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Article

Correlation of docetaxel administration duration, dosage, and patient age with epiphora severity: a retrospective observational study in breast cancer patients

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ABSTRACT

Epiphora, or excessive tearing, is a frequent yet under-recognised adverse effect of docetaxel, a taxane-based chemotherapeutic agent used in breast cancer treatment. Inflammatory and fibrotic changes within the lacrimal drainage system are hypothesised as the primary mechanisms. This study aimed to evaluate the correlation between docetaxel administration duration and epiphora severity, alongside the impact of cumulative dosage and patient age. A retrospective observational study was conducted at Mohammad Hoesin Hospital Palembang, involving 25 breast cancer patients who reported epiphora during docetaxel chemotherapy. Patients with pre-existing ocular conditions, prior lacrimal surgery, or concurrent use of epiphora-inducing medications were excluded. Epiphora severity was assessed using the Munk score, and statistical analyses included Pearson s correlation and multiple regression. Findings demonstrated a strong positive correlation between epiphora severity and docetaxel duration ($r = 0.645$, $p < 0.05$), cumulative dosage ($r = 0.618$, $p < 0.05$), and patient age ($r = 0.703$, $p < 0.05$). Limitations include the retrospective design, small sample size, and subjective assessment tools. These results emphasise the importance of monitoring for epiphora during docetaxel therapy, with early ophthalmologic intervention recommended. Further prospective studies are needed to clarify pathophysiological mechanisms and optimise management strategies for chemotherapy-induced epiphora.

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Introduction

Epiphora, or excessive tearing, is a common yet underrecognized adverse effect of chemotherapy that can significantly impact patients quality of life (Kintzel et al., 2006; Stoicescu et al., 2023). It results from increased tear production or impaired tear drainage due to lacrimal system dysfunction (Kashkouli et al., 2016; Schaefer & Schaefer, 2020). Among chemotherapeutic agents, taxane-based drugs such as docetaxel have been increasingly implicated in causing epiphora through lacrimal drainage obstruction (Gupta & Gupta, 2021; Maganti et al., 2021; Sohrevardi et al., 2024). Studies suggest that up to 30% of patients receiving docetaxel experience epiphora to some degree, though the condition is frequently underreported in clinical settings (van Eijk et al., 2022).

Docetaxel is a widely used chemotherapeutic agent for breast cancer (Crown et al., 2004; Figgitt & Wiseman, 2000; Lyseng-Williamson & Fenton, 2005; Smith et al., 2002), acting by stabilizing microtubules and preventing mitotic cell division (Hernández-Vargas et al., 2007; Mann et al., 2020; Noguchi, 2006; Shalli et al., 2005). However, its effects extend beyond tumor suppression, as it can induce systemic toxicity, including ophthalmologic complications (Dalvin et al., 2018; Fraunfelder et al., 2014; Grant & Schuman, 1993; Schmid et al., 2006). In particular, docetaxel is known to cause lacrimal drainage obstruction due to inflammatory and fibrotic changes in the lacrimal duct epithelium, leading to tear retention and chronic tearing (Esmaeli, Burnstine, et al., 2003; Esmaeli, Hidaji, et al., 2003; Gupta & Gupta, 2021). The underlying pathophysiological mechanisms involve direct cytotoxicity, chronic inflammation, and fibrosis within the lacrimal drainage system, contributing to progressive obstruction over the course of treatment (Ogawa et al., 2021; Pakdel & Kashkouli, 2009).

The Munk score was used to determine the intensity of the epiphora (Munk score: 0, no epiphora; 1 for occasional epiphora requiring dabbing <2 times/day; 2 for dabbing 2 4 times/day; 3 for dabbing 5 10 times/day and 4 for dabbing >10x/day or constant epiphora. The Munk score is widely used to assess disorders of the lacrimal drainage system. Although this method is subjective, according to some authors it allows relatively easy identification of patients with mild symptoms (Sieśkiewicz et al., 2021).

G McGwin et al reported that Docetaxel mostly used for breast cancer (48,8%) and were more likely to include lacrimal conditions with PRRs 2,47 (proportionate reporting ratio) compared to paclitaxel used (McGwin Jr et al., 2023). Dacryostenosis the mostly addverse effect observed PRR 19,54, lacrimation increased PRRs 3,2 (McGwin Jr et al., 2023). Identifying the exact cause of epiphora is sometimes difficult and in some cases can only be confirmed by a stepwise approach to elimination of the causative factors for epiphora (Sodhi et al., 2022; Swampillai & McMullan, 2012).

Despite reports of docetaxel-induced epiphora, there remains a lack of comprehensive analysis regarding the factors influencing its severity. Prior studies have primarily focused on qualitative descriptions of the condition, without quantifying the correlation between treatment duration, cumulative dosage, and patient-specific risk factors such as age. Furthermore, limited data exist on the threshold duration of docetaxel therapy at which the risk of severe epiphora becomes clinically significant. Given the potential impact on visual function, quality of life, and even treatment adherence, understanding these associations is crucial for optimizing patient management.

This study aims to bridge the existing knowledge gap by evaluating the correlation between docetaxel administration duration and epiphora severity in breast cancer patients. Additionally, we investigate the role of cumulative dosage and patient age in exacerbating epiphora symptoms. We hypothesize that prolonged docetaxel exposure, higher cumulative dosage, and advanced patient age are independently associated with increased severity of epiphora. Furthermore, we aim to identify a threshold duration beyond which the likelihood of severe epiphora significantly increases, thereby providing critical insights into preventive and therapeutic strategies for affected patients.

Methods

Cross sectional study design with correlation approach in breast cancer patient using docetaxel with epiphora complaint in Mohammad Hoesin Hospital Palembang that met the inclusion and exclusion criteria within March 2022 until August 2022. Epiphora degree based on Munk's score. Statistical Analysis using SPSS with chi square and McNemar to bivariate analysis and multiple linear regression for multivariate analysis.

This study employs a cross-sectional design with a correlational approach to assess the relationship between docetaxel treatment duration and epiphora severity in breast cancer patients. A cross-sectional design was chosen due to its feasibility in analyzing multiple variables within a defined study period. Although a longitudinal design may provide more insights into symptom progression, our study aims to establish an initial correlation that can inform future prospective research.

The study was conducted at Mohammad Hoesin Hospital Palembang, with breast cancer patients undergoing docetaxel chemotherapy as the target population. A purposive sampling technique was used to select patients meeting specific clinical criteria, ensuring the inclusion of individuals with documented complaints of epiphora. The sample size was determined based on statistical power calculations, considering an expected correlation coefficient of 0.6, a significance level ( ) of 0.05, and a statistical power ( ) of 0.8.

Patients were included if they were diagnosed with breast cancer and received docetaxel chemotherapy, reported symptoms of epiphora during or after treatment and had no prior history of lacrimal drainage disorders before chemotherapy initiation. Patients were excluded if they had pre-existing ocular surface diseases (e.g., dry eye syndrome, blepharitis), underwent prior lacrimal surgery or had a history of nasolacrimal duct obstruction, were receiving other medications known to induce epiphora (e.g., epidermal growth factor receptor inhibitors) and had received previous radiation therapy to the head and neck region.

Epiphora severity was assessed using both subjective and objective methods. The Munk score was used for patient-reported symptom severity, while the fluorescein dye disappearance test (FDDT) was performed to objectively evaluate lacrimal drainage function. Data on docetaxel administration, including duration and cumulative dosage, were collected from medical records.

Descriptive statistics were used to summarize baseline characteristics. Pearson s correlation and multiple linear regression analysis were employed to assess relationships between docetaxel treatment duration, cumulative dosage, patient age, and epiphora severity. To ensure validity, normality and linearity assumptions were tested prior to conducting Pearson s correlation. If data were found to be non-normally distributed, Spearman s rank correlation was used instead. Confounding variables such as age, dosage, and pre-existing conditions were controlled using multivariate regression analysis.

The study was approved by the hospital s ethics committee, and all patients provided informed consent before participation. Confidentiality and data protection protocols were strictly maintained throughout the study.

Results and Discussion

Result

The majority of the subjects were aged ≤50 years as many as 21 (84%) subjects. The most dose of docetaxel was 70 mg in 20 (80%) subjects. The duration of docetaxel administration was 2, 4 and 6 cycles where most of the subjects had received docetaxel for 2 cycles, namely 21 (84%) subjects. The highest degree of epiphora based on Munk's score was grade 1, namely 18 (72%) subjects can be seen in Table 2.

Table 1. Shapiro-wilk Test of Normality

Data	p-value
Age	.006
Docetaxel dose	.000
Docetaxel duration	.000

Table 2. Baseline Characteristics of Breast Cancer Patient

Baseline Characteristics	n (%)	Median (min-max)
Age		45 (23-64) years
50 years	21(84%)	
>50 years	4(16%)	
Breast Cancer Type		
Invasive ca Mammae	25 (100%)	

Baseline Characteristics	n (%)	Median (min-max)
Docetaxel dose		70 (40-114) mg
40 mg	1 (4%)	
70 mg	20 (80%)	
72 mg	2 (8%)	
99 mg	1 (4%)	
114 mg	1 (4%)	
Docetaxel Duration		6 (6-18) weeks
2 cycles	21(84%)	
4 cycles	3(12%)	
6 cycles	1(4%)	
Munk Score		1 (0-2)
0	4(16%)	
1	18(72%)	
2	3(12%)	

In this study, subjects aged 50 years, there were 18(85.7%) subjects who received docetaxel for 2 cycles, 2 (9.5%) subjects received docetaxel for 4 cycles and 1 (4.8%) subject received docetaxel for 6 cycles, whereas in subjects aged >50 years, 3 (75%) subjects received docetaxel for 2 cycles and 1 (25%) subject received docetaxel for 4 cycles.

Table 3. Identification of the effect of duration of docetaxel administration in breast cancer patients who experience epiphora

	Docetaxel Duration (Weeks)		
	2 cycles	4 cycles	6 cycles
Age			
50 years	18 (85,7%)	2 (9,5%)	1 (4,8%)
>50 years	3 (75%)	1 (25%)	0 (0%)
Breast Cancer Type			
Invasive Ca Mammae	21 (84%)	3 (12%)	1 (4%)

In this study, the most Docetaxel was given with a dose of 70mg, namely in 18 patients given for 2 cycles, one patient with Docetaxel 40mg was given for 2 cycles, two patients were given Docetaxel 72mg for 2 cycles while one patient was given Docetaxel 99mg and 114 mg for 4 cycles respectively (Figure 1).

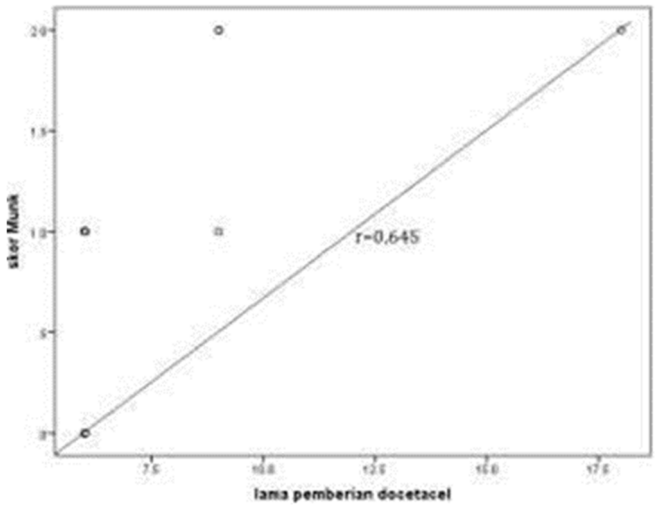

Figure 1 Correlation of duration of docetaxel administration to the degree of epiphora

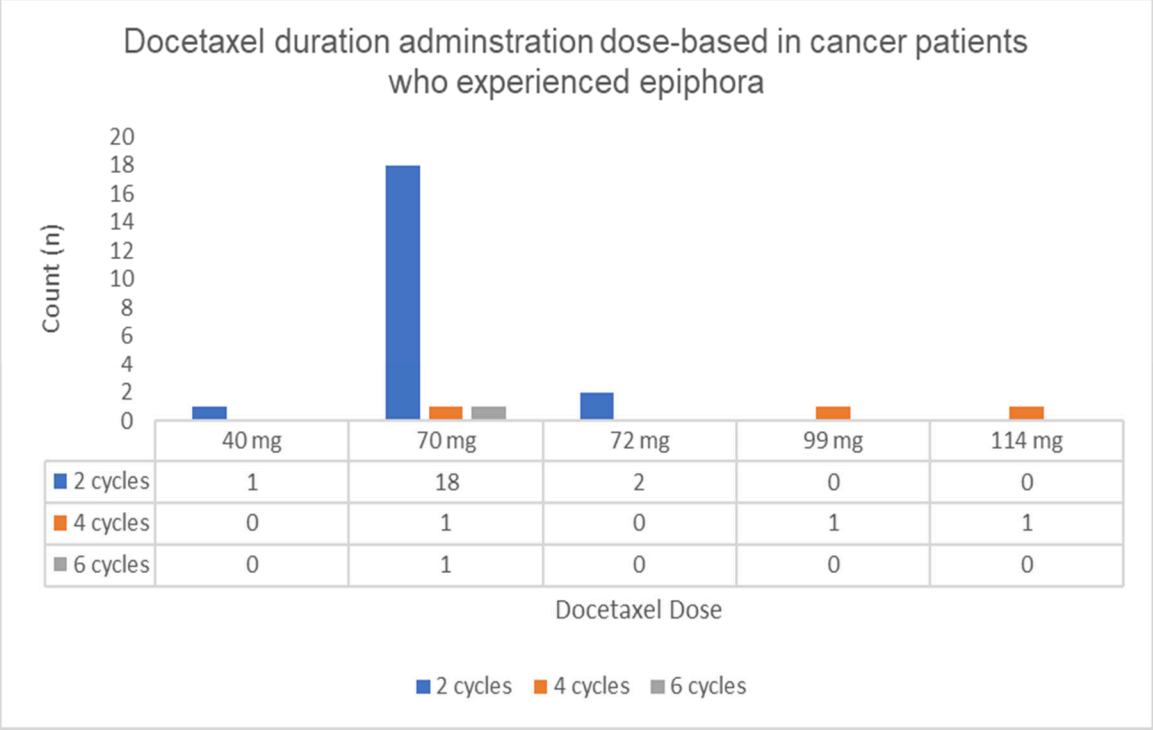

Figure 2 Docetaxel dose and duration

The results of the correlation test showed that there was a significant correlation (p=0.021) between the duration of docetaxel administration and the degree of epiphora with a strong correlation (r=0.645). Can be seen in Table 3. Correlation graph can be seen in Figure 2.

Table 4. Correlation of duration of docetaxel administration to the degree of epiphora

	Docetaxel Duration (Weeks)			P	r
	2 cycles	4 cycles	6 cycles		
Munk Score				0,021	0,645
0	4 (100%)	0 (0%)	0 (0%)		
1	17 (94,4%)	1 (5,6%)	0 (0%)		
2	0 (0%)	2 (66,7%)	1 (33,3%)		

Factors that correlate with the degree of epiphora based on the Munk Score in breast cancer patients can be seen in Table 4. It was found that the degree of epiphora was strongly correlated (r=0.703) with age, strongly correlated (r=0.618) with docetaxel dose, and strongly correlated (r=0.634) with docetaxel administration time.

Table 5. Multivariate linear regression analysis of factors associated with Munk's score (degree of epiphora) in breast cancer patients

	B	SE	Beta	P	r
Constant	1.325	0.252	5.269	0.000	
Age	0.018	0.004	4.423	0.000	0.703
Docetaxel Dose	0.011	0.003	3.513	0.002	0.618
Docetaxel duration	0.076	0.027	2.822	0.011	0.634

Discussion

Most of the subjects were aged 50 years, consisting of 21 (84%) subjects with a median of 45 years. The most dose of docetaxel was 70 mg in 20 (80%) subjects. The most duration of docetaxel administration was 2 cycles (84%). The highest degree of epiphora based on Munk's score was grade 1 (72%). A similar study conducted by Ma et al in 2020 found that out of 200 breast cancer patients

who received docetaxel therapy, 22(48.9%) subjects were aged <40 years, 38 (64.4%) subjects were aged 41-50 years, 33 (55.9%) of the subjects aged 51-60 years and 37 (18.5%) of the subject were >60 years old (Ma et al., 2020). In a meta-analysis conducted by Stoicescu et al in 2021, it was found that from 15 studies, 6 studies examined the relationship between dry eyes and treatment docetaxel based on weekly docetaxel administration with an average dose of 33.6 mg/m2 ± 2, and 9 studies of docetaxel therapy given once every 1 cycle with an average dose of 26.11 mg/m2 ± 26.11 (Stoicescu et al., 2021).

In this study, subjects aged 50 years, there were 18 (85.7%) subjects who received docetaxel for 2 cycles, 2(9.5%) subjects received docetaxel for 4 cycles and 1 (4.8%) subject received docetaxel for 6 cycles, whereas in subjects aged >50 years, 3 (75%) subjects received docetaxel for 2 cycles and 1 (25%) sample received docetaxel for 4 cycles. A similar study conducted by Erna et al also found that 16 (20%) subjects received chemotherapy duration of 2 cycles, 4 cycles and 5 cycles respectively, 20 (25%) subjects received 3 cycles of chemotherapy and 12 (15%) of the subject received 6 cycles of therapy.6 Research conducted by Ma et al in 2020 stated that 107 (53.5%) of the subjects had been given docetaxel for 4 cycles and 93 (46.5%) of the subjects received >4 cycles of therapy (Ma et al., 2020). Rzeszotarska et al in 2019 stated that the duration of docetaxel administration was carried out based on an indication of the severity of breast cancer but this poses a risk for several eye-related conditions such as conjunctivitis, epiphora and other dry eye syndromes (Rzeszotarska et al., 2019).

In this study, the results of the correlation test showed that there was a significant correlation (p=0.021) between the duration of docetaxel administration and the degree of epiphora with a strong correlation (r=0.645). In line with this study, Ma et al in 2020 found that there was a significant relationship between the duration of docetaxel administration and a strong correlation (r>0.6). A systematic review study conducted by Canino et al in 2022 also concluded that the longer the docetaxel chemotherapy cycle, the higher the risk of experiencing dry eye syndrome (Canino et al., 2022). Consistent with this study, Stoicescu et al 2021 found that there was a significant relationship in multivariate analysis with high correlation strength (r> 6) between the incidence of epiphora and the duration of docetaxel administration and concluded that the longer docetaxel is given, the more at risk of experiencing epiphora (Stoicescu et al., 2021).

Epiphora is associated with repeated weekly docetaxel administration and long chemotherapy cycles. These adverse effects can interfere with activities of daily living and have a negative impact on quality of life. Epiphora may be an adverse effect of medication that goes unreported because of the lack of recognition by clinicians and the embarrassment of sufferers associated with epiphora that appears to be out of control. The use of weekly docetaxel chemotherapy increased; therefore, sufferers must be given information to recognize and report signs and symptoms of epiphora (Kintzel et al., 2006).

Canino et al in 2022 stated that epiphora and conjunctivitis were side effects (> 5%) caused by administration of pertuzumab chemotherapy combined with trastuzumab and chemotherapeutic agents from the taxane group. The length of the chemotherapy cycle and the dose of chemotherapy are the triggering factors for side effects on the eye (Canino et al., 2022). Galindo-Fereiro et al in 2021 also found a significant correlation between the duration of docetaxel use and the incidence of epiphora on the upper and lower eyelids and concluded that it induces significant inflammation and stromal fibrosis in the mucous layer of the lacrimal drainage apparatus (Galindo-Ferreiro et al., 2021).

Conclusion

Our study establishes a significant correlation between the duration of docetaxel administration and the severity of epiphora in breast cancer patients. These findings highlight the importance of recognizing chemotherapy-induced ophthalmologic side effects and their potential impact on patient well-being. Given that epiphora can interfere with daily activities and diminish quality of life, routine ophthalmologic assessment should be considered for patients undergoing prolonged docetaxel therapy. Clinicians should be aware of this adverse effect and proactively counsel patients about its potential onset and severity.

Furthermore, our findings underscore the need for preventive measures, such as early detection of mild epiphora, timely referral to ophthalmologists, and potential modifications in chemotherapy regimens for patients at high risk of severe epiphora. Future research should explore targeted interventions to mitigate epiphora severity, including the role of corticosteroids, lacrimal stents, or alternative chemotherapeutic strategies that minimize ocular toxicity. By integrating ophthalmologic monitoring into oncology care, treatment adherence and overall patient comfort can be improved, ultimately optimizing outcomes for breast cancer patients receiving docetaxel.

References

Canino, F., Omarini, C., Cerma, K., Moscetti, L., Tornincasa, A., Trudu, L., Dominici, M., & Piacentini, F. (2022). Ocular toxicity in breast cancer management: manual for the oncologist. *Clinical Breast Cancer*, *22*(4), 289 299.

Crown, J., O Leary, M., & Ooi, W.-S. (2004). Docetaxel and paclitaxel in the treatment of breast cancer: a review of clinical experience. *The Oncologist*, *9*(S2), 24 32.

Dalvin, L. A., Shields, C. L., Orloff, M., Sato, T., & Shields, J. A. (2018). Checkpoint inhibitor immune therapy: systemic indications and ophthalmic side effects. *Retina*, *38*(6), 1063 1078.

Esmaeli, B., Burnstine, M. A., Ahmadi, M. A., & Prieto, V. G. (2003). Docetaxel-induced histologic changes in the lacrimal sac and the nasal mucosa. *Ophthalmic Plastic & Reconstructive Surgery*, *19*(4), 305 308.

Esmaeli, B., Hidaji, L., Adinin, R. B., Faustina, M., Coats, C., Arbuckle, R., Rivera, E., Valero, V., Tu, S., & Amir Ahmadi, M. (2003). Blockage of the lacrimal drainage apparatus as a side effect of docetaxel therapy. *Cancer: Interdisciplinary International Journal of the American Cancer Society*, *98*(3), 504 507.

Figgitt, D. P., & Wiseman, L. R. (2000). Docetaxel: an update of its use in advanced breast cancer. *Drugs*, *59*, 621 651.

Fraunfelder, F. T., Fraunfelder, F. W., & Chambers, W. A. (2014). *Drug-Induced Ocular Side effects: clinical ocular toxicology E-Book: clinical ocular toxicology*. Elsevier Health Sciences.

Galindo-Ferreiro, A., de Prado Otero, D. S., Marquez, P. I. G., & Schellini, S. (2021). Recurrent and recalcitrant upper lid cicatricial entropion following combined chemotherapy: Clinical and pathology correlation. *Saudi Journal of Ophthalmology*, *35*(4), 347 349.

Grant, W. M., & Schuman, J. S. (1993). *Toxicology of the eye: effects on the eyes and visual system from chemicals, drugs, metals and minerals, plants, toxins and venoms; also systemic side effects from eye medications* (Vol. 1). Charles C Thomas Publisher.

Gupta, N., & Gupta, N. (2021). Anatomy of Lacrimal Drainage System. *Endoscopic Dacryocystorhinostomy*, 9 21.

Hernández-Vargas, H., Palacios, J., & Moreno-Bueno, G. (2007). Molecular profiling of docetaxel cytotoxicity in breast cancer cells: uncoupling of aberrant mitosis and apoptosis. *Oncogene*, *26*(20), 2902 2913.

Kashkouli, M. B., Zolfaghari, R., Es haghi, A., Amirsardari, A., Abtahi, M. B., Karimi, N., Alemzadeh, A., & Aghamirsalim, M. (2016). Tear film, lacrimal drainage system, and eyelid findings in subjects with anophthalmic socket discharge. *American Journal of Ophthalmology*, *165*, 33 38.

Kintzel, P. E., Michaud, L. B., & Lange, M. K. (2006). Docetaxel-associated epiphora. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, *26*(6), 853 867.

Lyseng-Williamson, K. A., & Fenton, C. (2005). Docetaxel: a review of its use in metastatic breast cancer. *Drugs*, *65*, 2513 2531.

Ma, J., Pazo, E. E., Zou, Z., & Jin, F. (2020). Prevalence of symptomatic dry eye in breast cancer patients undergoing systemic adjuvant treatment: A cross-sectional study. *The Breast*, *53*, 164 171.

Maganti, N., Pathak, C. A., & Burkat, C. N. (2021). Canalicular Stenosis Secondary to Chemotherapeutic Agents. *Advances in Ophthalmology and Optometry*, *6*, 379 389.

Mann, J., Yang, N., Montpetit, R., Kirschenman, R., Lemieux, H., & Goping, I. S. (2020). BAD sensitizes breast cancer cells to docetaxel with increased mitotic arrest and necroptosis. *Scientific Reports*, *10*(1), 355.

McGwin Jr, G., Contorno, T., Vicinanzo, M. G., & Owsley, C. (2023). The Association Between Taxane Use and Lacrimal Disorders. *Current Eye Research*, *48*(9), 873 877.

Noguchi, S. (2006). Predictive factors for response to docetaxel in human breast cancers. *Cancer Science*, *97*(9), 813 820.

Ogawa, Y., Kawakami, Y., & Tsubota, K. (2021). Cascade of inflammatory, fibrotic processes, and stress-induced senescence in chronic GVHD-related dry eye disease. *International Journal of Molecular Sciences*, *22*(11), 6114.

Pakdel, F., & Kashkouli, M. B. (2009). Lacrimal drainage obstruction associated with topical and systemic medications. *Journal of Ophthalmic & Vision Research*, *4*(4), 270.

Rzeszotarska, A., Stodolska-Nowak, A., Kufel-Grabowska, J., Nowakowski, B., & Koci cki, J. (2019). Ocular side effects of the taxane-based chemotherapy do only vascular disorders matter? *OncoReview*, *9*(3 (35)), 59 63.

Schaefer, J. L., & Schaefer, D. P. (2020). Acquired causes of lacrimal system obstructions. In *Smith and Nesi s Ophthalmic Plastic and Reconstructive Surgery* (pp. 521 543). Springer.

Schmid, K. E., Kornek, G. V, Scheithauer, W., & Binder, S. (2006). Update on ocular complications of systemic cancer chemotherapy. *Survey of Ophthalmology*, *51*(1), 19 40.

Shalli, K., Brown, I., Heys, S. D., & Schofield, C. A. (2005). Alterations of -tubulin isotypes in breast cancer cells resistant to docetaxel. *The FASEB Journal*, *19*(10), 1299 1301.

Sie kiewicz, A., yso , T., Rogowski, M., Bielecki, M., Gindzienska-Sieskiewicz, E., Olszewska, E., & Bielecki, P. (2021). Assessment of lacrimal duct patency in patients undergoing endoscopic medial maxillectomy. *Journal of Clinical Medicine*, *10*(2), 245.

Smith, I. C., Heys, S. D., Hutcheon, A. W., Miller, I. D., Payne, S., Gilbert, F. J., Ah-See, A. K., Eremin, O., Walker, L. G., & Sarkar, T. K. (2002). Neoadjuvant chemotherapy in breast cancer: significantly enhanced response with docetaxel. *Journal of Clinical Oncology*, *20*(6), 1456 1466.

Sodhi, M., Yeung, S. N., Maberley, D., Mikelberg, F., & Etminan, M. (2022). Risk of ocular adverse events with taxane-based chemotherapy. *JAMA Ophthalmology*, *140*(9), 880 884.

Sohrevardi, S. M., Zangeneh, M., Owliaey, H., & Sheikhpour, E. (2024). The Evaluation of Ocular Toxicity of Chemotherapy Drugs. *Iranian Journal of Pediatric Hematology and Oncology*, *14*(4), 300 309.

Stoicescu, E. A., Burcea, M., Iancu, R. C., Zivari, M., Popa Cherecheanu, A., Bujor, I. A., Rastoaca, C., & Iancu, G. (2021). Docetaxel for breast cancer treatment-side effects on ocular surface, a systematic review. *Processes*, *9*(7), 1086.

Stoicescu, E. A., Iancu, R. C., Cherecheanu, A. P., & Iancu, G. (2023). Ocular adverse effects of anti-cancer chemotherapy. *Journal of Medicine and Life*, *16*(6), 818.

Swampillai, A. J., & McMullan, T. F. (2012). Epiphora. *British Journal of Hospital Medicine*, *73*(Sup11), C162 C165.

van Eijk, M., Vermunt, M. A. C., van Werkhoven, E., Wilthagen, E. A., Huitema, A. D. R., & Beijnen, J. H. (2022). The influence of docetaxel schedule on treatment tolerability and efficacy in patients with metastatic breast cancer: a systematic review and meta-analysis of randomized controlled trials. *BMC Cancer*, *22*(1), 104.