

RESEARCH ARTICLE

A survey of carboplatin desensitization therapy in Japan: A multicenter retrospective study

Hiroaki Komatsu¹  | Koji Matsumoto²  | Mitsunori Morita² |
Takayuki Nagasawa³ | Hiroshi Nishio⁴ | Jiro Suzuki⁵ | Shin Nishio⁶  |
Hisanori Kobara⁷ | Mayu Yunokawa⁸ | Kazuya Ariyoshi⁹ | Takashi Hirayama¹⁰ |
Hideki Tokunaga¹¹ | Masayo Ukita¹² | Kaori Yoriki¹³ | Mayuyo Mori-Uchino¹⁴ |
Akiko Furusawa¹⁵ | Shinichi Togami¹⁶ | Hiroko Nakamura¹⁷ | Mitsuya Ishikawa¹⁸ |
Toyomi Satoh¹⁹

Correspondence

Hiroaki Komatsu, Department of
Obstetrics and Gynecology, Tottori
University School of Medicine, 36-1,
Nishicho, Yonago, Tottori 683-8504,
Japan.

Email: komatsu.h.med@gmail.com

Koji Matsumoto, Department of
Medical Oncology, Hyogo Cancer
Center, 13-70, Kitaoji-cho, Akashi,
Hyogo 673-8558, Japan.

Email: kojmatsu2@hyogo-cc.jp

Abstract

Introduction: Hypersensitivity reactions (HSRs) to chemotherapy are serious adverse events associated with cancer drug therapy and can occur with any anti-tumor drug. This study investigated the safety and efficacy of carboplatin desensitization therapy in Japan and established a method for treating carboplatin HSRs.

Methods: Patients diagnosed with gynecological (ovarian, endometrial, or cervical) cancers who underwent carboplatin desensitization therapy between 2016 and 2020 at the Gynecologic Cancer Study Group of Japan Clinical Oncology Group were included. The carboplatin desensitization therapy at each institution and the implementation cases were registered in an online case report form.

Results: This retrospective study enrolled 136 patients (ovarian, 108; endometrial, 17; and cervical cancer, 11). Pre-existing allergies were present in 37 (27.2%) patients, and 32 (23.5%) patients exhibited prodromal symptoms during treatment before HSR onset. Erythema was the most common symptom at HSR onset, affecting 93 (68.4%) patients, followed by itching in 72 (52.9%) patients and decreased oxygen saturation in 43 (31.6%) patients. Loss of consciousness occurred in three (2.2%) patients. The most common timing of HSR onset was during the first recurrence treatment (47%). The mean total carboplatin dose until HSR onset was 7331 (2620–18,282) mg, and the mean number of doses was 14 (4–63). Desensitization treatment was completed in 75% of cases, and breakthrough HSRs occurred in 25% (34/136). No deaths occurred in the study cohort. The risk factors for HSRs were not identified.

Conclusion: Although carboplatin desensitization therapy has high success rates in Japan, erythema and pruritus are important HSRs to consider.

For Affiliation refer page on 7

This is an open access article under the terms of the [Creative Commons Attribution](https://creativecommons.org/licenses/by/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2024 The Authors. *Cancer Medicine* published by John Wiley & Sons Ltd.

KEYWORDS

carboplatin, desensitization, erythema, hypersensitivity reaction, pruritus

1 | INTRODUCTION

The platinum and taxane combination regimen is the primary treatment method for both initial and recurrent cases of gynecologic cancers.^{1–7} Carboplatin, in particular, was introduced in 1989 as a treatment for ovarian cancer and has become a popular choice mainly because its therapeutic effect is comparable to that of cisplatin and it has fewer adverse events. However, hypersensitivity reactions (HSRs) have been reported in patients receiving multiple cycles of chemotherapy with carboplatin.⁸ The frequency of HSRs varies among different reports, and few detailed causes or risk factors have been reported.⁹ Previously, Altwerger et al.,¹⁰ Suggimoto et al.,¹¹ and Joly et al.¹² reported germline BRCA mutations, carboplatin dosage, and regimen type and age >70 years, respectively, as risk factors for HSRs. Although patients with a history of allergies are more susceptible to HSRs, the number of such cases is unknown.^{13–15}

HSRs can severely impact vital signs, potentially leading to shock. Re-administration of carboplatin after HSRs can lead to death.¹⁶ In addition, HSRs prevent the use of platinum drugs in patients with platinum-sensitive relapsed disease despite the possibility of a successful platinum regimen. This may impact patients' prognoses. Carboplatin desensitization therapy has been used for HSRs in recent years, and several reports have been published.^{17–26} However, no fixed method of administration has been established because the reports were from single centers, included a small number of cases, and used various methods. Furthermore, due to the complexity of the administration system at each facility, a certain method of administration has not been established.

This study aimed to investigate the therapy completion rate, frequency of breakthrough HSRs, and factors associated with their onset in patients treated with carboplatin desensitization therapy. We defined HSRs that occurred

during the desensitization treatment period as breakthrough HSRs.

2 | METHODS

Patients who underwent carboplatin desensitization therapy for gynecological (cervical, uterine body, primary ovarian, fallopian tube, and peritoneal) cancers at the participating centers of the Gynecologic Cancer Study Group of the Japanese Clinical Oncology Group (JCOG) between January 2016 and December 2020 were included. The indication for desensitization therapy is left at the discretion of the gynecologic or medical oncologist at each facility and approved for implementation. A patient record form created using Google Forms was sent to each facility, and the cases were registered online. Each facility was asked to enter a case number to verify the case details.

For each facility, the carboplatin solution, administration rate, dilution method (e.g., 1/1000, 1/100, 1/10, or undiluted solution), and place of administration (including a private room, large room, intensive care unit, or outpatient clinic) were recorded. The typical treatment protocol was to administer the therapy for 1 h per session for 4 h (Figure 1).

The individual case questionnaire included details about age, type of cancer, FIGO stage, presence of allergies, HSR onset information, number of doses of the platinum regimen (including conventional, dose-dense, or weekly regimen), total dose, presence of suspected symptoms at the time of treatment one cycle prior to the treatment in which HSRs were diagnosed, symptoms before HSR onset timing, symptoms, response to HSR onset, number of desensitization therapies administered, prophylactic agents, duration of administration, and HSR recurrence.

The primary endpoints were the completion rate of carboplatin desensitization therapy and the frequency of breakthrough HSRs in patients treated with desensitization therapy. Secondary endpoints were the development

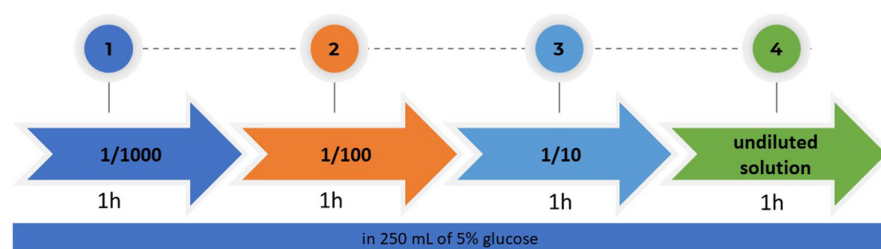


FIGURE 1 Typical scheme of carboplatin de-sensitization. Solutions with 1/1000, 1/100, and 1/10 dilutions of carboplatin and an undiluted solution were prepared in 250 mL of 5% glucose.

of carboplatin HSRs and their associated factors. Cases of complete treatment included those in which the planned desensitization therapy was administered or discontinued due to disease progression. Risk factors for the development of breakthrough HSRs were extracted using multivariate analysis.

This study was approved by the Ethics Committee of the Tottori University Hospital (IRB number 21-018) and all participating facilities. The requirement for obtaining informed consent was waived owing to the retrospective nature of the study.

2.1 | Statistical analyses

Continuous data are presented as mean and standard deviation. Categorical data are presented as numbers and frequencies. Multivariate analysis using logistic regression analysis was performed. Statistical significance was

set at p values of <0.05 . All statistical analyses were performed using the GraphPad Prism 8.3 software (GraphPad Software, Inc., La Jolla, CA, USA).

3 | RESULTS

Twenty facilities participated in the study. A total of 136 patients (ovarian cancer, 108; endometrial cancer, 17; cervical cancer, 11) were enrolled in this retrospective study (Table 1). A total of 638 cycles of desensitizing therapy were administered. All centers used a four-step method starting with a 1000-fold dilution. Solutions with 1/1000, 1/100, and 1/10 dilutions of carboplatin and an undiluted solution were prepared in 250 mL of 5% glucose. Each solution was administered as a 1-h intravenous infusion (4-step 4-h protocol).¹⁸ Sixteen facilities (80%) administered the therapy in a large room and 4 (20%) in an observation room. In 64% of the facilities,

TABLE 1 Patient characteristics.

	Total (<i>n</i> = 136)	Ovarian (<i>n</i> = 108)	Endometrial (<i>n</i> = 17)	Cervical (<i>n</i> = 11)
Age (years)	54 (27–82)	54 (27–82)	56 (32–81)	45 (29–58)
Height (cm)	156 (132–169)	156 (132–168)	156 (145–162)	158 (152–169)
Body weight (kg)	54 (39–100)	51 (32–89)	62 (42–100)	58 (47–67)
Stage				
I	16	6	3	7
II	4	3	0	1
III	75	69	5	1
IV	39	28	9	2
Unknown	2	2	0	0
Carboplatin dosage regimen				
Conventional	99	72	16	11
Dose-dense	31	30	1	0
Weekly	6	6	0	0
Allergy				
Yes	37 (27.2%)	32 (29.6%)	0	5 (45.5%)
No	99 (72.8%)	76 (70.4%)	17 (100%)	6 (54.5%)
Suspected symptoms of previous treatment				
Yes	32 (23.5%)	25 (23.1%)	3 (17.6%)	4 (36.4%)
No	104 (76.5%)	83 (76%)	14 (82.4%)	7 (63.6%)
Breakdown of suspected symptoms of previous treatment				
Erythema	19	14	2	3
Itching	18	13	2	3
Nausea and vomiting	5	5	0	0
Dyspnea	4	4	0	0
Other	5	4	1	0

physicians were on call in the wards, 25% were on call at the bedside, and the remainder appeared to be called in the event of an emergency.

Overall, 37 (27.2%) patients had preexisting allergies and 32 (23.5%) exhibited prodromal symptoms in the previous cycle when the HSR occurred. The most common symptoms were erythema and itching.

At HSR onset, erythema was the most common symptom, occurring in 93 (68.4%) patients, followed by itching in 72 (52.9%) and hypoxia in 43 (31.6%) patients (Table 2). Loss of consciousness occurred in three patients (2.2%). The timing of HSR onset was first-line

treatment in 31 (22.8%) patients, second-line treatment in 63 (47.1%), and third-line treatment or later in 41 (30.1%). The mean total carboplatin dose until HSRs appeared was 7331 (2620–18,282) mg, and the mean number of doses was 14 (4–63) (Table 3). HSRs occurred more frequently after the eighth cycle of treatment administration (Figure 2).

Desensitization therapy was completed in 75% of patients, with 25% (34/136) experiencing breakthrough HSRs (i.e., HSRs that occurred during the desensitization treatment period) (Table 4). Among these patients, 29% (10/34) of patients met all the diagnostic criteria

TABLE 2 Common symptoms at HSRs.

	Total (n = 136)	Ovarian (n = 108)	Endometrial (n = 17)	Cervical (n = 11)
Erythema				
All	93 (68.4%)	71	13	10
<10%	45	35	6	4
10%–30%	18	13	2	3
≥30%	16	10	4	2
Unknown	14	13	1	0
Itching				
Yes	72 (52.9%)	53	10	9
Sensory disturbance				
Yes	24 (17.6%)	23	1	0
Nausea and vomiting				
All	37 (27.2%)	31	3	3
Mild	31	25	3	3
Severe	4	4	0	0
Unknown	2	2	0	0
Dyspnea				
All	43 (31.6)	37	3	3
Mild (SpO ₂ 90–95%)	27	21	3	3
Moderate (SpO ₂ < 90%)	7	7	0	0
Severe	1	1	0	0
Unknown	8	8	0	0
Systolic blood pressure values				
91–100 mmHg	1	1	0	0
81–90 mmHg	7	7	0	0
71–80 mmHg	6	6	0	0
≥70 mmHg	4	4	0	0
Unknown	5	4	1	0
Chest discomfort				
Yes	24 (17.6%)	22	0	2
Unconsciousness				
Yes	3 (2.2%)	3	0	0

TABLE 3 Mean number of carboplatin doses and total number of carboplatin doses until HSR appearance.

	Total (136)	Ovarian (n = 108)	Endometrial (n = 17)	Cervical (n = 11)
Total carboplatin dose until HSR appearance (mg) average	7331 (2620–18,282)	7398 (2620–18,282)	7611 (4728–13,390)	5948 (2756–12,199)
Total number of carboplatin doses until HSR appearance (n) average	14 (4–63)	14 (4–63)	14 (8–18)	12 (8–21)

Abbreviation: HSR, Hypersensitivity reaction.

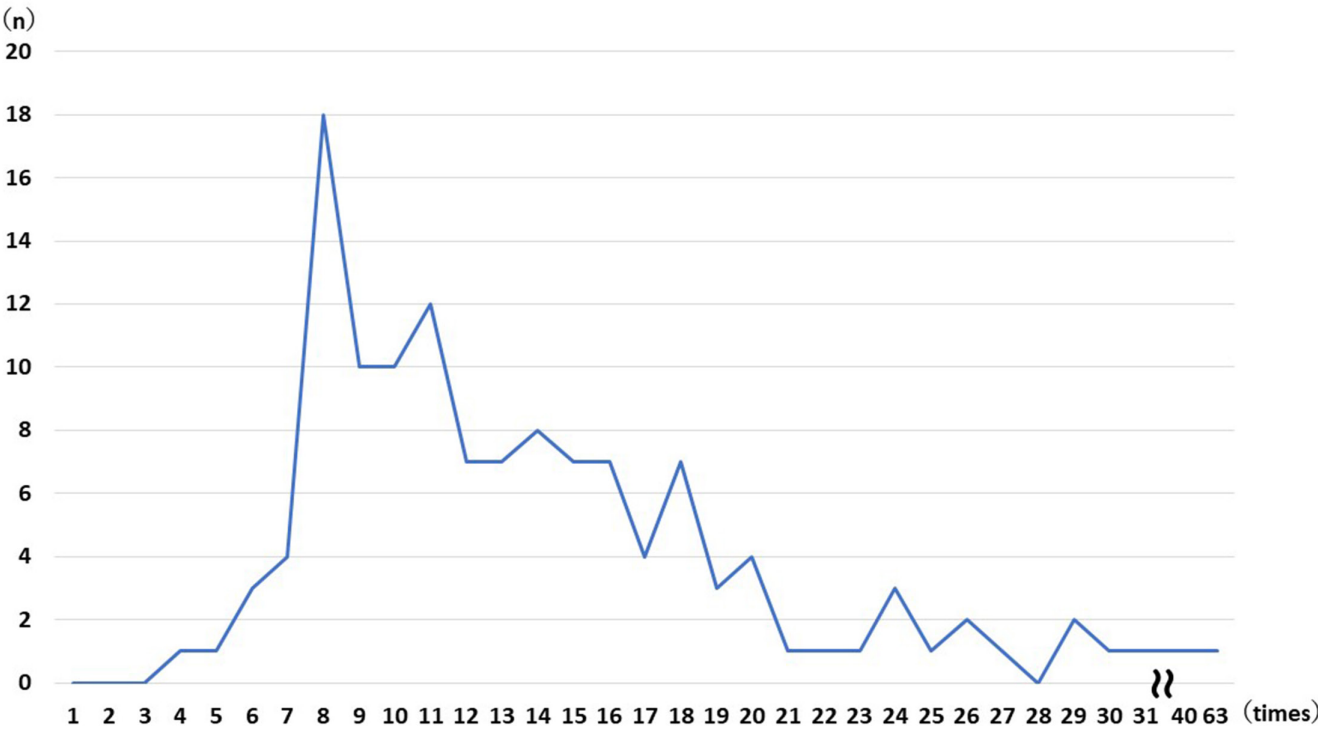


FIGURE 2 Number of carboplatin treatment courses until HSRs. HSRs occurred more frequently after the eighth cycle of treatment administration. HSRs, hypersensitivity reactions.

TABLE 4 Treatment complete rate.

	Total (136)	Ovarian (n = 108)	Endometrial (n = 17)	Cervical (n = 11)
Treatment complete rates	102 (75.0%)	83 (76.9%)	14 (82.4%)	5 (45.5%)
Reason for discontinuation				
Progression of disease	30 (20.1%)	23 (18.8%)	4 (23.5%)	3 (28.3%)
Breakthrough HSRs	34 (25.0%)	25 (33.7%)	3 (17.6%)	6 (63.6%)
Patient wishes	6 (4.4%)	3 (2.8%)	3 (17.6%)	0
Others	4 (2.9%)	3 (2.8%)	1 (5.9%)	0

Abbreviation: HSRs, Hypersensitivity reactions.

for anaphylaxis.²¹ The median number of desensitization treatments was 3, with some patients receiving up to 22 courses (Figure 3). No HSR-related mortality was observed. Risk factors for HSRs were not identified in this study (Table 5).

4 | DISCUSSION

Our study is one of the largest studies on carboplatin desensitization. This study showed that the main symptoms at HSR onset were erythema and itching. The completion

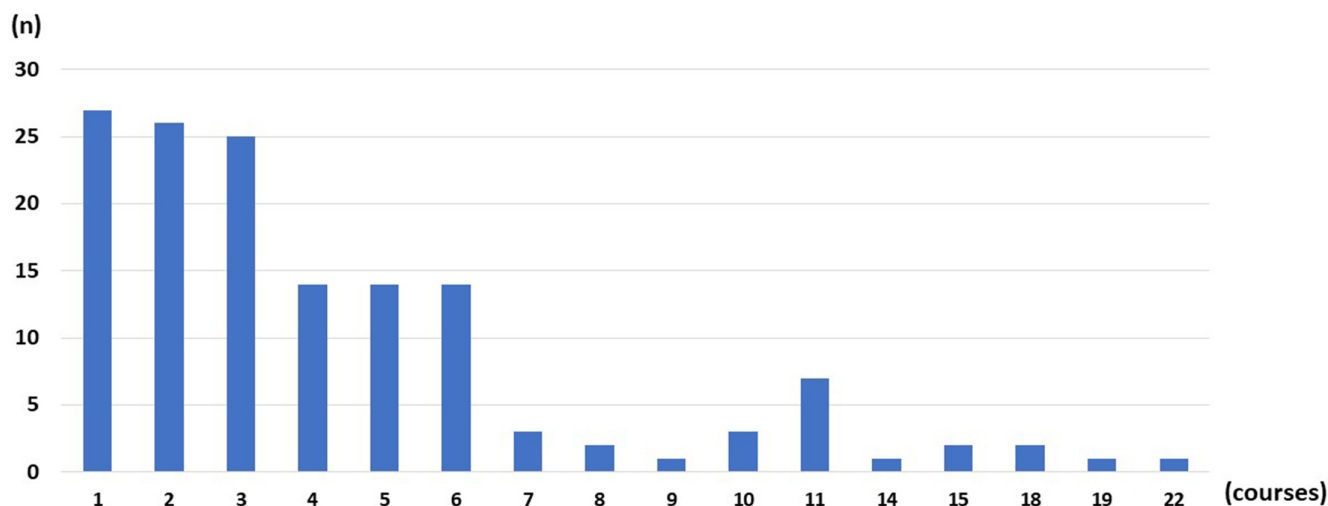


FIGURE 3 Number of carboplatin desensitization treatment courses. The median number of treatment courses was 3; some patients received up to 22 courses.

	Odds ratio	95% CI	p-value
Age (54 years)	1.263	0.478–3.424	ns
Allergy (drugs)	1.219	0.349–3.793	ns
Suspected symptoms of previous treatment	0.462	0.099–1.579	ns
NAC-IDS or PDS	0.557	0.204–1.529	ns
Timing of treatment	0.932	0.310–3.303	ns

TABLE 5 Risk factors for HSRs.

rate was 75%, indicating that the four-step carboplatin desensitization regimen was safe and feasible. However, the risk factors for breakthrough HSR development could not be determined.

Regarding symptoms preceding HSR diagnosis, erythema and itching, which can be considered prodromal symptoms, were observed in approximately 20% of patients during the course of treatment before HSR onset. However, in some centers, these symptoms could be considered HSRs, making it challenging to distinguish between them. In this study, the symptoms spontaneously resolved, and carboplatin therapy was continued even after symptom onset because the symptoms were not considered severe. Based on these results, we believe that early diagnosis of HSRs may be difficult, especially when only accompanied by atypical prodromal symptoms.

At HSR onset, erythema followed by itching appeared as a prodromal symptom. Erythema usually occurs in less than 10% of the body, and the appearance of symptoms may be missed owing to clothing. Altwerger et al.¹⁶ reported that the frequency of erythema on the palms was 30.3%, which was lower than that observed in our study; however, no generalized erythema was reported. They also reported pruritis in 51.5% of their patients, which

was comparable with the results observed in the present study. Owing to the presence of hypoxia and hypotension as symptoms other than erythema, desensitization should be performed in an environment where epinephrine can be administered immediately. In this study, we also examined the location and system of desensitization administration and conducted a subgroup analysis.

The mean total dose of carboplatin at HSR onset was approximately 7000 mg, and the mean number of courses was 14. These were similar regardless of carcinoma type and were predictors of HSR onset when carboplatin combination therapy was used. It should be noted that the earliest symptoms of HSR onset occurred in the fourth course, and the latest occurred in the 63rd course; thus, they may still occur after long-term treatment.

The treatment completion rate for desensitization administration was 75%, which was lower than that reported by another study. Yamamoto et al.²⁵ reported a treatment completion rate of 93.4%, which can vary greatly depending on the definition of treatment completion. The primary endpoint of their study was the success rate of carboplatin desensitization administration, which was calculated as the percentage of patients who completed all planned cycles

among all patients and the percentage of completed carboplatin desensitization cycles out of the total number of cycles. However, our treatment completion rate is the percentage of patients who completed treatment without breakthrough HSRs, which may explain the difference. The differences in cancer type, small number of cervical cancer cases, and response rate to platinum as a treatment for recurrence may have had an impact. Breakthrough HSRs were observed in 25% of patients, which was comparable to that reported by Altwerger et al. (14/56). We did not analyze the details of the occurrence of breakthrough HSRs in this study. We would like to address this in future studies. The presence or absence of allergy was not reliably ascertained. Because a drug or food allergy does not manifest unless ingested, it is not possible to reliably identify whether the patient has a true allergy.²⁶

Risk factors for HSRs could not be identified. Although the frequency of allergy varies with drug interactions, the findings of Joly et al.²⁶ are worth noting. HSR onsets may be influenced by the individual's allergic constitution and the frequency of prior supportive care, such as antihistamines and steroids. Future studies should further investigate these factors.

4.1 | Limitations and strengths

This study had some limitations. First, this was a retrospective study and was prone to various biases. We are currently planning to conduct a prospective study and look forward to future research in this area. Second, the diagnostic criteria for HSRs have not been clearly established. It would be desirable to have a research plan that clearly defines the frequency of occurrence based on diagnostic criteria for anaphylaxis or the measurement of tryptase levels at the event. Current CTCAE (ver.5) has three possible terms refuting HSR, including “allergic reaction,” “infusion-related reaction,” and “anaphylaxis.” “Allergic reaction” and “infusion-related reaction” are graded according to the intervention used for their management. “Anaphylaxis” is only classified as grade 3 or 4. Therefore, relatively mild but potentially dangerous reactions are difficult to grade using the CTCAE. The World Allergy Organization (WAO) Anaphylaxis Guidelines require skin (and/or mucosa) symptoms plus at least one other systemic symptom for the diagnosis of anaphylaxis. Consequently, if a patient experiences only generalized urticaria during carboplatin infusion, a diagnosis of anaphylaxis cannot be made using the WAO criteria. Usually, such patients are treated as those with HSR. This is also why only 29% of the patients who received desensitization fulfilled the anaphylaxis criteria. Third, the multicenter approach of this study was a limitation because of variations in desensitization protocols across institutions.

One of the strengths of this study is that it is one of the largest case analyses to date and includes more than 100 reported cases.

5 | CONCLUSION

This study revealed that more than 20% of patients had prodromal symptoms when carboplatin was administered before one of the treatments, leading to an HSR diagnosis. Additionally, the main symptoms of carboplatin treatment HSR onset were erythema and itching. The completion rate of carboplatin desensitization therapy using the four-step method was 75%, indicating that the regimen was safe and feasible, even for patients with HSRs. We are preparing to conduct a prospective multi-institutional study on carboplatin desensitization in Japan.

AUTHOR CONTRIBUTIONS

Hiroaki Komatsu: Data curation (equal); project administration (equal); writing – original draft (lead); writing – review and editing (equal). **Koji Matsumoto:** Conceptualization (equal); data curation (equal); supervision (equal); writing – review and editing (equal). **Mitsunori Morita:** Data curation (equal); writing – review and editing (equal). **Takayuki Nagasawa:** Data curation (equal). **Hiroshi Nishio:** Data curation (equal); writing – review and editing (equal). **Jiro Suzuki:** Data curation (equal); writing – review and editing (equal). **Shin Nishio:** Data curation (equal); supervision (equal). **Hisanori Kobara:** Conceptualization (equal). **Mayu Yunokawa:** Data curation (equal). **Kazuya Ariyoshi:** Data curation (equal). **Takashi Hirayama:** Data curation (equal). **Hideki Tokunaga:** Data curation (equal). **Masayo Ukita:** Data curation (equal). **Kaori Yoriki:** Data curation (equal). **Mayuyo Mori-Uchino:** Data curation (equal). **Akiko Furusawa:** Data curation (equal). **Shinichi Togami:** Data curation (equal). **hiroko nakamura:** Data curation (equal). **Mitsuya Ishikawa:** Data curation (equal); supervision (equal); writing – review and editing (equal). **Toyomi Satoh:** Supervision (equal); writing – review and editing (equal).

AFFILIATIONS

¹Department of Obstetrics and Gynecology, Tottori University School of Medicine, Yonago, Tottori, Japan

²Department of Medical Oncology, Hyogo Cancer Center, Akashi, Hyogo, Japan

³Department of Obstetrics and Gynecology, Iwate Medical University School of Medicine, Morioka, Iwate, Japan

⁴Department of Obstetrics and Gynecology, Keio University School of Medicine, Tokyo, Japan

⁵Department of Obstetrics and Gynecology, The Jikei University School

of Medicine, Tokyo, Japan

⁶Department of Obstetrics and Gynecology, Kurume University School of Medicine, Kurume, Japan

⁷Department of Obstetrics and Gynecology, Shinshu University, Nagano, Japan

⁸Department of Gynecology, The Cancer Institute Hospital of JFCR, Tokyo, Japan

⁹Department of Gynecology Service, National Kyushu Cancer Center, Fukuoka, Japan

¹⁰Department of Obstetrics and Gynecology, Juntendo University Hospital, Tokyo, Japan

¹¹Department of Gynecology, Tohoku University Graduate School of Medicine, Sendai, Japan

¹²Department of Gynecology and Obstetrics, Graduate School of Medicine, Kyoto University, Kyoto, Japan

¹³Department of Obstetrics and Gynecology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan

¹⁴Department of Obstetrics and Gynecology, Faculty of Medicine, The University of Tokyo, Tokyo, Japan

¹⁵Department of Gynecology, Tokyo Metropolitan Cancer and Infectious Diseases Center, Komagome Hospital, Tokyo, Japan

¹⁶Department of Obstetrics and Gynecology, Faculty of Medicine, Kagoshima University, Kagoshima, Japan

¹⁷Department of Obstetrics and Gynecology, National Hospital Organization Kure Medical Center and Chugoku Cancer Center, Kure, Japan

¹⁸Department of Gynecology, National Cancer Center Hospital, Tokyo, Japan

¹⁹Department of Obstetrics and Gynecology, Institute of Medicine, University of Tsukuba, Tsukuba, Japan

ACKNOWLEDGMENTS

We would like to express our sincere gratitude to the people who provided data for case collection at the participating JCOG and associated facilities.

CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest.

FUNDING INFORMATION

This study received no funding.

ETHICS APPROVAL STATEMENT

The study was approved by the Ethics Committee of Tottori University (IRB number: 21-018).

PATIENT CONSENT STATEMENT

The requirement for obtaining informed consent was waived owing to the retrospective nature of the study. Patient consent was obtained by opt-out.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Hiroaki Komatsu  <https://orcid.org/0000-0002-4507-6848>

Koji Matsumoto  <https://orcid.org/0000-0003-1907-0247>

Shin Nishio  <https://orcid.org/0000-0003-2526-630X>

REFERENCES

1. Parmar MK, Ledermann JA, Colombo N, et al. Paclitaxel plus platinum-based chemotherapy versus conventional platinum-based chemotherapy in women with relapsed ovarian cancer: the ICON4/AGO-OVAR-2.2 trial. *Lancet*. 2003;361(9375):2099-2106. doi:[10.1016/S0140-6736\(03\)13718-X](https://doi.org/10.1016/S0140-6736(03)13718-X)
2. Pfisterer J, Plante M, Vergote I, et al. Gemcitabine plus carboplatin compared with carboplatin in patients with platinum-sensitive recurrent ovarian cancer: an intergroup trial of the AGO-OVAR, the NCIC CTG, and the EORTC GCG. *J Clin Oncol*. 2006;24(29):4699-4707. doi:[10.1200/JCO.2006.06.0913](https://doi.org/10.1200/JCO.2006.06.0913)
3. Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. *J Clin Oncol*. 2010;28(20):3323-3329. doi:[10.1200/JCO.2009.25.7519](https://doi.org/10.1200/JCO.2009.25.7519)
4. Kitagawa R, Katsumata N, Shibata T, et al. Paclitaxel plus carboplatin versus paclitaxel plus cisplatin in metastatic or recurrent cervical cancer: the open-label randomized phase III trial JCOG0505. *J Clin Oncol*. 2015;33(19):2129-2135. doi:[10.1200/JCO.2014.58.4391](https://doi.org/10.1200/JCO.2014.58.4391)
5. Nomura H, Aoki D, Takahashi F, et al. Randomized phase II study comparing docetaxel plus cisplatin, docetaxel plus carboplatin, and paclitaxel plus carboplatin in patients with advanced or recurrent endometrial carcinoma: a Japanese gynecologic oncology group study (JGOG2041). *Ann Oncol*. 2011;22(3):636-642. doi:[10.1093/annonc/mdq401](https://doi.org/10.1093/annonc/mdq401)
6. Hoskins PJ, Swenerton KD, Pike JA, et al. Paclitaxel and carboplatin, alone or with irradiation, in advanced or recurrent endometrial cancer: a phase II study. *J Clin Oncol*. 2001;19(20):4048-4053. doi:[10.1200/JCO.2001.19.20.4048](https://doi.org/10.1200/JCO.2001.19.20.4048)
7. Miller DS, Filiaci VL, Mannel RS, et al. Carboplatin and paclitaxel for advanced endometrial cancer: final overall survival and adverse event analysis of a phase III trial (NRG oncology/GOG0209). *J Clin Oncol*. 2020;38(33):3841-3850. doi:[10.1200/JCO.20.01076](https://doi.org/10.1200/JCO.20.01076)
8. Tonkin KS, Rubin P, Levin L. Carboplatin hypersensitivity: case reports and review of the literature. *Eur J Cancer*. 1993;29A(9):1356-1357. doi:[10.1016/0959-8049\(93\)90093-u](https://doi.org/10.1016/0959-8049(93)90093-u)
9. Markman M, Kennedy A, Webster K, et al. Clinical features of hypersensitivity reactions to carboplatin. *J Clin Oncol*. 1999;17(4):1141. doi:[10.1200/JCO.1999.17.4.1141](https://doi.org/10.1200/JCO.1999.17.4.1141)
10. Altwerger G, Florsheim EB, Menderes G, et al. Impact of carboplatin hypersensitivity and desensitization on patients with recurrent ovarian cancer. *J Cancer Res Clin Oncol*. 2018;144(12):2449-2456. doi:[10.1007/s00432-018-2753-y](https://doi.org/10.1007/s00432-018-2753-y)
11. Sugimoto H, Iwamoto T, Murashima Y, Tabata T, Sagawa N, Okuda M. Risk factors contributing to the development of carboplatin-related delayed hypersensitivity reactions in Japanese patients with gynecologic cancers. *Cancer Chemother Pharmacol*. 2011;67(2):415-419. doi:[10.1007/s00280-010-1338-5](https://doi.org/10.1007/s00280-010-1338-5)

12. Joly F, Ray-Coquard I, Fabbro M, et al. Decreased hypersensitivity reactions with carboplatin-pegylated liposomal doxorubicin compared to carboplatin-paclitaxel combination: analysis from the GCG CALYPSO relapsing ovarian cancer trial. *Gynecol Oncol*. 2011;122(2):226-232. doi:[10.1016/j.ygyno.2011.04.019](https://doi.org/10.1016/j.ygyno.2011.04.019)
13. Makrilia N, Syrigou E, Kaklamanos I, Manolopoulos L, Saif MW. Hypersensitivity reactions associated with platinum antineoplastic agents: a systematic review. *Metal-Based Drugs*. 2010;2010:1-11. doi:[10.1155/2010/207084](https://doi.org/10.1155/2010/207084)
14. Navo M, Kunthur A, Badell ML, et al. Evaluation of the incidence of carboplatin hypersensitivity reactions in cancer patients. *Gynecol Oncol*. 2006;103(2):608-613. doi:[10.1016/j.ygyno.2006.04.002](https://doi.org/10.1016/j.ygyno.2006.04.002)
15. Markman M, Zanotti K, Peterson G, Kulp B, Webster K, Belinson J. Expanded experience with an intradermal skin test to predict for the presence or absence of carboplatin hypersensitivity. *J Clin Oncol*. 2003;21(24):4611-4614. doi:[10.1200/JCO.2003.05.539](https://doi.org/10.1200/JCO.2003.05.539)
16. Altwerger G, Gressel GM, English DP, et al. Platinum desensitization in patients with carboplatin hypersensitivity: a single-institution retrospective study. *Gynecol Oncol*. 2017;144(1):77-82. doi:[10.1016/j.ygyno.2016.09.027](https://doi.org/10.1016/j.ygyno.2016.09.027)
17. Rose PG, Fusco N, Smrekar M, Mossbruger K, Rodriguez M. Successful administration of carboplatin in patients with clinically documented carboplatin hypersensitivity. *Gynecol Oncol*. 2003;89(3):429-433. doi:[10.1016/S0090-8258\(03\)00178-1](https://doi.org/10.1016/S0090-8258(03)00178-1)
18. Takase N, Matsumoto K, Onoe T, et al. 4-step 4-h carboplatin desensitization protocol for patients with gynecological malignancies showing platinum hypersensitivity: a retrospective study. *Int J Clin Oncol*. 2015;20(3):566-573. doi:[10.1007/s10147-014-0731-1](https://doi.org/10.1007/s10147-014-0731-1)
19. Lee CW, Matulonis UA, Castells MC. Rapid inpatient/outpatient desensitization for chemotherapy hypersensitivity: standard protocol effective in 57 patients for 255 courses. *Gynecol Oncol*. 2005;99(2):393-399. doi:[10.1016/j.ygyno.2005.06.028](https://doi.org/10.1016/j.ygyno.2005.06.028)
20. Castells MC, Tennant NM, Sloane DE, et al. Hypersensitivity reactions to chemotherapy: outcomes and safety of rapid desensitization in 413 cases. *J Allergy Clin Immunol*. 2008;122(3):574-580. doi:[10.1016/j.jaci.2008.02.044](https://doi.org/10.1016/j.jaci.2008.02.044)
21. Vetter MH, Khan A, Backes FJ, et al. Outpatient desensitization of patients with moderate (high-risk) to severe platinum hypersensitivity reactions. *Gynecol Oncol*. 2019;152(2):316-321. doi:[10.1016/j.ygyno.2018.10.037](https://doi.org/10.1016/j.ygyno.2018.10.037)
22. Confino-Cohen R, Fishman A, Altaras M, Goldberg A. Successful carboplatin desensitization in patients with proven carboplatin allergy. *Cancer*. 2005;104(3):640-643. doi:[10.1002/cncr.21168](https://doi.org/10.1002/cncr.21168)
23. Nishimura M, Sakai H, Onoe T, et al. 4-step, 2-h carboplatin desensitization in Japanese patients with ovarian cancer: a prospective study. *Int J Clin Oncol*. 2021;26(8):1553-1560. doi:[10.1007/s10147-021-01935-7](https://doi.org/10.1007/s10147-021-01935-7)
24. Cardona V, Ansotegui IJ, Ebisawa M, et al. World allergy organization anaphylaxis guidance 2020. *Arerugi*. 2020;13(10):100472. doi:[10.1016/j.waojou.2020.100472](https://doi.org/10.1016/j.waojou.2020.100472)
25. Yamamoto A, Kamoi S, Matsuda S, Kawase R, Nakanishi K, Suzuki S. Efficacy and adverse events of carboplatin desensitisation therapy for gynaecological cancer: a retrospective study. *Medicines (Basel)*. 2022;9(4):26. doi:[10.3390/medicines9040026](https://doi.org/10.3390/medicines9040026)
26. Gorgulu Akin B, Erkoc M, Korkmaz ET, et al. Rapid drug desensitization with platin-based chemotherapy: analysis of risk factors for breakthrough reactions. *World Allergy Organ J*. 2022;15(1):100619. doi:[10.1016/j.waojou.2021.100619](https://doi.org/10.1016/j.waojou.2021.100619)

How to cite this article: Komatsu H, Matsumoto K, Morita M, et al. A survey of carboplatin desensitization therapy in Japan: A multicenter retrospective study. *Cancer Med*. 2024;13:e6968. doi:[10.1002/cam4.6968](https://doi.org/10.1002/cam4.6968)