



# Scalp Hypothermia (Penguin Cold Caps) in Preventing Alopecia in Cancer Patients

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## SUMMARY

Cancer morbidity and mortality are severe public health problems that are increasing day by day. In addition to their benefits of some methods, such as chemotherapy and radiotherapy, which are applied for cancer treatment, there are some side effects and complications, such as skin reactions, hair loss, fatigue, vomiting and loss of appetite. In this article, one of these complications and affecting more than half of the patients who receive cancer treatment alopecia will be mentioned. Alopecia may be temporary or permanent, but it has been stated by health professionals that this problem is often ignored. Alopecia affects body image in individuals, increases the level of stress, causes anxiety and depression and even individuals are exposed to stigma. The emergence of these problems in the patient also affects the quality of life negatively. To prevent alopecia, which can be seen especially due to chemotherapy, the process of cooling the scalp has started to be applied about 50 years ago and the materials used thanks to the changing materials science have been developed. In this study, the efficacy of scalp hypothermia (Penguin Cold Caps) in the prevention of alopecia, which is frequently seen due to chemotherapy, has been evaluated and it is aimed to investigate the relevant studies.

**Keywords:** Alopecia; cancer; hypothermia; patient; scalp.

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## Introduction

Cancer, which arises from the deterioration of health that is defined as a complete physical, social and mental wellness, is a globally important public health problem with its high mortality and increasing prevalence.[1,2] The risk of cancer is increased by negative lifestyles, such as smoking, drinking, bad dietary habits, physical inactivity, obesity, unhealthy sexual life and reproductive changes (e.g., miscarriages, late first birth) and exposure to environmental carcinogenic substances. As fertility decreased especially in developed countries and death rates decreased based on advanced diagnosis and treatment opportunities, the increase in the elderly population that lives with various chronic diseases (e.g.,

stroke, heart disease, diabetes, cancer) also contributes to the increased prevalence of cancer in patients.[3-11]

Cancer is held responsible for the death of one in every four people in the United States of America (USA), and it is even projected to become more prevalent than heart disease in the future. The World Health Organization (WHO) also stated that cancer has a significant place worldwide, new cases will be added in the next 20 years with an increase of 70%, it is the second among the causes of death, and it was responsible for the death of 8.8 million people in the year 2015. [1,8,12] Each year in Europe, in parallel to the WHO and USA statistics, new cases of cancer increase (about 3.7 million), and cancer is found to lead to 20% of the deaths (1.9 million).[13]

Received: December 31, 2019

Accepted: January 13, 2020

Online: February 24, 2020

Accessible online at:

[www.onkder.org](http://www.onkder.org)

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As in the entire world, cancer-related morbidity and mortality rates are high also in Turkey.[14,15] According to the 2016 results of the Turkish Statistical Institute, 174,000 people were newly diagnosed with cancer every year, and 80,577 of these people died.[16,17]

Today, the treatment of cancer involves surgery, chemotherapy, radiotherapy, immunotherapy, hormone therapy, targeted therapies and gene therapy (biological therapies). In addition to the advantages of all treatment methods, temporary or permanent side effects, such as skin reactions, loss of hair, fatigue, vomiting and loss of appetite and complications, may occur based on the medicine that is used, as well as the characteristics of the patient.[18-21] This review article aimed to investigate whether or not using Scalp Hypothermia (Penguin Cold Caps), which is an alternative treatment for chemotherapy-related alopecia (loss of hair), especially in cancer patients, is effective in preventing hair loss and examined studies that have been carried out on this topic.

Chemotherapy regimens involve a complicated process that has a high incidence of morbidity and mortality. Several drugs show toxic effects even in therapeutic doses.[22] Chemotherapy causes several side effects that negatively affect the quality of life of individuals, such as immunosuppression, neutropenia, anemia, diarrhea, constipation, dyspnea, chest pain, pain, nausea, vomiting, fatigue, alopecia, myalgia, stomatitis, and hand, foot and mouth disease.[23-26]

### **Alopecia**

Although alopecia is rarely reported in clinical studies as significant toxicity, it affects a large proportion of individuals who receive cancer treatment as 65% and may be temporary or permanent. This problem, which affects the body image of individuals with cancer significantly, is usually neglected by healthcare professionals.[27,28] If alopecia is resolved in the next 3-6 months after chemotherapy ended, it is known as "temporary alopecia," while it is known as "permanent alopecia" if the hair is not replaced for a time longer than six months.[28]

The main cause of alopecia is the damage to healthy cells, including hair-producing cells created by chemotherapy, which is aimed to kill the cancer cells that become abnormal by modifications, grow and spread rapidly.[29] The hair loss table, which varies from hair thinning to baldness, occurs in different periods from on to four weeks after the start of chemotherapy, and the hair loss progresses. In this process, individuals frequently complain about that groups of hair fall while washing or combing, as well

as the feeling of sensitivity and itching.[29,30] Studies report hair loss only in the front part of the head in women and a loss in a broader area of the body in men.[31,32] Although there are advancements in treatment and care for side effects, such as emesis, pain, thrombosis, hematopoietic cytopenia, xerostomia and infection, improvements to the desired extent have not been achieved in the prevention and treatment of alopecia.[33] However, it is possible to reduce hair loss by adjusting the dose programs and combinations of cytotoxic agents, applying low doses through an extended time period and changing the ways of administering these agents.[33,34]

Considering the effects of hair on body image and women especially as a symbol of health, attractiveness and femininity, hair loss causes anxiety and stress in the individual, individuals are exposed to self-alienation in addition to stigma, and quality of life is affected negatively.[35-39] In 65-85% of the patients who experience chemotherapy-related alopecia, [40] it was reported that sexual lives are affected negatively in addition to low self-image and depression and deterioration in physical, cognitive, emotional and social functions.[40,41] Two different studies with similar results reported that more than half of patients considered alopecia to be the most traumatic aspect of the treatment process, [39,42] and some patients even thought about refusing treatment due to this side effect.[42] Patients who were informed about this issue beforehand made psychological preparations by shortening their hair before alopecia kicked in and stated that they were not satisfied new tissue and color of their hair, which grew after completing the treatment process.[36] Thus, it was understood that the negative perceptions that the individual is exposed to, unpreparedness and limited social support increased alopecia-related issues even further.[43]

In the literature, hair loss is discussed concerning death, old age, sexuality, attractiveness, loss of uniqueness and an appearance of disease.[44-46] In recent years, healthcare professionals have tried to reduce the negative effects of alopecia on the individual by taking mechanical, physical and biological precautions.

### **Scalp Hypothermia**

To prevent chemotherapy-related alopecia, the procedure of cooling the scalp by reducing the temperature of the skin has been used since the 1970s.[47] In that period, broken pieces of ice that were placed into plastic bags emerged as a promising method. With the development of the methodology of this technique since then, the main principle of hypothermia

treatment has stayed the same due to its successful outcomes.[32-48] With the effects of vasoconstriction, scalp hypothermia is based on the principle of slowing down the intrafollicular metabolism by reducing the perfusion of the scalp, thus hair follicles. [44,49-51] Advantages and disadvantages of cooling the scalp are shown in Table 1. Today, it was seen that cooling down the scalp is the most effective protective intervention during chemotherapy with positive outcome rates of 50% to 80%.[41]

If studies that investigated whether or not scalp hypothermia is effective are examined, van den Hurk et al. (2012), who discussed the positive outcomes of such implementations found that there was no need for wigs or head covers in 81% of 53 patients who received scalp hypothermia therapy during chemotherapy treatment. [52] Another similar study applied scalp hypothermia on 1411 patients in the last session of chemotherapy, and it was seen that there was no need for wigs of head covers in 50% of the patients.[53] In addition to these positive outcomes, undesired side effects, although at low rates, may be encountered in the form of headache, sense of coldness, nausea, needle phobia, claustrophobia and increased distress.[47,54-57] Moreover, this treatment may have contraindications for patients with the common cold, cold agglutinin disease, cryofibrinogenemia and post-traumatic cold dystrophia, and rarely those with metastasis in the scalp. As tumor cells that take root from the scalp will not be affected by chemotherapy sufficiently during hypothermia, there might be a chance of relapse of the tumor after the treatment. [58] For example, the study by Rugo et al. (2017) in the USA reported that they needed to stop the implementation in four patients (3.8%) due to headache and three patients (2.8%) due to common cold among their 106 patients in the scalp hypothermia group.[59]

A non-pharmacological method that is currently used in scalp hypothermia and found to be successful in preventing alopecia is the method of Penguin Cold Caps. The project of the Penguin Cold Cap Registry was started in 2010 by the University of California San Francisco (UCSF).[60] In the study by Rice et al. (2018), where the effectiveness and tolerability of scalp hypothermia were assessed using Penguin Cold Caps in breast cancer patients, hair loss was assessed by both the patients and implementers every 3-4 weeks during chemotherapy and at least one month after completing chemotherapy. The patients assessed their own hair loss (five-point Dean's scale), satisfaction levels (VAS; Visual Analog Scale, 0-100 points) and their tolerances for the severity of headache, scalp pains and other side effects using VAS-like scales.[60] In general, it was found that Penguin Cold Caps application successfully prevented chemotherapy-related alopecia in 61% of the patients, and this effect was specific to the treatment regimen that was applied (Docetaxel/carboplatin/trastuzumab 100%, Docetaxel/cyclophosphamide 84%, Docetaxel/cyclophosphamide 50%, Paclitaxel/Doxorubicin/cyclophosphamide 43%, Doxorubicin/cyclophosphamide/Paclitaxel 20%). The most frequently observed side effect of the application was headache by 78.5%. It was seen that the satisfaction levels of the patients who completed the scalp cooling treatment varied in the range of 74%-100%, scalp hypothermia by Penguin caps was effective in reducing alopecia, especially for non-anthracycline short regimens, it was tolerated well and assessed to be a positive practice by most patients.[60]

In another randomized controlled study where the effectiveness of the Penguin Cold Caps system and the views of female patients on it were investigated, gel

**Table 1** Advantages and disadvantages of the cooling the scalp. [47,53,54,57,57,64,65]

| <b>Scalp cooling</b>   |   |
|--|---|
| <b>Advantages</b>  | <b>Disadvantages</b>  |
| Enables to protect your hair more.   | Extends your hospitalization period.  |
| Reduces the need for wig or headscarf.   | Does not guarantee the protection of hair; outcomes are uncertain.  |
| Even if you have hair loss during the treatment, scalp cooling enables a faster regrowth.    | Hair quality may reduce.  |
| Provides some opportunities for doing something against the boldness.                        | The cooling applied may cause headaches or dizziness, especially for the first 15 minutes.  |
| Scalp cooling can increase satisfaction in the individuals concerning its positive outcomes. | If the scalp cooling fails, it may cause extra disappointment.  |
|  | Unintended side effects can be faced, such as the sense of coldness, common cold, nausea, trypanophobia, claustrophobia and increased distress. |

head covers were changed three times in a total of two hours to keep the temperature of the scalp below  $-18^{\circ}\text{C}$  in the treatment group, and the patients were assessed by surveys and photographs through their chemotherapy cycles (5 Fluorouracil  $600\text{ mg/m}^2$ , Epirubicin  $50\text{ mg/m}^2$ , Cyclophosphamide  $600\text{ mg/m}^2$ ). While there was no significant hair loss in 30% of the 10 patients in the treatment group, there was mild hair loss in 40% and severe hair loss in 20%. While all the control group patients (5 patients) needed wigs, there was no need for it in 70% of the treatment group patients.[54]

In the study by Katsimbri et al. (2000), 30 minutes before starting the chemotherapy treatment (at least one of taxanes, anthracyclines or etoposide drugs), Crylon Gel caps made out of polyurethane material were used on patients to keep the temperature of the scalp at  $-15^{\circ}\text{C}$ , the caps were changed at every 35 minutes during two hours of chemotherapy, and cap treatment continued for two hours after the chemotherapy treatment ended. Hair loss was assessed on five levels; not needing wigs was considered to be a success in patients who were divided into four groups based on their drug combinations, and a success rate of 81% was achieved in general.[61]

A similar study was carried out by Kargar et al. (2011), and the results of 31 patients who accepted using Penguin Cold Caps and 32 patients who refused it were compared. In their study, the entire process lasted 120 minutes from 15 minutes before starting chemotherapy in a way to keep the scalp temperature under  $-20^{\circ}\text{C}$  and keep each cap in contact for 45 minutes. There were significant differences in the 2<sup>nd</sup>-6<sup>th</sup> cycles between the two groups of patients who were assessed based on the Alopecia Guidelines by WHO. There was no significant hair loss or mild hair loss in 77.4% of the patients in the hypothermia group. Severe or complete alopecia was observed in 22.6% of the experiment group and 61.3% of the control group. Accordingly, it was concluded that the Penguin Cold Caps method was an effective method in preventing chemotherapy-related alopecia.[62]

Cigler et al. (2015) applied scalp hypothermia down to  $-32^{\circ}\text{C}$  by Penguin Cold Caps (polyurethane filled with cryogenic insulation material) on women with early-stage breast cancer who received adjuvant chemotherapy treatment with docetaxel and cyclophosphamide. The process of cooling the scalp was started 50 minutes before the chemotherapy, and the caps were changed every 30 minutes during chemotherapy infusion and for four hours after completion. The women were asked to avoid hair products that contain alcohol or peroxide, wash their hair at most two times every week with shampoo and lukewarm

water using gentle motions, avoid hair dyes and not use hairdryers, hair straighteners or curling irons from two weeks before chemotherapy and up to four months after the completion of the treatment. Alopecia was assessed by Dean's Scale before each chemotherapy session and after chemotherapy in varying intervals between three weeks and three months. It was reported that no patients quit the treatment due to reasons like side effects, they tolerated the scalp cooling process well, and successful results (65% excellent, 25% good, 10% medium/bad hair loss) were obtained.[63] The results of the studies related to scalp cooling according to the type of chemotherapy and their results are summarized in Table 2.

## Conclusion

Consequently, it is highly important for healthcare professionals to show a proactive and supportive attitude towards prevention, treatment and care for chemotherapy-related alopecia and develop the coping strategies of the patients. Non-pharmacologic methods that develop through time and alternative medical practices are a significant part of nursing care, and these will provide important contributions in the improvement of the outcomes of treatment and care. It is believed that, for preventing alopecia, studies with large samples and well-organized methodologies should be conducted. We are of the opinion that the evidentiality of this practice may be increased by conducting future studies on scalp cooling practices, such as those that involve Penguin Cold Caps with different types of cancer and new drug combinations, with caps containing different materials and considering different time intervals/temperatures.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

**Financial Support:** No financial support or assistance from any person or organization was received for this study.

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**Table 2** Studies and results of the scalp cooling according to chemotherapy type. [52-54,60-63,65-68]

| Writer/s                | Study type/<br>number of cases                          | Cancer type  | Chemotherapy<br>type   | Scalp cooling<br>system duration  | Results<br>obtained   |
|-------------------------|---|--|--|---|---|
| Katsimbri et al. (2000) | Clinical study-<br>57 patients                          | Lung cancer,<br>unknown primary<br>cancer and<br>breast cancer | At least one of among<br>taxanes, anthracyclines<br>or etoposide medicines   | -It was started to apply<br>Crylon Gel 30 minutes<br>before starting<br>chemotherapy.<br>-The caps changed in<br>every 35 minutes during<br>the two-hour-long<br>chemotherapy.<br>-It was continued to the<br>cap application until two<br>hours after the end of<br>the treatment. | It was gained 81% success<br>in general from this<br>application in which the<br>efficiency of the method<br>is different from the<br>medicine combinations.  |
| Peck et al. (2000)      | Randomized<br>controlled trial<br>(RCT)<br>-10 patients | Breast cancer  | 5 Fluorouracil 600 mg/m <sup>2</sup> ,<br>Epirubicin 50 mg/m <sup>2</sup> ,<br>Cyclophosphamide<br>600 mg/m <sup>2</sup>       | To the intervention group,<br>-It was applied gel cap<br>for two hours and<br>10 minutes in total during<br>the chemotherapy.<br>It was changed three<br>times periodically.<br>-The patients were<br>evaluated during the<br>chemotherapy cycles.                                  | From 10 patients in the<br>intervention group, it was<br>observed that<br>-30% had no significant<br>hair loss,<br>-40% had slight hair loss,<br>-20% had severe hair loss.<br>-All of the control group<br>(five patients) were<br>in need of a wig,<br>-70% of the intervention<br>group was not in need of<br>a wig. |
| Kargar et al. (2011)    | Semi-experimental<br>study<br>-63 patients              | -  | The patients had been<br>using Taxol, ABVD and BEP;<br>Cyclophosphamide,<br>Adriamycin and Vincristine,<br>plus, Prednisolone. | 15 minutes before<br>starting chemotherapy,<br>each cap was<br>applied in a way to keep<br>the scalp under -20 OC and<br>to be in contact with the scalp<br>for 45 minutes. The total<br>transaction was applied for<br>120 minutes.  | -In 77.4% of the group<br>(experimental) to whom it<br>was applied hypothermia,<br>it was seen no hair loss or<br>a slight hair loss.<br>-Severe or complete<br>alopecia; it was seen in<br>22.6% of the experimental<br>group and 61.3% of the<br>control group.   |

Table 2 Cont.

| Writer/s                   | Study type/<br>number of cases                     | Cancer type  | Chemotherapy<br>type  | Scalp cooling<br>system duration  | Results<br>obtained   |
|----------------------------|--|--|---|---|---|
| van den Hurk et al. (2012) | Observational and randomized study<br>-53 patients | Breast, prostate, lung, ovary and gastrointestinal one collateral cancer           | Combined with docetaxel or other cytotoxics as the 3-week only agent to which it was applied intravenously. | The method was started 30 minutes before the chemotherapy infusion and applied until 45 or 90 minutes after the end of the infusion.  | It was identified in 81% of 53 patients to whom it was applied scalp hypothermia during chemotherapy that it is not needed any wig or headscarf after the treatment.<br>-It was seen that the need for wig or headscarf went away in 50% of those who had undergone scalp hypothermia.<br>-It was identified that the headscarf usage rate was significantly increased because of higher dose and shorter infusion duration, advanced age, woman gender and the hairs, which are not Western-European type, as well as the chemotherapy type. |
| van den Hurk et al. (2012) | Clinical study<br>-1411 patients                   | Breast, woman genital cancer, gastrointestinal/ collateral, lung, prostate, other. | (FEC, AC, AC/D, AC/T, TAC, Db, FAC, FEC/D, TCarbo, T, Irino and other)*                                     | While the cooling duration before the average infusion was 38 minutes, the cooling duration after the average infusion was 90 minutes. The average number of cooling sessions was four. | -No patients had left the application because of reasons, such as side effects, and they tolerated the scalp cooling practice well.<br>-It was obtained successful results (65% excellent, 25% good, 10% medium/ severe level hair loss)<br>-It was seen 50% or lower hair loss in 67 out of 101  |
| Gigler et al. (2015)       | Clinical study<br>-20 patients                     | Early period breast cancer   | Adjuvant chemotherapy with docetaxel and cyclophosphamide   | The scalp cooling practice was started 50 minutes before the chemotherapy; the caps were changed every 30 minutes until four hours during and after the chemotherapy infusion.          |   |
| Rugo et al. (2017)         | Prospective cohort study                           | Phase I or II breast cancer  | Adjuvant or neoadjuvant chemotherapy regimens   | It was started 30 minutes before every chemotherapy   |   |



**Table 2** Cont.

| Writer/s           | Study type/<br>number of cases | Cancer type   | Chemotherapy<br>type  | Scalp cooling<br>system duration                                       | Results<br>obtained   |
|--------------------|--------------------------------|---------------|---|--|---|
| Rice et al. (2018) | Record study<br>-103 patients  | Breast cancer | and chemotherapy regime<br>which was planned to<br>complete within six months<br>without successive or<br>combined anthracycline<br>and a taxane. | cycle, and it was held 90<br>to 120 minutes after the<br>chemotherapy. | <p>patients in the cooling group.</p> <p>-It was seen more hair loss in all the patients in the control group.</p> <p>-The rate of the patients who say that they consider themselves less attractive is more in the control group (56.3%) than in the group who have undergone scalp cooling (27.3%).</p> <p>-It was needed to stop the application because of that it was seen headache in four out of 106 patients (3.8%) and it was seen common cold in three out of 106 patients (2.8%).</p> <p>Generally, it was avoided successfully from alopecia due to chemotherapy in 61% of the patients.</p> <p>-Effect is peculiar to the regime: TCH 100%, TCx4 84%, TCx5-6 50%, P/AC 43%, AC/P 20%.</p> <p>-The most frequently seen toxicity is a headache (78.5%).</p> <p>-The satisfaction rate of those who completed scalp cooling was varied between 74%-100%.</p> <p>-Especially for the short</p> |

Table 2 Cont.

| Writer/s                | Study type/<br>number of cases  | Cancer type  | Chemotherapy<br>type  | Scalp cooling<br>system duration   | Results<br>obtained   |
|-------------------------|---|--|---|--|---|
| Kinoshita et al. (2019) | Multi-centered<br>controlled study<br>-48 patients  | Phase I/II primary<br>breast cancer<br>(more than half of<br>the patients in all<br>groups are Phase II. | The target regimens<br>which was planned to<br>receive four cures of<br>adjuvant/neoadjuvant<br>chemotherapy;<br>AC (doxorubicin 60<br>mg/m <sup>2</sup> +cyclophosphamide<br>600mg/m <sup>2</sup> ),<br>EC (epirubicin 100 mg/m <sup>2</sup> +<br>cyclophosphamide<br>600 mg/m <sup>2</sup> ),<br>TC (docetaxel 75 mg/m <sup>2</sup> +<br>cyclophosphamide<br>600 mg/m <sup>2</sup> ) ya da FEC<br>(fluorouracil 500 mg/m <sup>2</sup><br>+epirubicin 100 mg/m <sup>2</sup> +<br>cyclophosphamide<br>500 mg/m <sup>2</sup> ) | Scalp hypothermia was<br>started 30 minutes before<br>the chemotherapy infusion,<br>and it was continued<br>until for at least 90 minutes<br>after the end of the<br>chemotherapy. | regimes without<br>anthracycline, it was<br>identified that penguin<br>and scalp hypothermia are<br>efficient in reducing<br>alopecia and was<br>well-tolerated.<br>-All patients who<br>completed this application<br>recommended the<br>Penguin.<br>-The number of patients<br>who did not develop<br>alopecia is more in the<br>scalp cooling group<br>(experimental) than in the<br>control group.<br>-The state of $\geq 50$<br>increase in hair volume in<br>12 weeks after the<br>chemotherapy. It was<br>identified as follows:<br>-85.7% in the<br>experimental group,<br>-50.0% in the control<br>group.<br>-It did not develop any<br>severe side effects on<br>scalp hypothermia in any<br>patient.<br>Of the 13 studies,<br>-It was identified that four<br>studies (31%) indicated<br>that the scalp cooling is<br>related to significant<br>healings in life quality |
| Marks et al. (2019)     | Systematic<br>review<br>-Four randomized<br>controlled study<br>-Eight cohort study<br>-One sectional study | -  | -   | -  |   |



**Table 2** Cont.

| Writer/s             | Study type/<br>number of cases | Cancer type                     | Chemotherapy<br>type        | Scalp cooling<br>system duration  | Results<br>obtained  |
|----------------------|--------------------------------|---------------------------------|-----------------------------|---|--|
| Bajpai et al. (2020) | RCT<br>-51 patients            | Non-metastatic<br>breast cancer | Anthracycline<br>and taxane | This method was started<br>30 minutes before every<br>chemotherapy cycle, and<br>the scalp heat was protected<br>during the chemotherapy<br>application. It was started the<br>cooling practice 90 minutes<br>after the completion of<br>scalp cooling. | measurements,<br>-It was identified that<br>eight studies (62%)<br>indicated that it is not<br>significant or there is no<br>healing, and<br>-One study (7.7%) reached<br>a mixed conclusion.<br>-It was seen that more hair<br>was protected at a<br>significantly high rate in<br>the experimental group<br>who had undergone scalp.<br>Hypothermia than in the<br>control group.<br>-It was identified that hair<br>loss was significantly<br>lower in the experimental<br>group. |

\*ABVD: Adoxorubicin, bleomycin, vinblastine, dacarbazine; BEP: Bleomycin, etoposide, platinum; FEC: 5 Fluorouracil, epirubicin, cyclophosphamide; AC/D: Adriamycin, cyclophosphamide /docetaxel; AC/T: Adriamycin, cyclophosphamide/paclitaxel; TAC: Docetaxel, doxorubicin, cyclophosphamide; Db: Mono and combination chemotherapy; FAC: Fluorouracil, Adriamycin and Cytosar; FEC/D: 5 fluorouracil, epirubicin, cyclophosphamide/docetaxel; TCarbo: Paclitaxel and carboplatin; I: Irinotecan; T: Paclitaxel

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