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Dermatological care for skin undergoing cancer treatment

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A B S T R A C T

The World Health Organization defines cancer as a group of diseases characterized by the uncontrolled growth of cells. Worldwide, it is estimated that there will be 19.3 million new cases in 2020. Risk factors in Portugal include alcohol, tobacco, excess weight and physical inactivity, highlighting the importance of early diagnosis for a favorable prognosis. Treatments vary, resulting in various adverse effects, particularly on the skin, such as xerosis, hyperpigmentation, hand-foot syndrome, sensitivity to light and itching, requiring care before, during and after treatments. This includes hygiene, moisturizing and sun protection. The careful choice of dermatological products is essential to minimize the adverse effects of treatments. Corrective make-up can help improve patients' quality of life by concealing certain skin alterations. This literature review aims to understand the skin changes inherent to cancer, the drugs that potentiate them and to explore the dermatological care available. To achieve this objective, a bibliographic search was carried out in different databases including Pubmed and google scholar, official entities such as the World Health Organization, the National Health Service and the library of the Coimbra School of Health Technology. Using keywords such as cancer, cosmetics, skin care, dermatology, quality of life, cancer treatments, considering a study period of the last 5 years. Drugs used in clinical practice were discussed, such as Apalutamide, Brigatinib, Capecitabine, Cetuximab, Erlotinib, Gefitinib, Panitumumab, Sorafenib associated with their adverse effects, promoting a better understanding of treatments and their effects, focusing on the needs of cancer patients. The promotion of well-being and adherence to treatment are facilitated by a careful approach to the choice of cosmetic and dermatological products, as discussed. Knowledge of dermatological toxicities is essential for improving the quality of life and therapeutic adherence of cancer patients.

Keywords: Cancer treatments; Dermatology; Quality of life; Skin care.

INTRODUCTION

The term “cancer” has the capacity to arouse concern in a significant number of individuals and at the same time awaken negative memories for those who have previously shared experiences associated with this term. According to the World Health Organization, cancer is a large group of diseases that can start in almost any organ or tissue in the body. This occurs when cells grow uncontrollably, crossing their usual boundaries and invading adjacent parts of the body and/or spreading to other organs (1).

This highly prevalent pathology is the second leading cause of death in Portugal and worldwide. According to data from the International Cancer Research Agency Globocan, 60,467 thousand new cases were recorded in 2020. Worldwide, it is estimated that there were 19.3 million new cases (2).

In Portugal, the main risk factors associated with this condition include excessive alcohol and tobacco consumption, being overweight and physical inactivity. Early diagnosis, through screening programs, leads to earlier decision-making and, consequently, contributes to a more favorable prognosis (1) (3).

There are different treatment plans, each of which includes different therapies, resulting in equally different modes of action. The manifestation of this pathology generates various complications, including influencing the integrity of our skin and mucous membranes. The influence of these therapies on the skin varies between patients, as individual responses can differ (4). It is worth noting that, regardless of the response, side effects resulting from treatment are common, especially when it comes to chemotherapy, radiotherapy or biological therapy (5).

Various skin manifestations are observed, the most prevalent of which are characterized by dryness, hyperpigmentation, greater sensitivity to light, hand-foot syndrome (redness and pain in the hands and feet) and itching all over the body. Symptoms such as pain, redness, heat, dryness and itching are common in areas that have previously undergone radiotherapy (6) (7). Skin undergoing this type of treatment is more sensitive to small changes, resulting in the need for specialized attention and a personalized approach to pre-treatment, during and post-treatment care.
Dermatological skin care covers several essential areas, such as personal hygiene, cleansing, moisturizing and the application of photoprotection (5). These changes impose the need to consciously adapt the dermatological routine in response to the challenges imposed by this specific context. To this end, this article will present various precautions that can be adopted to mitigate and improve these conditions.

Just as there are products that improve skin conditions, it is essential to recognize the existence of substances that, conversely, can aggravate the unwanted adverse effects of different therapies. For this reason, care must be taken when advising on the use of certain products (5) . To this end, it is essential to acquire a more detailed knowledge of the variety of dermatological products available to us, to achieve the most favorable results possible.

In the complex and challenging scenario of cancer treatment, promoting well-being and improving patients' quality of life plays a fundamental role. Corrective make-up can be used to achieve this, as it can conceal most skin alterations (8). The careful choice of cosmetic and dermatological products is crucial, as it can considerably influence the skin's response to ongoing treatments, playing an important role in promoting adherence (5) (9). The purpose of this article is to understand the skin changes inherent to cancer and the cytotoxic drugs that potentiate them, exploring the different dermatological treatments available.

MATERIAL AND METHODS

This article is a literature review (10), for the purpose of writing it, we selected full-text, open-access articles published in Portuguese and English on the subject in question. The research was carried out considering a study period of the last 5 years.

The research was carried out using different databases such as Pubmed and Google Scholar, as well as official entities such as the World Health Organization, the National Health Service and the Library of the Coimbra School of Health Technology. Using keywords such as: Cancer treatments; Dermatology; Quality of life; Skin care. The articles used in this study were selected according to the Prisma Flowchart (Diagram 1) below and after applying the inclusion criteria mentioned above. At the same time, a search was carried out using the name of each drug individually to find detailed information on each one. To detail the research, a prism and a table were drawn up covering all the articles selected for the study.

It is essential to emphasize that, in accordance with Helsinki law, all copyrights were respected during the research process (11). Ensuring that all the authors of review articles, dissertations and relevant works used in the preparation of the article are duly cited throughout, demonstrating total academic integrity and avoiding any form of plagiarism.

RESULTS/ DISCUSSION

The following table (Table 1) summarizes the results obtained from the bibliographical research, providing a comprehensive overview of the studies analyzed, which were used as a basis for the discussion.

Table 1- Table of results

Author/ Year	*Type of study*	*Objective of study*	*Results/ Conclusions*
Dreno B, Khosrotehrani K, De Barros Silva G, Wolf JR, Kerob D, Trombetta M, et al. (2023) (9)	Systematic review	Analyze new skin toxicities associated with oncology drugs and evaluate the role of dermo-cosmetics in improving patient outcomes and minimizing interruptions in cancer treatment. Provide general recommendations on skin care and factors to consider when using dermocosmetics for different types of skin toxicity.	Skin toxicities can lead to treatment interruption, resulting in sub-optimal results. Dermocosmetics with dermatologically active ingredients improve skin disease systems, minimize alterations in the skin barrier and provide photoprotection, making them essential for preventing skin toxicities.

Pons Benavent M, Porcar Saura S, Bou Boluda L. (2023) (12)	Case study	It aims to provide information on the characteristics of these frequent adverse effects, to correct their diagnostic and therapeutic approach.	Some patients have reported intense itching and general discomfort. Sometimes it is necessary to withdraw the medication and simultaneously subject patients to a short period of systemic corticosteroids to resolve these effects.
Barbieri MA, Sorbara EE, Cicala G, Santoro V, Cutroneo PM, Franchina T, et al. (2022) (13)	Original article	The aim of this study was to highlight all Adverse Drug Reactions associated with tyrosine kinase inhibitors approved for non-small cell lung cancer and reported in the Adverse Drug Reaction Reporting system. Consequently, put in all the complete reports in the National Pharmacovigilance Network database.	The largest number of cases were related to skin diseases such as irritation, dermatitis and skin toxicity. They recognized other gastrointestinal, liver and respiratory risks, as well as infections.
Iscan D, Tolay R, Bayram E, Demir T, Bicakci S. (2023) (14)	Case study	Monitoring of colon cancer disorders, particularly related to neurotoxicity.	Common side effects of capecitabine include nausea, gastrointestinal effects (vomiting and diarrhea), dermatological effects (hand-foot syndrome and changes in skin pigmentation). The neurological effects of capecitabine are very rare.
Lugtenberg RT, Boers-Doets CB, Witteveen PO, Van Herpen CML, Wymenga & ANM, De Groot JWB, et al. (2020) (15)	Original article	The main objective of this study is to obtain information on the different skin care products used against skin reactions in patients with metastatic colorectal cancer undergoing treatment with cetuximab.	For the patients, the skin reactions did not affect the continuity of therapy with cetuximab. Xerosis, rash, itching and cracks usually appear in the first few weeks of treatment and increase over time. The most commonly used skin products were moisturizers and antibiotics, the use of which gradually increased.
Acikgoz Y, Bal O, Ucar G, Durnali A, Ergun Y, Dirikoc M, et al. (2021) (16)	Original article	To explore the predictive role of clinical and baseline inflammation-related and other hematological parameters for cetuximab-induced skin toxicity. They also aimed to analyze the survival outcomes of these patients according to risk categories.	Cutaneous toxicity from cetuximab can reduce quality of life and adherence to treatment. Identifying patients at higher risk of skin toxicity improves adherence and treatment success. The platelet/lymphocyte ratio and red blood cell status are reliable indicators of these patients.
Uchino T, Fujino H, Kamiya D, Suzuki T, Miyazaki Y, Asada K, et al. (2020)(17)	Original article	It aimed to investigate the relationship between erlotinib-related dry skin and changes in intercellular lipid composition and stratum corneum structure.	Treatment with erlotinib can cause rash, itching, dry skin and acne, which worsen over time. Emollients and topical steroids are the main options for treating skin toxicity.

Singh S, Sadhukhan S, Sonawane A. (2023)(18)	Article from a medical journal	They investigated the groundbreaking discoveries made over the last 20 years and discussed the efforts currently underway to circumvent chemotherapy resistance. They also highlighted the new challenges, limitations and future directions for the development of improved therapeutic approaches.	The preclinical study showed that several drug-related adverse effects are generated by gefitinib including nausea, peripheral edema, decreased appetite and rash.
Lavery MJ, Forsyth L, Hindle E. (2021)(19)	Case study	The aim of this study is to verify the cutaneous manifestations secondary to Panitumumab therapy and to retrospectively analyze the last four patients who received Panitumumab therapy at the corresponding institution.	Patients treated with panitumumab usually present with a painful acneiform rash that begins on the head and neck, progressing to the trunk and extremities. Dermovat cream is effective in the initial treatment and can avoid the use of oral antibiotics. Months later, an eczematous rash with digital fissures may appear. Discontinuation of panitumumab is rare, dose reduction and the use of topical corticosteroids can control dermatitis and symptoms.
Nakata K, Komori T, Saso K, Ota H, Kagawa Y, Morita S, et al. (2021)(20)	Original article	The aim of this trial was to evaluate the efficacy and safety of preventive antibiotic treatment with clarithromycin to avoid the skin toxicities of panitumumab.	Preventive treatment included moisturizers and topical steroids applied daily, which are complicated and uncomfortable. To simplify care, it was planned to use prophylactic oral clarithromycin, daily moisturizer and topical sunscreen, without daily steroids.
Lee YS, Jung YK, Kim JH, Cho SB, Kim DY, Kim MY, et al. (2020)(21)	Systematic review	In the present study, the aim was to investigate the role of urea cream in preventing the hand-foot skin reaction or improving the severity of the hand-foot skin reaction.	Hand-foot skin reaction is the most common adverse event during treatment with sorafenib in patients with hepatocellular carcinoma. Treatment with urea cream can be considered for prophylaxis or improvement of the condition in patients treated with sorafenib. Urea cream reduced the development of grade II hand-foot skin reaction within two weeks.
Wang L, Chen M, Ran X, Tang H, Cao D. (2023)(22)	Systematic review	Show promising results for the targeted treatment of hepatocellular carcinoma and other types of cancer by nanomedicines based on sorafenib. Prospects, challenges and future	Poor aqueous solubility, low bioavailability, unfavorable pharmacokinetic properties and side effects limit the clinical application of the drugs. They studied alternatives, such as drug

		opportunities for the development of sorafenib-based drug delivery are presented.	release mechanisms, to improve biopharmaceutical properties.
Mohiuddin AK (2019) (23)	Systematic review	Explore the various formulas for the skin, exploring the importance of these products in maintaining skin health throughout life. The article addresses how skin care varies with age and the specific needs of different areas of the skin.	In young people, environmental factors such as UV radiation are paramount, in older people ageing and prolonged exposure are more important. Aging skin is more susceptible to clinical problems, requiring special care to avoid diseases and systemic and pharmacological complications.
Khan AD, Alam MN. (2019) (24)	Systematic review	To make people aware of the various harmful effects of cosmetics and the chemicals used in their production.	Cosmetic products can present health risks and recurring adverse effects are attributed to the toxic substances commonly found in their formulations.
Piquero-Casals J, Morgado-Carrasco D, Granger C, Trullàs C, et al. (2021) (25)	Systematic review	A review of the use of urea in dermatology, discussing its mechanism of action, safety profile and frequent indications.	Urea is crucial for regulating keratinocyte proliferation, maintaining the skin barrier and defending against microbes. It is well tolerated and widely used as a moisturizer and keratolytic in dermatological treatments, being indicated for xerosis, psoriasis, ichthyosis and seborrheic dermatitis.
Anoop TM, Joseph P R, PN M, KP P, Gopan G, Chacko S (2021) (26)	Original article	To determine the spectrum of skin toxicities in patients receiving systemic chemotherapy and targeted agents for breast cancer patients.	Skin toxicities are common after systemic chemotherapy. Early recognition of the cutaneous side effects of these agents and prompt early interventions can reduce significant morbidity, cosmetic disfigurement, treatment interruptions and psychological distress in women treated for breast cancer.

Prevention is fundamental in all pathologies, a concept that also applies to the progression of skin toxicity. Dermatological diseases have a major impact on patients' quality of life, influencing both physical and psychological aspects. Cancer therapy has improved survival, with chemotherapy, radiotherapy and biological therapy protocols contributing to these positive results. However, these treatments often result in toxicity, especially dermatological toxicity, which needs special attention due to its frequency and impact on patients' physical and psychosocial health. This can lead to undesirable clinical results or even the discontinuation of treatment.

Chemotherapy treatments using molecularly targeted drugs, epidermal growth factor receptor inhibitors and tyrosine kinase inhibitors, can cause unfavorable skin effects. These effects diminish patients' quality of life, and even with optimized management, can lead some patients to discontinue treatment. Sometimes these molecules are used alone or in combination therapy, for example with radiotherapy and immunotherapy.

In order to provide a clear and organized overview of the most used drugs in current therapy and their associated toxicity effects, a table (Table 2) was constructed compiling this information. This table serves as a guide for health professionals in identifying the associated adverse effects, promoting a more effective and patient-centered approach.

Table 2- Molecules used in practice and their effects

Drug	*Therapeutic indication and classification*	*Dermatological toxicity*
Apalutamide (12)	It is an androgen receptor inhibitor; its anti-tumor activity is based on decreasing cell proliferation and cell apoptosis. It is used to treat hormone-sensitive metastatic prostate cancer in combination with androgen deprivation therapy in adult men.	Common side effects include intense pruritus, edema and skin rashes.
Brigatinib (13)	An anaplastic lymphoma kinase inhibitor. Used to treat non-small cell lung cancer.	The largest number of cases presented skin irritation, dermatitis and skin toxicity.
Capecitabine (14)	It produces 5-fluorouracil (which can be administered orally), which acts as an antimetabolite to inhibit cell growth by interfering with DNA and RNA synthesis. They are often used to treat solid tumor cancers, such as breast cancer and gastrointestinal tumors.	Common side effects of capecitabine include dermatological side effects, including hand-foot syndrome and altered skin pigmentation.
Cetuximab (15)(16)	This is an IgG1 monoclonal antibody that binds to the epidermal growth factor receptor and competitively inhibits epidermal growth factor binding. The drug is administered via intravenous infusion Use in metastatic colorectal cancer (without mutation) and head and neck cancer.	Causes dermatological disorders such as desquamation, acneiform rash, dermatitis, xerosis, pruritus, rash, nail changes, acne vulgaris, skin fissures and alopecia.
Erlotinib (17)	It is an inhibitor of the tyrosine kinase receptor (regulates the differentiation, survival and proliferation of cells) of the epidermal growth factor. Used to treat non-small cell lung cancer.	They have various skin diseases that impair the skin's barrier function such as rash (most common), itching, dry skin (characterized by rough, scaly or friable skin, accompanied by a loss of skin elasticity and itching) and acne. This increased with increasing time after the start of erlotinib administration.
Gefitinib (18)	It is the first of the first generation of epidermal growth factor receptors, a multi-target tyrosine kinase inhibitor used for the treatment of non-small cell lung cancer. When combined with cytotoxic chemotherapy, it is highly effective.	It can generate several drug-related adverse effects, including peripheral edema and rash.
Panitumumab (19) (20)	This is an IgG2 monoclonal antibody used to treat metastatic carcinomas.	It triggers various events such as skin toxicities, from painful acneiform eruptions (in this case starting on the head and neck and progressing to the trunk and extremities), pruritic xerosis and painful fissures.

Sorafenib (21) (22)	Sorafenib is a multi-target tyrosine kinase inhibitor, which has been used mainly in the treatment of advanced hepatocellular carcinoma and kidney cancer. It is a molecularly targeted chemotherapy drug that can inhibit angiogenesis and tumor cell proliferation, leading to improved overall survival in patients with hepatocellular carcinoma (HCC).	Hand-foot skin reaction (HFSR) is the most common adverse event during treatment with sorafenib in patients with hepatocellular carcinoma; rashes also occur.

After analyzing the different compounds used in the oncology clinic, a few toxicities were shown to be prevalent, not only dermatological, but also at hepatic, respiratory and intestinal levels. The most common include fatigue, diarrhea, nausea, anorexia, weight loss, constipation, joint and muscle pain, hot flashes, headaches and dizziness. Among dermatological toxicities, the most prevalent include pruritus, photosensitivity, xerosis, papules and pustules, dermatitis, hand-foot syndrome and nail and hair changes (alopecia). Some molecules, due to their pharmacokinetic properties and undesirable side effects, limit their clinical application (21) (22).

Although dermatological issues may seem secondary due to the severity of toxicities, they are significant and can lead to treatment discontinuation. The body image and discomfort associated with these conditions can emotionally impact patients, making the involvement of dermatologists in treatment teams crucial. Healthcare professionals should be informed about the care needed to mitigate these conditions and improve patients' quality of life.

The term “dermatological care” encompasses a diversity of care from skin, nails and hair, all of which are affected during cancer treatments. Many patients find the visible changes more distressing than the physical symptoms (9). Environmental factors, such as radiation and pollution, are important and should be considered, as they make the skin more sensitive and susceptible to aggression. The prevention and treatment of dermatological toxicities involves basic care such as cleansing, moisturizing, restoring and sun protection, which are essential to prevent progression to more damaging conditions (12)(26)(23).

Formulations with urea, ceramides, lipid-regenerating substances, neutral pH, emollient and non-comedogenic products should be favored (17)(24). Depending on the purpose, urea can be used in different concentrations, from 2% to 10% to moisturize and optimize the skin's barrier function, from 10% to 30% for high-concentration moisturizers and keratolytics, and 30% for keratolytics and removal of necrotic tissue (25). Moisturizing creams, deodorants and shampoos should be adapted to something milder. There are products aimed at this public through specific ranges for fragile and sensitive skin, which should be free of fragrances or perfumes, irritants such as alcohol-based lotions, avoiding possible inflammation. Sometimes it is necessary to use pharmacological agents such as topical corticosteroids, oral and topical antibiotics, antihistamines to treat and prevent some of the dermatological adverse effects (15)(16)(17).

Skin care is essential at all stages of life but needs change with age and health conditions. Currently, emollients and topical steroids are the main treatment options for skin toxicity (18). The use of topical corticosteroids is useful in the initial treatment, providing clinical improvement without the need for oral antibiotics, although they are sometimes necessary (19)(21).

Topical photoprotection should be applied daily, regardless of specific skin conditions. In addition, there is systemic photoprotection, which includes supplements such as carotenoids, antioxidants, polyphenols, aimed at neutralizing the damage caused by UV radiation, and is an increasingly used therapy (20). To guarantee complete protection, it is important to adopt additional measures, such as wearing hats, appropriate clothing and controlling the time of sun exposure.

The use of urea has proven to be very positive as it is a hygroscopic molecule present in the epidermis as a component of the natural moisturizing factor, in dermatological formulations, urea can be used for prophylaxis or improvement of skin reactions, such as hand-foot syndrome, xerosis, dermatitis and dermatoses, which are the most common adverse events (22). In addition, urea can increase the absorption of certain topical medications into the skin and nails and is one of the main causes of dose reduction or discontinuation in some patients (25).

Additional measures can be taken, such as the use of corrective make-up, which can significantly improve patients' quality of life by helping to camouflage scars and skin disfigurements. Make-up not only improves physical appearance but also contributes positively to patients' psychological well-being. Despite the benefits of chemotherapy, changes in body image negatively affect the quality of life of cancer patients, making it essential to find mechanisms like this to facilitate adaptation to this major change (26). Many cosmetics contain toxic ingredients that can cause serious damage to the skin, so it is essential to make people aware of their harmful effects (24)(25).

Investing in prevention and promoting healthy lifestyles are important aspects that contribute to a better quality of life. Although cancer treatments are essential for patients' survival, they bring with them undesirable dermatological adverse effects, so proper dermatological care is essential to minimize these effects and improve patients' quality of life.

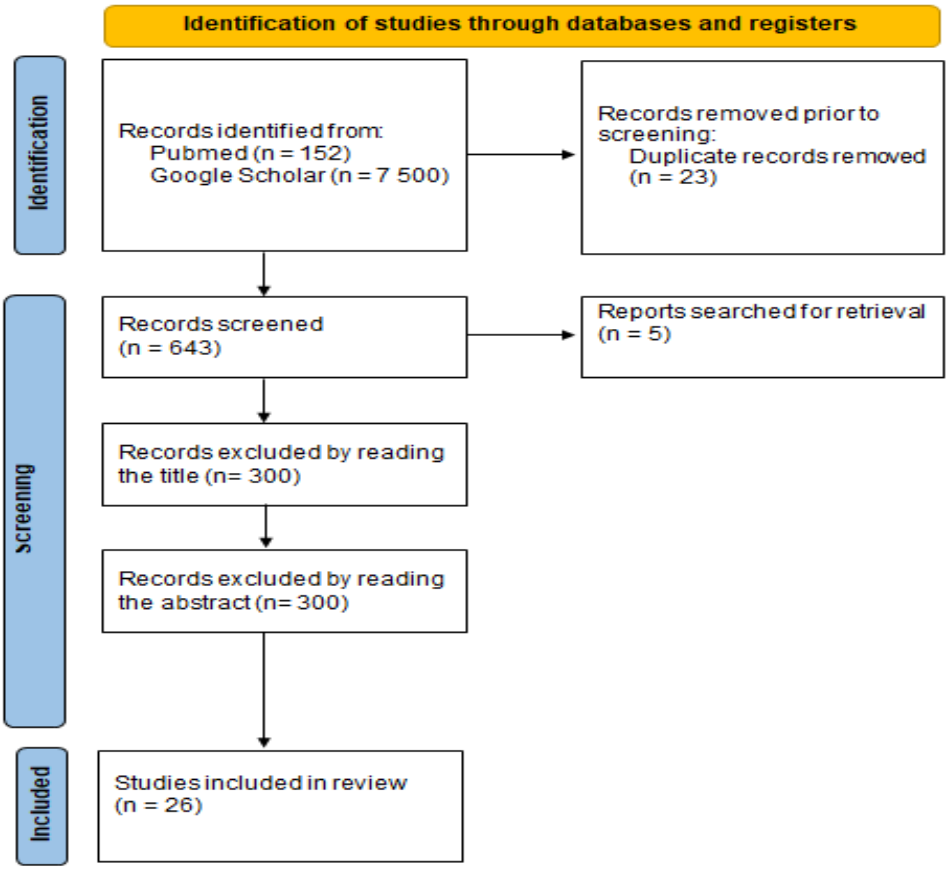

*Diagram 1- **Prisma Flowchart***

CONCLUSION

The study achieved its objectives, covering everything from the skin changes inherent in cancer to the drugs that cause them, and the care required. The study has some limitations, as only some of the drugs used in current cancer therapy were covered, focusing on those that currently cause the most dermatological affections, such as pruritus, photosensitivity, xerosis, dermatitis, hand-foot syndrome, among others, due to their pharmacological characteristics. It is crucial to know the skin changes inherent to cancer to maintain the quality of life of cancer patients, as well as to identify some of the drugs that potentiate them. In this way, they can be alerted to the careful choice of skin care products, combined with appropriate preventive and therapeutic measures, which can mitigate the negative impacts of these adverse effects.

Awareness of specific care and the inclusion of specialized professionals can result in better clinical outcomes and quality of life for these patients. The work of healthcare professionals is fundamental to reducing drug-related problems, preventing adverse effects and demonstrating benefits through their intervention. This highlights the desirability and need to implement more information in this area, promoting beneficial results.

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