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Impact of Oncological Treatments on Reproductive Capacity: Alternatives to Minimize Risks and the Role of DEX Immunotherapy

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ABSTRACT

Fertility preservation in cancer patients is an increasingly relevant challenge due to the gonadotoxic effects of conventional treatments, such as chemotherapy and radiotherapy. This article reviews current options for fertility preservation and explores the potential of DEX immunotherapy as a less invasive alternative. Initially, an overview of cancer incidence in fertile age and the importance of addressing reproductive concerns in this population group is presented. Subsequently, the negative impacts of conventional treatments on reproductive capacity are analyzed and strategies to minimize these risks, such as reducing treatment intensity and using cryopreservation techniques, are discussed DEX immunotherapy stands out as a promising option, with a lower risk of gonadotoxicity compared to traditional treatments. This immunological approach allows to specifically target cancer cells, reducing damage to reproductive cells and offering better fertility preservation in young patients. Finally, the article addresses future research needs and practical guidelines for clinicians, highlighting the importance of a multidisciplinary approach that integrates fertility preservation options in cancer treatment.

It is concluded that, although DEX immunotherapy is a viable alternative, it is essential to promote further research and develop specific clinical protocols to maximize its effectiveness and safety in terms of long-term reproductive health.

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Introduction

Overview of Cancer in Patients of Childbearing Age

Cancer in people of childbearing age, both men and women, poses a unique challenge, as these patients are often faced with the dilemma of undergoing treatments that may compromise their reproductive capacity in the long term. The incidence of cancer in young adults is not as high as in older people; however, treatment side effects, especially those affecting fertility, require special attention in this population. Young patients with ovarian cancer, for example, experience elevated rates of fertility preservation complications due to the direct impact of treatments on ovarian tissue [1]. 1.2. Importance of fertility preservation in oncological treatment Fertility preservation is critical for young patients facing a cancer diagnosis. Conventional treatments such as chemotherapy and radiotherapy can severely damage reproductive cells, thus reducing the chances of having biological children in the future. Fertility preservation techniques not only contribute to protecting the reproductive capacity of patients, but also have a significant impact on their psychological well-being and quality of life by offering an option to fulfil their fertility wishes after treatment [2,3]. Research has shown that fertility preservation counselling before treatment considerably improves the quality of life of young women with cancer, helping them to cope with the emotional and physical effects of the disease and its treatments [3]. 1.3. Objective of the review the main objective of this review is to analyse the effects of conventional cancer treatments on the reproductive capacity of patients of childbearing age and to explore alternatives to minimise these impacts, such as cycle reduction and the incorporation of treatments that include cytoprotective mechanisms, less harmful to fertility. In addition, the potential of DEX immunotherapy as an innovative strategy in fertility preservation in young patients with cancer will be discussed. This review highlights the need for multidisciplinary strategies that integrate both fertility preservation and cancer treatment options to improve long-term outcomes in these patients [4]. 1.4. Ethical and practical considerations in fertility preservation For physicians, the decision to refer young cancer patients to fertility preservation programs involves both ethical and practical considerations. Evidence suggests that early referral to fertility preservation options by oncologists is crucial to improve reproductive outcomes in patients who are at risk of fertility loss due to aggressive treatments [5]. However, many patients do not receive this information in a timely manner, limiting their ability to make informed decisions before starting treatment [6,7]. These

decisions reflect an ethical dimension in clinical practice, where lack of adequate information and guidance could harm patients' reproductive future.

Epidemiology of Cancer in Childbearing Age

Cancer Incidence in Young Adults

Cancer in adults of childbearing age has shown an increase in incidence in recent years, especially in some specific types of cancer. In Canada, for example, a cancer surveillance project reported a significant incidence in this population, highlighting the importance of more precise and specific monitoring for young adults [8]. Likewise, in the United States, data suggest that cancer in adolescents and young adults represents a considerable proportion of new diagnoses, with types such as melanoma, lymphoma, thyroid cancer and testicular cancer being predominant in this group [9].

Despite representing a lower percentage compared to cancer rates at older ages, cancer in young adults has unique implications due to the potential consequences on fertility and long-term quality of life [11]. These statistics reflect the need for increased awareness and targeted strategies for early detection in young people, especially since these patients are less likely to perceive early symptoms as signs of cancer [12].

Types of Cancer and their Specific Effects on Fertility

Among the most common cancers in young adults are breast cancer, lymphoma, melanoma, and thyroid cancer, all of which may require intensive treatments that directly impact fertility [12]. In men, testicular cancer and some types of lymphoma are particularly prevalent and directly affect reproductive function. Necessary treatments, such as chemotherapy and radiation therapy, often have long-lasting side effects on sperm production and overall reproductive capacity [10].

The impact on fertility varies depending on the type of cancer and the treatment needed. In women, treatment for breast cancer, one of the most common types of cancer in this population, frequently includes chemotherapy and hormonal therapy, both of which have the potential to decrease ovarian reserve [13]. Furthermore, gynecological cancer, such as cervical cancer and ovarian cancer, represents an additional challenge, as it directly affects the reproductive organs, complicating fertility preservation options [11].

Difficulties in Early Detection and the Impact on Quality of Life

Early detection of cancer in young people presents significant challenges due to the low prevalence and lack of specific screening programs for this population. In many cases, initial symptoms are wrongly associated with less serious conditions, which delays diagnosis and, consequently, treatment and fertility preservation options [9]. Lack of timely diagnosis in this group can lead to more aggressive treatments, which in turn reduces the chances of preserving fertility and significantly affects quality of life [8]. Delayed detection also has an impact on the psychological well-being of young patients, as they face both the burden of a life-threatening illness and limitations on their future plans to start a family. Evidence shows that young adults with cancer often experience greater emotional impact related to infertility secondary to treatments, affecting their quality of life and long-term emotional recovery [14].

Importance of Cancer Staging and Its Relationship to Fertility Preservation

Cancer staging at diagnosis is crucial to determine both the prognosis and the most appropriate type of treatment for each patient. In the case of patients of childbearing age, this assessment has additional relevance, since early stages may allow for less invasive treatments, which offer a better chance of preserving fertility [10,13]. However, when cancer is diagnosed at advanced stages, more aggressive treatments become inevitable, increasing the risk of infertility.

Some studies highlight that advanced therapies, such as immunotherapy combinations involving dendritic cells and CIK cells, may offer a less damaging alternative to fertility, while improving survival rates without compromising quality of life as much [12]. This is particularly relevant in the context of oncology for young adults, as it provides hope in terms of preserving fertility while effectively fighting cancer.

Impact of Conventional Treatments on Fertility

Mechanisms of Fertility Impairment

Conventional cancer treatments, such as chemotherapy and radiotherapy, can have a devastating impact on fertility due to their effect on reproductive cells. Chemotherapy, particularly when it includes alkylating agents, is known to be toxic to the gonads, affecting both egg production in women and sperm quality and quantity in men [15]. These agents have a direct effect on the DNA of reproductive cells, increasing the risk of ovarian failure in young women and azoospermia in men, which can result in permanent infertility in many cases [16].

On the other hand, radiotherapy, especially when administered to areas close to the reproductive organs, can damage gonadal tissue irreversibly. Radiation to the pelvic region, in particular, is highly damaging and can affect both the ovaries and testicles, causing long-lasting damage and significantly reducing the chances of fertility in young patients [17]. Furthermore, studies have shown that exposure to high doses of radiation considerably increases the risk of developing premature ovarian failure and decreased ovarian reserve [18]. (Table 1)

Table 1: Adverse Effects on Fertility from Conventional Cancer Treatments

Type of Treatment	Effects on Male Fertility	Effects on Female Fertility	Duration of Effect
Chemotherapy	Potential Azoospermia, Reduced Spermatogenesis	Risk of Premature Ovarian Failure	Long Term, with Possibility of Irreversibility Depending on dose and duration
Radiotherapy	Potential Damage to Testicular Tissue	Possible Reduction in Ovarian Reserve	Long Term, with the Possibility of Irreversibility, Especially in Pelvic Treatments
Hormonal Therapy	Changes in Sperm Production	Possible Reduction in Ovarian Reserve	Varies Depending on the Treatment
Surgery on Reproductive Organs	Direct Loss of Reproductive Capacity	Direct Loss of Reproductive Capacity	Permanent if it Affects Reproductive Organs

Table 1: This Table Shows how Conventional Treatments May Compromise Fertility Through Direct Effects on Reproductive Cells, with Potential Long-Term Impacts.

Specific Risks According to Type of Treatment

The risk of infertility varies depending on the type of treatment received and the individual sensitivity of the patient. In the case of chemotherapy, alkylating agents, such as cyclophosphamide, are especially dangerous for fertility due to their ability to damage the DNA of germ cells. In young women, this treatment can induce premature ovarian failure, limiting the chances of subsequent pregnancy [19]. In men, the use of alkylating agents is associated with a significant reduction in sperm production and with possible irreversible damage to spermatogonial cells [15].

Regarding radiotherapy, the damage depends on the dose and location of the treatment. Radiation to the pelvic area can directly affect reproductive organs, while radiation to other areas, such as the brain, can alter hormonal function, impacting fertility through indirect mechanisms [20].18 Additionally, patients receiving radiotherapy to the pelvic area have an increased risk of gonadal damage, which further complicates the chances of maintaining fertility after treatment [21].

Long-Term Effects of Cancer Treatments on Fertility

The effects of cancer treatments are not only immediate, but can also have long-term consequences on fertility and overall reproductive health. Research suggests that cancer survivors in adolescence and young adulthood are at increased risk for infertility and may experience difficulties achieving successful pregnancies in adulthood [22]. Furthermore, exposure to chemotherapy and radiation therapy during these critical stages of development can lead to accelerated reproductive aging, affecting reproductive capacity at early ages [20].

Cohort studies have shown that young people who survived childhood or adolescent cancer face elevated rates of reproductive complications and may be less likely to conceive without assistance [23]. This long-term impact on fertility not only affects the biological aspects of reproduction, but also the psychological and social aspects of patients, who may experience feelings of loss and anxiety related to their expectations of forming a family in the future [21].

Considerations in Fertility Management during Conventional Treatments

For young cancer patients, it is essential to have management strategies that seek to preserve fertility before starting conventional treatments. Fertility preservation has become a priority in the comprehensive management of cancer in adolescents and young adults, and techniques such as egg and sperm cryopreservation offer alternatives for those who wish to keep their reproductive options open [15].

However, there are barriers and challenges in the implementation of these techniques. Often, the lack of adequate information and counseling on fertility preservation options limits patients' access to these procedures, especially when the diagnosis is urgent and treatment must be started quickly [17]. In addition, the costs of preservation procedures are not always covered by health systems, which represents an additional difficulty for patients and their families [22].

Minimizing Reproductive Risks during Treatment

Reduction of Treatment Intensity

One of the strategies to minimize reproductive risks during cancer treatment is to reduce the intensity of treatment, either by decreasing the number of chemotherapy cycles or adjusting the radiation dose. Reducing the intensity may decrease damage to reproductive cells and reduce the risk of premature ovarian failure and azoospermia in young patients. However, this approach has limitations, as excessive reduction in dose or number of cycles could compromise the effectiveness of cancer treatment [24].

The benefits of reducing treatment intensity must be carefully balanced against the potential risks of reduced efficacy in controlling cancer. In some cases, oncologists may opt for a lower dose or fewer cycles in low-risk patients or in early stages of the disease, as long as this does not jeopardize long-term survival [25]. However, in highly aggressive cancers, this strategy may not be feasible and alternatives should instead be considered to protect fertility without compromising oncologic treatment [26].

Protective Measures and Fertility Preservation Options

Cryopreservation Techniques for Sperm, Eggs and Embryos

Cryopreservation is the most established and widely used technique to preserve fertility in cancer patients. It consists of freezing reproductive cells, such as sperm, eggs and embryos, before starting treatment. In the case of men, sperm cryopreservation is an effective and simple option that allows storing semen samples for future use. In women, egg or embryo cryopreservation is a viable option, although it requires a prior ovarian stimulation process, which can delay the start of cancer treatment [27].

Cryopreservation techniques offer a safe option for patients who wish to maintain their reproductive potential after cancer treatment. However, in very young patients or those with advanced cancers requiring immediate treatment, cryopreservation may not be feasible due to the time required for ovarian stimulation in women or the lack of reproductive maturity in some cases [28]. (Table 2)

Table 2: Strategies for Fertility Preservation in Cancer Patients

Strategy	Description	Advantages	Limitations
Sperm/Egg	Storage of Reproductive Cells	Safe Procedure, High Effectiveness	It Requires Time and Reproductive Maturity
Use of GnRH	Protection of Ovaries by Inducing Hibernation	Possible Reduction of Ovarian Damage during Chemotherapy	Variable Efficacy Depending on the type of Cancer and the Individual Response of each Patient
DEX	Use of Agents Directed Against Cancer Cells	Less Damage to Reproductive Cells	None Specified
Reduction of Treatment Intensity	Adjustment of Therapy Cycles or Doses to Minimize Damage to Germ Cells	Lower Potential Risk to Fertility	Requires Rigorous Clinical Criteria to Avoid Compromising the Efficacy of Treatment

Table 2: Comparison of Strategies for Fertility Preservation, Highlighting Potential Benefits and Limitations of Each Approach

Use of Hormonal and Non-Hormonal Protection Strategies during Treatment

Hormonal strategies, such as the use of gonadotropin-releasing hormone (GnRH) analogues, are employed in some patients to protect the ovaries during chemotherapy. These drugs induce a state of "hibernation" in the ovaries, which may reduce the impact of chemotherapy on ovarian function. Although data on their efficacy are mixed, some studies have shown a decreased risk of ovarian failure in women treated with GnRH during chemotherapy [26,29].

In addition to hormonal strategies, there are non-hormonal methods of protection, such as the use of tissue protectors or precision radiotherapy techniques that limit exposure to the reproductive organs. These techniques seek to minimize direct damage to the ovaries or testicles during treatment, thus reducing the risk of infertility without affecting the effectiveness of the oncological treatment [30].

Precision and Biological Therapy Approaches Such as DEXy Immunotherapy

Biological and precision therapy offer a promising approach to reduce gonadotoxicity in young cancer patients. Unlike traditional chemotherapy, which affects both cancer cells and healthy cells, biological precision therapy of the immunotherapy type , uses targeted agents that attack specific cancer cells with fewer side effects on other tissues in the body. This allows for better protection of reproductive cells and a lower chance of infertility [25].

Targeted therapies, such as tyrosine kinase inhibitors and monoclonal antibodies, have been shown to reduce the risk of ovarian failure and azoospermia compared to conventional chemotherapy alkylating agents [30]. However, these therapies are not available for all cancer types, and in some cases, high cost and limited availability may restrict their use [31]. As precision medicine continues to evolve, more biologic therapy options are likely to emerge that may offer less damaging alternatives to fertility. (Table 3)

Table 3: Comparison between DEX Immunotherapy and Conventional Treatments in Terms of Fertility

Type of Treatment	Potential Risk of	Impact on Ovarian Reserve and	Level of Systemic Damage
DEX	Low Potential	Minimum	Low
Chemotherapy	Potentially High, with Systemic Impact	Significant Reduction	Potentially High
Radiotherapy	Potentially High, Especially in Pelvic Treatments	Possible Serious Damage, Especially to the Pelvic Region	Potentially High

Table 3: Comparison between DEX immunotherapy and Conventional Treatments in Terms of Reproductive Function Preservation, Highlighting the Potentially Lower Gonadotoxicity of DEX.

Potential role of DEX Immunotherapy in Fertility Preservation

Introduction to DEX Immunotherapy and Its Potential in Fertility Preservation

Dendritic) immunotherapy cell-based Exosome DEX immunotherapy has been proposed as a promising therapy in the treatment of advanced cancers due to its ability to stimulate a specific immune response against tumor cells. Unlike conventional treatments such as chemotherapy and radiotherapy, which affect both cancer cells and healthy cells, DEX immunotherapy uses components of the immune system to specifically attack malignant cells, which could significantly reduce side effects and the risk of gonadotoxicity in young patients [32].

This therapy, not being cytotoxic to the same degree as traditional chemotherapeutic agents, offers the possibility of effectively treating cancer while preserving the functionality of reproductive cells. Some studies suggest that DEX immunotherapy could be a viable option for cancer patients who wish to preserve their fertility, especially those who require prolonged treatments [33].

Mechanism of Action of DEX Immunotherapy and Its Advantages for Fertility Preservation

DEX immunotherapy is based on the use of dendritic cells and exosomes to present tumor-specific antigens to the immune system, thereby triggering an immune response directed against cancer cells without damaging other tissues. This mechanism of action is different from that of chemotherapy, which causes direct damage to all rapidly dividing cells, including germ cells. Consequently, the use of DEX immunotherapy reduces the risk of ovarian and testicular damage compared to conventional treatments [34,35].

Furthermore, DEX therapy can be customized to fit the characteristics of each patient's tumor, allowing for greater precision in treatment and a reduction in unwanted side effects, including those affecting fertility. This specificity of immunotherapy could offer a considerable advantage in young patients, who often experience a significant emotional burden due to the possibility of losing their reproductive capacity due to oncological treatments [36]. (Table 4)

Table 4: Clinical Effects of DEX Immunotherapy on Fertility Preservation

Effect of DEX	Mechanism of Action	Potential Benefit in Fertility	Clinical Evidence
Protection of Reproductive Cells	Targeted Attack on Tumor Cells	Less Damage to Reproductive Cells	Studies in Preclinical Models and Reviews
Reduction of Systemic Toxicity	Minimizes Side Effects on Unaffected Organs	Lower Risk of Ovarian Failure	Preliminary Results in Cohort Studies
Personalization of Treatment	Specific Adaptation to the Patient's Immunological Profile	Additional Protection for Fertility	Data in Development, Ongoing Studies

Table 4: Mechanisms of Action of DEX Immunotherapy and its Potential Benefits in Fertility Preservation

Clinical Evidence and Current Studies on DEX Immunotherapy

in Young Patients

To date, there are several ongoing clinical studies investigating the use of DEX immunotherapy in the treatment of different types of cancer. Although specific data on its effectiveness in preserving fertility are still limited, preliminary results indicate that this therapy may offer a less invasive and less harmful alternative in terms of reproductive health [37]. A recent analysis highlights that patients treated with DEX immunotherapy experience fewer fertility-related side effects compared to those treated with conventional chemotherapy, which represents an important advance in reproductive oncology [29].

Furthermore, some studies have evaluated the long-term effects of immunotherapy on reproductive function and have found no significant evidence of gonadal damage, suggesting that DEX therapy could be a viable option for patients interested in preserving their fertility [38]. However, further specific studies are required to confirm these findings and determine best practices to maximize the benefits of this therapy in terms of fertility preservation.

Future Prospects and Development of Treatment Protocols Including Dex Immunotherapy

The development of treatment protocols incorporating DEX immunotherapy and personalized medicine approaches represents a significant opportunity to improve treatment options in young cancer patients. The possibility of combining this therapy with other fertility preservation strategies, such as cryopreservation or the use of GnRH analogues, could further increase the likelihood of patients maintaining their reproductive capacity after treatment [29,33].

Furthermore, the implementation of DEX immunotherapy in clinical practice could transform the approach to oncology in patients of childbearing age, allowing effective cancer treatment without compromising reproductive health. Future research should focus on establishing specific protocols for young patients and on evaluating the effectiveness of DEX immunotherapy in combination with other fertility preservation techniques to maximize outcomes [30,34].

Future Directions and Clinical Implications

Research Needs and Gaps

There are significant gaps in research on the impact of DEX immunotherapy on the reproductive health of young cancer patients. Despite advances in reproductive oncology, additional studies are needed to comprehensively evaluate how DEX may influence fertility preservation and long-term gonadal function [36]. Future research should focus on identifying optimal doses and assessing the safety and effectiveness of DEX compared to other fertility preservation approaches. It is also crucial to investigate how DEX interacts with other preservation techniques, such as cryopreservation, and determine whether their combination can improve fertility outcomes in young patients [37,39].

Another relevant aspect for future research is the long-term impact of DEX on fertility in patients who have achieved cancer remission. Current studies have not provided sufficient data on how this therapy might affect patients in terms of reproductive function in the years following treatment, which is a priority in oncofertility research [38]. (Table 5)

Table 5: Future Directions and Research Needs in Oncofertility with DEX Immunotherapy

Research Area	Specific Objective	Potential Importance in Fertility Preservation	Current Obstacles
Optimal Dosage of DEX	Identify Ideal Treatment Levels	Maximize Efficacy and Minimize Adverse Effects	Limited Data, Individual Variability
Interaction with	Evaluate Synergy between DEX and	Increase Potential Success in Fertility Preservation	Lack of Longitudinal Studies and Lack of Standard Combination Protocols
Long-term Effects on Fertility	Post-DEX Reproductive Function Monitoring	Ensuring Long-Term Reproductive Health	Resources For Long-Term Studies

Table 5: Key Research Areas in the Use of DEX Immunotherapy for Fertility Preservation, Addressing Objectives and Current Challenges, Especially in Combination with Cryopreservation Techniques.

Practical Guidelines for Clinicians

For clinicians, it is essential to have clear protocols and practical guidelines that integrate fertility assessment in young cancer patients and consider the use of DEX as a viable option. It is recommended that all patients of childbearing potential receive fertility counselling before starting treatment and are informed about available preservation options, including immunotherapy therapies such as DEX [40]. This is especially relevant in cases where conventional treatments, such as chemotherapy, may compromise fertility in the long term.

The proposed protocols should also include a comprehensive assessment of reproductive health before treatment, in order to adapt preservation options according to the individual characteristics and preferences of each patient [41]. In addition, long-term follow-up of patients treated with DEX is suggested to monitor their reproductive function and assess possible adverse effects. These guidelines should be based on international recommendations and the most recent advances in oncofertility , adapting to the particularities of each case [42].

Conclusion

This article has explored fertility preservation options in young cancer patients, highlighting the impact of conventional treatments and the potential of DEX immunotherapy. DEX emerges as a promising alternative that could reduce gonadotoxicity compared to traditional chemotherapy, offering a less invasive option to preserve fertility while effectively treating cancer [43,45]. However, the implementation of this therapy still requires further research and the development of specific clinical protocols.

Continued research into DEX and its impact on reproductive health, as well as into the integration of fertility preservation strategies into oncologic treatment, is critical. Clinicians should adopt a patient-centered approach, offering early, personalized fertility counseling and exploring innovative options such as DEX. This approach will not only improve patient health outcomes, but will also contribute to a better long-term quality of life for

those who wish to preserve their reproductive capacity [44,47]. (Figure: 1)

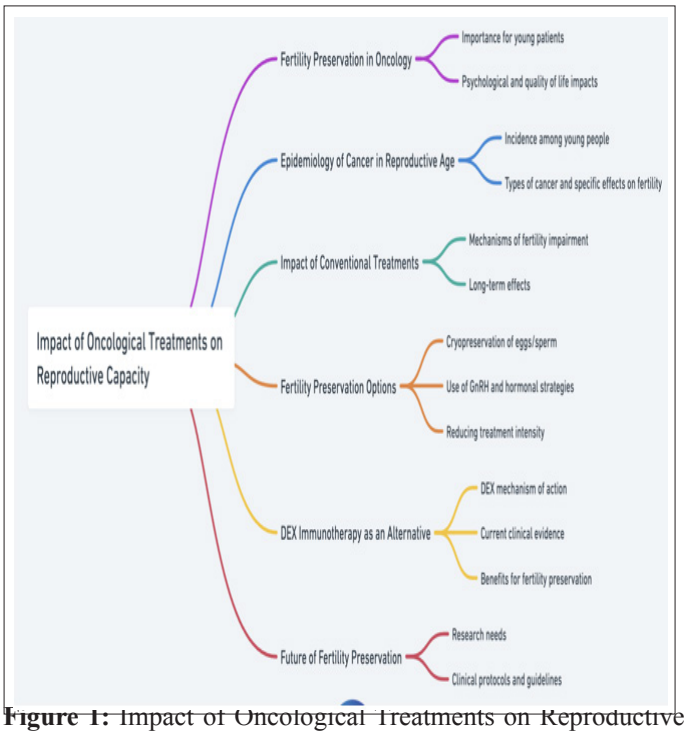

Figure 1: Impact of Oncological Treatments on Reproductive Capacity and Fertility Preservation

Figure 1: This Mind Map Summarizes the Main Factors and Approaches for Fertility Preservation in Young Cancer Patients. It Highlights the Impact of Conventional Treatments, Preservation Alternatives, and the Potential of DEX Immunotherapy as a Less Harmful Option for Fertility. Additionally, it outlines Future Research Needs and the Importance of Clinical Protocols in Oncofertility.

Abbreviations:

- **DEX:** Dendritic Cell-based Exosome Immunotherapy
- **GnRH:** Gonadotropin-Releasing Hormone
- **CIK:** Cytokine-Induced Killer Cells
- **Cryo:** Cryopreservation Techniques
- **IVF:** In Vitro Fertilization
- **QoL:** Quality of Life
- **OGRD:** Orlando Global Research and Development
- **USA:** United States of America
- **SKN:** St. Kitts and Nevis
- **JSMR:** Journal of Sexual Medicine & Research

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