A SYSTEMATIC REVIEW ON MYC INHIBITION IN THE TREATMENT OF BREAST CANCER

By

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A thesis submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of
Bachelor of Pharmacy

School of Pharmacy
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Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing degree at BRAC University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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Approval

The thesis/project titled “a systematic review on MYC inhibition in the treatment of Breast Cancer” submitted by Kyazze Kevin (21146063) of Spring, 2021 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy on 06-Feb-2025.

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Ethics Statement

This project does not involve any kind of animal and human trial.

Abstract

Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body. Breast cancer originates from the breast tissue especially from the inner lining of milk ducts or the lobules that supply the ducts with milk. The MYC gene plays a central role in the proliferation and malignant transformation of animal and human cells. Most of the human malignancies have been reported to have amplification or over expression of this gene. Use of MESH terms like MYC and Breast cancer were used in the selection of studies which fit the selection criteria for inclusion. It was found out that drug molecules like OMO-103, MYCi975, 3'UTRMYC-18 with OMO-103 showing a 49% reduction in tumor volume reduction as well as other molecular targets like Prox1 in combination with existing chemotherapy have showed promising prognosis in the treatment of breast cancer by reducing the overexpression and amplification of MYC gene and its downstream processes.

Keywords: MYC oncogene; Breast cancer; MYC amplification; MYC overexpression; Hazard Ratio (HR); Tumor volume.

Dedication

I dedicate this thesis to my mother, Nakkazi Christine and to my wife, Nanfuka Milly, without whom, my dream of becoming a pharmacist would have died.

Acknowledgement

Heartfelt gratitude to my supervisor, Ms. Namara Mariam Chowdhury, Senior Lecturer, School of Pharmacy, Brac University, who accepted the responsibility and task to guide me through the completion of this thesis.

I express my sincere thanks to all my faculties who have labored tirelessly to teach, guide and instill knowledge and life skills to me throughout this academic journey period. For all their efforts, I cannot say enough thanks. I will always be grateful.

Lastly but not the least, all thanks, honor, glory and power belong to the Almighty God, who in Him, I live and have my being.

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List of Acronyms

A	Alisertib
BC	Breast Cancer
CT	Computational Tomography
ELISA	Enzyme Linked Immunosorbent Assay
FDR	False Discovery Rate
GFP	Gene Functional Similarity
GSEA	Gene Set Enrichment Assay
GWC	Gene Wide Code
HER2-	Human Growth Factor Receptor 2 Negative
HR	Hazard ratio
HR+	Hormone Receptor Positive
Mg	milligrams
miR	microRNA
mTORi	mammalian Target of Rapamycin
MYC	Myelocytomatosis
P	Paclitaxel
PCR	Polymerase Chain Reaction
PFS	Progression Free State
PTEN	Phosphatase and Tensin Homolog

RNA-seq	RNA-sequencing
TNBC	Tripple Negative Breast Cancer
RECIST	Response Evaluation Criteria in Solid Tumors
FISH	Fluorescence In-Situ Hybridization
WGS	Whole Gene Sequencing
WHO	World Health Organization

Chapter 1

Introduction

1.1 Cancer

According to the National Cancer Institute (2021), cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body. It can start from anywhere in the body. In normal cases, cells grow and multiply according to the body's individual requirements after which they die when they become old or damaged and are replaced by new cells. However, in the case of cancer this normal process of death and replacement is disrupted and cells never die leading to proliferation of abnormal, damaged and even normal cells forming tumors and lumps of tissues.

The abnormal proliferation of cells is referred to as tumor. It is however crucial to distinguish between benign and malignant tumors. With benign tumors there is no invading of surrounding tissues and no spreading to distant areas while as with malignant tumors, cells are capable of invasion and spreading to other body parts (Cooper, 2000).

1.2 Types of Cancer

According to the Cleveland clinic (2021), there are over 100 types of cancer and are usually categorized according to where they start in the body and the types of tissues they affect. There are 3 broad classifications; solid, blood and mixed cancers. Solid cancers are the most common making about 80% to 90% of all cases and include cancers like carcinomas that affect the epithelial tissues like the skin, colon, breast and the sarcoma cancers that affect tissues like the bones and connective tissues. Secondly are the blood cancers that start in the blood cells or the lymphatic system; these include cancers like leukemia, lymphomas and multiple myelomas.

Finally, the third classification is mixed cancers which consist of both the solid and the blood cancers and examples include the carcinoma-sarcomas and adenosquamous carcinoma.

1.3 Grading of Cancer

According to Cancer Research UK (n.d.), cancer can be graded in 2 ways, using the TNM (Tumor Node Metastasis) method and the number system. The number system is the most common, where cancer is divided into 4 stages which is also sometimes written in roman numerals i.e. from stage 1 to stage 4, with stage 1 meaning that the cancer is small and contained within the organ, stage 2 meaning the tumor is larger but has not yet spread, stage 3 meaning that the cancer is larger and may have started to spread into surrounding tissues and stage 4 also called secondary or metastatic cancer meaning that the cancerous cells have started to spread from where it originally started to another body organ. The TNM method or system where T, describes tumor size, N describes if there are any cancer cells in the lymph nodes and M which describes whether the cancer has spread or not is also used. With the numbers attached which signify the severity of the cancer for instance T can be from 0 to 4, N from 0 to 3 and M either 0 or 1 with M0 for instance signifying that the cancer has not spread and M1 signifying that the cancer has spread.

1.4 Causes of Cancer

According to the Mayoclinic (2024), cancer is caused by mutation(changes) to the DNA within cells. Inside the cell DNA are numerous genes that contain instructions that control and regulate the normal functioning of the cells and any errors in the gene sequences due to mutations can result in the cell abnormal functioning which predisposes a person to cancer.

According to Stanford healthcare (n.d.), there is no one single cause of cancer rather a number of factors in combination, interact together and produce cancer. These factors mainly include genetic, environmental and constitutional individual characteristics. Since the main cause of

cancer is mutation in the genes, there are 3 main genes that are mainly involved in cancer and these include oncogenes which regulate normal growth and any mutation in them leads to production of abnormal cells, tumor suppressor genes which have the ability to recognize abnormal and damaged cells and initiate corrective action and mismatch repair genes which recognize errors during DNA replication and correct them and any mutations in any of the those genes leads to cancer.

1.5 Symptoms of Cancer

According to WHO Office for Africa (2024), cancer signs to look for include unusual bleeding, blood in the urine or stool, discharge from any part of the body, sore throat which does not heal, bowel or bladder habits, changes in the consistency, color, shape of stool, lump in the breast or other parts of the body, nagging cough which does not go way and sputum with blood among others. In case of the above signs a person is strongly advised to go for screening and testing of cancers in order to get early treatment as much as possible.

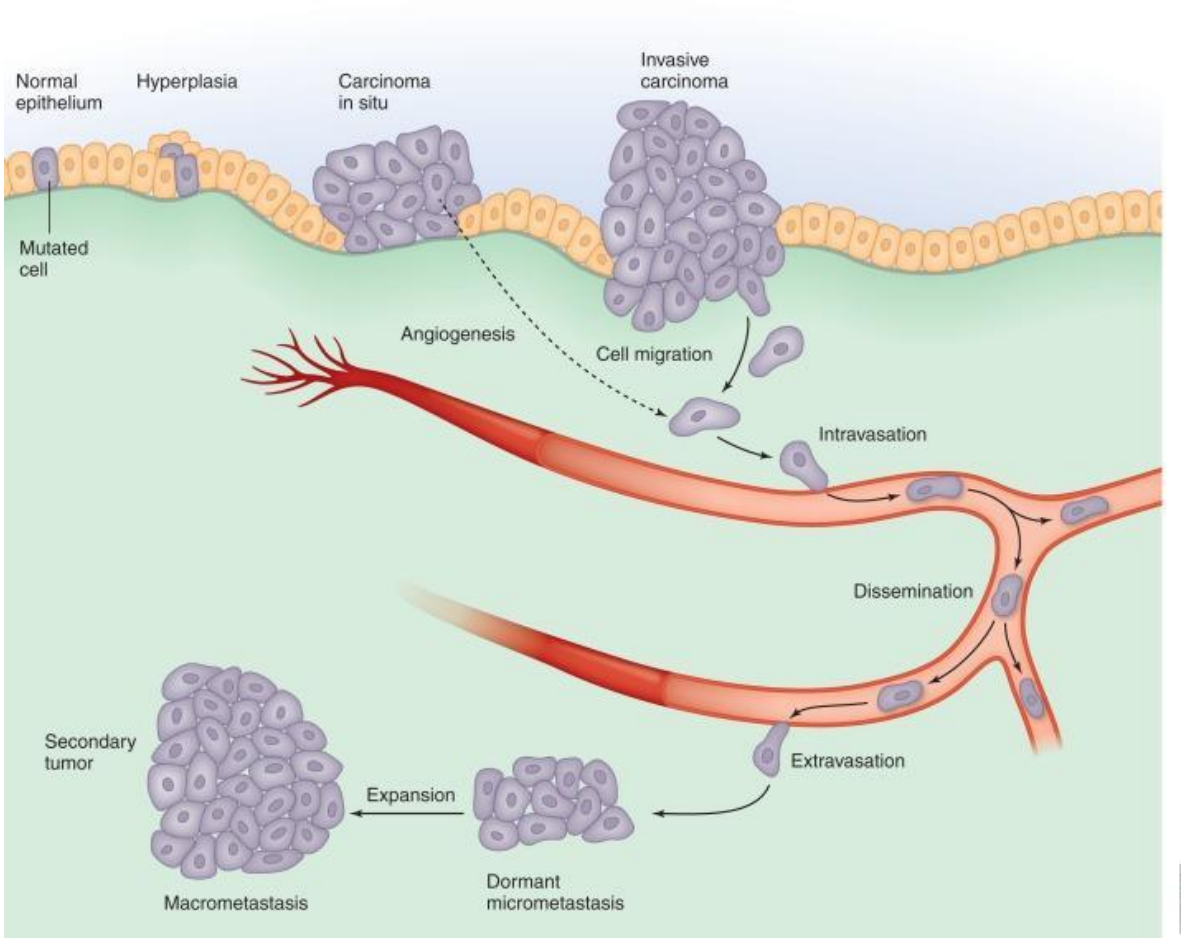

Figure 1. Cancer pathogenesis and development

1.6 Cancer pathogenesis

Figure 1above shows the cancer progress which involves first initiation, promotion, progression and later metastasis with initiation involving mutation in the normal cells, promotion involving proliferation of the abnormal cells, progression involving angiogenesis, invasion and mechanisms to avoid cellular process destruction and metastasis involving spread to other parts of the body.

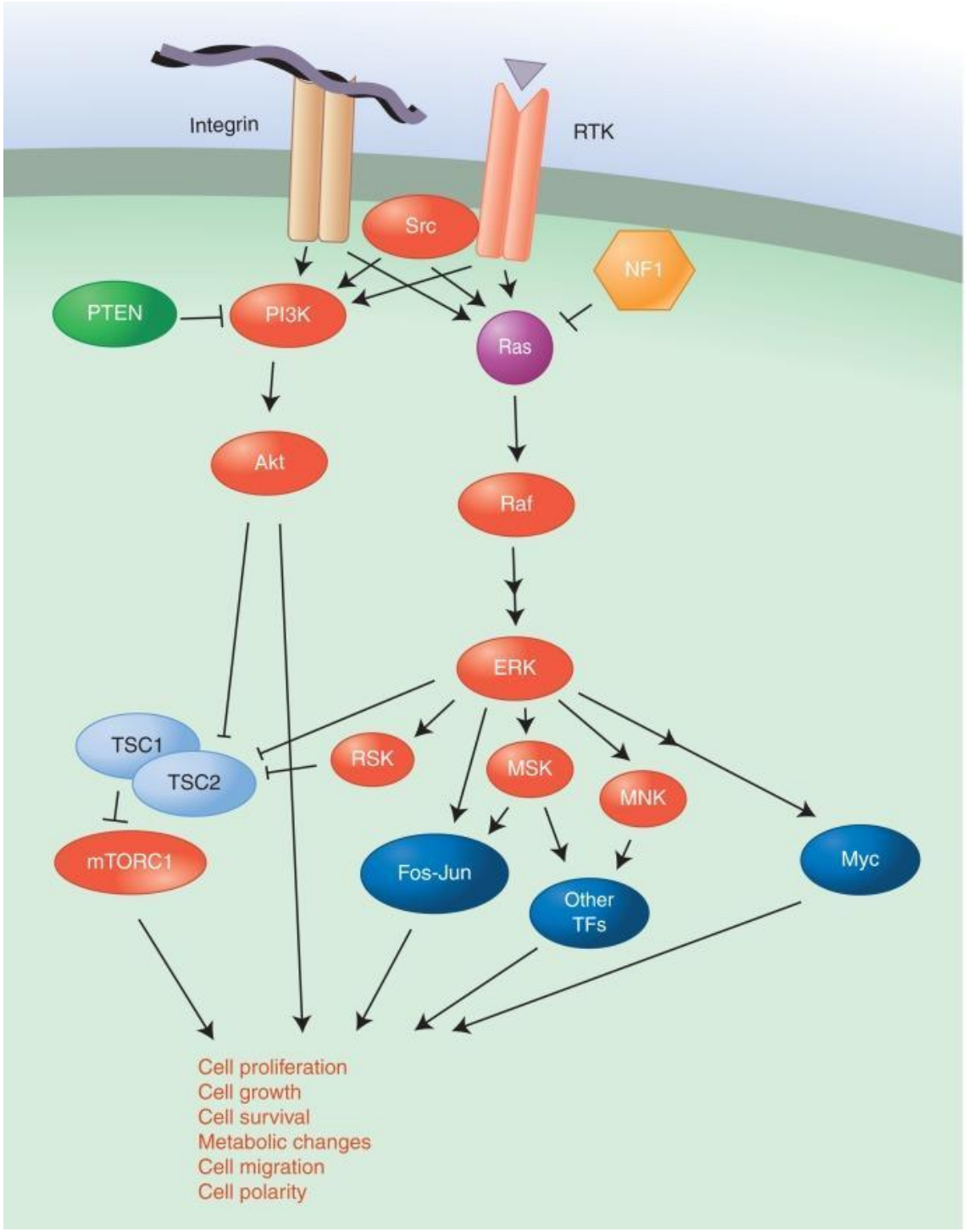

Figure 2. Different signaling pathways of cancer

Since the discovery of oncogenes (MYC, RAS, BRAF, KIT) among others and tumor suppressor genes (TP53, BRCA1 and PTEN), signaling pathways involving these genes play major roles in regulating and controlling important prosurvival and progrowth cellular

processes. (Yip and Papa, 2021). Several pathways are involved in the signal transduction of cancer as shown in Figure 2 however, the P13K-Akt and Ras-ERK pathways are some of the examples of the oncogenic signaling pathways and in these pathways, many genes are commonly incorporated in the P13K-aKT and Ras-ERK pathways. Growth factors and cytokine on the receptors cause the activation of these pathways. The P13K-Akt pathways can be activated also when there are mutations in the gene sequences that lead to production of proteins involved in this pathway for example the PTEN and INPP4B tumor suppressors among others. (Sever and Brugge, 2015). The Ras-ERK pathway is also activated by mutations in Ras or its downstream target Raf. (Yang & Wu, 2024). Furthermore, the transcription factor Myc is a downstream target of Ras-ERK signaling and many other pathways (Nie et al., 2012).

1.7 Cancer prevention and treatment

According to the American Cancer Society (2024), there are several approaches for cancer treatment depending on the cancer types, the treatment goals, how advanced the cancer is and the treatment types that are available and accessible. In addition to that, many procedures and drugs are available as shown in the Figure 3 with a lot of drugs still under study. Some of the local treatments available include therapies like the surgery and the radiation which treat cancers in specific parts of the body and also the systemic therapies which can treat cancers almost anywhere in the body including metastatic cancers and these include the chemotherapy and the targeted or the immunotherapy

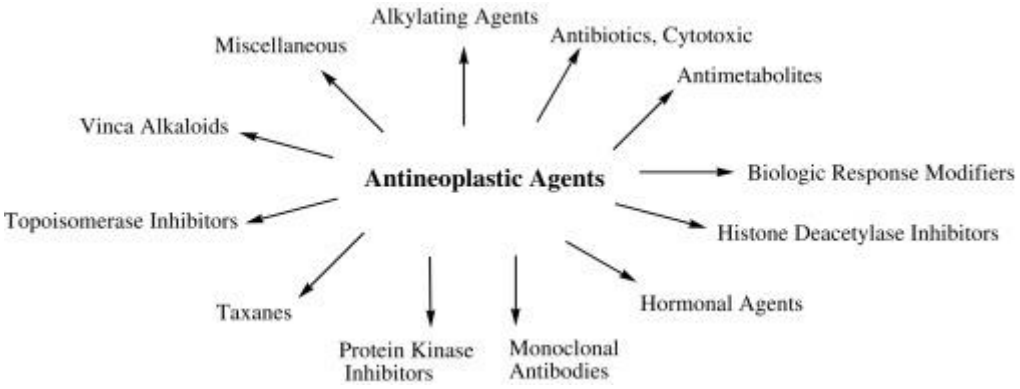

Figure 3. Different Anticancer agents

Cancer prevention measures among many include; lifestyle modification like cessation of smoking, maintaining a healthy weight, exercising regularly, eating healthy diet, drinking alcohol in moderation, protection from sun for example use of sunscreens, protection from infections especially on viral infections, and getting screening tests regularly for early cancer detection and treatment (Siteman Cancer Center, n.d.).

1.8 Breast Cancer

Nowadays, breast cancer is the most frequently diagnosed life-threatening cancer in women and the leading cause of death among women. It is reported that the incidence of breast cancer increases per year by 1% despite the advances in screening and the treatment options available. Of all the people diagnosed with breast cancer, only less than 1% are males implying that women are more at risk of developing breast cancer than men. (Breast Cancer Facts and Statistics 2025, n.d.;Giaquinto et al., 2024).

These cancers originate from the breast tissue especially from the inner lining of milk ducts or the lobules that supply the ducts with milk. It is a heterogeneous disease in which genetic and environmental factors are involved. Early breast cancer is considered curable but patients with locally advanced or metastatic BC have poor prognosis with survival rates approximately 2-4

years. Based on molecular and histological evidence, it can be categorized into 3 groups; BC expressing hormone receptors (Estrogen receptors (ER+) or progesterone receptors (PR+), BC expressing human epidermal receptors (HER+) and Triple Negative BC (TNBC) which do not express Estrogen Receptors (ER), progesterone receptors or HER2 receptors (Barzaman et al., 2020).

1.9 The MYC gene

The MYC gene was discovered by Bishop and colleagues in the late 1970s (Bishop, 1982) and it plays a central role in the proliferation and malignant transformation of animal and human cells. Most of the human malignancies have been reported to have amplification or over expression of this gene (Nesbit et al., 1999).

Recently, it has been shown in several studies that cMYC gene regulates growth both in the areas of cell size and tissue cell differentiation thus it plays a vital role in most aspects of cellular function like replication, growth, metabolism, differentiation and apoptosis (Dang et al.,1999).

The cMYC gene is most transcribed into 3 major transcripts that start from different initiating sites yielding 3 major proteins named cMYC-1, cMYC-2, cMYC-3 with the most abundant being cMYC-2 (Benassayag et al., 2005). With its over expression it has been reported in several studies that most of the resistant cancer treatments are associated with cMYC amplification and/overexpression, making it an ideal target in the treatment of cancers. However, there is a still a mystery of how the gene mechanisms can be altered to bring about the therapeutic effect by targeting the gene.

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1.10 Objectives of the study

The goal of the systematic review is to systematically analyze the MYC through already established studies of how well it can be interrupted to bring about treatment of advanced prognosis of breast cancer in addition to already existing medications which sometimes are suffering resistance due to the MYC overexpression or amplification. To achieve this goal a number of objectives were set to guide the conducting of this systematic review which include;

- To assess the efficacy of therapeutic strategies targeting the MYC oncogene in cancer patients.
- To summarize the types of interventions used to inhibit MYC.
- To evaluate the safety profiles of these interventions.

Chapter 2

Methodology

2.1 Search strategy

Comprehensive search strategy using keywords and MeSH terms related to MYC:

("MYC oncogene" OR "MYC inhibition" OR "MYC targeting" OR "MYC small molecules" OR "MYC RNA interference" OR "MYC monoclonal antibodies") AND ("cancer" OR "breast cancer" OR "lung cancer" OR "leukemia") AND ("treatment outcome" OR "tumor response" OR "survival" OR "safety")

2.2 Inclusion criteria

Adult cancer patients (≥18 years) with tumors characterized by MYC overexpression (defined as 2-fold or greater expression compared to normal tissue) in diseases such as; breast cancer, non-small lung cancer, acute myeloid leukemia.

2.3 Exclusion criteria

Studies not specifically focusing on MYC or MYC-targeted therapies., non-cancer studies (e.g., studies focusing on MYC in non-tumorigenic contexts), non-peer-reviewed articles, editorials, and opinion pieces without sufficient data, studies with participants receiving treatments that could confound results (e.g., other targeted therapies without prior washout periods)

Parameter	Inclusion Criteria	Exclusion Criteria
Patients/Cell lines	Patients at any stage with BC/ BC cell lines	Patients without BC/ Cell lines without BC
Intervention	Small molecules, RNA interference, monoclonal antibodies, combination therapy targeting the MYC oncogene	Studies not targeting the MYC oncogene
Comparator	Groups receiving standard treatment/Placebo group/Control group	No placebo/Control group
Outcome	MYC amplification/overexpression/ apoptosis induction/tumor volume reduction/PFS	Lack of detailed MYC amplification/PFS/ apoptosis induction/ tumor volume reduction
Study design	RCT, Preclinical studies, Clinical studies, case-control studies, cohort studies	Abstracts, Literature review, No full texts, systematic reviews, reviews

Table 1. PICOS table

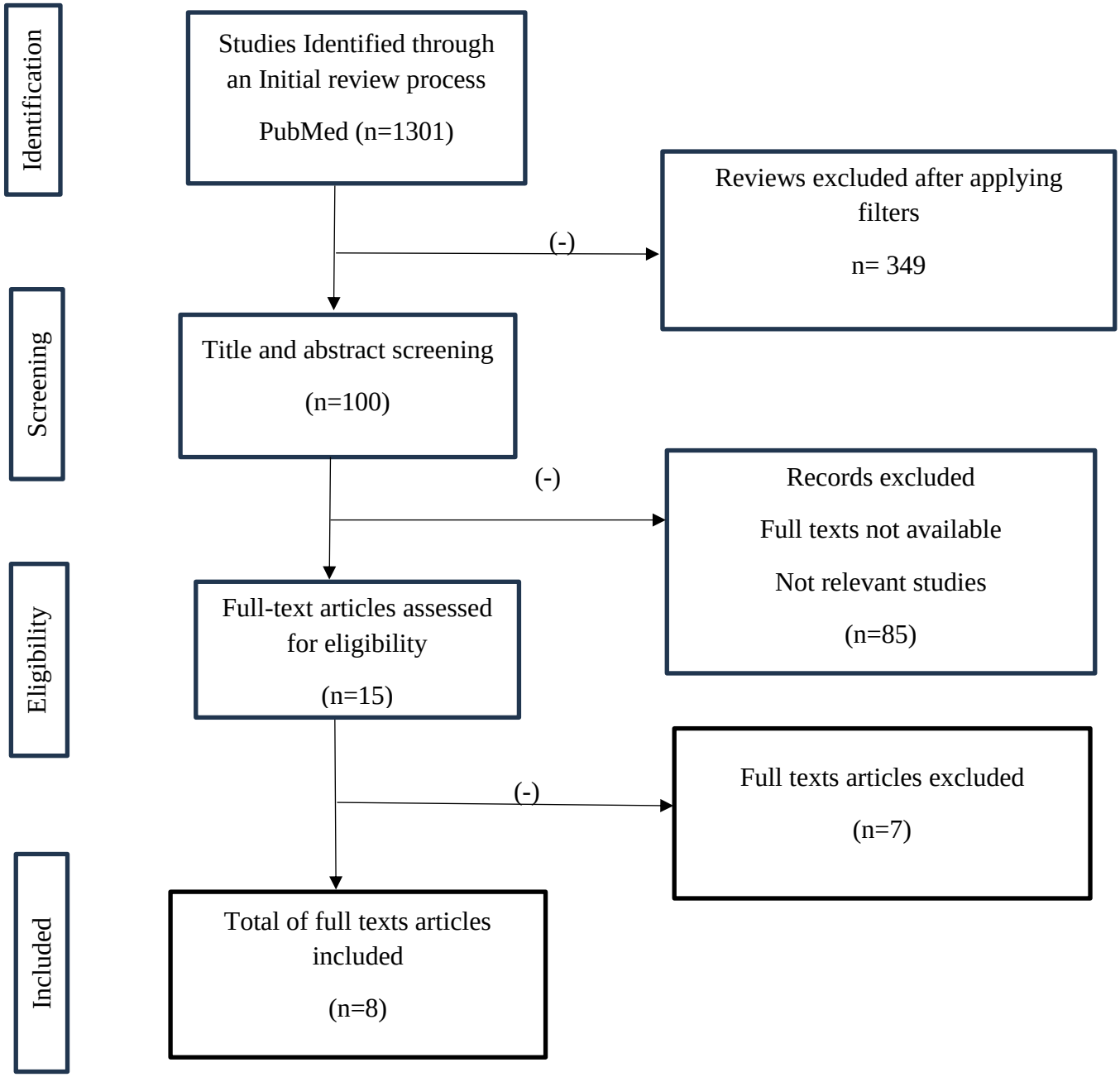

Figure 4. Prisma flow diagram

Chapter 3

Results

Study	Population	Intervention/Comparator	Primary Outcomes	Effect Measure	Potential Use
Prox1 (PMC10377922) (Michail et al.,2023)	Breast cancer cell lines	Prox1 application vs. control	Quantification of c-MYC positive cells over all cells in Prox1 and GFP infected MDA-MB-251 cells	(GFP:28.78+/-5.604% vs Prox1: 15.71+/-5.74% p< 0.05) for p<0.05, results are significant	Novel molecular mechanism of Prox1 which mediates tumor suppressive functions in breast tissue which can be widely used as well in other cancer conditions
Alisertib Trial (JCO.2023.41.16) (Byron et al.,2023)	HR+, HER2-negative, TN MBC patients	Alisertib + paclitaxel vs. paclitaxel alone	Measurement of PFS (Progression Free State) by GSEA (Gene Set Enrichment Analysis) considering it benefit for PFS >= 6 months and not benefit for < 6 months	Benefit from A+P, was associated with enrichment for MYC targets and UPR compared with benefit from P	A added to P, can improve PFS in patients with HR+, her2-, and TN MBC compared to P alone
MicroRNAs (13058-019-1098-z) (Wang et al., 2019)	Triple-negative breast cancer	PTEN vs hsa miR-4324, hsa miR-125b, hsa miR-145, hsa miR-381, hsa miR136	Quantification of MYC using GSEA and GWC (Genome Wide Connectivity)	% survival of 205 TNBC samples was with HR=2.12, P=0.012, For 44 TNBC samples was with	PTEN low levels together with the 5 other microRNAs are drivers rather than surrogates of poor prognosis

				HR=3.28, p=0.024	
Trastuzumab Trial (30.2125) (Perez et al., 2011)	Early-stage HER2+ breast cancer	MYC status in trastuzumab-treated patients vs patients with chemotherapy alone	FISH (Fluorescence In-Situ Hybridization) method with MYC: CEP8 ratio, average MYC copies/nucleus and exploratory polysomy 8	Patients with both chemotherapy and trastuzumab had less events compared to those with chemotherapy alone. (HR=0.35, p=0.001, HR=0.48, p=0.001) Patients with MYC copies/ nucleus<=0.5 and > 0.5 had HR=0.52, p=0.002 and HR=0.48, p=0.02	MYC amplification may have an additional benefit of adjuvant trastuzumab in patients with early-stage HER-2 positive breast cancer if constant MYC overexpression goes without promotion of growth factors by making the tumors to be more sensitive to apoptotic stimuli or chemotherapy
OMO-103 (4159-024-02805-1) (Garralda et al., 2024)	Solid tumor cells	OMO-103 in patients with solid tumor cells	Measure of preliminary antitumor activity using CT (Computed tomography) scans, Guardant Assay and RECIST (Response Evaluation Criteria in	1 patient showed 49% reduction in total tumor volume at best response and 8 patients showed stable disease	Safety and tolerability of the drug promising with dose level at 6.48 mg/kg. Encouraging signs of drug activity based on clinical response.

			Solid Tumors)		
MYC i975 (PMC9374613) (Tang et al., 2022)	TNBC cells	MYCi975 vs control	Measurement of antiproliferative and apoptosis inducing effects of MYCi975 using IC50 value inhibition, western blotting and ELISA	Response to MYCi975 decreased as MYC levels increased; Western blotting (p=0.00.047, r=-0.5835), ELISA (p=0.001, r=-0.767) IC50 values ranged from 2.49 -7.7 micrometers. Apoptosis inducing ranged from 0 to 80% with greater effect in TNBC than no TNBC cells with (p=0.041 and 0.001) respectively	Combination therapy with Paclitaxel, doxorubicin can have better therapeutic outcome
MYC and mTOR inhibitors (37642941) (Bhin et al., 2023)	Breast cancer	MYC activation and mTOR inhibitor resistance vs control	Mutiomic analysis of MYC amplification on mTORi resistance using LC-WGS (Low Coverage Whole Gene Sequencing) and RNA-	MYC focal amplifications in resistant tumors with CN (Copy Number) ratio of 10 controls, 6 sensitive and 13 control and MYC mRNA expression across 9 controls, 10 sensitive and 14 resistances	Combination therapy with MYC inhibitors in mTOR inhibitors treatments can confer greater prognosis in treatment of mTOR inhibitors resistant tumors

		seq methods	with Pearson correlation analysis between the 2 being with values (R=0.85, p=1.75 x10 ^-8)		
3'UTR MYC-18 (PMC11311709) (Awah et al., 2024)	TNBC	3’UTRMYC-18 and control	MYC mRNA degradation measurement using transcript quantification like quantitative PCR and tumor and animal weight measurement	Nonsense triggered mediated decay at an extremely high level (p=6.1 x10^-8 and FDR=5.3 x10^-6). Treated group survival compared with control improved significantly with p< 0.0001. 3’UTRMYC-18 and nanocage showed 80% reduction in tumor volume compared to controls	Potential therapeutic for TNBC and metastatic cancers

Table 2. Table of results

Intention to treat	Unique ID	Study ID	Experimental	Comparator	Outcome	Weight	D1	D2	D3	D4	D5	Overall

	Michail et al.,2023	Preclinical study 1	Prox1	Control	cMYC quantification	1						
	Byron et al.,2023	Clinical trial p2	A+P	P alone	PFS measurement	1						
	Wang et al.,2019	Preclinical study 2	Micro-RNAs	Control	MYC quantification	1						
	Perez et al.,2011	Clinical trial p3	MYC status vs Trastuzumab and Chemotherapy	MYC status vs Chemotherapy alone	MYC quantification	1						
	Garralda et al.,2024	Clinical trial p1	OMO-103	control	Anti-tumor activity measurement	1						
	Tang et al.,2023	Preclinical study 3	MYCi975	Control	Antiproliferative and apoptosis measurement	1						

	Bhin et al., 2023	Preclinical study 4	MYC activation and mTORi resistance	Control	MYC amplification in mTORi resistance	1						
	Awah et al.,2024	Preclinical study 5	3’UTR MYC-18	Control	MYC-mRNA degradation	1						

Table 3. Table showing risk of bias

 Low risk

 Some concerns

 High risk

D1 Randomization process.

D2 Deviations from intended interventions.

D3 Missing outcome data.

D4 Measurement of outcome data.

D5 Selection of the reported results.

3.1 Risk of bias

According to the study's intention, each of the 8 studies consisting of this systematic review was relevant and based on the thorough evaluation of the studies' methodology information, 3 were regarded as having an overall "Low risk" studies.(Wang et al.,2019, Perez et al., 2011, Tang et al.,2022),4 studies had some concerns due to inadequacy of information in some of their domains and one study had High risk due to inadequacy of information in several domains and having a High risk in the domain of deviation from intended intervention which led to its overall score of having High risk.

The rating "Low risk" signifies that the study had minimal issues and the conclusions that were made are more likely to be valid, conversely a "High risk" implies that there were major flaws in the study that may certainly introduce bias in the outcome making it unreliable and lastly the rating "some concerns" shows that there was lack of transparency in the study or inadequacy of some information.

All the domains' evaluations were same for all the studies, with domain1(Randomization process), since most of the studies were preclinical studies, the randomization process is not applicable, however some studies the randomization process was clearly outlined while one study there were some concerns in the randomization process as it was not stated clearly (Byron et al.,2023).

With Domain2 (Deviation from intended interventions), 6 studies showed Low risk while one study showed some High risk (Byron et al.,2023).

With Domain3 (Missing of outcome data), no study showed High risk however only 2 studies (Byron et al.,2023, Wang et al.,2019) showed Low risk and the rest showed some concerns

With Domain4(Measurement of outcome data), 2 studies showed some concerns (Michail et al., 2023 and Wang et al., 2019) while the rest showed Low risk

With Domain5(Selection of the reported results), no study showed High risk, 3 studies showed some concerns (Byron et al.,2023, Bhin et al.,2023 and Awah et al.,2024) while the rest showed Low risk.

Chapter 4

Discussion

Michail et al., (2023), showed that Prox1 had antitumorigenic effect by direct repression of cMYC transcription and its downstream target genes with sufficient suppression of cMYC amplification with $p< 0.05$ which is significant values for the conclusion that Prox1 promises better prognosis in the treatment of BC through cMYC suppression.

A combination of Alisertib and paclitaxel showed increased benefit to patients receiving treatment from this therapy compared to patients receiving treatment form only chemotherapy of Paclitaxel alone with more enrichment for MYC targets and UPR hence a synergy derived from these 2 therapies gave more benefit in treating Progress Free State in patients hence a promising combination therapy (Byron et al., 2023).

Wang et al., (2019), identified that the loss of PTEN with other microRNAs defined a certain type of TNBC, with positive correlation and $p=0.012$ for 205 TNBC patients' samples and $p=0.024$, for 44 TNBC patients' samples which are significant in the overexpression and amplification of MYC gene which leads to the aggressive TNBC hence targets at these molecules could significantly increase prognosis in the treatment of TNBC by interfering with MYC amplification and overexpression.

Perez et al., (2011), demonstrated that treatment with Trastuzumab together with chemotherapy in patients with early stage HER2 + BC showed less events with HR=0.3and $p=0.001$ compared to patients undergoing chemotherapy alone with HR=0.48 and $p=0.001$. This was due to also co-amplification of MYC with MYC copies per nucleus ≥ 0.5 with HR=0.52 and $p=0.002$ in patients with combination therapy compared to patients with chemotherapy alone with HR=0.48 and $p=0.02$ showing benefit of adjuvant Trastuzumab in patients with early stage HER2+ BC with the amplification making the tumors more sensitive to apoptotic stimuli or

chemotherapy as long as the limit did not exceed that which could promote Growth Factor activation.

OMO-103 drug exhibited safety and tolerability with dose level at 6.48 mg/kg in the phase 1 clinical trial hence proving the drug safety in the patients hence showing a stable disease state in the patients whom among them 1 showed a 49% reduction in total tumor volume proving that phase II could proceed with these earlier preliminary efficacy results of antitumor activity. (Garralda et al., 2024)

Tang et al., 2022, demonstrated that MYCi975 showed decreased MYC levels with p=0.047 and IC50 inhibition values ranging from 2.49-7.7μm and apoptosis induction ranging from 0 to 80% with greater effect in patients with TNBC with p=0.041 and p=0.001 in patients without TNBC. However, a combination therapy with Paclitaxel, Doxorubicin would have better therapeutic significance.

Bhin et al., (2023), showed that mTORi resistance therapy was majorly due to the amplification of the MYC gene despite the fact that mTOR pathway was targeted effectively by the mTORi and thus showed MYC amplification in patients showing resistance to mTORi treatment sighting out that targeting the MYC inhibition in these patients would prove a better remedy in the improved prognosis of mTORi resistance BC types.

Awah et al., (2024), demonstrated that the molecule 3'UTR MYC-18 could lead to the degradation of the MYC mRNA with significant p value=6.1×10^{-8} in patients treated group compared to the control group in the treatment of TNBC through the nonsense triggered mediated decay hence the molecule 3'UTR MYC-18 has a potential for improved diagnosis in TNBC patients.

Chapter 5

Conclusions

The studies majorly showed that MYC amplification ultimately causes poor prognosis in BC and molecular targets and molecules that caused degradation in the MYC amplification through degradation, induced tumor volume and increased apoptosis patients and cell lines under study except one study that showed that trastuzumab in combination with chemotherapy increased MYC copies per nucleus which increased the sensitivity of tumor cells towards chemotherapy at a level below which MYC amplification can cause Growth Factor activation.

Chapter 6

Future Prospects

The preclinical studies as well as the early phase clinical trials showed promising results towards the targeting of the MYC oncogene though proper Pharmacokinetics properties of these drug molecules need to be studied further in order to formulate products which are not only bioavailable but it can effectively reach the MYC oncogene target.

Further research has to be studied to identify drug molecules that can effectively target receptor targets like PTEN and the submicroRNAs that define MYC amplification in TNBC.

Lastly but not the least advanced stages of clinical trials beyond phase1 should be carried out to determine the efficacy as well as the safety of these promising drug molecules which calls for governments and non-government organizations as well as interested parties to fund the quick promising MYC inhibition therapy in the treatment of BC which not only wipes the women population but can cause potential death in men as well which can hinder social, political and economic development worldwide.

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