A multicentre study to determine the efficacy and patient acceptability of the Paxman Scalp Cooler to prevent hair loss in patients receiving chemotherapy

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Summary Alopecia is a distressing and common side-effect of chemotherapy, especially anthracycline- and taxane-containing regimen. A series of studies and reviews have considered scalp cooling as a means of reducing this side-effect without a definitive result. The aim of the study was to determine the efficacy and patient acceptability of scalp cooling using the Paxman Scalp Cooler. This was an open, non-randomised, observational study conducted at eight sites involving 94 patients. Alopecia was assessed using the World Health Organisation (WHO) grading system. Patient acceptability was assessed by questionnaire. Results were compiled by Scalp Cooling Assessment Groups using data from eight centres in the UK collected between 1997 and 2000. Use of the Paxman Scalp Cooler was adjudged a success for 89% of all patients using the WHO grading system for alopecia and for 87% of patients being specifically administered the commonly used 5-fluorouracil, epirubicin and cyclophosphamide (FEC) regimen. When asked about degrees of comfort during the scalp-cooling process, 85% of patients described it as very comfortable, reasonably comfortable or comfortable, with only 15% of patients reporting a description of uncomfortable or very uncomfortable. Scalp cooling using the Paxman Scalp Cooler was found to be an effective technique with minimal side-effects for patients treated with commonly prescribed alopecia-inducing chemotherapy drugs.

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Keywords Scalp cooling; Alopecia-inducing chemotherapy; Efficacy; Patient acceptability; Multicentre evaluation


Das Ziel der vorliegenden Studie war es, den Einsatz speziell des Paxman Kopfhautkühlgeräts auf seine Wirksamkeit und Akzeptanz durch die Patienten zu untersuchen. Es handelte sich um eine offene, nicht randomisierte Beobachtung von 94 Patienten aus acht verschiedenen Gesundheitsinstitutionen. Haarausfall wurde dabei nach den Kriterien der Weltgesundheitsorganisation (WHO) definiert und bewertet, während der Grad der Akzeptanz des Gerätes durch die Patienten mit einem Fragebogen erfasst wurde. Die Daten von acht Gesundheitszentren im
Introduction

The trauma of hair loss

Alopecia (hair loss) is a common side-effect of chemotherapy treatment. Throughout history, luxuriant hair has been symbolic of good health, strength and sexual attractiveness. Conversely, loss of hair gives rise to perceptions of ageing, illness and loss of attractiveness. Batchelor (2001), in one of the most recent and comprehensive surveys of the literature on hair loss during cancer chemotherapy, notes that historically, shaving of the head has often been associated with mourning or entering a religious order. Enforced cutting or shaving of the head even in modern times is employed as a sign of contempt and degradation.

Ever since the increased use of drugs in the treatment of cancer in the 1970s, the distressing side-effects of alopecia have been recognised. Those reporting one of the earliest studies on the subject went so far as to say 'it may be one of the most traumatic psychological side-effects that cancer patients will experience' (Baxley et al., 1984, p. 501), a suggestion seemingly borne out in a recent study by Münstedt et al. (1997) when 47% of the patients surveyed stated that alopecia was the most traumatic side-effect of chemotherapy. Indeed, occasionally alopecia can even generate sufficient anxiety for some patients to consider rejection of potentially curative treatment (Tierney and Taylor, 1991). Psychological distress is generally considered to be worse for females rather than males: adult males seem to cope more easily—no doubt because male baldness, even in young males, is more socially acceptable (Batchelor 2001). However, this easy assumption may be questionable (Baxley et al., 1984). Children are particularly vulnerable to the stigma of sudden hair loss (Reid, 1997).

Alopecia is usually reversible, and wigs are made routinely available to patients receiving National Health Service in patient treatment. Doctors and nurses may become inured to the sight of many bald patients and consider alopecia as a price well worth paying for treatment of a life-threatening disease. There is evidence that some patients share this view. One of the first studies into 'body image' of patients concluded that although subjects with alopecia decreased their social activities compared with those not experiencing alopecia, hair loss 'had an unexpectedly small effect' on body image, possibly due to the patients' ability to adapt to the change (Wagner and Bye, 1979). Nevertheless, there is sufficient first-hand testimony, to the initial trauma at least, of sudden and dramatic hair loss (Clement Jones, 1985, cited in Williams et al., 1999) for the probability to feature in any psychosocial assessment of a cancer patient (Ehmann et al., 1991; Nicholas and Veach, 2000). However, even those actively prepared for hair loss can be left feeling unprepared:

All of a sudden, it is one day.
You go into that shower, And you start to wash your hair,
And then you come out and you have no hair,
And the hair is all over the shower, the tub, the walls,
The hands, your body, I mean, you just can’t.
That was the most traumatic thing in the world. (Williams et al., 1999, p. 1465)

The causes of alopecia during chemotherapy

Chemotherapy in the treatment of cancer relies for its effectiveness on the ability of the drugs to attack rapidly dividing cells which may be
both malignant and, unfortunately, normal. At any one time, around 85–90% of human hair follicles are in a state of rapid growth. Certain drugs, or generally high-dose chemotherapy, lead to partial or total atrophy of the hair root bulb, causing the hair shaft to break off spontaneously, or when it is washed or combed (Cline, 1984). The hair may also be weakened, by a narrowing of the hair shaft adjacent to the scalp—this has been suggested as associated most frequently with standard dose chemotherapy (Pickard-Holley, 1995).

It is apparent that alopecia, though a frequent side-effect of chemotherapy, varies in incidence and degree with the drug or combination of drugs administered. Batchelor (2001, p. 150) states that ‘the literature varies greatly in the categorisation of which agents cause severe, moderate or mild alopecia’. Degree of hair loss is also route, dose and schedule dependent. Some agents do not cause alopecia at all, whilst for example, 100% alopecia has been reported for a control group treated with doxorubicin (Giaccone et al., 1988).

Reduction of alopecia during chemotherapy—scalp cooling

Measures to reduce or eliminate alopecia during chemotherapy have been investigated since the 1960s with varying degrees of success. They have included mechanical methods such as tourniquets, and physical methods such as scalp cooling and use of biological agents. In recent times, scalp cooling and physical methods such as tourniquets, have largely been superseded by specially designed cryogel caps. In general, these are simpler to prepare, more comfortable and do not melt. More recent commercially available systems use cooled air blown over the scalp, or as in the Paxman Scalp Cooler, liquid coolant circulated through a refrigeration unit attached to a special cap. Most studies show some success in hair preservation, but the different techniques used, and the variety of chemotherapy regimens adopted, makes comparisons and firm conclusions difficult. Some studies have reported considerable success (e.g. Anderson et al., 1981; Lemenager et al., 1997), whereas other workers have asserted that the evidence is so inconclusive as to question whether scalp cooling is worthwhile, or of only limited use (Tierney, 1987; Tollenaar et al., 1994).

There are few studies comparing different methods of scalp cooling, but one study has suggested that cold air circulation is more effective than cryogel packs, as a lower temperature can be maintained for a longer period (Hillen et al., 1990). Dougherty (1996) reported a study in which gel packs and a thermocirculator machine were employed; there seemed to be little difference in effectiveness or patient acceptability, but samples were small.

It does seem clear from reported results that scalp cooling is particularly effective when a patient is treated with anthracyclines (such as doxorubicin or epirubicin), which are normally particularly aggressive depilators. This was also the conclusion of Noble-Adams (1998) who noted lower success rates when using cyclophosphamide, either used alone or in combination, possibly due to its relatively long half-life. For example, David and Speechley (1987) reported that 70% of a group of 54 patients had no hair loss following treatment with doxorubicin in conjunction with scalp cooling using gel packs, but only 23% of 31 patients treated with doxorubicin and cyclophosphamide in combination were similarly fortunate. An interaction between the two drugs may lead to a decrease in the rate of metabolism and excretion of doxorubicin (Middleton et al., 1985).

David and Speechley also showed a clear diminution in effectiveness of scalp cooling when patients
were suffering from a malfunctioning liver, and this is reported elsewhere in the literature (Anderson et al., 1981; Robinson et al., 1987). Again slowing metabolism and excretion of the drug seems the likely cause. However, other studies have obtained very good hair preservation despite a high incidence of liver metastases (Lemenager et al., 1997; Katsimbri et al., 2000).

Possible concerns related to scalp cooling

Theoretically, tumour cells, which have seeded in the scalp, might not receive adequate treatment during scalp cooling, allowing them to grow later. Cases of scalp metastases have been reported (Middleton et al., 1985) in a few patients who received scalp cooling and were being treated for metastatic breast cancer. However, there are no reported incidences of scalp metastases in the literature after scalp cooling in patients receiving adjuvant breast cancer chemotherapy (Lemenager et al., 1997; Tollenaar et al., 1994).

Some side-effects have been reported in studies, including headaches, dizziness and nausea. Tierney (1987) reports some extreme reactions of patients (‘worse than the treatment itself’). Some methods of scalp-cooling require close supervision, and Tierney is further concerned by the additional workload for nurses and time for treatment.

A potential disadvantage of scalp cooling is the length of time required for patients to remain in the oncology clinic, in addition to the duration of the chemotherapy regimen, which cannot be avoided. For the patients themselves, this may be an acceptable inconvenience in order to prevent hair loss. The nursing staff may need to re-arrange clinic times in busier units due to a limited number of patient beds being available. It may be necessary to set up a protocol in clinics where scalp-cooling facilities are insufficient for all eligible patients, in order that as many as possible may be offered the choice of preventing or reducing hair loss. Several minutes may be taken to switch on the equipment, check that temperatures are within the required parameters and fit the cap. This particular method of scalp cooling has a minimal effect on nursing time because the same cap remains on the patient’s head throughout the procedure, unlike the commonly used gel cap method, where several caps have to be changed at regular intervals. Once in place, the cost of operating the system would equate to that of a domestic refrigerator, and is therefore, relatively inexpensive.

Study design

Aim of the study

- To assess the efficacy of scalp cooling to reduce alopecia for women undergoing treatment for breast cancer using the Paxman Scalp Cooler.
- To assess patient views on the comfort and acceptability of scalp cooling using the Paxman Scalp Cooler.

Intervention: The Paxman Scalp Cooler

The Paxman Scalp Cooler (Fig. 1) employs a powerful refrigerated cooling system, which rapidly reduces the temperature of a liquid coolant to a pre-set temperature reading −5°C. When this has been reached, electronic sensors monitor and control the coolant to read between −4°C and −5°C. The coolant is pumped at low pressure through a scalp-cooling cap which is colour coded for size and consists of a triple layered, spiral wound tube shaped to the contours of the patient’s head. Coolant passes through the chambers extracting heat from the patient’s scalp. Inlets and outlets were positioned at the crown of the cap and have simple push-in connectors to connect the cap to the coolant lines.

![Figure 1](image_url) Patient who used the system successfully. The photograph was taken following chemotherapy treatment.
Patient characteristics and recruitment

Results were compiled by the Scalp Cooling Assessment Groups from eight centres in the UK from which data were collected between 1997 and 2000. All patients were female and being treated for breast cancer in the adjuvant or palliative setting, as outpatients. They were selected for possible recruitment to the trial according to disease type and Consultant approval. Suitable patients were then given the option to receive scalp-cooling with their chemotherapy treatment as part of a trial. In each hospital that submitted information, staff and those patients who received scalp cooling, were asked to complete questionnaires for a period of time during which the scalp-cooling system was being assessed prior to its general introduction. Each centre returned questionnaires for all patients who received scalp cooling during the evaluation period of the system and recruitment varied across the eight sites. Data were collected using standard forms, which were compiled onto a database for review. The study was intended to be observational, and therefore, only descriptive statistics have been employed.

Cookridge Hospital submitted results from 31 patients, the Berkshire Cancer Centre submitted results from 20 patients, Derriford Hospital submitted results from 13 patients, Newham Hospital submitted results from eight patients, Peterborough submitted results from six patients, Ross Hall Hospital submitted results from one patient, Halifax General Hospital submitted results from 13 patients and the Royal Hospital Haslar submitted results from two patients.

Various drug regimens were given by each hospital according to the policy for treatment of breast cancer with chemotherapy. Epirubicin regimens as single agent or in combination, were administered to 72 patients (77%), with 62 patients from this group (66% of the total) receiving the commonly used 5-fluorouracil, epirubicin and cyclophosphamide (FEC) regimen at doses of epirubicin ranging from 60 to 75 mg/m². Doxorubicin regimens as single agent or in combination, were administered to 11 patients (12%) at doses ranging from 30 to 60 mg/m². Five patients (5%) were administered docetaxel single agent at doses from 75 to 100 mg/m², five patients (5%) were administered the cyclophosphamide, methotrexate and 5-fluorouracil (CMF) regimen, and one patient (1%) was administered the mitozantrone, mitomycin C and methotrexate (MMM) regimen.

Those patients accepting scalp cooling were invited to comment on their experience with the cooler. Degree of alopecia was routinely assessed as part of standard clinical practice at the hospitals involved. All patients whose data are included in this report gave verbal consent.

Each patient who received scalp cooling was assessed at the end of the chemotherapy treatment and all results submitted during this period were included in the study and compiled in a database for ease of analysis. It was felt that all suitable patients should be offered scalp cooling. Patients declining scalp cooling from the outset, did so from their own choice and the incidence of alopecia in this group, was not documented.

Scalp temperature testing and evaluation

There are some suggestions in the literature that a scalp temperature below 22°C is required for hair preservation (Gregory et al., 1982; Bülow et al., 1985) and Bülow et al. demonstrated that a subcutaneous temperature below 22°C corresponds to an epidermal temperature of 19°C. Hillen et al. (1990) attributed the success of their air-cooling method in part to achieving epidermal temperatures below 15°C.

In order to verify the temperatures attained with the system, scalp surface temperature tests were undertaken in room temperatures of 23–25.4°C on three volunteers not included in the study. A Grant 12000 Series Squirrel-Metre Logger Instrument specially developed for monitoring body surface temperatures was used. The average scalp temperature of the three volunteers recorded, was 15.5°C but variations from 11.3°C to 18.9°C were observed from probes positioned in four areas of the scalp, one on the crown, one on either side of the head and one at the back of the head, demonstrating that it was not possible to achieve an even temperature reduction. Temperatures recorded on the crown tended to be higher, reading an average of 16.5°C, which is a degree higher than those recorded at other sites. One of the volunteers was bald and the test results clearly indicated slightly lower temperatures overall when no hair is present, reading an average scalp temperature of 15.2°C, probably due to the direct contact of the cap on the skin and no insulating effect from the hair.

These results indicate that the equipment used in the study reduced scalp temperatures within an acceptable range, to an optimum level for alopecia prevention and tolerable levels of coldness for the patient, where no area of the scalp tested had a temperature above 19°C.

Study procedure

A cooling cap of the correct size was selected to ensure good contact with the scalp for the most
effective cooling. It is important to achieve a snug fit in order to avoid patchy alopecia associated with loosely fitted caps. The scalp cooler was switched on 1 h before use and allowed to reach its operating temperature. The patient’s hair was dampened, and a small amount of conditioner was applied before fitting the cap, in order to achieve a closer contact with the scalp. A pre-cooling time of 15–20 minutes was recommended to allow time for an adequate reduction in scalp temperature. The cap remained on the scalp during the infusion period, which varied according to regimen, and then for the recommended time after infusion of the agent causing the alopecia. The same cooling cap was worn throughout the whole period of pre-cooling, infusion and post-infusion cooling.

The participating hospitals were asked to complete report forms detailing the drug regimen and exact cooling time for each patient. Recommendations for post-infusion cooling times were based on peak plasma concentrations, drug half-life, potential interactions and the experience of users of the Paxman Scalp Cooler. A post-infusion cooling time of 2 hours was recommended for the majority of patients in this study. However, low-dose, single-agent doxorubicin given at 40 mg/m² and below, had a recommended post-infusion cooling time of 1 ½ hours, as did single-agent epirubicin at doses of 50 mg/m² and below. Regimes containing doxorubicin in combination with cyclophosphamide were recommended a post-infusion cooling time of 3 hours. Thus, the time ranged from 1 ½ to 3 hours according to the regimen being used and the following considerations:

(i) The degree of protection against hair loss is inversely proportional to the dose of alopecia inducing drug being administered (Tollenaar et al., 1994); therefore high-dose single-agent or combination regimens would have a longer post-infusion cooling time than low-dose regimens.

(ii) As already noted, the pharmacokinetic profile of a particular drug may be altered by the addition of another agent in a combination regimen (Middleton et al., 1985). It follows that a drug combination, for example of doxorubicin and cyclophosphamide, would have a longer recommended post-infusion cooling time than the same dose of doxorubicin being administered as single-agent therapy.

Assessment of hair loss

Measurement of the degree of hair loss was determined in each centre on completion of treatment using the World Health Organisation (WHO) criteria for alopecia (World Health Organisation, 1979) (Table 1). Photographs were provided which best described the hair condition associated with each grade and showed the head and scalp area in a selection of patients who were not included in the study, both before and after treatment. They showed overall thinning of the hair rather than patchy hair loss. The photographs were used together with WHO grades for alopecia and the final grading assessment was made by nurses from the scalp-cooling study groups. Success was defined as the patient not requiring a wig (grades 0, 1 and 2).

Patients were asked to complete their own report forms in order to assess the general attitude to the scalp cooling process and the degree of acceptance and comfort levels. They were first asked to assess separately the comfort levels and acceptability of the cooling cap.

Also, patients were asked about their attitude to scalp cooling as a whole; as regards comfort, whether they felt cold, and whether they experienced any headaches or other side-effects, or suffered boredom. Finally, patients were given an opportunity to record any relevant comments of their own.

Results

Efficacy

A total of 94 patients being treated for breast cancer were included in the study aged from 28 to 61 with a mean age of 44 years. Table 2 shows the assessment of hair loss by degree for all 94 patients in the study. Since 62 of the patients (66%) were being treated with the extensively used FEC regimen, the table shows the results for this group separately.

A total of 83 of all patients were assessed as having grade 0, 1 or 2 hair loss. This suggests a
success rate for the procedure of 89%. The figures for those being treated with the FEC regimen were 54% and 87%. Ten out of 11 patients treated with doxorubicin single agent or in combination achieved success, as did all five patients treated with docetaxel. Four out of five patients receiving CMF and the one patient receiving the MMM regimen were successful. Only five (5%) patients discontinued scalp cooling before the end of the treatment cycles in this study and all were recorded as treatment failures. Reasons given for discontinuation were that one patient had found the treatment uncomfortable, another three patients lost a considerable amount of hair after the first and second cycles and in one other patient the reason was not documented.

### Comfort and acceptability

Patients were asked to assess their levels of comfort and acceptability during the scalp-cooling period. Results are shown in Table 3. Out of the 94 patients, 80, or 85% of the total, said they were very comfortable, reasonably comfortable or comfortable. The same patients were asked if they found the procedure to be acceptable or unacceptable and 100% acceptability was reported.

### Side-effects

Patients were asked about side-effects during the scalp-cooling period including whether they felt cold or suffered from headaches or boredom. Ninety patients out of a total number of 94 patients responded with results as shown in Table 4. Four patients failed to complete this part of the questionnaire. The side-effects reported were found to be minor and reversible with coldness alleviated by a blanket and headaches usually treated with commonly prescribed painkillers.

### Discussion

#### Hair loss

Some results were particularly noteworthy. Two of the most commonly used drugs, doxorubicin and epirubicin, are from the anthracycline group of antibiotics. As noted earlier, anthracyclines are
normally particularly aggressive depilators. Doxorubicin, even in lower doses of 25–30 mg/m², is often not associated with severe hair loss, but Giaccone et al. (1988) reports that 100% of patients in a control group receiving doses ranging from 30–70 mg/m², developed alopecia. A more recent study by Ridderheim et al. (2003) evaluates patients receiving a regimen containing 25 mg/m² doxorubicin. There is no control group in this study, but one out of the eight patients who received scalp cooling developed alopecia after the second cycle of treatment. Without scalp cooling, doxorubicin treatment leads to severe and usually total alopecia (Benjamin, 1975). Reported levels of complete alopecia when using epirubicin range from 25% to 100% (Cerasasimo and Hong, 1986). All eight patients in the study treated with epirubicin, and seven out of eight treated with doxorubicin, were recorded as 'successes'. These results seemingly confirm conclusions from the literature that scalp cooling is particularly effective when used with this group of drugs. Although the combination of an anthracycline with cyclophosphamide did reduce success from these high levels, the 87% success rate with the FEC regimen patients using the cooler compares favourably, for example, with the results of studies by David and Speechley (1987) discussed earlier.

All five patients treated with the taxane-based regimen, docetaxel, were reported as successes. Docetaxel-induced alopecia is normally observed in 70–80% of patients at the doses used (Lemenager et al., 1997). There are only a limited number of studies for taxane-based chemotherapies, and post-infusion cooling times in these studies vary from 30 minutes to 2 hours (Katsimbri et al., 2000; Lemenager et al., 1997; Ridderheim et al., 2003). Since the infusion times of these therapies are much longer than those of the anthracyclines, it would be beneficial to determine an optimum post-infusion cooling time in order to reduce the total amount of time spent in the chemotherapy unit, especially as taxane use is increasing due to recent recommendations.

It is recognised that CMF and MMM regimens are associated with low rates of alopecia, but all results received were included in the study for completeness.

### Comfort, acceptability, and side-effects

Questionnaires were designed to enable the patients to describe their feelings towards scalp cooling as accurately as possible and to gauge a tolerance level which was acceptable in the context of scalp cooling. A cap could be described as uncomfortable, but the discomfort experienced may be acceptable to a patient who wishes to avoid the hair loss associated with chemotherapy treatment. If responses from patients had indicated poor comfort levels, this would, no doubt, have resulted in more patients withdrawing from the procedure. It is reasonable to deduce from the results that minor discomfort is outweighed by the potential benefits.

Results obtained from patients themselves appear to indicate high levels of comfort and acceptability with evidence of only minor and reversible side-effects. Indeed, 85% of patients reported an acceptable or higher degree of overall comfort throughout the cooling period. Headaches at some time during any of the treatment cycles, were reported by 29 patients (32%). It would appear from the few patients who discontinued treatment in this study, that effective protection against hair loss was an acceptable exchange for the prolongation of the treatment.

Liver function was not recorded for the patients in this particular study, but it would be a useful inclusion in further studies to indicate whether metabolism of particular drug regimens are more affected than others by the presence of liver metastases.

None of the patients developed scalp metastases during the study period, however, there are concerns regarding a potential risk in the adjuvant setting where treatment is given with curative

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<th>Yes</th>
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<td>Did you feel cold?</td>
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<td>58</td>
<td>38</td>
<td>42</td>
</tr>
<tr>
<td>Did you need a blanket to keep warm?</td>
<td>26</td>
<td>29</td>
<td>64</td>
<td>71</td>
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<td>Did you suffer from headache at any time during cooling?</td>
<td>29</td>
<td>32</td>
<td>61</td>
<td>68</td>
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<tr>
<td>Did you suffer from adverse feelings or other bad effects caused by cooling?</td>
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<td>10</td>
<td>81</td>
<td>90</td>
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<tr>
<td>Did you suffer from boredom during cooling?</td>
<td>29</td>
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intent. They will only be addressed by a clinical trial involving long-term follow-up with large patient numbers. In the metastatic setting, where treatment is generally given with palliative intent, hair loss is a constant reminder of disease and quality of life issues need to be addressed in this group.

Future work

- 'It is anticipated that further studies using the Paxman Scalp Cooler will involve a far higher proportion of the taxane based regimens'.
- Patients followed up to document incidence of scalp metastases.
- Liver function monitored and analysed.
- Trials to determine optimum scalp cooling times, which maintain efficacy whilst reducing the time spent by both staff and patients.

Conclusion

Based on literature standards for comparison, the results suggest that scalp cooling with the Paxman Scalp Cooler is an effective and seemingly well-tolerated technique for the prevention and reduction of alopecia. Its use should be seriously considered to improve the quality of life of all suitable cancer patients receiving chemotherapy.

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