge            | 7 (4)                  |
| Expired                       | 14 (7)                 |
| Ambulatory status at discharge|                        |
| Improved                      | 47 (26)                |
| Stationary                    | 126 (69)               |
| Aggravated                    | 9 (5)                  |

ECOG : Eastern Cooperative Oncology Group

**Table 5. Preoperative and postoperative ambulatory function evaluation using the nurick score**

| Preoperative Nurick score | Postoperative Nurick score (number of patients) |
|---------------------------|-----------------------------------------------|
| 1→1 (12)                  | 2→1 (4) 3→1 (0) 4→1 (0) 5→1 (0)               |
| 1→2 (1)                   | 2→2 (47) 3→2 (3) 4→2 (1) 5→2 (1)               |
| 1→3 (0)                   | 2→3 (2) 3→3 (18) 4→3 (8) 5→3 (6)               |
| 1→4 (2)                   | 2→4 (0) 3→4 (0) 4→4 (17) 5→4 (24)              |
| 1→5 (1)                   | 2→5 (1) 3→5 (0) 4→5 (2) 5→5 (32)               |

Grade 0 : Signs or symptoms of root involvement but without evidence of spinal cord disease. grade 1 : Signs of spinal cord disease but no difficulty in walking. grade 2 : Slight difficulty in walking that did not prevent full-time employment. grade 3 : Difficulty in walking that prevented full-time employment or the ability to perform all housework but that was not severe enough to require someone else’s help to walk. grade 4 : Able to walk with someone else’s help or the aid of a frame. grade 5 : Chair bound or bedridden. improved ambulatory function. no change of ambulation. aggravated ambulatory function.

The life expectancy of most MSCC patients is in general relatively short, depending on the type of primary tumor and visceral metastasis, bone metastasis. However, Tokuhashi score has six prognostic factors. Additionally, performance status, number of metastases in the vertebral body and Frankel grade are included. In our study, both scoring systems are significant prognostic predictors on postoperative survival, but they are not significant on postoperative ambulatory function. On multivariate analysis, only Tomita scoring system was a statistically significant predictor of postoperative survival. We speculated that there might be some confounding bias with other variables in Tokuhashi scoring system, such as performance status, number of metastases in the vertebral body and Frankel grade. Therefore, there could have been significant influence on patient's survival on univariate analysis.

Most studies revealed that ambulatory function at time of diagnosis is the most important predictor for the postoperative ambulatory outcome. The most important prognostic indicator for the prediction of ambulatory outcome is patients' pretreatment ambulatory status. If a patient can walk at the start of therapy he or she will probably retain this ability. We also confirmed these results and favorable postoperative results. However, preoperative ambulatory status was not a statistically significant predictor of survival in this present study. We found that ECOG performance
status is most important predictable factor for both postoperative survival and ambulatory function. In this regard, preoperative ECOG performance status should be evaluated in metastatic spinal tumor.

A thoracic location of the metastatic tumor has been reported to be associated with worse functional outcomes. The reason may be that thoracic spinal canal is narrower, making the spinal cord more vulnerable to injury. However, survival and ambulatory function according to tumor location showed no statistically significant difference in our study.

There have been numerous studies of post-radiotherapy or postoperative prognostic factor in metastatic spinal tumor. However, there have been a few studies about prognostic factor of postoperative survival and ambulatory function. Clinical outcome and survival after palliative surgery for spinal metastases has been reported by Hirabayashi et al. These authors found that survival was significantly associated with the anatomic site of primary carcinoma and postoperative ambulation. Our findings were somewhat different. We added preoperative variables (preoperative ECOG, Nurick, Tomita and Tokuhashi score) and excluded postoperative variables in order to remove the confounding error such as operation. Moreover, by a resident registration number, the survival data of patients were obtained from the Ministry of Public Administration and Security as a government agency. Thus, our data are accurate without recall bias (such as letter surveys and telephone documentation). On this score, the merits of our study may be some reduced bias and gap analysis between postoperative survival and ambulation.

This study is limited by retrospective design and long period included (21 years). During this period, there were differences in various surgical techniques. Patient selection and differences in surgical skill and decision between surgeons are also limitations which might have affected the confounding

| Table 6. Univariate analysis for postoperative ambulatory status (logistic regression) |
|----------------------------------|-------------------|-----------------|-----------------|-----------------|-----------------|
| Potential prognostic factor | Odds ratio (95% CI) | p value |
| Age | | |
| 1≤60 | 1.0 | 0.248 |
| 2>60 | 1.586 (0.725-3.466) | 0.248 |
| Gender | | |
| 1 male | 1.0 | 0.338 |
| 2 female | 1.482 (0.663-3.309) | 0.248 |
| Group of primary tumor | | |
| 1 very rapid growth | 1.0 | 0.078 |
| 2 rapid growth | 0.545 (0.143-2.074) | 0.248 |
| 3 moderate growth | 2.100 (0.665-6.633) | 0.248 |
| 4 slow growth | 2.504 (0.762-8.230) | 0.248 |
| 5 very slow growth | 2.715 (0.985-9.524) | 0.248 |
| Location of spinal metastases | | |
| 1 cervical | 1.0 | 0.501 |
| 2 cervico-thoracic | 1.800 (0.184-17.567) | 0.248 |
| 3 thoracic | 3.234 (0.087-114.256) | 0.248 |
| 4 thoraco-lumbar | 3.309 (0.399-27.463) | 0.248 |
| 5 lumbar | 2.250 (0.200-25.369) | 0.248 |
| 6 cervico-thoraco-lumbar | 0.750 (0.060-9.319) | 0.248 |
| 7 others | 0.567 (0.024-2.456) | 0.248 |
| Interval between primary and spinal metastases diagnosis | | |
| 1 previous diagnosis of MSCC | 1.0 | 0.276 |
| 2 under 12 months | 0.855 (0.285-2.564) | 0.276 |
| 3 under 24 months | 2.055 (0.764-5.525) | 0.276 |
| 4 over 25 months | 1.720 (0.574-5.152) | 0.276 |
| Preoperative treatment | | |
| 1 absence | 1.0 | 0.496 |
| 2 presence | 0.770 (0.362-1.636) | 0.496 |
| OP extent of spinal metastases | | |
| 1 no removal | 1.0 | 0.971 |
| 2 only biopsy | 0.875 (0.245-87.256) | 0.971 |
| 3 partial removal | 0.784 (0.345-124.586) | 0.971 |
| 4 subtotal removal | 0.663 (0.149-2.947) | 0.971 |
| 5 total removal | 0.726 (0.290-1.815) | 0.971 |
| Surgical approach | | |
| 1 anterior | 1.0 | 0.084 |
| 2 posterior | 1.444 (0.148-14.139) | 0.084 |
| 3 combine | 4.155 (0.522-33.049) | 0.084 |
| ECOG performance status before surgery | | |
| 1 restricted in physically | 1.0 | <0.001* |
| 2 capable of all self care | 0.472 (0.028-7.853) | <0.001* |
| 3 only limited self care | 4.630 (0.562-38.171) | <0.001* |
| 4 completely disabled | 42.857 (5.224-351.611) | <0.001* |
| Ambulatory function before surgery | | |
| 1 able to walk | 1.0 | <0.001* |
| 2 not able to walk | 29.677 (9.756-90.280) | <0.001* |
| Tomokuhashi score group | | |
| 1 score 2-8 | 1.0 | 0.008 |
| 2 score 9-11 | 5.953 (0.758-46.741) | 0.008 |
| 3 score 12-15 | 1.091 (0.106-11.262) | 0.008 |
| Tomita score group | | |
| 1 score 2-3 | 1.0 | 0.34421 |
| 2 score 4-5 | 2.838 (0.321-25.091) | 0.34421 |
| 3 score 6-7 | 3.659 (0.431-31.065) | 0.34421 |
| 4 score 8-10 | 5.094 (0.628-41.339) | 0.34421 |

Group of primary tumor 1 : lung, stomach, 2 : liver, gallbladder, unidentified, 3 : Others, 4 : kidney, uterus, 5 : breast, prostate, thyroid. p-values were obtained from the multivariate analysis performed with the logistic regression. *Statistically significant value. CI : confidence interval, ECOG : Eastern Cooperative Oncology Group
factors. However, we have performed metastatic spinal surgery of decompression and stabilization under same indication and one institution.

CONCLUSION

In summary, survival after metastatic spinal tumor surgery was shown to be influenced by preoperative ECOG performance status and Tokuhashi score. Tokuhashi score might be more reliable predictor of prognosis in our patients’ survival than Tokuhashi score. The ambulatory functional outcomes after metastatic spinal tumor surgery were influenced by preoperative ambulatory status and preoperative ECOG performance status. These results indicate that prompt decompressive surgery may improve patient’s survival and gait before general condition and ambulatory function of patient become worse.

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Table 7. Multivariate analysis for postoperative ambulatory status (logistic regression)

| Potential prognostic factor | Odds ratio (95% CI) | p-value |
|----------------------------|---------------------|---------|
| Group of primary tumor     |                     |         |
| 1 very rapid growth        | 1.0                 | 0.80    |
| 2 rapid growth             | 0.352 (0.040-3.114) |         |
| 3 moderate growth          | 3.061 (0.319-29.329)|         |
| 4 slow growth              | 2.172 (0.273-17.309)|         |
| 5 very slow growth         | 1.417 (0.545-6.524) |         |
| Surgical approach          |                     |         |
| 1 anterior                 | 1.0                 | 0.466   |
| 2 posterior                | 2.777 (0.523-14.762)|         |
| 3 combine                  | 1.528 (0.070-33.423)|         |
| ECOG performance status before surgery |       |         |
| 1 restricted in physically  | 1.0                 | 0.016   |
| 2 capable of all self care | 0.312 (0.016-6.005)|         |
| 3 only limited self care   | 1.406 (0.117-16.890)|         |
| 4 completely disabled      | 9.843 (0.578-167.647)|        |
| Ambulatory function before surgery |       |         |
| 1 able to walk             | 1.0                 | 0.026   |
| 2 not able to walk         | 5.603 (1.224-25.653)|         |
| Tokuhashi score group      |                     |         |
| 1 score 2-8                | 1.0                 | 0.866   |
| 2 score 9-11               | 0.788 (0.033-18.900)|         |
| 3 score 12-15              | 0.540 (0.029-10.178)|         |

p-values were obtained from the multivariate analysis performed with the logistic regression. *Statistically significant value. CI : confidence interval, ECOG : Eastern Cooperative Oncology Group.
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