

Comprehensive Online Management Based on Cloud Platform for Breast Cancer Patients Using Dual-Targeted Therapy with Macromolecular Monoclonal Antibodies

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Abstract

Objective: The purpose of the study was to explore the application effects of the cloud platform-based comprehensive online management for breast cancer patients using dual-targeted therapy with macromolecular monoclonal antibodies. **Methods:** 120 breast cancer patients treated by dual-targeted therapy with macromolecular monoclonal antibodies were managed by a cloud platform from March to November 2019. Comprehensive online management included consultation about drugs and side effects and frequently asked questions in the dual-targeted therapy with macromolecular monoclonal antibodies. **Results:** In the consultation about drugs and side effects, there were five patients with fever, neutrophil, cough, and fatigue; 24 with diarrhea; 25 with nausea; 11 with oral mucosal inflammation; 10 with rashes and dry skin; 8 with insomnia; and 1 with palpitation. Moreover, 110 patients with anxiety about the missed or delayed treatment were properly handled. **Conclusion:** The comprehensive online management of dual-targeted therapy with macromolecular monoclonal antibodies based on the cloud platform is helpful to satisfy the at-home breast cancer patients' needs, ensure the continuity of dual-targeted therapy with macromolecular monoclonal antibodies for breast cancer patients, prevent misinformation, alleviate patients' negative psychological emotions, and reduce patients' economic losses. The online cloud platform integrated management model is crucial for managing patients with breast cancer treated by dual-targeted therapy.

Keywords

Breast Cancer, Dual-Targeted Therapy with Macromolecular Monoclonal

1. Introduction

Breast cancer is one of the most common malignancies and has the highest incidence and mortality rate among women worldwide. According to the latest cancer statistics in 2018 [1], 24.3 percent of cancer affecting women worldwide was breast cancer, and about 15 percent of women cancer patients died for it. Human epidermal growth factor receptor-2 (HER-2) gene amplification or overexpression among breast cancer patients presents 25% to 30% [2] [3]. The survival rate of HER-2 positive breast cancer patients was significantly increased with the utilization of the anti-HER targeted drugs, such as Trastuzumab and Pertuzumab [4] [5]. On the one hand, Trastuzumab can significantly reduce the recurrence and metastasis of HER-2 positive breast cancer. On the other hand, 25% of patients with early HER-2 positive breast cancer still had recurrence or metastasis even after standard treatment with Trastuzumab [6]. Theoretically, the combination of Pertuzumab and Trastuzumab can block signal transduction at the source and inhibit the growth of tumor cells. Compared to Trastuzumab alone, postsurgical early HER-2 positive breast cancer patients with a dual-targeted regimen of Trastuzumab and Pertuzumab reported a 24% lower risk of recurrence; and lymph node positive subgroup recurrence was reduced by 28% [7] [8]. Therefore, dual-targeted therapy with macromolecular monoclonal antibodies is vital to HER-2 positive breast cancer patients. However, dual-targeted therapy with macromolecular monoclonal antibodies requires long times, high costs, and active cooperation for patients and families. Thus, scientific and reasonable comprehensive online management for these patients is essential.

We recruited patients who received dual-targeted therapy with macromolecular monoclonal antibodies in a hospital from March to November 2019. Comprehensive online management included consultation about drugs and side effects and frequently asked questions in the dual-targeted therapy with macromolecular monoclonal antibodies.

2. Methods

2.1. Setting and Sample

From March to November, 2019, 120 HER-2 positive breast cancer patients who had been diagnosed by pathology at Sun Yat-sen University Cancer Center were recruited in this study. A positive HER-2 was defined as an evaluation of a validated test, with an immunohistochemical (IHC) score of 3+ or in situ hybridization (ISH) ratio ≥ 2.0 [9]. Inclusion criteria: 1) patients with clinically confirmed breast cancer; 2) using dual-targeted therapy with macromolecular monoclonal antibodies; 3) HER-2 positive; 4) Patients with good cognitive ability; 5) informed consent of patients and their families. Exclusion criteria: 1) history of cognitive

impairment or mental illness; 2) Combined with other malignant tumors. Among the 120 participants, there were 118 women and two men. The mean age of the participants was 52 years old. All 120 patients were treated with the combination of Pertuzumab and Trastuzumab.

Ethical approval for this study was obtained from the Research Ethics Unit at Sun Yat-sen University Cancer Center (approval number GYX2020-002).

2.2. Comprehensive Online Management Based on Cloud Platform

Comprehensive online management was applied to breast cancer patients who used dual-targeted therapy with macromolecular monoclonal antibodies. The management was conducted through the WeChat official account, including “Cloud Follow-up System” and “Cloud Clinic,” to release the information about treatment and medication (dosage and combined medication), consultation, and answer questions that might help patients solve adverse drug reactions according to their situation. Online management contents are as follows:

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Trastuzumab and Pertuzumab must be administered sequentially in any order; the other targeted drug should be used only when no adverse effects occur in the first drug.

1) Dose

The initial dose of Trastuzumab was 8 mg/kg by body weight (intravenous infusion for 90 minutes). In the following times, Trastuzumab was calculated by 6 mg/kg (intravenous infusion 30 to 90 minutes) every three weeks. The initial Pertuzumab was administered intravenously for 60 minutes at an initial dose of 840 mg; then, it was then administered through intravenous infusion for 30 to 60 minutes at a dose of 420 mg every three weeks.

2) Effects of Other Drugs

For patients receiving Anthracycline, Pertuzumab and Trastuzumab should be used only after the usage of Anthracycline has been completed. Pertuzumab and Trastuzumab should be started on the first day of the first cycle of treatment with taxanes. Even though the chemotherapy regimen was discontinued, the dual-targeted therapy should continue for one year.

For metastatic breast cancer, Pertuzumab is used in combination with Trastuzumab and docetaxel until disease progression or unacceptable toxicity occurs. Even if docetaxel therapy is discontinued, dual-targeted therapy of Pertuzumab and Trastuzumab therapy can continue.

2.3. Consultation and FAQ

2.3.1. Misses or Delayed Treatment

The regular interval for treatment is three weeks. Under normal circumstances, patients should follow the doctors' advice to receive dual-targeted treatment with macromolecular monoclonal antibodies according to the treatment intervals. Patients cannot stop the therapy or change the interval.

For patients treated with a combination of Trastuzumab and Pertuzumab, if the interval is less than six weeks, 6 mg/kg Trastuzumab and 420 mg Pertuzumab should be given intravenously as soon as possible rather than waiting until the next scheduled time of therapy. If the interval is more than six weeks, the 8 mg/kg Trastuzumab and 840 mg Pertuzumab should be re-administered. The maintenance of 6 mg/kg Trastuzumab and 420 mg Pertuzumab should be re-administered every three weeks.

In this study, 110 patients consulted about delayed therapy. However, their intervals between the two treatments were less than six weeks. The patients' anxiety was relieved, and no economic loss was caused.

2.3.2. Fever, Neutrophil, Cough, and Fatigue

Side effects of the dual-targeted therapy with macromolecular monoclonal antibodies include fever, neutrophil, cough, and fatigue.

We guided the patient to obey protective isolation home temperature surveillance, go to the nearest hospital for blood tests, and be careful of the indicators or signs of infection. It is needed to use granulocyte stimulating factor to increase granulocytes and broad-spectrum antibiotics as directed.

Patients with neutrophils have a decreased immunity and are particularly susceptible to infection. These patients must wear masks and take precautions when going out. They should engage in regular and light aerobic exercise, such as Yoga, walking, and Tai Chi. They can also sing and paint to enhance their physique and immunity. Patients should pay attention to proper rest, not staying up late, and not being too tired. Appropriate physical exercise can help relax mood, enhance fitness, and improve immunity. Adequate sleep can make the body increase the secretion of sleep factors so that leukocytosis occurs and liver detoxification is enhanced, killing some of the invasion of viruses and bacteria to a certain extent.

In this study, five patients reported neutrophil, and one patient was treated with granulocyte count (GMF) and recovered. Another patient stayed at home for seven days, then went to the local hospital and found the neutrophil numbers returned to normal range. Three patients with fever, neutrophil, weakness, and cough were recovered after treatment.

2.3.3. Diarrhea

Pertuzumab can cause secretory diarrhea, and most patients were on Grade I (less than four stools per day) and Grade II (4 - 6 stools per day), but a few patients may have severe grade III diarrhea (≥ 7 stools per day). All cases occurred in the early stage of treatment. The incidence will decrease with the follow-up treatment. Therefore, we should inform the patient at home to closely observe the changes in vital signs, fever, shortness of breath, and other symptoms and guide the patient to eat a low-fiber, high-protein diet with adequate liquid intake and avoid irritant flatulent food. Patients should stay in bed when diarrhea is severe. Timely supplement of water and nutrition, prevent fluid and electrolyte disorders, check biochemical routine, blood routine in the nearest hospitals, and

intravenous nutrition support might be used when needed.

There were 18 participants with Grade I diarrhea, four with grade II diarrhea, and two with grade III diarrhea. We released the information on the treatment prevention of diarrhea-related knowledge through WeChat so that patients could consult with healthcare givers through the “follow-up system” and “cloud consulting room” about medication and treatment methods. Patients with Grade I and II diarrhea, were controlled with diet and antidiarrheal. Patients with grade III diarrhea were recommended to the nearest hospital for blood routine and biochemical examination. Although hypokalemia occurred, the diarrhea symptoms were controlled after treatment with antidiarrheal, oral, intravenous potassium supplementation, and parenteral nutrition. There was no fever, shortness of breath, shortness of breath, and other symptoms.

2.3.4. Nausea

We served online consultation with healthcare givers to help patients with anti-nausea prescribed medication, instruct patients to have more meals a day but less food at each, choose attractive food and avoid sweets, fried or greasy foods. Patients should drink more water in small amounts and multiple times. Patients should not drink much water at once. Patients need to rest after meals but do not stay in bed too long. Patients were suggested to avoid unpleasant smells. Fresh air may help relieve gastrointestinal symptoms. In this study, 25 patients were instructed to ventilate their rooms at least 2-3 times a day for more than 30 minutes each time and dress in appropriate clothes when the temperature changed to avoid colds and flu [10].

2.3.5. Oral Mucositis

Patients were guided to perform oral care using gargle after meals and before bed. Gargle and oral care can keep the mouth clean, make the microorganisms living in the mouth fall off to prevent infection, and control oral ulcers.

Patients should use mucosal protection or repair agents such as sucralfate and oral mucosa to form complex formations to reduce external damage to the oral mucosa and promote oral mucosal repair and regeneration under the guidance of healthcare givers [11] [12].

Tips of diet for oral care: Patients with mucositis should eat light and easily digestible food. Semi-liquid and liquid diets with high protein foods, such as milk, porridge, soy milk, and noodles, are appropriate. Patients should avoid spicy and stimulating food. Adequate sleep can also be conducive to oral mucositis recovery. In this study, oral mucositis was repaired gradually among eleven patients, and no oral infection occurred.

2.3.6. Skin Rashes and Dry Pruritus

We instructed patients to cut the nail short to prevent the rash from breaking and festering during the night. We also instructed patients to pay attention to personal hygiene and change clothes frequently. Patients should use warm water instead of hot showers, avoid alkaline or irritant soaps and lotion, choose mild

baby shower lotions, use creams to alleviate the symptoms of dry skin after showers; wear loose and breathable cotton clothes to keep the skin clean; pay attention to keeping quilts, pillows, towels, pillowcases clean.

Tips of diet for skincare: patients are advised to develop good eating habits. Diet should be light and easy to digest, including fresh fruits and green leafy vegetables rich in vitamin A (such as apples, pears, bananas, apricots, tomatoes, carrots) and vitamin C (strawberries, kiwis, guavas) as natural laxatives. At the same time, patients were told the dietary taboos during treatment: like spicy or greasy food. In addition, the stimulation from wine, strong tea, coffee should be avoided. Patients need to consult online and use allergy medications under health-care givers' supervision if necessary. The symptoms of skin rash and skin pruritus improved in 10 patients in this study.

2.3.7. Anxiety and Insomnia

Breast cancer patients frequently suffer anxiety, depression, fear, worry, and other negative psychological symptoms. These negative psychological symptoms could damage the immune system, reduce immunity, and affect breast cancer prognosis. Therefore, we must pay attention to patients' psychological changes. Through online psychological counseling, timely response to patients' questions and emotions, encourage patients to view the disease and life in positive ways and help patients adjust their psychological conditions in time, patients could keep calm minds. Besides, listening to soothing music, Baduanjin (traditional Chinese exercise) could help adjust the body, regulate breath and heart, physiologically dredge the meridians and collaterals of the human body, and ensure the smooth flow of Qi and blood [13], so the body's immune system could keep strong. There are some valuable tips: 1) dealing with negative emotions. Please do not pay too much attention but meditate that these are some of life's challenges, and we need to overcome them; 2) self-motivation. We should think that everyone has unique abilities; suffering is an essential experience, believing that we can do it; 3) positive thinking. Patients should look on the positive side from a broader perspective and affirm self-abilities; 4) sleeping environment should be quiet, shade, and comfortable. Behaviors before going to bed are mainly to promote blood circulation and eliminate fatigue, such as feet bath hot bath. There should be no strenuous exercise within 2 hours before bed; 5) patients should avoid caffeine, spicy, greasy food, or over-eating 2 hours before bed. Patients should pay attention to the evaluation of sleep status. If there are any performance of insomnia, early guidance should be given to patients. Recommendations of standard psychobehavioral therapy for patients with chronic insomnia should be given [14] [15]. Patients can use the "Cloud Clinic" online system for online appointments to obtain sleeping pills' guidance.

2.3.8. Palpitation

Patients were instructed to closely observe the possible cardiac toxicity of Trastuzumab and take immediate measures to protect their hearts. At the same time,

cardiac function tests should be performed as routines before medication and dynamically monitored during treatment, such as every three months. If the patient has asymptomatic cardiac dysfunction, the number of tests should increase to every 6 - 8 weeks a time to ensure patients' safety [16]. Patients were told to observe vital signs, heart rate changes, reasonable arrangements for daily living and diet, and avoid fatigue. If cardiac symptoms aggravate, patients should get a timely diagnosis and treatment to re-check ECG and echocardiography.

3. Results

Breast cancer patients treated by dual-targeted therapy with macromolecular monoclonal antibodies are administrated through WeChat Cloud Clinic and Cloud Follow-up System. Among the 120 patients, 5 reported fever, neutrophil, cough, and fatigue, 24 reported diarrhea, 25 reported nausea, 11 reported oral stomatitis, 10 reported skin rashes, and dry, itchy skin, and 8 reported insomnia, 1 patient reported palpitation (Table 1).

110 patients with anxiety about missed or delayed therapies were well treated and resolved throughout the consultation. There were 58 patients whose dual-targeted therapy with macromolecular monoclonal antibodies with treatment delay. However, the interval between the two treatments was less than six weeks, reducing the patients' anxiety and not increasing their financial burdens.

4. Discussion

4.1. Advantages of Online Management

In this study, information was pushed, and questions are answered online through cloud platforms such as WeChat. Cloud Clinic and Cloud Follow-up System can timely release the information of macromolecular monoclonal antibodies dual-targeted therapy. It is helpful not only to solve the common problems of patients but also to help patients actively deal with their particular problems, reflecting the trend of personalized care.

The online management model helped patients solve complex problems in

Table 1. The results of the comprehensive online management.

Interrogation content	n	Percentage (%)
fever, neutrophil, cough, and fatigue	5	4.1
diarrhea	24	20.0
nausea	25	20.8
oral stomatitis	11	9.2
skin rashes, and dry, itchy skin	10	12.0
insomnia	8	6.7
palpitation	1	0.8
	120	100

real-time, meet self-treatment needs at home, reduce patients' commute between home and hospital, and improve patients' self-care ability. It also saves the hospital's human, material, and financial resources [17].

4.2. Humane Care, Nurse-Patient Communication and Improvement of Patients' Compliance

Through intercommunication, patients feel valued by timely feedback, guidance, and treatment. The online management of breast cancer patients treated by dual-targeted therapy with macromolecular monoclonal antibodies provided individualized guidance for different patients, met patients' health knowledge needs and greatly enhanced the interaction between healthcare givers and patients. It also shortened the distance between healthcare givers and patients, improved patients' compliance, improved the status of nurses in maintaining health, enriched the professional connotation of nurses, and improved the sense of responsibility of nurses [18].

4.3. Development of Continuing Care

With the development of continuous care, more and more patients are included in the follow-up. Based on regular returns to the hospital, through telephone, WeChat, video, and other means of communication, healthcare givers could understand the rehabilitation of patients. Many patients visit online to read popular science articles and consult with caregivers, effectively promoting "cloud consulting," which lays the cornerstone for the future development of continuing care.

5. Conclusions

Despite the increasing use of dual-targeted therapy with macromolecular monoclonal antibodies in breast cancer, there is a lack of support for preventing, monitoring, and managing side effects, especially significant for Chinese patients [19]. The limited data on the safety of dual-targeted therapy among Chinese breast cancer patients brought challenges to safety management in China. In addition, attention should be paid to the adverse reactions associated with macromolecular monoclonal antibodies such as Trastuzumab and Pertuzumab.

These drugs only have data in clinical trials. The natural side effects require follow-up to determine. The prevention and management of side effects are crucial for the prognosis, treatment continuity, and quality of life. Therefore, we should fully understand the possible side effects of different targeted therapies. Early detection, prevention, monitoring of the changes of symptoms and indicators of patients before and after treatment and during treatment, timely adoption of reasonable and practical measures to maintain the application of targeted therapy with macromolecular monoclonal antibodies as far as possible are necessary to the maximum antitumor effect of macromolecular monoclonal antibodies targeting therapy. Pertuzumab, a macromolecular monoclonal antibody

targeting drug, was used in clinical in our department in March 2019. The nursing of dual-targeted therapy with macromolecular monoclonal antibodies needs to be standardized. The online management of dual-targeted therapy with macromolecular monoclonal antibodies for breast cancer patients is helpful for learning.

6. Limitation

This study only required short online management time, and failed to observe the long-term effect of cloud platform on patients. Also only patients receiving dual-target therapy were selected, and the cloud platform could be extended to other treatment methods and other diseases in the future.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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