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Review Article

Effectiveness and Safety of Common Non-Oncologic Pharmaceuticals in Cancer Management: A Systematic Review

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Abstract

Background. De novo anticancer drug development is lengthy, costly, and risky, motivating cautious evaluation of off-label use of common non-oncologic agents where mechanistic plausibility and clinical signals exist.

Objectives. To synthesize the effectiveness and safety of frequently repurposed non-oncologic drug classes in oncology and to identify priorities for practice and research.

Methods. A PRISMA-guided systematic review (2015–2025) screened titles/abstracts and full texts in duplicate, with standardized extraction and narrative/thematic synthesis. Records identified: 1,699; duplicates removed: 119; other removals (missing metadata): 33; records screened: 1,547; excluded at title/abstract: 956; reports sought: 591; not retrieved: 410; assessed for eligibility: 181; included: 181. Outcomes included OS, PFS/DFS, ORR, QoL, and CTCAE-graded toxicities.

Results. Antihypertensives comprised the largest class, followed by antidiabetics, statins, anti-inflammatories/aspirin, antibiotics, antidepressants, and anthelmintics; lung, breast, colorectal, pancreatic, and ovarian cancers were most represented. Signals suggest possible benefit for overall survival and mortality, with limited and inconsistent evidence for PFS/DFS and ORR; QoL was rarely reported. Outcome definitions, progression ascertainment, censoring rules, exposure metrics (dose, duration, timing), and reporting completeness were heterogeneous, constraining meta-analytic pooling and causal inference.

Conclusion. Generalized repurposing for oncology is not supported at this time beyond established non-oncologic indications. Biologically coherent, low-toxicity signals, most consistently for β-blockade and RAAS modulation, and more variably for metformin, statins, and aspirin, justify targeted, rigorously designed evaluation in prospective trials and robust observational emulations, with harmonized endpoints and systematic CTCAE capture. Equity-by-design, common data elements, preregistration, and data/code sharing are essential to accelerate credible, practice-informing evidence.

Keywords: Non-Oncologic Agents, Effectiveness and Safety, Cancer Management

1. Introduction

Developing a new anticancer agent is long, uncertain, and capital-intensive, with high late-stage attrition and unforeseen toxicities despite extensive investigations.[1–5] These constraints slow patient access, strain health-system budgets, and exacerbate global distributive discrepancies. For the management of these drawbacks, a judicious off-label use of non-oncologic medicines, or drug repurposing, offers a pragmatic path for appropriate options. Indeed, such pharmaceuticals have established manufacturing, human pharmacokinetic and pharmacodynamic evidences, and baseline safety, leading to faster lower-cost deployment when supported by mechanistic plausibility (*e.g.*, metabolic, vascular, or immunologic effects).[6–8]

However, promoting off-label strategies must, follow a rigorous framework. Evidence hierarchies should privilege randomized data, where available, while robust observational emulations and prospective registries generate decision-grade real-world evidence.[9] Dosing and scheduling require oncology-specific optimization; drug–drug interactions and overlapping toxicities demand proactive pharmacovigilance.

In fact, off-label implementation of non-oncologic pharmaceuticals in the management of cancer is accelerating, propelled by mechanistic plausibility such as the metformin's modulation of the Adenosine Monophosphate-activated Protein Kinase (AMPK) and the Mechanistic Target of Rapamycin (mTOR) signaling, the statins' inhibition of the mevalonate/prenylation axis, the β-adrenergic blockade with propranolol in vascular sarcomas, and Non-Steroidal Anti-Inflammatory Drug (NSAID)-mediated suppression of the COX-2 (Cyclooxygenase-2) and PGE_2 (prostaglandin E_2) pathway, together with signals emerging from real-world cohorts and pragmatic use.[10–18]

In addition, mechanism-Based,[16–20] as well as hypothesis-driven[21–24] and strategic[18,25,26] repurposing of non-oncologic medicines namely metformin, renin-angiotensin system (RAS) inhibitors, β-blockers, statins, and aspirin/NSAIDs, has broadened in scope as a pragmatic strategy to enhance effectiveness, tolerability, and affordability of cancer care, particularly in resource-constrained settings.

Mechanistically, these agents modulate cross-cutting pathways as exemplified by tumor metabolism and insulin resistance,[27–30] tumor microenvironment and stromal remodeling,[31–34] and neuro-immune-inflammatory signaling,[35–37] that could synergize with standard oncologic therapies.

Consequently, off-label use should be overseen by multidisciplinary tumor boards with protocolized eligibility and monitoring, transparent informed consent, and adherence to national regulation. Framed as "evidence-generating care," this approach treats off-label prescribing as a structured strategy to convert mechanistic and real-world signals into patient benefit while curbing the costs, timelines, and safety risks of de novo development.

This systematic review will critically synthesize the clinical effectiveness, overall survival, progression-free/disease-free survival, and objective response rate and safety, including Common Terminology Criteria for Adverse Events (CTCAE)-graded toxicities and drug-drug interactions, of commonly repurposed non-oncologic drug classes used in oncology. It will investigate on the sources of heterogeneity and based on these insights, will delineate an applied research agenda.

2. Methodology

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) framework was employed as guide in the development of this systematic review. Using the PRISMA guidelines to plan, conduct, and report a systematic review ensures scientific transparency and reproducibility.

2.1. Data sources and search strategy

In order to ensure the transparency and reproducibility of the comprehensive studies search for the systematic review of the effectiveness and safety of common non-oncologic pharmaceuticals in cancer management, it was suitable to use the Boolean logic as operational information retrieval system based on the following keyword: ''anticancer effect of antibiotics'', ''anticancer use of antidiabetics'', ''anticancer use of antidepressants'', ''anticancer effect of anthelmintic'', ''antihypertensive use in cancer'', ''anticancer effect of statins'' and ''anticancer effect of anti-inflammatories''. This systematic search was conducted for the last decade in French and/or English in two (02) databases: PubMed and Google Scholar.

2.2. Eligibility criteria and selection process

At first glance, studies published in English and/or French between 2015 and 2025 on clinical trials, cohort studies and case reports – on investigating common non-oncologic drugs use in cancer treatment – on the evaluation of the effectiveness, safety, or outcomes of common non-oncologic pharmaceuticals for cancer therapy, were included. However, studies focusing exclusively on non-cancer conditions - in vitro or animal studies not relevant to human cancer treatment - articles without abstract and full-text free access were excluded. In the present work the phrases ''common non-oncologic pharmaceuticals'' and ''common off-label drugs'' stand for the common drugs such as antibiotics, antidiabetics, antidepressants, anthelmintic, antihypertensive, statins and anti-inflammatories reproposed for oncologic purpose.

Moreover, on the 6th of August 2025, the research was conducted by using the following Boolean search string (''anticancer effect of antibiotics'' OR ''anticancer use of antidiabetics'' OR ''anticancer use of antidepressants'' OR ''anticancer effect of anthelmintic'' OR ''antihypertensive use in cancer'' OR ''anticancer effect of statins'' OR ''anticancer effect of anti-inflammatories'') for both databases (PubMed and Google Scholar).

Furthermore, after an automatic screening via ChatGPT 5 Thinking, two reviewers (LZ and MSZ) independently identified articles and reviewed them sequentially (titles,

abstracts, then full texts) for inclusion (Figure 1). For articles without an abstract, or without sufficient information in the abstract to make decision, the full text and, if necessary, supplementary material were reviewed.

2.3. Data Extraction and Analysis Procedure

For transparency purpose, three reviewers (LZ, AO and MSZ) independently performed data extraction from the included studies. Extracted data covered study contexts, design, population characteristics, clinical trials, cohort studies and case reports – studies investigating off-label drug use in cancer treatment – evaluation of the effectiveness, safety, or outcomes of off-label drugs for cancer therapy, were examined. Data were exported to Zotero software and duplicates were removed. The next stage in the selection process involved a thorough review of the abstracts of eligible articles. Studies without abstracts or with irrelevant information were then excluded. The final selection of studies included in this review was made through a comprehensive evaluation of the full texts.

The final included studies full texts were thoroughly reviewed based on the inductive thematic analysis and narrative synthesis and then presented under key sub-themes relevant to this systematic review.

3. Results

3.1. Articles Reviewed and Included in the Study

Figure 1 presents the flowchart diagram of the selection process for the studies included in this systematic review. This flowchart indicates the different stages of the search strategy as described in the methodology section used for cleaning up and excluding duplicates, review systematic and meta-analysis articles. In addition, titles and abstracts were included in the literature review. Then, during the full-text assessment, all records exhibiting ambiguous data or lacking sufficient information to satisfy the predefined inclusion criteria were excluded in accordance with the PRISMA guidelines. Therefore, one hundred and eighty-one (181) relevant articles were finally included for this systematic review (Figure 1 and Table 1).

3.2. Profile of Included Studies: Oncologic Indications and Non-Oncologic Drug Classes

Table 1 catalogues the 181 studies detailing study design, cancer type and anatomical site, and the common non-oncologic pharmacotherapies investigated. Thus, the cardiometabolic agents, *i.e.*, antihypertensives (n=108), are the most frequently used, mainly the β-blockers (*e.g.*, propranolol), the renin–angiotensin system drugs (ARBs/ACEIs), and the thiazide diuretics. The antidiabetics (n=31) were also often used, metformin and insulin being the most representative.

The other classes of pharmaceuticals, such as anti-inflammatories (n=8; aspirin and NSAIDs), statins **(**n=5), antidepressants (n=4), antibiotics (n=3), and a single anthelmintic (n=1; mebendazole), were not used such much. In addition, mixed-class combinations (n=21) were also used and include antidiabetics + antihypertensives (n=5), antidiabetics + statins (n=3), antihypertensives + statins (n=5), antihypertensives + anti-inflammatories (n=3). Study designs span randomized control trials (RCTs), prospective / retrospective cohorts, case-control studies, case series / reports, and early-phase clinical trials across diverse cancer sites (lung, pancreatic, breast, colorectal, ovarian, hepatocellular, melanoma, head-and-neck, prostate, primary brain tumors, hemangiomas, and “various” metastatic settings).

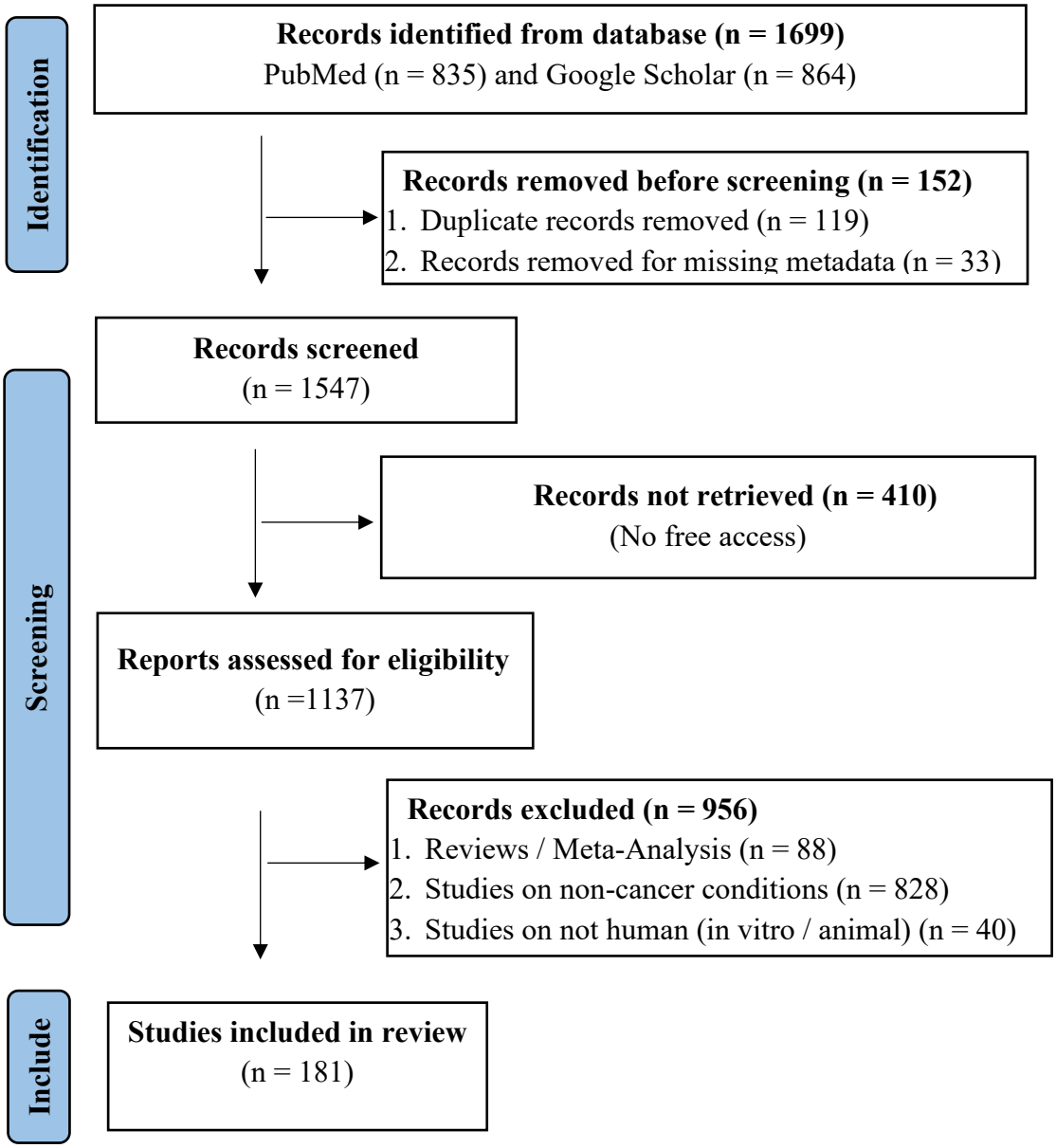

Figure 1: PRISMA Flow Diagram displaying the study selection process.

This diagram summarizes the consecutive phases of the systematic review process, including the identification of records through database searching, removal of duplicates, screening of titles and abstracts, assessment of full-text articles for eligibility, and final inclusion of studies in the qualitative synthesis, in accordance with PRISMA 2020 guidelines.

Table 1: Distribution of Included Studies Across Off-Label Drug Classes

#	Title	Authors & Year	Study Design	Cancer Site (s)	Off-Label Drug(s)
	Anthelmintic (n = 1)				
1	A phase 2a clinical study on the safety and efficacy of individualized dosed mebendazole in patients with advanced gastrointestinal cancer	S. Mansoori *et al.,* 2021[21]	Not specified	VMC[10]	Mebendazole
	Anti-inflammatories (n = 8)				
2	Antiplatelet drugs and breast cancer risk in a large nationwide Danish case-control study	Manon Cairat *et al.,* 2023[38]	Case-control study	Breast cancer	Aspirin
3	Aspirin as a neoadjuvant agent during preoperative chemoradiation for rectal cancer	Angelo Restivo *et al.,* 2015[39]	Randomized controlled trial	Colorectal cancer	Aspirin
4	Association of Low-Dose Aspirin and Survival of Women with Endometrial Cancer	Koji Matsuo *et al.,* 2016[40]	Retrospective cohort	Endometrial cancer	Aspirin
5	Effect of low-dose aspirin use on survival of patients with gastrointestinal malignancies; an observational study	M. A. Frouws *et al.,* 2017[41]	Registry study	Colorectal cancer	Aspirin
6	Effects of postoperative non-steroidal anti-inflammatory drugs on long-term survival and recurrence of patients with non-small cell lung cancer	Wensheng Jiang *et al.,* 2018[42]	Retrospective study	NSCLC[7]	NSAID[6]
7	Hitting the bull's-eye in metastatic cancers—NSAIDs elevate ROS in mitochondria, inducing malignant cell death	Stephen John Ralph *et al.,* 2015[43]	Not specified	VMC[10]	NSAID[6]
8	Prevalence of renal insufficiency and factors associated among selected cancer patients on chemotherapy at Ocean Road Cancer Institute in Tanzania: a cross-sectional study	Hamidu N. Rajabu *et al.,* 2024[44]	Not specified	Renal cell carcinoma	NSAID[6]
9	The association of aspirin use with overall survival of patients with inoperable non-small cell lung cancer: a retrospective study	Min-Chun Chuang *et al.,* 2021[45]	Randomized controlled trial	NSCLC[7]	Aspirin
	Antibiotics (n = 3)				
10	Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study	Nicole M. Kuderer *et al.,* 2020[46]	Cohort study	Breast cancer	Azithromycin
11	Efficacy and safety of concurrent anti-Cancer and anti-tuberculosis chemotherapy in Cancer patients with active Mycobacterium tuberculosis: a retrospective study	Tomonori Hirashima *et al.,* 2018[47]	Retrospective study	Lung cancer	Rifampicin
12	The characteristics and clinical course of patients with melioidosis and cancer	Tej Shukla *et al.,* 2024[48]	Cohort study	Various cancers	STZ,[9] Trimethoprim

#	Title	Authors & Year	Study Design	Cancer Site (s)	Off-Label Drug(s)
	Antibiotics; Antihypertensives (n = 1)				
13	Evaluation of a Comprehensive Skin Toxicity Program for Patients Treated with Epidermal Growth Factor Receptor Inhibitors at a Cancer Treatment Center	Zizi Yu *et al.,* 2020[49]	Clinical trial	Colorectal cancer	Tetracycline, Doxycycline, ARB[2]
	Antibiotics; Statins (n =1)				
14	SARS-CoV-2-related pneumonia can be successfully managed in patients with metastatic neuroendocrine tumors: a critical point of view	F. Spada *et al.,* 2020[50]	Randomized controlled trial	VMC[10]	Azithromycin, Statins
	Antidepressants (n =4)				
15	Case-specific potentiation of glioblastoma drugs by pterostilbene	Linnéa Schmidt *et al.,* 2016[51]	Not specified	Primary brain tumors	Sertraline
16	Enhancing Duloxetine with Mirogabalin for Treating Taxane-Induced Peripheral Neuropathy in Advanced Lung Cancer	Yasuhiro Nakajima et al. 2025[52]	Retrospective cohort	Lung cancer	Duloxetine
17	Implementing Pre-Emptive Pharmacogenetics: Impact of Early Pharmacogenetic Screening in a Pediatric Oncology Cohort of 1,151 Subjects	Emma C. Bernsen *et al.,* 2025[53]	Retrospective cohort	Various cancers	Amitriptyline, Paroxetine
18	Risk factors and pharmacotherapy for chemotherapy-induced peripheral neuropathy in paclitaxel-treated female cancer survivors: A retrospective study in Japan	Shiori Hiramoto *et al.,* 2021[54]	Retrospective cohort	Breast cancer	Duloxetine
	Antidiabetics (n = 31)				
19	A malignant cause of hypoglycaemia: a metastatic insulin-secreting pancreatic neuroendocrine carcinoma	Mark Anthony Sandoval *et al.,* 2016[55]	Not specified	Pancreatic cancer	Insulin
20	Association between Metformin Use and Survival in Nonmetastatic Rectal Cancer Treated with a Curative Resection: A Nationwide Population Study	Young-Jun Ki *et al.,* 2017[56]	Cohort study	Colorectal cancer	Metformin
21	Association of Metformin Use with Cancer-Specific Mortality in Hepatocellular Carcinoma After Curative Resection: A Nationwide Population-Based Study	Young-Seok Seo *et al.,* 2016[57]	Retrospective cohort	Hepatocellular carcinoma	Metformin
22	Body Mass Index Influences the Salutary Effects of Metformin on Survival After Lobectomy for Stage I NSCLC	Sai Yendamuri *et al.,* 2019[58]	Cohort study	NSCLC[7]	Metformin
23	Case Report: Diazoxide-induced diabetic ketoacidosis in a patient with insulinoma	Run Ting Chin *et al.,* 2025[59]	Case report	Pancreatic cancer	Insulin
24	Changing Insulinoma Management Due to Incidentally Discovered Metastasis: A Case Report	Riya Madan *et al.,* 2020[60]	Case report	Pancreatic cancer	Insulin
25	Clinical outcomes of 20 Japanese patients with insulinoma treated with diazoxide	Yoshihiro Niitsu *et al.,* 2019[61]	Retrospective study	Pancreatic cancer	Insulin

#	Title	Authors & Year	Study Design	Cancer Site (s)	Off-Label Drug(s)
26	Clinical significance of glycemic parameters on venous thromboembolism risk prediction in gastrointestinal cancer	Fiorella Guadagni *et al.,* 2017[62]	Prospective cohort	VMC[10]	Insulin
27	Diagnosis and Treatment Course of Insulinoma Presenting as Hypoglycemia Unawareness Using a Factory-Calibrated Continuous Glucose Monitoring System	Azusa Aida *et al.,* 2022[63]	Case report	Pancreatic cancer	Insulin
28	Effect of metformin on the survival of patients with ALL who express high levels of the ABCB1 drug resistance gene	Christian Ramos-Peñafiel *et al.,* 2018[64]	Clinical trial	Leukemia	Metformin
29	Effects of 2-year calorie restriction on circulating levels of IGF-1, IGF-binding proteins and cortisol in nonobese men and women: a randomized clinical trial	Luigi Fontana *et al.,* 2016[65]	Randomized controlled trial	Various cancers	Insulin
30	Effects of Brief Adjunctive Metformin Therapy in Virologically Suppressed HIV-Infected Adults on Polyfunctional HIV-Specific CD8 T Cell Responses to PD-L1 Blockade	Glen M. Chew *et al.,* 2021[66]	Clinical trial	Various cancers	Metformin
31	Examining the relationship between metformin dose and cancer survival: A SEER-Medicare analysis	Lisa Scarton *et al.,* 2022[67]	Retrospective cohort	Lung cancer	Metformin
32	Giant left pheochromocytoma with vascular anomalies and pelvic horseshoe kidney: a case report	Emily Biben *et al.,* 2023[68]	Randomized controlled trial	Ovarian cancer	Metformin, Insulin
33	Impact of metformin use on the recurrence of hepatocellular carcinoma after initial liver resection in diabetic patients	Wei-Ru Cho *et al.,* 2021[69]	Retrospective cohort	Hepatocellular carcinoma	Metformin
34	Inhibition of Protein Phosphatase 2A Sensitizes Mucoepidermoid Carcinoma to Chemotherapy via the PI3K-AKT Pathway in Response to Insulin Stimulus	Limin Liu *et al.,* 2018[70]	Not specified	VMC[10]	Insulin
35	Metformin Downregulates the Expression of Epidermal Growth Factor Receptor Independent of Lowering Blood Glucose in Oral Squamous Cell Carcinoma	Wei-Ming Wang *et al.,* 2022[71]	Not specified	HNSCC[5]	Metformin
36	Metformin Enhances Cisplatin-Induced Apoptosis and Prevents Resistance to Cisplatin in Co-mutated KRAS/LKB1 NSCLC	Massimo Moro *et al.* 2018[72]	Clinical trial	NSCLC[7]	Metformin
37	Metformin effects on biochemical recurrence and metabolic signaling in the prostate	Brian Winters *et al.* 2015[73]	Case-control study	Prostate cancer	Metformin, Insulin
38	Metformin enhances the response to radiotherapy in diabetic patients with rectal cancer	Bo Young Oh *et al.* 2016[74]	Case-control study	Colorectal cancer	Metformin
39	Metformin selectively inhibits metastatic colorectal cancer with the KRAS mutation by intracellular accumulation through silencing MATE1	Jinye Xie *et al.,* 2020[10]	Not specified	Colorectal cancer	Metformin

#	Title	Authors & Year	Study Design	Cancer Site (s)	Off-Label Drug(s)
40	Metformin use and incidence cancer risk: evidence for a selective protective effect against liver cancer	Harvey J. Murff *et al.,* 2018[30]	Randomized controlled trial	Lung cancer	Metformin
41	Metformin, Diabetes, and Survival among U.S. Veterans with Colorectal Cancer	Jessica K. Paulus *et al.,* 2016[75]	Randomized controlled trial	Colorectal cancer	Metformin
42	Overcoming acquired resistance to PD-1 inhibitor with the addition of metformin in small cell lung cancer (SCLC)	Yeseul Kim *et al.,*2021[76]	Not specified	SCLC[8]	Metformin
43	PPARγ Agonist Pioglitazone in Combination with Cisplatinum Arrests a Chemotherapy-resistant Osteosarcoma PDOX Model	Takashi Higuchi *et al.,* 2020[77]	Randomized controlled trial	Sarcoma	Pioglitazone
44	Phase 1 lead-in to a phase 2 factorial study of temozolomide plus memantine, mefloquine, and metformin as postradiation adjuvant therapy for newly diagnosed glioblastoma	Stefania Maraka *et al.,* 2019[78]	Not specified	Primary brain tumors	Metformin
45	Plasma levels of the proprotein convertase furin and incidence of diabetes and mortality	C. Fernandez *et al.,* 2018[79]	Prospective cohort	Various cancers	Insulin
46	Prognostic value of metformin for non-small cell lung cancer patients with diabetes	Tongbai Xu *et al.,* 2018[80]	Retrospective study	NSCLC[7]	Metformin
47	The preventive effect of metformin on progression of benign prostate hyperplasia: A nationwide population-based cohort study in Korea	Yehee Hong *et al.,* 2019[81]	Prospective cohort	Prostate cancer	Metformin
48	Thymic emigration patterns in patients with type 2 diabetes treated with metformin	Grzegorz Dworacki *et al.,* 2015[82]	Case-control study	Various cancers	Metformin
49	Unusual presentation of an insulinoma in an elderly male patient	M. Adarsh *et al.,* 2021[83]	Case report	Pancreatic cancer	Insulin
	Antidiabetics; Anti-inflammatories (n = 1)				
50	Metformin for patients with metastatic prostate cancer starting androgen deprivation therapy: a randomised phase 3 trial of the STAMPEDE platform protocol	Silke Gillessen *et al.,* 2025[84]	Randomized controlled trial	Prostate cancer	Metformin, Aspirin, NSAID[6]
	Antidiabetics; Antihypertensives (n = 5)				
51	A Randomized Phase II Study of Metformin plus Paclitaxel/Carboplatin/Bevacizumab in Patients with Chemotherapy-Naïve Advanced or Metastatic Nonsquamous NSCLC[7]	Kristen A. Marrone *et al.,* 2018[85]	Randomized controlled trial	NSCLC[7]	Metformin, Insulin, ARB[2]
52	Contributing factors for menopausal symptoms after surgical staging for endometrial cancer	Koji Matsuo *et al.,* 2016[86]	Retrospective study	Endometrial cancer	HCT[4], Insulin
53	Metformin induces a fasting- and antifolate-mimicking modification of systemic host metabolism in breast cancer patients	Elisabet Cuyàs *et al.,* 2019[28]	Randomized controlled trial	Breast cancer	Metformin, ARB[2]

#	Title	Authors & Year	Study Design	Cancer Site (s)	Off-Label Drug(s)
54	Phase I study of metformin in combination with carboplatin/paclitaxel chemotherapy in patients with advanced epithelial ovarian cancer	K. Esther Broekman *et al.,* 2020[87]	Clinical trial	Ovarian cancer	Metformin, ARB[2]
55	Survival impact and toxicity of metformin in head and neck cancer: An analysis of the SEER-Medicare dataset	William A. Stokes *et al.,* 2018[88]	Prospective cohort	HNSCC[5]	Metformin, ARB[2]
	Antidiabetics; Antihypertensives; Anti-inflammatories (n =1)				
56	Acute kidney injury and long-term renal effects of alectinib in anaplastic lymphoma kinase-positive non-small cell lung carcinoma: a case report	Marco van Londen *et al.,* 2022[89]	Case report	NSCLC[7]	Enalapril, Metformin, Naproxen, ARB[2]
	Antidiabetics; Antihypertensives; Statins; Anti-inflammatories (n = 1)				
57	Increased tumor response to neoadjuvant therapy among rectal cancer patients taking angiotensin-converting enzyme inhibitors or angiotensin receptor blockers	Zachary S. Morris *et al.,* 2016[90]	Not specified	Colorectal cancer	ARB[2], Metformin, Aspirin, Statins
	Antidiabetics; Statins (n = 3)				
58	Differential and Joint Effects of Metformin and Statins on Overall Survival of Elderly Patients with Pancreatic Adenocarcinoma: A Large Population-Based Study	Jian-Yu E *et al.,* 2017[91]	Prospective cohort	Pancreatic cancer	Metformin, Statins
59	Metformin Use Is Associated with Longer Progression-Free Survival of Patients with Diabetes and Pancreatic Neuroendocrine Tumors Receiving Everolimus and/or Somatostatin Analogues	Sara Pusceddu *et al.,* 2018[92]	Retrospective study	Pancreatic cancer	Metformin, Insulin, Statins
60	Providers' mediating role for medication adherence among cancer survivors	Justin G. Trogdon *et al.,* 2021[93]	Retrospective cohort	Lung cancer	Insulin, Statins
	Antihypertensives (n = 108)				
61	A Case of Superficial Kaposiform Hemangioendothelioma Treated with Oral Propranolol Combined with Topical Sirolimus	Nan Dang *et al.,* 2024[94]	Not specified	Sarcoma	Propranolol
62	A successful pregnancy in a patient with secondary hypertension caused by adrenal adenoma: a case report	Xin Zhang *et al.,* 2019[95]	Case report	Renal cell carcinoma	Nifedipine
63	AGTR1 promotes lymph node metastasis in breast cancer by upregulating CXCR4/SDF-1α and inducing cell migration and invasion	Yuxi Ma *et al.,* 2019[96]	Not specified	Breast cancer	Losartan
64	Airway obstruction as the primary manifestation of infantile thyroid hemangioma	Yujian Liang *et al.,*. 2020[97]	Case report	Thyroid cancer	Propranolol
65	Analysis of factors affecting the therapeutic effect of propranolol for infantile haemangioma of the head and neck	Jian-Yong Dong *et al.,* 2017[98]	Not specified	HNSCC[5]	Propranolol

#	Title	Authors & Year	Study Design	Cancer Site (s)	Off-Label Drug(s)
66	Analysis of factors associated with hiccups based on the Japanese Adverse Drug Event Report database	Ryuichiro Hosoya *et al.,* 2017[99]	Not specified	Various cancers	ARB[2]
67	Angiotensin II enhances the proliferation of Natural Killer/T-cell lymphoma cells via activating PI3K/Akt signaling pathway	Gui-Hua Zhang *et al.,* 2020[100]	Not specified	Lymphoma	Losartan
68	Angiotensin converting enzyme inhibitors and risk of lung cancer: population-based cohort study	Blánaid M. Hicks *et al.,* 2018[101]	Cohort study	Lung cancer	ARB[2]
69	Angiotensin-Receptor Blockers Prevent Vestibular Schwannoma-Associated Hearing Loss	Samuel Early et al. 2025[102]	Clinical trial	Various cancers	ARB[2], Losartan
70	Antihypertensive medication use and ovarian cancer survival	Tianyi Huang et al. 2021[103]	Prospective study	Ovarian cancer	ACEI[1], Beta-blocker
71	Assessment of Quality of Life and Treatment Outcomes of Patients with Persistent Postchemotherapy Alopecia	Azael Freites-Martinez et al. 2019[104]	Retrospective cohort	Various cancers	Spironolactone
72	Association Between Angiotensin II Receptor Blockers and the Risk of Lung Cancer Among Patients with Hypertension From the Korean National Health Insurance Service-National Health Screening Cohort	Sungji Moon et al. 2020[105]	Retrospective cohort	Lung cancer	ARB[2]
73	Association Between Urinary Catecholamine Excretion and Urine Volume	Michael Haap et al. 2019[106]	Not specified	Primary brain tumors	ACEI[1]
74	Association between Concomitant Use of Hydrochlorothiazide and Adverse Chemotherapy-Related Events among Older Women with Breast Cancer Treated with Cyclophosphamide	Christine D. Hsu et al. 2020[107]	Cohort study	Breast cancer	HCT[4]
75	Association between Use of Hydrochlorothiazide and Risk of Keratinocyte Cancers in Kidney Transplant Recipients	Thibault Letellier et al. 2020[108]	Cohort study	Pancreatic cancer	HCT[4]
76	Association of Hydrochlorothiazide Use and Risk of Malignant Melanoma	Anton Pottegård et al. 2018[109]	Case-control study	Melanoma	HCT[4]
77	Association of RAAS inhibitors on osteoporosis and fracture risk in the hypertensive population-A prospective population-based cohort study in Lanzhou, China	Hongtao Yin et al. 2024[110]	Prospective cohort	Various cancers	ARB[2]
78	Associations between initiating antihypertensive regimens on stage I-III colorectal cancer outcomes: A Medicare SEER cohort analysis	Rajesh Balkrishnan et al. 2021[111]	Retrospective cohort	Colorectal cancer	ACEI[1] Beta-blocker
79	Associations between short-term efficacy and clinical characteristics of infantile hemangioma treated by propranolol	Changhua Wu et al. 2019[112]	Retrospective study	Various cancers	Propranolol
80	Associations of Angiotensin-Converting Enzyme Inhibitor or Angiotensin Receptor	Theodore M. Brasky et al. 2021[113]	Prospective study	Colorectal cancer	ARB[2]

#	Title	Authors & Year	Study Design	Cancer Site (s)	Off-Label Drug(s)
	Blocker Use with Colorectal Cancer Risk in the Women's Health Initiative				
81	Beta blocker and steroid therapy in the treatment of infantile hepatic hemangioendothelioma	Zeynep Canan Özdemir et al. 2017[114]	Not specified	Thyroid cancer	Beta-Blocker, Propranolol
82	Beta-adrenergic receptor blockers and liver cancer mortality in a national cohort of hepatocellular carcinoma patients	Ruzan Udumyan et al. 2020[115]	Retrospective cohort	Hepatocellular carcinoma	Beta-Blocker
83	Calcium Channel Blocker Versus Renin-Angiotensin System Inhibitor in Risk of Kidney Cancer Among Patients with Hypertension: A Propensity Score-Matched Cohort Study	Minji Jung et al. 2024[116]	Retrospective cohort	Renal cell carcinoma	ARB[2]
84	Case Report: Giant Paraganglioma of the Skull Base with Two Somatic Mutations in SDHB and PTEN Genes	Ailsa Maria Main et al. 2022[117]	Case report	HNSCC[5]	Labetalol
85	Case report: Alectinib-associated intestinal ulceration and colitis in a patient with NSCLC[7] and effective treatment with Mesalazine	Zijian Qiu et al. 2025[118]	Case report	NSCLC[7]	ARB[2]
86	Change of serum cytokine profiles by propranolol treatment in patients with infantile hemangioma	Sayaka Tani et al. 2019[119]	Not specified	Various cancers	Propranolol
87	Clinical Features, Prognostic Factors, and Treatment Interventions for Ulceration in Patients with Infantile Hemangioma	Esteban Fernández Faith et al. 2021[120]	Retrospective cohort	Various cancers	Propranolol
88	Clonidine suppression testing for pheochromocytoma in neurofibromatosis type 1	WingYee Wan et al. 2019[121]	Not specified	Various cancers	Clonidine
89	Comparison of diagnostic evaluations for cough among initiators of angiotensin converting enzyme inhibitors and angiotensin receptor blockers	Mugdha Gokhale et al. 2016[122]	Not specified	Lung cancer	ARB[2], ACEI[1]
90	Comparison of efficacy and safety between benidipine and hydrochlorothiazide in fosinopril-treated hypertensive patients with chronic kidney disease: protocol for a randomised controlled trial	Cheng Xue et al. 2017[123]	Randomized controlled trial	Renal cell carcinoma	HCT[4], ACEI[1] Fosinopril
91	Computed tomography combined with confirmatory tests for the diagnosis of aldosterone-producing adenoma	Shihan Chen et al. 2021[124]	Retrospective study	Various cancers	Captopril
92	Daily Lisinopril vs Placebo for Prevention of Chemoradiation-Induced Pulmonary Distress in Patients with Lung Cancer (Alliance MC1221): A Pilot Double-Blind Randomized Trial	Terence T. Sio et al. 2019[125]	Randomized controlled trial	Lung cancer	Lisinopril
93	Does Angiotensin-Converting Enzyme Inhibitor and β-Blocker Use Reduce the Risk of Primary Liver Cancer? A Case-Control Study Using the U.K. Clinical Practice Research Datalink	Katrina Wilcox Hagberg et al. 2016[126]	Case-control study	Hepatocellular carcinoma	ACEI[1]

#	Title	Authors & Year	Study Design	Cancer Site (s)	Off-Label Drug(s)
94	Early propranolol treatment of infantile hemangiomas improves outcome	Ana Giachetti et al. 2023[127]	Retrospective cohort	Sarcoma	Propranolol
95	Effect of Oral Propranolol on Periocular Infantile Capillary Hemangioma: Outcomes Based on Extent of Involvement	Kavya M. Bejjanki et al. 2021[128]	Retrospective study	Various cancers	Propranolol
96	Effect of Propranolol on 18F-Fluorodeoxyglucose Uptake in Brown Adipose Tissue in Children and Young Adults with Neoplastic Diseases	Samuel L. Brady et al. 2021[129]	Cohort study	Various cancers	Propranolol
97	Effect of intrathecal morphine and epidural analgesia on postoperative recovery after abdominal surgery for gynecologic malignancy: an open-label randomised trial	Preben Kjølhede et al. 2019[130]	Randomized controlled trial	Various cancers	Clonidine
98	Effective Management of Advanced Angiosarcoma by the Synergistic Combination of Propranolol and Vinblastine-based Metronomic Chemotherapy: A Bench to Bedside Study	Eddy Pasquier et al. 2016[131]	Not specified	VMC[10]	Propranolol
99	Effectiveness of fixed Doses of Propranolol in the Treatment of Hemangiomas Regardless of Child's weight gain: A case report	Jaime Anger et al. 2019[132]	Case report	Various cancers	Propranolol
100	Efficacy and Safety of Topical Timolol for the Treatment of Infantile Hemangioma in the Early Proliferative Stage: A Randomized Clinical Trial	Fania Z. Muñoz-Garza et al. 2021[133]	Randomized controlled trial	Various cancers	Propranolol
101	Efficacy and safety of standard dose triple combination of telmisartan 80 mg/amlodipine 5 mg/chlorthalidone 25 mg in primary hypertension: A randomized, double-blind, active-controlled, multicenter phase 3 trial	Eun Joo Cho et al. 2023[134]	Randomized controlled trial	Leukemia	Chlorthalidone, Telmisartan, Amlodipine
102	Efficacy of Eplerenone in the Management of Mineralocorticoid Excess in Men with Metastatic Castration-resistant Prostate Cancer Treated with Abiraterone Without Prednisone	David Gill et al. 2017[135]	Retrospective cohort	Prostate cancer	Spironolactone, Eplerenone
103	Efficacy of infantile hepatic hemangioma with propranolol treatment: A case report	Mu-Chieh Tsai et al. 2019[136]	Case report	Various cancers	Propranolol
104	Efficacy of losartan plus modified Folfirinox Versus Modified Folfirinox in advanced pancreatic cancers: A randomized clinical trial (AFPAC Study)	Anant Ramaswamy et al. 2025[137]	Randomized controlled trial	Pancreatic cancer	ARB[2], Losartan
105	Endoscopic variceal ligation combined with carvedilol versus endoscopic variceal ligation combined with propranolol for the treatment of oesophageal variceal bleeding in cirrhosis: study protocol for a multicentre, randomised controlled trial	Yiling Li et al. 2025[138]	Randomized controlled trial	Hepatocellular carcinoma	Beta-blocker, Propranolol, Carvedilol
106	Evaluation of antihypertensive medications use and survival in patients	Rūta Everatt et al. 2024[24]	Retrospective cohort	Ovarian cancer	ACEI[1], Beta-blocker

#	Title	Authors & Year	Study Design	Cancer Site (s)	Off-Label Drug(s)
	with ovarian cancer: a population-based retrospective cohort study				
107	Evaluation of various confirmatory tests for the diagnosis of aldosterone-producing adenoma	Satoshi Kidoguchi et al. 2020[139]	Not specified	Various cancers	Captopril
108	Expression and function of ABCG2 and XIAP in glioblastomas	Ivette F. Emery *et al.,* 2017[140]	Not specified	Primary brain tumors	ARB[2]
109	High expression of CD44v9 and xCT in chemoresistant hepatocellular carcinoma: Potential targets by sulfasalazine	Fumitaka Wada et al. 2018[141]	Not specified	Hepatocellular carcinoma	ARB[2]
110	Histopathological analysis of spontaneous large necrosis of adrenal pheochromocytoma manifested as acute attacks of alternating hypertension and hypotension: a case report	Nobumasa Ohara et al. 2016[142]	Randomized controlled trial	Various cancers	ARB[2]
111	Huge fetal hepatic Hemangioma: prenatal diagnosis on ultrasound and prognosis	Li Jiao-Ling et al. 2018[143]	Not specified	Various cancers	Propranolol
112	Hydrochlorothiazide use and risk of nonmelanoma skin cancer: A nationwide case-control study from Denmark	Sidsel Arnspang P. *et al.,* 2018[144]	Case-control study	Various cancers	HCT[4]
113	Hydrochlorothiazide use is strongly associated with risk of lip cancer	A. Pottegård *et al.,* 2017[145]	Case-control study	Various cancers	HCT[4]
114	Hypertension, use of antihypertensive medications, and risk of epithelial ovarian cancer	Tianyi Huang et al. 2016[146]	Prospective cohort	Ovarian cancer	Beta-Blocker
115	Impact of Angiotensin I-converting Enzyme Inhibitors and Angiotensin II Type-1 Receptor Blockers on Survival of Patients with NSCLC	Lili Miao et al. 2016[147]	Retrospective study	NSCLC[7]	ARB[2]
116	Impact of Angiotensin Receptor Blockers, Beta Blockers, Calcium Channel Blockers and Thiazide Diuretics on Survival of Ovarian Cancer Patients	Min Ae Cho et al. 2020[148]	Retrospective study	Ovarian cancer	ARB[2], Beta-Blocker
117	Impact of renin angiotensin system inhibitors on survival of patients with metastatic non-small cell lung cancer	Nadiye Sever et al. 2025[149]	Randomized controlled trial	NSCLC[7]	Beta-blocker, ARB[2]
118	Individualized dosing of oral propranolol for treatment of infantile hemangioma: a prospective study	Arun Prasad et al. 2019[150]	Prospective study	Various cancers	Propranolol
119	Infantile Subglottic Hemangioma: A Case Report Infantile Subglottic Hemangioma: A Case Report	Richa Baniya et al. 2024[151]	Case report	Various cancers	Propranolol
120	Infantile hemangiomas: risk factors for complications, recurrence and unaesthetic sequelae	Letícia Gaertner Mariani et al. 2022[152]	Retrospective cohort	HNSCC[5]	Propranolol
121	Inhibition of β2-adrenergic receptor reduces triple-negative breast cancer brain metastases: The potential benefit of perioperative β-blockade	Cecilia Choy et al. 2016[153]	Retrospective study	Breast cancer	Propranolol

#	Title	Authors & Year	Study Design	Cancer Site (s)	Off-Label Drug(s)
122	Long-term exposure to antihypertensive drugs and the risk of cancer occurrence: evidence from a large population-based study	Matteo Franchi et al. 2024[154]	Cohort study	Various cancers	Beta-blocker
123	Long-term neurocognitive functioning of children treated with propranolol or atenolol for infantile hemangioma	Mireille M. Hermans et al. 2023[155]	Clinical trial	Various cancers	Beta-blocker, Propranolol, Atenolol
124	Losartan May Not Prevent Vestibular Schwannoma Growth or Related Hearing Loss During Observation	Benjamin D. Lovin et al. 2024[156]	Randomized controlled trial	Various cancers	losartan
125	Management of severe hypertension due to lenvatinib in patients with advanced thymic carcinoma: A case report	Kinnosuke M. et al. 2022[157]	Case report	Lung cancer	Azilsartan, Amlodipine
126	Neonatal giant hepatic hemangioma: A case report	Zhenwei Zhu et al. 2018[158]	Case report	Various cancers	Propranolol
127	Oral propranolol combined with topical timolol for compound infantile hemangiomas: a retrospective study	Jing Ge et al. 2016[159]	Retrospective study	Various cancers	Propranolol
128	Oral propranolol for the treatment of infantile haemangiomas in Singapore	Joanne Mui Ching Tan et al. 2021[160]	Retrospective cohort	HNSCC[5]	Beta-Blocker, Propranolol
129	Our Experience in Treating Infantile Hemangioma: Prognostic Factors for Relapse After Propranolol Discontinuation	Hiba Zaaroura et al., 2025[161]	Retrospective cohort	Various cancers	Propranolol
130	Phase I Clinical Trial of Combination Propranolol and Pembrolizumab in Locally Advanced and Metastatic Melanoma: Safety, Tolerability, and Preliminary Evidence of Antitumor Activity	Shipra Gandhi et al. 2021[162]	Clinical trial	Melanoma	Propranolol
131	Postdiagnostic use of antihypertensive medications and survival in colorectal, lung, corpus uteri, melanoma and kidney cancer patients with hypertension	Rūta Everatt et al. 2025[163]	Cohort study	Lung cancer	ARB[2], Beta-blocker
132	Practical surgical technique using the SMISS approach for lip reduction in involuted lip infantile hemangiomas	Qianyi Chen et al. 2024[164]	Retrospective study	Various cancers	Propranolol
133	Propranolol as an effective therapy for infantile haemangioma of the urinary bladder	Taha Anwar et al. 2019[165]	Not specified	Bladder/urothelial cancer	Propranolol
134	Propranolol for Off-label Treatment of Patients with Melanoma: Results From a Cohort Study	Vincenzo De Giorgi *et al.*, 2018[166]	Randomized controlled trial	Melanoma	Propranolol
135	Propranolol induced G0/G1/S phase arrest and apoptosis in melanoma cells via AKT/MAPK pathway	Chengfang Zhou et al. 2016[167]	Not specified	Melanoma	Propranolol
136	Propranolol treatment for infantile hemangioma: a case series of sixty-two patients	Giovanna Stringari et al. 2016[168]	Case series	Various cancers	Propranolol
137	Prospective pilot trial with combination of propranolol with chemotherapy in patients with epithelial ovarian cancer and	Lois M. Ramondetta et al. 2019[169]	Clinical trial	Ovarian cancer	Beta-Blocker, Propranolol, ARB[2]

#	Title	Authors & Year	Study Design	Cancer Site (s)	Off-Label Drug(s)
	evaluation on circulating immune cell gene expression				
138	Rare airway tumor in a previously healthy adolescent successfully treated with endoscopic resection and oral propranolol	Alexander I. et al. 2023[170]	Case report	Various cancers	Propranolol
139	Rebound Growth of Infantile Hemangiomas after Propranolol versus Atenolol Treatment: A Retrospective Study	Shoham Baruch et al. 2024[171]	Retrospective study	Various cancers	Propranolol; Atenolol
140	Regulatory/modulatory effect of prune essence concentrate on intestinal function and blood lipids	Hui-Fang Chiu et al. 2017[172]	Randomized controlled trial	Various cancers	ARB[2]
141	Renin-Angiotensin-Aldosterone System-based Antihypertensive Agents and the Risk of Colorectal Cancer Among Medicare Beneficiaries	Phyo T. Htoo et al. 2019[173]	Cohort study	Colorectal cancer	ARB[2], Beta-Blocker
142	Renin-angiotensin system inhibitors improve the survival of cholangiocarcinoma: a propensity score-matched cohort study	Xiao-Xu Zhu et al. 2023[174]	Retrospective cohort	Cholangio-carcinoma	ARB[2]
143	Repurposing existing medications as cancer therapy: design and feasibility of a randomized pilot investigating propranolol administration in patients receiving hematopoietic cell transplantation	Jennifer M. Knight et al., 2018[25]	Randomized controlled trial	Multiple myeloma	Propranolol
144	Response to angiotensin blockade with irbesartan in a patient with metastatic colorectal cancer	M. R. Jones et al., 2016[175]	Not specified	Colorectal cancer	Irbesartan
145	Retrospective analysis of neoplasms in patients using angiotensin receptor blockers	Arvind Kumar Sharma et al. 2024[176]	Retrospective study	Various cancers	ARB[2], ACEI[1], Beta-blocker,TelmisartanCandesartan
146	Risk of Nonmelanoma Skin Cancer in Association with Use of Hydrochlorothiazide-Containing Products in the United States	Efe Eworuke et al. 2021[177]	Retrospective cohort	Various cancers	HCT[4]
147	Risk of squamous cell carcinoma of the lip and cutaneous melanoma in older Australians using HCT: A population-based case-control study	Benjamin Daniels et al. 2020[178]	Case-control study	Melanoma	HCT[4]
148	Safety and effectiveness of oral propranolol for infantile hemangiomas started before 5 weeks and after 5 months of age: an Italian multicenter experience	Maya El Hachem et al. 2017[179]	Retrospective cohort	Various cancers	Propranolol
149	Success in the use of oral propranolol in the treatment of infantile hemangioma in nasal tip - Report of two cases	Mariana Carvalho Costa et al. 2020[180]	Not specified	VMC[10]	Beta-Blocker, Propranolol
150	Successful re-administration of Pazopanib in a patient with metastatic renal cell carcinoma and a history of Pazopanib-induced nephrotic syndrome: a case report	So-Yeon Jeon et al. 2019[181]	Case report	Lung cancer	Amlodipine

#	Title	Authors & Year	Study Design	Cancer Site (s)	Off-Label Drug(s)
151	Successful treatment of an exudative choroidal hemangioma with oral propranolol in a 10-year-old boy	Bliss E. O'Bryhim et al. 2019[182]	Clinical trial	Various cancers	Propranolol
152	Systemic β-Adrenergic Receptor Activation Augments the ex vivo Expansion and Anti-Tumor Activity of Vγ9Vδ2 T-Cells	Forrest L. Baker et al., 2019[183]	Randomized controlled trial	Various cancers	Beta-Blocker, Bisoprolol
153	The Role of the Pharmacist in the Treatment of Patients with Infantile Hemangioma Using Propranolol	Saul Castaneda et al. 2016[184]	Prospective study	Various cancers	Propranolol
154	The Use of Antihypertensive Medication and the Risk of Breast Cancer in a Case-Control Study in a Spanish Population: The MCC-Spain Study	Inés Gómez-Acebo et al. 2016[185]	Case-control study	Breast cancer	Beta-Blocker
155	Risk of squamous cell carcinoma of the lip and cutaneous melanoma in older Australians using hydrochlorothiazide: A population-based case-control study.	Benjamin *et al.,* 2020[186]	A population-based case-control study	Melanoma	hydrochlorothiazide
156	The Use of Telmisartan and the Incidence of Cancer	Koray T. et al., 2016[187]	Cohort study	Lung cancer	ARB[2], Telmisartan
157	The effect of propranolol on the prognosis of hepatocellular carcinoma: A nationwide population-based study	Ping-Ying Chang et al. 2019[188]	Cohort study	Hepatocellular carcinoma	Beta-Blocker, Propranolol
158	The use of drugs acting on the renin-angiotensin system and the incidence of pancreatic cancer	Victoria Mandilaras et al. 2017[189]	Case-control study	Pancreatic cancer	ARB[2]
159	Timed sequential therapy of the selective T-type calcium channel blocker mibefradil and temozolomide in patients with recurrent high-grade gliomas	Matthias Holdhoff et al. 2017[190]	Cohort study	Primary brain tumors	ARB[2]
160	To compare intralesional and oral propranolol for treating periorbital and eyelid capillary hemangiomas	Aditi Mehta et al. 2019[191]	Randomized controlled trial	Various cancers	Propranolol
161	Total Neoadjuvant Therapy with Folfirinox in Combination with Losartan Followed by Chemoradiotherapy for Locally Advanced Pancreatic Cancer: A Phase 2 Clinical Trial	Janet E. Murphy et al., 2019[192]	Clinical trial	Pancreatic cancer	Losartan
162	Treatment failure with propranolol for subglottic haemangioma	Zhaobo Liu et al. 2019[193]	Not specified	Various cancers	Propranolol
163	Ultrasound and MRI findings as predictors of propranolol therapy response in patients with infantile hemangioma	Hee Jin Park et al. 2021[194]	Retrospective study	Various cancers	Propranolol
164	Use of N-nitrosodimethylamine (NDMA) contaminated valsartan products and risk of cancer: Danish nationwide cohort study	Anton Pottegård et al. 2018[195]	Cohort study	Colorectal cancer	Valsartan
165	Use of hydrochlorothiazide and risk of skin cancer: a nationwide Taiwanese case-control study	Anton Pottegård et al. 2019[196]	Case-control study	Melanoma	HCT[4]
166	Use of liothyronine without levothyroxine in the treatment of mild consumptive hypothyroidism caused by hepatic hemangiomas	Shinji Higuchi et al. 2017[197]	Not specified	Thyroid cancer	Propranolol

#	Title	Authors & Year	Study Design	Cancer Site (s)	Off-Label Drug(s)
167	Use of non-selective β-blockers is associated with decreased tumor proliferative indices in early stage breast cancer	Alexa Montoya et al., 2017[26]	Retrospective study	Breast cancer	Beta-Blocker, Propranolol
168	Utility of the ACE Inhibitor Captopril in Mitigating Radiation-associated Pulmonary Toxicity in Lung Cancer: Results From NRG Oncology RTOG 0123	William Small et al. 2018[198]	Randomized controlled trial	NSCLC[7]	ACEI[1] Captopril
	Antihypertensives; Anti-inflammatories (n = 3)				
169	Antihypertensive treatments and risks of lung Cancer: a large population-based cohort study in Hong Kong	Jinhui Li et al. 2021[199]	Retrospective cohort	Lung cancer	Aspirin, ARB[2]
170	Pancreatic resection with perioperative drug repurposing of propranolol and etodolac - the phase II randomized controlled PROSPER trial	Felix J. Hüttner et al. 2025[200]	Randomized controlled trial	Pancreatic cancer	Propranolol, COX-2[3]
171	Perioperative COX-2 and β-Adrenergic Blockade Improves Metastatic Biomarkers in Breast Cancer Patients in a Phase-II Randomized Trial	Lee Shaashua et al. 2017[201]	Randomized controlled trial	Breast cancer	Propranolol, COX-2[3]
	Antihypertensives; Statins (n = 5)				
172	Assessment of concomitant non-oncologic medication in patients with surgically treated renal cell carcinoma: impact on prognosis, cell-cycle progression and proliferation	Eva Neumann et al. 2019[202]	Not specified	Renal cell carcinoma	ARB[2], Statins
173	Enteroids to Study Pediatric Intestinal Drug Transport	Eva J. Streekstra et al. 2024[203]	Not specified	Breast cancer	Rosuvastatin, Propranolol, Enalapril, Statins
174	Multicenter, Phase III, Randomized, Double-Blind, Placebo-Controlled Trial of Pravastatin Added to First-Line Standard Chemotherapy in Small-Cell Lung Cancer (LUNGSTAR)	Michael J. Seckl et al. 2017[204]	Randomized controlled trial	SCLC[8]	Pravastatin, Statins, ARB[2]
175	Nonadherence to Statins and Antihypertensives and Hospitalizations Among Elderly Medicare Beneficiaries with Incident Cancer	Ishveen Chopra et al. 2017[205]	Retrospective study	Breast cancer	Statins, ARB[2]
176	Severe adverse cutaneous reactions induced by gefitinib combined with antihypertensive and antihyperlipidemic drugs in lung cancer: a case report	Xiao Shen et al. 2022[206]	Case report	Lung cancer	Rosuvastatin, Simvastatin, Nifedipine, Valsartan, Statins
	Statins (n = 5)				
177	Randomized phase 2 study of valproic acid combined with simvastatin and gemcitabine/nab-paclitaxel-based regimens in untreated metastatic pancreatic adenocarcinoma patients: the VESPA trial study protocol	Alfredo Budillon et al. 2024[207]	Randomized controlled trial	Pancreatic cancer	Simvastatin, Statins

#	Title	Authors & Year	Study Design	Cancer Site (s)	Off-Label Drug(s)
178	Simvastatin delays castration-resistant prostate cancer metastasis and androgen receptor antagonist resistance by regulating the expression of caveolin-1	Yingying Gao et al. 2019[208]	Retrospective study	Prostate cancer	Simvastatin, Statins
179	Statin use is associated with improved survival in ovarian cancer: A retrospective population-based study	Alexandra Couttenier et al. 2017[209]	Retrospective cohort	Ovarian cancer	Rosuvastatin, Simvastatin, Statins
180	The Effect of Atorvastatin on Oncogenic miRNAs in Hematological Malignancies: A Central Study	Jood Hashem et al. 2024[210]	Cohort study	Leukemia	Atorvastatin, Statins
181	The Effect of Statins on Markers of Breast Cancer Proliferation and Apoptosis in Women with In Situ or Early-Stage Invasive Breast Cancer	Anam Kamal et al. 2024[211]	Clinical trial	Breast cancer	Simvastatin, Statins

3.3. Leading Non-Oncologic Pharmacotherapies Evaluated in Oncology (Top 10)

The ten most represented agents (Table 2) highlight the centrality of sympathetic/RAAS blockade and glucose-lowering therapy: propranolol leads (48 studies; 26.5%), followed by ARBs (19.9%), (class), metformin (16.0%), statins (class) **(**25; 13.8%**),** β-blockers (class) **(**21; 11.6%**),** insulin (16; 8.8%), hydrochlorothiazide **(**11; 6.1%), ACEIs (class) (9; 5.0%), aspirin (8; 4.4%), and losartan (6; 3.3%). This rank order highlights a literature concentrated on propranolol and RAAS modulation, with metformin as the leading non-oncologic metabolic agent, and a long-tail of other commonly prescribed medicines.

Table 2: Top 10 Off-label Drugs Across Included Studies

Off-label drug	Label	Count (studies)	Overall (%)
Propranolol	antihypertensive	48	26.5%
ARB (class)	antihypertensive	36	19.9%
Metformin	antidiabetic	29	16.0%
Statins (class)	statins	25	13.8%
Beta-blocker (class)	antihypertensive	21	11.6%
Insulin	antidiabetic	16	8.8%
Hydrochlorothiazide	antihypertensive	11	6.1%
ACE inhibitor (class)	antihypertensive	9	5.0%
Aspirin	anti-inflammatories	8	4.4%
Losartan	antihypertensive	6	3.3%

3.4. Distribution of Cancer Sites and Drug Classes Normalized

The distribution of the included studies (n = 181) across cancer sites (Figure 2 A) shows lung (all) as the largest site-specific share (17.9%), with substantial representation of breast (8.1%)**,** colorectal (7.7%)**,** pancreatic (7.6%)**,** and ovarian cancers (6.5%)**,** while heterogeneous cohorts under "various cancers" contribute to 22.4% of the normalized total. By class of drugs normalized (Figure 2 B), antihypertensives account for the majority (61.7%), followed by antidiabetics (7.7%)**,** statins (9.6%), anti-inflammatories (5.8), antibiotics (2.7%), antidepressants (2.0%), and anthelmintics (0.4%) Within sites, antihypertensives contribute notably to lung (13.8% of cells) and ovarian (6.1%), whereas antidiabetics feature in lung (5.5%) and pancreatic (5.0%) disease; statin-related entries appear in lung (3.3%), pancreatic (2.2%), and ovarian (1.7%) categories.

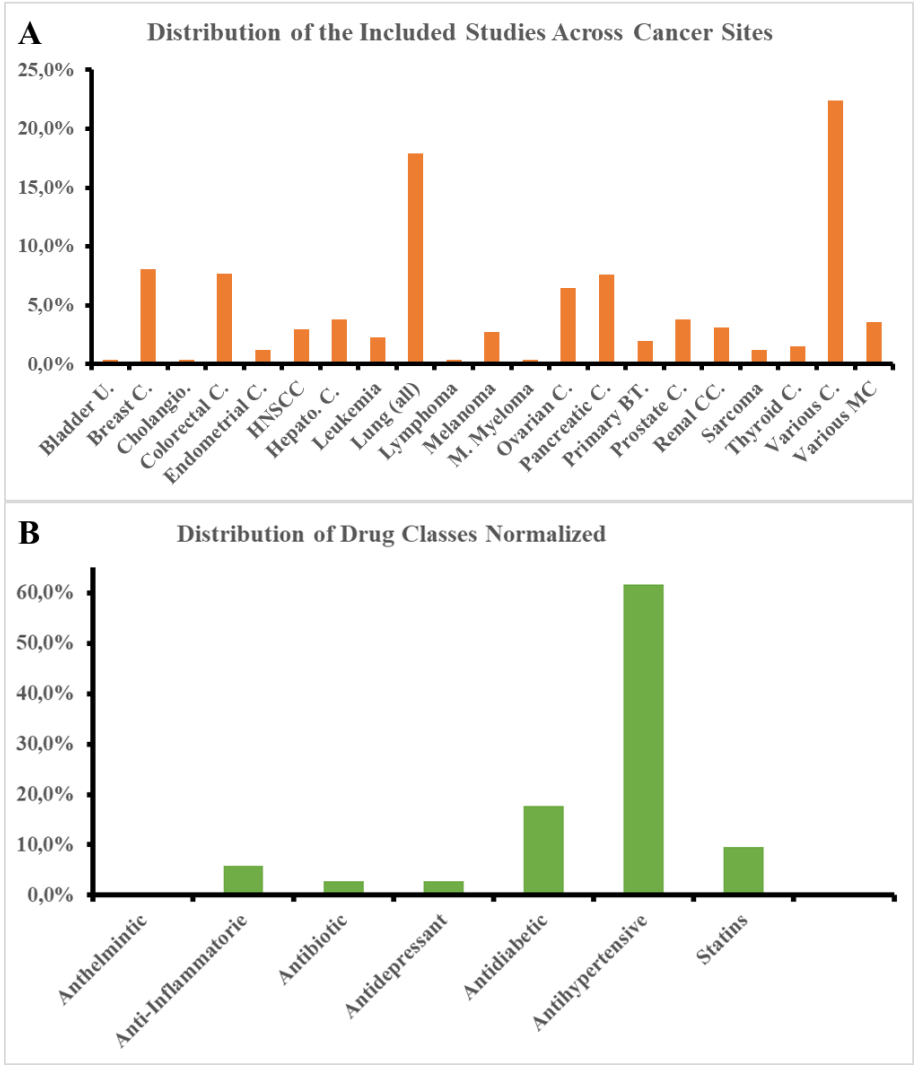

Figure 2: Distribution of Cancer Sites and Drug Classes Normalized

3.5. Outcome-Wise Evidence Reliability Assessment

Screening-level outcome coding (table 3) indicates moderate reliability signals favouring benefit for overall survival (OS) (15; 40% showing benefit) and mortality (16; 43.8% benefit), with recurrence likewise showing benefit signals (13; 38.5%) whereas similarly based mainly on observational designs; progression-free survival (PFS) (3 studies; 66.7% benefit) and Disease-free survival (DFS) (3; 100% benefit) are rated low due to very small numbers; objective response rate (ORR) (3; evenly split 33/33/33%) shows no consistent effect; quality of life **(**QoL) evidence is very low (2 studies with no consistent effect); and toxicity/safety shows a moderate reliability profile (12 studies) with mixed but interpretable signals. Overall, the evidence suggests hypothesis-generating benefits in survival-related outcomes, warranting study-level verification and, where feasible, meta-analytic synthesis.

Table 3: Synthesis of evidence reliability by outcome

Outcome	# Studies	Benefit (%)	No effect (%)	Harm (%)	Evidence Reliability Rating	Interpretation
DFS	3	100.0%	0.0%	0.0%	Low	Signals of benefit predominate.
Mortality	16	43.8%	6.2%	12.5%	Moderate	Signals of benefit predominate.
ORR	3	33.3%	33.3%	33.3%	Low	No consistent effect across studies.
OS	15	40.0%	6.7%	20.0%	Moderate	Signals of benefit predominate.
PFS	3	66.7%	33.3%	0.0%	Low	Mixed/uncertain evidence.
Quality of life	2	0.0%	0.0%	0.0%	Very low	No consistent effect across studies.
Recurrence	13	38.5%	15.4%	7.7%	Moderate	Signals of benefit predominate.
Toxicity/safety	12	25.0%	8.3%	8.3%	Moderate	Signals of benefit predominate.

Disease-free survival (DFS); Objective response rate (ORR); Overall survival (OS); Progression-free survival (PFS)

3.6. Adverse Event Reporting, Outcome Evidence, and Risk-of-Bias Assessment

The Safety/Adverse Events, the Outcomes Evidence Synthesis and the Risk of-Bias Assessment for all the included studies (n = 181) are been performed and reported respectively in appendix A, B and C.

In fact, appendix A consolidates, for each included study, the cancer site, repurposed non-oncologic drug(s), and Common Terminology Criteria for Adverse Events (CTCAE)-aligned adverse events with aspartate aminotransferase) and ALT **(**alanine aminotransferase) AST/ALT mapped to "AST increased/ALT increased", alongside reported AE frequency, severity (including flags for grade ≥3), and any treatment discontinuations due to AEs. This appendix is intended to surface cross-study pharmacovigilance signals, such as hepatic enzyme elevations, hypertension, neuropathy and infections, and to highlight reporting gaps relevant to benefit–risk appraisal.

The appendix B aggregates study-level clinical outcomes (OS, PFS, DFS, ORR, recurrence, mortality, QoL, toxicity) with their corresponding significance status and a brief, standardized conclusion label. Significance encodings (*e.g.*, P-value reported, Effect size reported, Not significant, Results not reported) are drawn automatically from abstracts/tags and therefore function as screening-level annotations rather than definitive adjudications. The goal is to enable rapid mapping of signal directionality (benefit/no effect/harm) by drug class and tumor type, while clearly marking entries that require full-text confirmation for meta-analytic use.

The appendix B provides a heuristic *Risk-of-Bias (*ROB) screen using abstract-level cues for randomisation, blinding, and outcome reporting (registered/prespecified), then synthesizes an overall ROB per pre-stated rules (e.g., High non-randomized designs; Low risk where randomisation/blinding and reporting were adequate; Some concerns otherwise). Because inputs are tag/abstract based, entries flagged as unclear or high risk should be validated against full texts. The table of this appendix is designed to prioritize studies for qualitative synthesis, sensitivity analyses, and potential exclusion where bias threatens internal validity.

4. Discussion

A panoramic overview of the therapeutic landscape is first provided and outcome distributions are described; the highest-priority class signals are then consolidated, reliability is integrated with safety and risk-of-bias appraisals, and practice guardrails with research priorities are articulated to convert signals into decision-grade evidence.

4.1. Panoramic Evidence Overview of the Therapeutic Landscape

The panoramic cartography base on the therapeutic landscape is heterogeneous. Cardiometabolic agents, *i.e.*, pharmaceuticals used to prevent or treat cardiovascular and metabolic disorders such as conditions involving blood pressure, lipids, glucose/insulin resistance, thrombosis, and obesity, dominate this therapeutic landscape. Typical pharmaceuticals such as propranolol (26.5%)**,** followed by ARBs (19.9%), metformin (16.0%), statins (13.8%), β-blockers (11.6%)**,** insulin (8.8%), hydrochlorothiazide (6.1%)**,** ACEIs (5.0%), aspirin (4.4%) and losartan (3.3%), Table 2.

In fact, in pancreatic ductal adenocarcinoma (PDAC), stromal modulation with angiotensin-receptor blockade has been explored alongside intensified chemotherapy. Early-phase data suggest higher downstaging and R0 resection rates in locally advanced disease; however, randomized data in advanced PDAC have not confirmed a PFS benefit, highlighting disease-setting specificity and the need for biomarker anchoring.[137,192]

Afterwards, co-administration of a short perioperative β-blockade and with COX-2 inhibitor has demonstrated modulation of dissemination-related biomarkers and signals compatible with improved disease-free outcomes in early breast cancer.[201]

In addition, for antiplatelet strategies, concurrent or neoadjuvant aspirin during chemoradiation in rectal cancer has been associated with improved tumor downstaging and survival signals, though definitive large RCTs are limited.[212–215] In metastatic melanoma, adding propranolol to anti-PD-1 therapy appears feasible with preliminary activity, warranting controlled evaluation.[162]

Subsequently, metformin shows context-dependent signals. Thus a PFS benefit has been suggested in advanced non-squamous NSCLC when combined with platinum-taxane-bevacizumab, whereas randomized trials in unresectable stage III NSCLC failed to show survival benefit when added to concurrent chemoradiotherapy, cautioning against routine use outside trials.[85,216–220]

Regarding the outcomes evidence, survival endpoints (OS, PFS, DFS) are the most frequently reported outcomes, whereas objective response rate and quality-of-life metrics are comparatively sparse and inconsistently defined (Table 3). This pattern highlights the largely associative nature of current evidence and the need for harmonized endpoints and consistent censoring rules before any quantitative synthesis.

Moreover, the Biological rationales are concordant with this landscape. Indeed, β-blockade targets stress-axis signaling and may enhance antitumor immune responses; RAAS inhibition can decompress desmoplastic stroma and improve perfusion; metformin engages AMPK/mTOR and tumor metabolism; statins influence the mevalonate pathway and membrane prenylation; and COX-2 inhibition modulates inflammation relevant to tumor progression, especially in the peri-treatment window.

Finally, population-based cohorts and meta-analyses suggest improved survival in ovarian cancer among statin users, with heterogeneity by histotype and lipophilicity class; prospective, biomarker-guided trials are warranted.[71,209,221]

4.2. Priority Signals by Drug Class

β-blockers, mainly propranolol, show convergent biologic and early clinical signals. In melanoma, early-phase work combining propranolol with PD-1 blockade suggests immunomodulatory synergy; perioperative β-blockade paired with COX-2 inhibition repeatedly attenuates pro-metastatic biomarker profiles in breast cancer. These findings justify focused, disease-specific randomized testing rather than class-wide generalization.[222–224]

Subsequently, RAAS inhibitors (ACEIs/ARBs) are supported by observational associations across select histologies (e.g., lung, ovarian, hepatobiliary), but confounding by indication and exposure misclassification remain material threats.[225–227] Translationally, losartan-containing total neoadjuvant strategies in pancreatic cancer demonstrate feasibility and encouraging R0 resection rates, although randomized data are mixed and do not yet establish consistent PFS/OS gains. Taken together, these findings support histology-specific development with careful causal design.[228–231]

Overall heterogeneity reflects differences in disease stage, treatment backbone, dosing/intensity and timing, and patient/tumor biology; the losartan-associated downstaging in Locally advanced pancreatic ductal adenocarcinoma (LAPC) versus null PFS in advanced PDAC illustrates setting-specific effects, while mixed NSCLC results with metformin highlight dependence on metabolic phenotypes and radiotherapy sequencing.[85,137,192,216]

Metformin, in particular, exhibits a large literature footprint with context-dependent effects. Population-based cohorts and some meta-analyses report survival advantages, often in patients with diabetes or selected histologies, whereas RCT-focused syntheses in non-diabetic NSCLC show no consistent OS/PFS benefit despite occasional gains in disease control. Effect modification by diabetes and tumor metabolic phenotype is plausible, pointing to target-trial emulation and biomarker-anchored subgrouping in future evaluations.[232–234]

Statins and aspirin/NSAIDs provide promising but non-definitive signals.[212–214] In ovarian cancer, several cohorts and reviews suggest improved survival among statin users, though heterogeneity by statin class, timing, and histotype limits inference. In rectal cancer, low-dose aspirin during neoadjuvant chemoradiation has been associated with deeper pathological responses in randomized settings, an observation warranting stratified confirmation.[235–239]

4.3. Outcomes, Safety and Risk of Bias

The reliability of the outcomes remained inconsistent, although time-to-event endpoints dominate, definitions, progression ascertainment, and censoring conventions vary across studies, limiting aggregation. Objective response is inconsistently reported, and quality-of-life outcomes remain under-measured. Hence, directional trends are favored over precise pooled effect estimates, and outcome harmonization is endorsed for all meta-analytic efforts.

Safety profiles largely mirror known class effects but are incompletely reported. Recurrent themes include hepatic enzyme elevations (AST/ALT), blood-pressure shifts under RAAS agents, neuropathy when antidepressants are used for chemotherapy-induced peripheral neuropathy, and infection risks with antibiotics. A notable harm signal links hydrochlorothiazide to keratinocyte cancers/melanoma, supporting dermatologic surveillance and tailored antihypertensive selection in oncology. Safety signals should be contextualized by population risk. For example, photosensitizing agents such as hydrochlorothiazide have been linked to higher risks of non-melanoma skin cancers in some light-skinned populations, with attenuated signals in certain Asian cohorts.[240–244]

AEs should be captured using standardized frameworks, with consistent grading, causality attribution and structured outcome reporting.[245–247]

Risk-of-bias concerns are common: confounding by indication, immortal-time and prevalent-user biases, and exposure misclassification in observational designs; and limited causal inference in single-arm, small early-phase trials. Causal inference is strengthened by target-trial emulation incorporating new-user, active-comparator cohorts; time-varying exposure models; negative-control outcomes/exposures; and validated instruments.

4.4. Clinical Implications and Good-Practice Guidance

Generalized off-label drug or repurposing medicines for oncology is not supported at this time; prescribing should be confined to established non-oncologic uses. Therefore, continuation of agents such as metformin, statins, or RAAS inhibitors is reasonable when clinically indicated for comorbidities, provided drug–drug interactions, organ function, and trial eligibility are considered. The most compelling near-term opportunities are context-specific and biology-anchored: perioperative stress-axis modulation (β-blocker ± COX-2 inhibitor) in curative-intent settings, and tumor-microenvironment targeting (e.g., losartan) in desmoplastic tumors, preferably within prospective trials. Clinicians should maintain vigilance for uncertain or adverse signals (*e.g.*, thiazide photosensitization-linked skin cancer; microbiome/infection considerations with antibiotics).

4.5. Research Priorities and Overall Implications

Overall comparability improves with prespecified definitions of OS, PFS/DFS, and ORR, aligned censoring rules, and tumor-specific endpoint conventions. DATECAN provides consensus definitions that support harmonized, interpretable time-to-event analyses across tumor types.[248]

For signals of association to be converted into practice-changing evidence, a coherent pathway is delineated, beginning with prospective, disease-specific trials justified pharmacokinetically and stratified by

biomarker-anchored subgroups. In parallel, rigorous observational emulations are to be conducted using new-user, active-comparator cohorts, with time-varying exposure modeled and negative-control outcomes/exposures and validated instruments incorporated. Endpoints are to be harmonized through prespecified OS and PFS/DFS definitions with systematic CTCAE capture. Adaptive or factorial platforms are required to test rational combinations (*e.g.*, losartan ± chemoradiation; propranolol ± checkpoint inhibitors). Equity and generalizability across age, comorbidity, and global settings are to be built in from the outset. Overall, biologically coherent, low-toxicity signals, most consistently for β-blockade and RAAS modulation, and more variably for metformin, statins, and aspirin, are judged to warrant targeted, rigorously designed evaluation rather than immediate clinical repurposing.

4.6. Methodologic Priorities for the Next Phase

The review's principal strengths, most notably a cross-class cartography of accessible, low-cost agents and a structured screening of efficacy and safety (OS, PFS/DFS, ORR; systematic CTCAE capture), are capitalized upon to support transparent prioritization by feasibility, biological plausibility, and anticipated public-health impact. Accepted constraints include the predominance of non-randomized designs; heterogeneity in endpoint definitions, ascertainment, censoring practices, and follow-up windows; variable operationalization of exposure (dose, duration, timing); and reliance on abstract-level data for several estimates.

Collectively, these features circumscribe claims and necessitate full-text verification before any meta-analysis, with explicit evaluation of confounding by indication, immortal-time and prevalent-user biases, time-varying confounding, selection and misclassification error, and the adequacy of active comparators.

On balance, biologically coherent, low-toxicity signals, most consistently for β-blockade and RAAS modulation, and more variably for metformin, statins, and aspirin, justify targeted, rigorously designed evaluation rather than immediate clinical repurposing. The guidance and methodological priorities delineated here should shape near-term trial portfolios and high-quality observational emulations, emphasizing prospective registration, harmonized core outcomes with systematic CTCAE capture, common data elements, and open data/code sharing to accelerate credible, decision-grade synthesis.

5. Conclusion

This systematic review detects biologically plausible, low-toxicity signals across several non-oncologic drug classes, yet the evidence base is largely composed of nonrandomized designs, non-uniform endpoint definitions and ascertainment. These limitations qualify causal inference and require more in-depth investigations before any quantitative synthesis, including explicit checks for confounding by indication, immortal-time and prevalent-user biases, time-varying exposure, and misclassification.

Safety findings broadly track class expected effects, although uneven reporting and a small number of potential harms (*e.g.*, hydrochlorothiazide-associated photosensitivity) warrant targeted monitoring. At present, across the board repurposing cannot be endorsed beyond established non-oncologic indications; continuation for primary indications remains reasonable with attention to drug–drug interactions and pharmacovigilance.

Methodological priorities include prospective, disease-specific trials with pharmacokinetic justification and biomarker-anchored subgroups; rigorous target-trial emulations in observational data (new-user, active-comparator cohorts; time-varying exposure; negative-control outcomes/exposures; validated instruments); and endpoint harmonization using prespecified OS/PFS/DFS definitions with systematic CTCAE capture. The most consistent opportunities for formal testing involve perioperative β-blockade (± selective COX-2 inhibition) and RAAS modulation (*e.g.*, losartan in desmoplastic tumors), ideally within adaptive or factorial platforms. Equity by design, common data elements, preregistration, and open data/code should be embedded from the outset to accelerate credible, decision-grade synthesis.

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LZ, AO, designed the study.

LZ, AO, MWO, MSZ, wrote the manuscript.

LZ, AO, MWO, MSZ, collected the data.

LZ, AO, MSZ, computerized the data.

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Appendix A: Included Studies – Safety/Adverse Events Table (n = 181)

Common Terminology Criteria for Adverse Events (CTCAE); Aspartate Aminotransferase (**AST**) and Alanine Aminotransferase (**ALT**) refer to the CTCAE AE terms **"AST increased"** and **"ALT increased."**

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Adverse Event (AE)	AE Frequency	Severity	Discontinuation due to AE
1	Samuel Early *et al.*, 2025	Various C.	ARB[3], Losartan	Hypertension			
2	Run Ting Chin *et al.*, 2025	Pancreatic C.	Insulin	Side Effects			
3	Zijian Qiu *et al.*, 2025	NSCLC[9]	ARB[3]	Adverse Events, Side Effects, CTCAE Reported		Grade ≥3 Reported	Reported (No Value Found)
4	Anant Ramaswamy *et al.*, 2025	Pancreatic C.	ARB[3], Losartan	Adverse Events, AST	72.7%, 95%, 73.2%		
5	Yiling Li *et al.*, 2025	Hepato. C.	Beta-blocker, Propranolol, Carvedilol	Adverse Events, ALT, AST, Hypertension			
6	Yasuhiro Nakajima *et al.*, 2025	Lung C.	Duloxetine	Neuropathy, Peripheral Neuropathy			Reported (No Value Found)
7	Nadiye Sever *et al.*, 2025	NSCLC[9]	Beta-blocker, ARB[3]	Ast	35.7%, 21.3%, 11%		
8	Emma C. Bernsen *et al.*, 2025	Various C.	Amitriptyline, Paroxetine	Alt, Ast	16%		
9	Silke Gillessen *et al.*, 2025	Prostate C.	Metformin, Aspirin, NSAID[8]	Adverse Events, ALT, AST	5%, 20%, 94%	Grade ≥3 Reported	
10	Hiba Zaaroura *et al.*, 2025	Various C.	Propranolol	Alt, Ast	12.6%, 57.8%		Reported (No Value Found)
11	Felix J. Hüttner *et al.*, 2025	Pancreatic C.	Propranolol, COX-2[4]	Adverse Events, Serious Adverse Events, AST	95%, 95%, 11.1%	Saes Reported	
12	Rūta Everatt *et al.*, 2025	Lung C.	ARB[3], Beta-blocker	ALT, Hypertension	95%, 95%, 95%		
13	Nan Dang *et al.*, 2024	Sarcoma	Propranolol				
14	Hongtao Yin *et al.,* 2024	Various C.	ARB[3]	Hypertension	95%		
15	Minji Jung *et al.,* 2024	Renal CC.	ARB[3]	Hypertension	95%, 95%, 95%		

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Adverse Event (AE)	AE Frequency	Severity	Discontinuation due to AE
16	Eva J. Streekstra *et al.,* 2024	Breast C.	Rosuvastatin, Statins Propranolol, Enalapril,	ALT, AST			
17	Rūta Everatt *et al.*, 2024	Ovarian C.	ACEI[1], Beta-blocker	Hypertension	95%, 95%, 47%		
18	Richa Baniya *et al.*, 2024	Various C.	Propranolol				
19	Matteo Franchi *et al.*, 2024	Various C.	Beta-blocker	ALT, AST, Hypertension	49.5%		
20	Benjamin D. Lovin *et al.*, 2024	Various C.	Losartan	AST	33%, 50%, 36%		
21	Qianyi Chen *et al.*, 2024	Various C.	Propranolol				
22	Hamidu N. Rajabu *et al.*, 2024	Renal CC.	NSAID[8]	AST, Hypertension	76.6%, 62.2%, 60%		
23	Alfredo Budillon *et al.*, 2024	Pancreatic C.	Simvastatin, Statins	Toxicity, ALT, AST	2023/04		
24	Shoham Baruch *et al.*, 2024	Various C.	Propranolol, Atenolol	ALT, AST	25%, 60%, 40%		25%
25	Arvind Kumar Sharma *et al,* 2024	Various C.	ARB[3], ACEI[1], Beta-blocker, Telmisartan, Candesartan	ALT, Hypertension	95%, 5%, 11.9%		
26	Jood Hashem *et al.*, 2024	Leukemia	Atorvastatin, Statins	Alt, Ast			
27	Anam Kamal *et al.*, 2024	Breast C.	Simvastatin, Statins	Adverse Event, Adverse Events, AST			
28	Tej Shukla *et al.*, 2024	Various C.	STZ[13], Trimethoprim	Infection	11%, 95%, 95%; 47/446, 17/47		
29	Manon Cairat *et al.*, 2023	Breast C.	Aspirin	Alt, Ast	95%, 2%, 2%		
30	Ana Giachetti *et al.*, 2023	Sarcoma	Propranolol	Alt	99%, 95%, 48%		
31	Eun Joo Cho *et al.*, 2023	Leukemia	Chlorthalidone, Telmisartan, Amlodipine	Adverse Event, Serious Adverse Event, AST, Hypertension	78.3%, 53.8%, 37.8%; 2/88	Saes Reported	78.3%
32	Emily Biben *et al.*, 2023	Ovarian C.	Metformin, Insulin	Hypertension	9%		9%

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Adverse Event (AE)	AE Frequency	Severity	Discontinuation due to AE
33	Mireille M. Hermans *et al.*, 2023	Various C.	Beta-blocker, Propranolol, Atenolol	Adverse Effects	19%, 19%		
34	Alexander I. Gipsman *et al.*, 2023	Various C.	Propranolol				
35	Xiao-Xu Zhu *et al.*, 2023	Cholangio-carcinoma	ARB[3]	Hypertension	56.9%, 95%, 95%		
36	Marco van Londen *et al.*, 2022	NSCLC[9]	Enalapril, Metformin, Naproxen, ARB[3]	Toxicity, AST, Acute Kidney Injury			
37	Ailsa Maria Main *et al.*, 2022	HNSCC[7]	Labetalol		40%; 246/146		
38	Azusa Aida *et al.*, 2022	Pancreatic C.	Insulin	ALT, AST, Hypoglycemia			
39	Lisa Scarton *et al.*, 2022	Lung C.	Metformin	Alt, Ast	38.5%, 95%, 95%		
40	Letícia Gaertner Mariani et al, 2022	HNSCC[7]	Propranolol		4%, 10%, 24%; 1/3		
41	Kinnosuke Matsumoto et al, 2022	Lung C.	Azilsartan, Amlodipine	Toxicity, ALT, AST, Hypertension		Grade ≥3 Reported	
42	Wei-Ming Wang *et al.*, 2022	HNSCC[7]	Metformin	Ast			
43	Xiao Shen *et al.*, 2022	Lung C.	Rosuvastatin, Statins Nifedipine, Valsartan,	AST, Hypertension			
44	S. Mansoori *et al.*, 2021	VMC[14]	Mebendazole	Adverse Effects, AST, Infection			
45	Tianyi Huang *et al.*, 2021	Ovarian C.	ACEI[1], Beta-blocker	ALT, Hypertension	95%, 95%, 95%		
46	Jinhui Li *et al.*, 2021	Lung C.	Aspirin, ARB[3]	Hypertension	95%, 95%, 95%		
47	Rajesh Balkrishnan *et al.*, 2021	Colorectal C.	ACEI[1], Beta-blocker		95%, 95%, 95%		
48	Theodore M. Brasky *et al.*, 2021	Colorectal C.	ARB[3]	ALT, AST, Hypertension	95%		

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Adverse Event (AE)	AE Frequency	Severity	Discontinuation due to AE
49	Esteban Fernández *et al.*, 2021	Various C.	Propranolol		75.0%, 95%, 95%		
50	Shihan Chen *et al.*, 2021	Various C.	Captopril	Hypertension	97.8%, 95.7%		
51	Kavya M. Bejjanki *et al.*, 2021	Various C.	Propranolol		41%, 59%, 59%		
52	Samuel L. Brady *et al.*, 2021	Various C.	Propranolol	AST	44%, 15%, 26%		
53	Glen M. Chew *et al.*, 2021	Various C.	Metformin	Infection	71%; 5/7		
54	Fania Z. Muñoz-Garza *et al.*, 2021	Various C.	Propranolol	Adverse Effects	0.5%, 0.5%, 80%		
55	Wei-Ru Cho *et al.*, 2021	Hepato. C.	Metformin	AST, Hepatitis	54.9%, 18.4%, 9%		
56	Joanne Mui Ching Tan *et al.*, 2021	HNSCC[7]	Beta-Blocker, Propranolol	AST	75.9%, 41.8%, 65.8%		
57	Yeseul Kim *et al.*, 2021	SCLC[12]	Metformin	AST			
58	Shipra Gandhi *et al.*, 2021	Melanoma	Propranolol	Adverse Event, Toxicities, Treatment-Related AE	44%, 78%		
59	Justin G. Trogdon *et al.*, 2021	Lung C.	Insulin, Statins	AST	80%		
60	Shiori Hiramoto *et al.*, 2021	Breast C.	Duloxetine	AST, Hypertension, Neuropathy, Peripheral Neuropathy			
61	Efe Eworuke *et al.*, 2021	Various C.	HCT[6]		95%, 95%, 95%		
62	Min-Chun Chuang *et al.*, 2021	NSCLC[9]	Aspirin	ALT, AST	95%, 95%, 95.0%		
63	Hee Jin Park *et al.*, 2021	Various C.	Propranolol		19/24, 6/14		
64	M. Adarsh *et al.*, 2021	Pancreatic C.	Insulin	AST			
65	Yujian Liang *et al.*, 2020	Thyroid C.	Propranolol				
66	Gui-Hua Zhang *et al.*, 2020	Lymphoma	Losartan	AST			
67	Sungji Moon *et al.*, 2020	Lung C.	ARB[3]	ALT, AST, Hypertension	95%, 95%, 95%		95%

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Adverse Event (AE)	AE Frequency	Severity	Discontinuation due to AE
68	Christine D. Hsu *et al.*, 2020	Breast C.	HCT[6]	Adverse Event, Adverse Events, Neutropenia, ALT, AST	95%, 27%, 11%		95%
69	Thibault Letellier *et al.*, 2020	Pancreatic C.	HCT[6]	AST, Hypertension	11%, 7%, 9%		
70	Ruzan Udumyan *et al.*, 2020	Hepato. C.	Beta-Blocker	Hypertension	93%		
71	Sayaka Tani *et al.*, 2019	Various C.	Propranolol				
72	Riya Madan *et al.*, 2020	Pancreatic C.	Insulin	AST, Hypoglycemia	30%		
73	Nicole M. Kuderer *et al.*, 2020	Breast C.	Azithromycin	ALT, AST, Infection	30%, 50%, 21%		
74	Zizi Yu *et al.*, 2020	Colorectal C.	Tetracycline, Doxycycline, ARB[3]	Toxicity, Toxicities, ALT, AST, Rash	90%, 9%, 34%		
75	Satoshi Kidoguchi *et al.*, 2020	Various C.	Captopril		22.0%		
76	Min Ae Cho *et al.*, 2020	Ovarian C.	ARB[3], Beta-Blocker		6.4%, 7.1%, 12.2%		
77	Jinye Xie *et al.*, 2020	Colorectal C.	Metformin	AST			
78	Takashi Higuchi *et al.*, 2020	Sarcoma	Pioglitazone	Toxicity, AST			
79	K. Esther Broekman *et al.*, 2020	Ovarian C.	Metformin, ARB[3]	Adverse Events, Toxicities, CTCAE Reported	28%	Grade ≥3 Reported	Reported (No Value Found)
80	Benjamin Daniels *et al.*, 2020	Melanoma	HCT[6]	ALT, Dermatitis	95%, 95%, 95%		
81	Benjamin *et al.*, 2020	Melanoma	HCT[6]	ALT, Dermatitis	95%, 95%, 95%		
82	F. Spada *et al.*, 2020	VMC[14]	Azithromycin, Statins	ALT, AST, Infection			
83	Mariana Carvalho Costa *et al.*, 2020	VMC[14]	Beta-Blocker, Propranolol	ALT			
84	Xin Zhang et al, 2019	Renal CC.	Nifedipine	ALT, AST, Hypertension			
85	Yuxi Ma *et al.*, 2019	Breast C.	Losartan	AST			
86	Azael Freites-Martinez *et al.*, 2019	Various C.	Spironolactone	Adverse Event, Adverse Events, AST	82%, 62%, 41%		
87	Eva Neumann *et al.*, 2019	Renal CC.	ARB[3], Statins		95%		

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Adverse Event (AE)	AE Frequency	Severity	Discontinuation due to AE
88	Michael Haap *et al.*, 2019	Primary BT.	ACEI[1]	AST, Hypertension	57%, 43%, 43%		
89	Changhua Wu *et al.*, 2019	Various C.	Propranolol				
90	Sai Yendamuri *et al.*, 2019	NSCLC[9]	Metformin				
91	Yoshihiro Niitsu *et al.*, 2019	Pancreatic C.	Insulin	Adverse Effects, Thrombocytopenia, AST			
92	WingYee Wan *et al.*, 2019	Various C.	Clonidine				
93	Terence T. Sio *et al.*, 2019	Lung C.	Lisinopril	Adverse Event, ALT, Acute Kidney Injury, Hypotension, Pneumonitis	62%, 86%	Grade ≥3 Reported	
94	Jaime Anger *et al.*, 2019	Various C.	Propranolol				
95	Preben Kjølhede *et al.*, 2019	Various C.	Clonidine	Adverse Event, Adverse Events, Serious Adverse Event, ALT		Saes Reported	
96	Mu-Chieh Tsai *et al.*, 2019	Various C.	Propranolol	Adverse Effects, ALT			
97	Arun Prasad *et al.*, 2019	Various C.	Propranolol	Side Effect, Side Effects	76%, 24%; 17/22, 5/22		
98	Elisabet Cuyàs *et al.*, 2019	Breast C.	Metformin, ARB[3]	ALT, AST			
99	Stefania Maraka *et al.*, 2019	Primary BT.	Metformin	Adverse Event, Toxicity, Toxicities, AST	66%, 43%		
100	Taha Anwar *et al.*, 2019	Bladder/urothelial cancer	Propranolol	ALT			
101	Lois M. Ramondetta *et al.*, 2019	Ovarian C.	Beta-Blocker, Propranolol, ARB[3]	AST	88.5%, 38.5%, 69%		
102	Phyo T. Htoo *et al.*, 2019	Colorectal C.	ARB[3], Beta-Blocker	ALT, Hypertension	95%, 95%, 95%		
103	Yingying Gao *et al.*, 2019	Prostate C.	Simvastatin, Statins	ALT, AST	82.1%, 80%		
104	So-Yeon Jeon *et al.*, 2019	Lung C.	Amlodipine	Adverse Effects, AST, Hypertension			Reported (No Value Found)
105	Bliss E. O'Bryhim *et al.*, 2019	Various C.	Propranolol				

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Adverse Event (AE)	AE Frequency	Severity	Discontinuation due to AE
106	Forrest L. Baker *et al.*, 2019	Various C.	Beta-Blocker, Bisoprolol	Toxicity, ALT	182%, 60%		
107	Ping-Ying Chang *et al.*, 2019	Hepato. C.	Beta-Blocker, Propranolol	ALT, AST, Hepatitis	22%, 95%, 95%		
108	Yehee Hong *et al.*, 2019	Prostate C.	Metformin	ALT			
109	Aditi Mehta *et al.*, 2019	Various C.	Propranolol	Side Effect, Side Effects, AST	11.67%, 21.71%		
110	Janet E. Murphy *et al.*, 2019	Pancreatic C.	Losartan	Toxicity, ALT, AST	16%, 84%, 86%		
111	Zhaobo Liu *et al.*, 2019	Various C.	Propranolol				
112	Anton Pottegård *et al.*, 2019	Melanoma	HCT[6]	ALT	95%, 95%, 95%		
113	Kristen A. Marrone *et al.*, 2018	NSCLC[9]	Metformin, Insulin, ARB[3]	Toxicity, AST	47%, 95%, 25%		
114	Blánaid M. Hicks *et al.*, 2018	Lung C.	ARB[3]		95%, 95%, 95%		
115	Anton Pottegård *et al.*, 2018	Melanoma	HCT[6]				
116	Christian Ramos-Peñafiel *et al.*, 2018	Leukemia	Metformin	AST	95%, 95%		
117	Wensheng Jiang *et al.*, 2018	NSCLC[9]	NSAID[8]		95%, 95%		
118	Tomonori Hirashima *et al.*, 2018	Lung C.	Rifampicin	Adverse Event, Adverse Events, AST, Pneumonitis, Colitis	36.7%, 67.9%, 16.7%; 24/6, 1/2	Grade ≥3 Reported	
119	Fumitaka Wada *et al.*, 2018	Hepato. C.	ARB[3]		5/7, 2/30		
120	Li Jiao-Ling *et al.*, 2018	Various C.	Propranolol	ALT, AST	64/10		
121	Sidsel Arnspang Pedersen *et al.*, 2018	Various C.	HCT[6]		95%, 95%, 95%		
122	Limin Liu *et al.*, 2018	VMC[14]	Insulin	AST			
123	Massimo Moro *et al.*, 2018	NSCLC[9]	Metformin	AST	95%, 75%, 0%		
124	Sara Pusceddu *et al.*, 2018	Pancreatic C.	Metformin, Insulin, Statins	AST, Hyperglycemia	6.5%, 95%, 95%		
125	Harvey J. Murff *et al.*, 2018	Lung C.	Metformin	AST	95%		

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Adverse Event (AE)	AE Frequency	Severity	Discontinuation due to AE
126	Zhenwei Zhu *et al.*, 2018	Various C.	Propranolol				
127	C. Fernandez *et al.*, 2018	Various C.	Insulin	AST			
128	Tongbai Xu *et al.*, 2018	NSCLC[9]	Metformin		95%		
129	Vincenzo De Giorgi *et al.*, 2018	Melanoma	Propranolol	AST	80%, 95%		
130	Jennifer M. Knight *et al.*, 2018	Multiple myeloma	Propranolol	ALT, AST, Hypotension	20%, 6%, 58%		92%
131	William A. Stokes *et al.*, 2018	HNSCC[7]	Metformin, ARB[3]	Toxicity, Toxicities, AST, Hypertension	65.6%, 57.7%, 73.4%		
132	Anton Pottegård *et al.*, 2018	Colorectal C.	Valsartan	ALT	95%, 95%		
133	William Small *et al.*, 2018	NSCLC[9]	ACEI[1], Captopril	Toxicity, ALT, Pneumonitis	23%, 14%; 3/13, 1/7		
134	Jian-Yong Dong *et al.*, 2017	HNSCC[7]	Propranolol	AST	91.72%, 97.63%, 98.48%		
135	Ryuichiro Hosoya *et al.*, 2017	Various C.	ARB[3]	Adverse Effects, ALT, AST	95%		
136	Young-Jun Ki *et al.*, 2017	Colorectal C.	Metformin	ALT, AST	95%, 95%, 95%		
137	Zeynep Canan Özdemir *et al.*, 2017	Thyroid C.	Beta-Blocker, Propranolol	Hypothyroidism	50%		
138	Fiorella Guadagni *et al.*, 2017	VMC[14]	Insulin	ALT, AST	42%, 21%, 79%		
139	Cheng Xue *et al.*, 2017	Renal CC.	HCT[6], ACEI[1], Fosinopril	AST, Hypertension			
140	Jian-Yu E *et al.*, 2017	Pancreatic C.	Metformin, Statins	ALT	7.56%, 35.84%, 19.45%		
141	M. A. Frouws *et al.*, 2017	Colorectal C.	Aspirin	AST	95%		
142	David Gill *et al.*, 2017	Prostate C.	Spironolactone, Eplerenone	Adverse Event, Adverse Events, Toxicity, Toxicities, AST			
143	Ivette F. Emery *et al.*, 2017	Primary BT.	ARB[3]	AST			
144	A. Pottegård *et al.*, 2017	Various C.	HCT[6]		95%, 95%, 95%		

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Adverse Event (AE)	AE Frequency	Severity	Discontinuation due to AE
145	Michael J. Seckl *et al.*, 2017	SCLC[12]	Pravastatin, Statins, ARB[3]	Adverse Event, Adverse Events, Toxicity, ALT, AST	43%, 57%, 13.2%		
146	Ishveen Chopra *et al.*, 2017	Breast C.	Statins, ARB[3]	AST	31.2%, 13.7%, 27.4%		
147	Lee Shaashua *et al.*, 2017	Breast C.	Propranolol, COX-2[4]	Adverse Event, AST			
148	Hui-Fang Chiu et al, 2017	Various C.	ARB[3]	ALT, AST	8.35%, 9.38%, 6.99%		
149	Maya El Hachem *et al.*, 2017	Various C.	Propranolol	Side Effect, Side Effects, Diarrhea, Constipation	91.8%, 42.6%, 67.7%		
150	Alexandra Couttenier *et al.*, 2017	Ovarian C.	Rosuvastatin, Simvastatin, Statins	ALT, AST	95%, 95%, 23%		
151	Victoria Mandilaras *et al.*, 2017	Pancreatic C.	ARB[3]		95%, 95%, 95%; 3/10		
152	Matthias Holdhoff *et al.*, 2017	Primary BT.	ARB[3]	Toxicity, Toxicities, ALT, AST, Hypertension		Grade ≥3 Reported	
153	Shinji Higuchi *et al.*, 2017	Thyroid C.	Propranolol	Hypothyroidism			Reported (No Value Found)
154	Alexa Montoya *et al.*, 2016	Breast C.	Beta-Blocker, Propranolol	AST	66%, 23%		
155	Mark Anthony Sandoval *et al.*, 2016	Pancreatic C.	Insulin	AST, Hypoglycemia			
156	Koji Matsuo *et al.*, 2016	Endometrial C.	Aspirin	AST, Hypertension	9.4%, 95%, 7.5%		
157	Young-Seok Seo *et al.*, 2016	Hepato. C.	Metformin	ALT, AST	95%, 95%		
158	Linnéa Schmidt *et al.*, 2016	Primary BT.	Sertraline	AST			
159	Mugdha Gokhale *et al.*, 2016	Lung C.	ARB[3], ACEI[1]	Side Effect	20%, 4.7%, 21.2%		
160	Koji Matsuo *et al.*, 2016	Endometrial C.	HCT[6], Insulin	Hypertension	91.1%, 60.2%, 65.8%		

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Adverse Event (AE)	AE Frequency	Severity	Discontinuation due to AE
161	Katrina Wilcox Hagberg *et al.*, 2016	Hepato. C.	ACEI[1]	ALT, AST, Hypertension	95%, 95%		
162	Eddy Pasquier *et al.*, 2016	VMC[14]	Propranolol	Alt, AST	100%		
163	Luigi Fontana *et al.*, 2016	Various C.	Insulin	AST, Weight Loss	25%, 0.8%, 0.7%		
164	Nobumasa Ohara *et al.*, 2016	Various C.	ARB[3]	Alt, Hypertension, Hypotension, Hemorrhage	2%; 40/25, 300/160		
165	Tianyi Huang *et al.*, 2016	Ovarian C.	Beta-Blocker	ALT, AST, Hypertension	95%, 95%, 95%		
166	Lili Miao *et al.*, 2016	NSCLC[9]	ARB[3]	AST	30%, 15%		
167	Zachary S. Morris *et al.*, 2016	Colorectal C.	ARB[3], Metformin, Aspirin, Statins	AST	52%, 17%, 24%		
168	Cecilia Choy *et al.*, 2016	Breast C.	Propranolol	AST	95%		
169	Bo Young Oh *et al.*, 2016	Colorectal C.	Metformin				
170	Jessica K. Paulus *et al.*, 2016	Colorectal C.	Metformin		10%, 95%, 22%		
171	Jing Ge *et al.*, 2016	Various C.	Propranolol	Adverse Effects, Side Effect, Side Effects, AST	0.5%, 100%, 1.1%; 89/89		
172	Chengfang Zhou *et al.*, 2016	Melanoma	Propranolol				
173	Giovanna Stringari *et al.*, 2016	Various C.	Propranolol	Adverse Effects, Hypotension, Hypoglycemia	95.2%		
174	M. R. Jones *et al.*, 2016	Colorectal C.	Irbesartan	Toxicity, ALT, AST			
175	Saul Castaneda *et al.*, 2016	Various C.	Propranolol	Adverse Effects, Side Effect, Side Effects, ALT	10%, 64%, 36%		
176	Inés Gómez-Acebo *et al.*, 2016	Breast C.	Beta-Blocker	ALT, AST, Hypertension	95%, 95%, 95%		
177	Koray Tascilar *et al.*, 2016	Lung C.	ARB[3], Telmisartan	AST, Hypertension	8%, 85%, 95%		
178	Angelo Restivo *et al.*, 2016	Colorectal C.	Aspirin	ALT, AST	67.6%, 43.6%, 46%		
179	Stephen John Ralph *et al.*, 2015	VMC[14]	NSAID[8]				

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Adverse Event (AE)	AE Frequency	Severity	Discontinuation due to AE
180	Brian Winters *et al.*, 2015	Prostate C.	Metformin, Insulin	ALT	45%		
181	Grzegorz Dworacki *et al.*, 2015	Various C.	Metformin				

ACEI[1] : Angiotensin-Converting Enzyme Inhibitors; **AE[2]**: Adverse Events; **ARB[3]** : Angiotensin II Receptor Blocker (AT_1 antagonists); **COX-2[4]** : Cyclo-Oxygenase-2 (enzyme)/COX-2-selective inhibitors; **DFS[5]**: Disease-free survival; **HCT[6]** : Hydrochlorothiazide; **HNSCC[7]** : Head and Neck Squamous Cell Carcinoma; **NSAID[8]** : Non-Steroidal Anti-Inflammatory Drug; **NSCLC[9]** : Non-Small Cell Lung Cancer; **OS[10]** : Overall survival; **PFS[11]**: Progression-free survival; **SCLC[12]** : Small Cell Lung Cancer; **STZ[13]** : Sulfamethoxazole; **VMC[14]** : Various Metastatic Cancer; **ORR[14]**: Objective response rate; **PVR[15]** : P-value reported**; RnP[16] :** Results not Reported; **Cancer Site[17] :** Various C. (Various Cancers), Pancreatic C. (Pancreatic Cancer), Hepato. C. (Hepatocellular Carcinoma), Lung C. (Lung Cancer), Prostate C. (Prostate Cancer), Renal CC. (Renal cell carcinoma), Breast C. (Breast Cancer), Colorectal C. (Colorectal cancer), Ovarian C. (Ovarian Cancer), Endometrial C. (Endometrial cancer), Thyroid C. (Thyroid Cancer), Primary BT. (Primary Brain Tumors),

Appendix B : Included Studies – Outcomes Synthesis

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Outcome Measure	Stat. Significance	Conclusion
1	Samuel Early *et al.*, 2025	Various C.	ARB[3], Losartan	RnP[16]	Significant	Insufficient information in abstract to conclude.
2	Run Ting Chin *et al.*, 2025	Pancreatic C.	Insulin	Mortality	RnP[16]	Outcome mentioned; significance not reported.
3	Zijian Qiu *et al.*, 2025	NSCLC[9]	ARB[3]	Recurrence, Toxicity/AE[2]	RnP[16]	Significant improvement in at least one reported outcome.
4	Anant Ramaswamy *et al.*, 2025	Pancreatic C.	ARB[3], Losartan	OS[10], Response rate	Effect size reported	Significant improvement in at least one reported outcome.
5	Yiling Li *et al.*, 2025	Hepato. C.	Beta-blocker, Propranolol, Carvedilol	Toxicity/AE[2]	RnP[16]	Significant improvement in at least one reported outcome.
6	Yasuhiro Nakajima *et al.*, 2025	Lung C.	Duloxetine	RnP[16]	PVR[15]	Significant improvement in at least one reported outcome.
7	Nadiye Sever *et al.*, 2025	NSCLC[9]	Beta-blocker, ARB[3]	OS[10]	RnP[16]	Outcome mentioned; significance not reported.
8	Emma C. Bernsen *et al.*, 2025	Various C.	Amitriptyline, Paroxetine	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Outcome Measure	Stat. Significance	Conclusion
9	Silke Gillessen *et al.*, 2025	Prostate C.	Metformin, Aspirin, NSAID[8]	OS[10], Toxicity/AE[2]	RnP[16]	Significant improvement in at least one reported outcome.
10	Hiba Zaaroura *et al.*, 2025	Various C.	Propranolol	Recurrence	Significant (PVR[15])	Effect reported with statistical detail; direction unclear.
11	Felix J. Hüttner *et al.*, 2025	Pancreatic C.	Propranolol, COX-2[4]	DFS[5], Toxicity/AE[2] Recurrence,		Outcome mentioned; significance not reported.
12	Rūta Everatt *et al.*, 2025	Lung C.	ARB[3], Beta-blocker	Mortality, Hazard ratio	Significant	Significant improvement in at least one reported outcome.
13	Nan Dang *et al.*, 2024	Sarcoma	Propranolol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
14	Hongtao Yin *et al.,* 2024	Various C.	ARB[3]	Hazard ratio	Not significant	No statistically significant effect reported.
15	Minji Jung *et al.,* 2024	Renal CC.	ARB[3]	Hazard ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
16	Eva J. Streekstra *et al.,* 2024	Breast C.	Rosuvastatin, Statins Propranolol, Enalapril,	RnP[16]	RnP[16]	Significant improvement in at least one reported outcome.
17	Rūta Everatt *et al.*, 2024	Ovarian C.	ACEI[1], Beta-blocker	Mortality, Hazard ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
18	Richa Baniya *et al.*, 2024	Various C.	Propranolol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
19	Matteo Franchi *et al.*, 2024	Various C.	Beta-blocker	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
20	Benjamin D. Lovin *et al.*, 2024	Various C.	Losartan	Hazard ratio	PVR[15]	Significant improvement in at least one reported outcome.
21	Qianyi Chen *et al.*, 2024	Various C.	Propranolol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
22	Hamidu N. Rajabu *et al.*, 2024	Renal CC.	NSAID[8]	RnP[16]	Significant	Insufficient information in abstract to conclude.
23	Alfredo Budillon *et al.*, 2024	Pancreatic C.	Simvastatin, Statins	OS[10], Response rate, Mortality		Outcome mentioned; significance not reported.

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Outcome Measure	Stat. Significance	Conclusion
24	Shoham Baruch *et al.*, 2024	Various C.	Propranolol, Atenolol	Odds ratio	Significant (PVR[15])	Effect reported with statistical detail; direction unclear.
25	Arvind Kumar Sharma *et al,* 2024	Various C.	ARB[3], ACEI[1], Beta-blocker, Telmisartan, Candesartan	Odds ratio	Effect size reported	Significant worsening or increased risk reported.
26	Jood Hashem *et al.*, 2024	Leukemia	Atorvastatin, Statins	OS[10]	RnP[16]	Significant improvement in at least one reported outcome.
27	Anam Kamal *et al.*, 2024	Breast C.	Simvastatin, Statins	Toxicity/AE[2]	PVR[15]	No statistically significant effect reported.
28	Tej Shukla *et al.*, 2024	Various C.	STZ[13], Trimethoprim	Odds ratio, Relative risk	Significant (PVR[15])	No statistically significant effect reported.
29	Manon Cairat *et al.*, 2023	Breast C.	Aspirin	Odds ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
30	Ana Giachetti *et al.*, 2023	Sarcoma	Propranolol	RnP[16]	PVR[15]	Significant improvement in at least one reported outcome.
31	Eun Joo Cho *et al.*, 2023	Leukemia	Chlorthalidone, Telmisartan, Amlodipine	Response rate, Toxicity/AE[2]	RnP[16]	Outcome mentioned; significance not reported.
32	Emily Biben *et al.*, 2023	Ovarian C.	Metformin, Insulin	RnP[16]	RnP[16]	Significant improvement in at least one reported outcome.
33	Mireille M. Hermans *et al.*, 2023	Various C.	Beta-blocker, Propranolol, Atenolol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
34	Alexander I. Gipsman *et al.*, 2023	Various C.	Propranolol	RnP[16]	RnP[16]	Significant improvement in at least one reported outcome.
35	Xiao-Xu Zhu *et al.*, 2023	Cholangio-carcinoma	ARB[3]	OS[10], PFS[11], Hazard ratio	Effect size reported	Significant improvement in at least one reported outcome.
36	Marco van Londen *et al.*, 2022	NSCLC[9]	Enalapril, Metformin, Naproxen, ARB[3]	Toxicity/AE[2]	RnP[16]	Outcome mentioned; significance not reported.
37	Ailsa Maria Main *et al.*, 2022	HNSCC[7]	Labetalol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
38	Azusa Aida *et al.*, 2022	Pancreatic C.	Insulin	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Outcome Measure	Stat. Significance	Conclusion
39	Lisa Scarton *et al.*, 2022	Lung C.	Metformin	OS[10]	Significant (PVR[15])	Effect reported with statistical detail; direction unclear.
40	Letícia Gaertner Mariani et al, 2022	HNSCC[7]	Propranolol	Recurrence	Significant (PVR[15])	Effect reported with statistical detail; direction unclear.
41	Kinnosuke Matsumoto et al, 2022	Lung C.	Azilsartan, Amlodipine	Toxicity/AE[2]	RnP[16]	Outcome mentioned; significance not reported.
42	Wei-Ming Wang *et al.*, 2022	HNSCC[7]	Metformin	RnP[16]	RnP[16]	Significant improvement in at least one reported outcome.
43	Xiao Shen *et al.*, 2022	Lung C.	Rosuvastatin, Statins Nifedipine, Valsartan,	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
44	S. Mansoori *et al.*, 2021	VMC[14]	Mebendazole	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
45	Tianyi Huang *et al.*, 2021	Ovarian C.	ACEI[1], Beta-blocker	Mortality, Hazard ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
46	Jinhui Li *et al.*, 2021	Lung C.	Aspirin, ARB[3]	Hazard ratio	Effect size reported	Significant improvement in at least one reported outcome.
47	Rajesh Balkrishnan *et al.*, 2021	Colorectal C.	ACEI[1], Beta-blocker	Mortality, Hazard ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
48	Theodore M. Brasky *et al.*, 2021	Colorectal C.	ARB[3]	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
49	Esteban Fernández *et al.*, 2021	Various C.	Propranolol	Hazard ratio	Effect size reported	Significant improvement in at least one reported outcome.
50	Shihan Chen *et al.*, 2021	Various C.	Captopril	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
51	Kavya M. Bejjanki *et al.*, 2021	Various C.	Propranolol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
52	Samuel L. Brady *et al.*, 2021	Various C.	Propranolol	RnP[16]	PVR[15]	No statistically significant effect reported.
53	Glen M. Chew *et al.*, 2021	Various C.	Metformin	PFS[11]	RnP[16]	Significant improvement in at least one reported outcome.

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Outcome Measure	Stat. Significance	Conclusion
54	Fania Z. Muñoz-Garza *et al.*, 2021	Various C.	Propranolol	Odds ratio	Not significant	No statistically significant effect reported.
55	Wei-Ru Cho *et al.*, 2021	Hepato. C.	Metformin	OS[10], Recurrence	Significant (PVR[15])	Significant improvement in at least one reported outcome.
56	Joanne Mui Ching Tan *et al.*, 2021	HNSCC[7]	Beta-Blocker, Propranolol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
57	Yeseul Kim *et al.*, 2021	SCLC[12]	Metformin	RnP[16]	RnP[16]	Significant improvement in at least one reported outcome.
58	Shipra Gandhi *et al.*, 2021	Melanoma	Propranolol	ORR[14], Response rate, Toxicity/AE[2]	Not significant	No statistically significant effect reported.
59	Justin G. Trogdon *et al.*, 2021	Lung C.	Insulin, Statins	RnP[16]	Significant	Significant improvement in at least one reported outcome.
60	Shiori Hiramoto *et al.*, 2021	Breast C.	Duloxetine			Significant worsening or increased risk reported.
61	Efe Eworuke *et al.*, 2021	Various C.	HCT[6]	Hazard ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
62	Min-Chun Chuang *et al.*, 2021	NSCLC[9]	Aspirin	OS[10], Mortality, Hazard ratio	Effect size reported	Significant improvement in at least one reported outcome.
63	Hee Jin Park *et al.*, 2021	Various C.	Propranolol	RnP[16]	PVR[15]	No statistically significant effect reported.
64	M. Adarsh *et al.*, 2021	Pancreatic C.	Insulin	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
65	Yujian Liang *et al.*, 2020	Thyroid C.	Propranolol	RnP[16]	RnP[16]	Significant improvement in at least one reported outcome.
66	Gui-Hua Zhang *et al.*, 2020	Lymphoma	Losartan	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
67	Sungji Moon *et al.*, 2020	Lung C.	ARB[3]	Hazard ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
68	Christine D. Hsu *et al.*, 2020	Breast C.	HCT[6]	Toxicity/AE[2], Risk ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
69	Thibault Letellier *et al.*, 2020	Pancreatic C.	HCT[6]	Hazard ratio	Effect size reported	Effect reported with statistical detail; direction unclear.

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Outcome Measure	Stat. Significance	Conclusion
70	Ruzan Udumyan *et al.*, 2020	Hepato. C.	Beta-Blocker	Mortality	Significant	Significant improvement in at least one reported outcome.
71	Sayaka Tani *et al.*, 2019	Various C.	Propranolol	RnP[16]	Significant	Significant improvement in at least one reported outcome.
72	Riya Madan *et al.*, 2020	Pancreatic C.	Insulin	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
73	Nicole M. Kuderer *et al.*, 2020	Breast C.	Azithromycin	Mortality, Odds ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
74	Zizi Yu *et al.*, 2020	Colorectal C.	Tetracycline, Doxycycline, ARB[3]	OS[10], Quality of life, Toxicity/AE[2],	Not significant	No statistically significant effect reported.
75	Satoshi Kidoguchi *et al.*, 2020	Various C.	Captopril	RnP[16]	RnP[16]	Significant improvement in at least one reported outcome.
76	Min Ae Cho *et al.*, 2020	Ovarian C.	ARB[3], Beta-Blocker	PFS[11], Hazard ratio, Recurrence,	PVR[15]	Significant improvement in at least one reported outcome.
77	Jinye Xie *et al.*, 2020	Colorectal C.	Metformin	OS[10], DFS[5]	RnP[16]	Outcome mentioned; significance not reported.
78	Takashi Higuchi *et al.*, 2020	Sarcoma	Pioglitazone	Toxicity/AE[2]	RnP[16]	Significant improvement in at least one reported outcome.
79	K. Esther Broekman *et al.*, 2020	Ovarian C.	Metformin, ARB[3]	Toxicity/AE[2]	PVR[15]	Effect reported with statistical detail; direction unclear.
80	Benjamin Daniels *et al.*, 2020	Melanoma	HCT[6]	Odds ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
81	Benjamin *et al.*, 2020	Melanoma	HCT[6]	Odds ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
82	F. Spada *et al.*, 2020	VMC[14]	Azithromycin, Statins	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
83	Mariana Carvalho Costa *et al.*, 2020	VMC[14]	Beta-Blocker, Propranolol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
84	Xin Zhang et al, 2019	Renal CC.	Nifedipine	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Outcome Measure	Stat. Significance	Conclusion
85	Yuxi Ma *et al.*, 2019	Breast C.	Losartan	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
86	Azael Freites-Martinez *et al.*, 2019	Various C.	Spironolactone	Toxicity/AE[2], Quality of life		Significant improvement in at least one reported outcome.
87	Eva Neumann *et al.*, 2019	Renal CC.	ARB[3], Statins	OS[10]	Significant (PVR[15])	Significant improvement in at least one reported outcome.
88	Michael Haap *et al.*, 2019	Primary BT.	ACEI[1]	RnP[16]	Significant (PVR[15])	Significant improvement in at least one reported outcome.
89	Changhua Wu *et al.*, 2019	Various C.	Propranolol	RnP[16]	Not significant	No statistically significant effect reported.
90	Sai Yendamuri *et al.*, 2019	NSCLC[9]	Metformin	OS[10], Recurrence, Hazard ratio	PVR[15]	Effect reported with statistical detail; direction unclear.
91	Yoshihiro Niitsu *et al.*, 2019	Pancreatic C.	Insulin	RnP[16]	PVR[15]	Insufficient information in abstract to conclude.
92	WingYee Wan *et al.*, 2019	Various C.	Clonidine	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
93	Terence T. Sio *et al.*, 2019	Lung C.	Lisinopril	Toxicity/AE[2], Quality of life	RnP[16]	Outcome mentioned; significance not reported.
94	Jaime Anger *et al.*, 2019	Various C.	Propranolol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
95	Preben Kjølhede *et al.*, 2019	Various C.	Clonidine	Toxicity/AE[2] Quality of life	Significant (PVR[15])	Significant improvement in at least one reported outcome.
96	Mu-Chieh Tsai *et al.*, 2019	Various C.	Propranolol	Recurrence	RnP[16]	Outcome mentioned; significance not reported.
97	Arun Prasad *et al.*, 2019	Various C.	Propranolol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
98	Elisabet Cuyàs *et al.*, 2019	Breast C.	Metformin, ARB[3]	RnP[16]	RnP[16]	Significant improvement in at least one reported outcome.
99	Stefania Maraka *et al.*, 2019	Primary BT.	Metformin	PFS[11], Toxicity/AE[2]	RnP[16]	Outcome mentioned; significance not reported.

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Outcome Measure	Stat. Significance	Conclusion
100	Taha Anwar *et al.*, 2019	Bladder/urothelial cancer	Propranolol	RnP[16]	RnP[16]	Significant improvement in at least one reported outcome.
101	Lois M. Ramondetta *et al.*, 2019	Ovarian C.	Beta-Blocker, Propranolol, ARB[3]	Quality of life	Significant (PVR[15])	Significant improvement in at least one reported outcome.
102	Phyo T. Htoo *et al.*, 2019	Colorectal C.	ARB[3], Beta-Blocker	Hazard ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
103	Yingying Gao *et al.*, 2019	Prostate C.	Simvastatin, Statins	Recurrence		Outcome mentioned; significance not reported.
104	So-Yeon Jeon *et al.*, 2019	Lung C.	Amlodipine	Recurrence	Not significant	Effect reported with statistical detail; direction unclear.
105	Bliss E. O'Bryhim *et al.*, 2019	Various C.	Propranolol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
106	Forrest L. Baker *et al.*, 2019	Various C.	Beta-Blocker, Bisoprolol	Toxicity/AE[2]	RnP[16]	Outcome mentioned; significance not reported.
107	Ping-Ying Chang *et al.*, 2019	Hepato. C.	Beta-Blocker, Propranolol	OS[10], DFS[5], Mortality	Significant (PVR[15])	No statistically significant effect reported.
108	Yehee Hong *et al.*, 2019	Prostate C.	Metformin	Hazard ratio	Effect size reported	Significant improvement in at least one reported outcome.
109	Aditi Mehta *et al.*, 2019	Various C.	Propranolol	RnP[16]	PVR[15]	Significant improvement in at least one reported outcome.
110	Janet E. Murphy *et al.*, 2019	Pancreatic C.	Losartan	OS[10], PFS[11], Toxicity/AE[2]	RnP[16]	Outcome mentioned; significance not reported.
111	Zhaobo Liu *et al.*, 2019	Various C.	Propranolol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
112	Anton Pottegård *et al.*, 2019	Melanoma	HCT[6]	Odds ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
113	Kristen A. Marrone *et al.*, 2018	NSCLC[9]	Metformin, Insulin, ARB[3]	OS[10], PFS[11], Toxicity/AE[2]	Not significant	No statistically significant effect reported.
114	Blánaid M. Hicks *et al.*, 2018	Lung C.	ARB[3]	Hazard ratio	Effect size reported	Effect reported with statistical detail; direction unclear.

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Outcome Measure	Stat. Significance	Conclusion
115	Anton Pottegård *et al.*, 2018	Melanoma	HCT[6]	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
116	Christian Ramos-Peñafiel *et al.*, 2018	Leukemia	Metformin	OS[10], Recurrence, Odds ratio	PVR[15]	Effect reported with statistical detail; direction unclear.
117	Wensheng Jiang *et al.*, 2018	NSCLC[9]	NSAID[8]	OS[10], PFS[11], DFS[5]	Significant	No statistically significant effect reported.
118	Tomonori Hirashima *et al.*, 2018	Lung C.	Rifampicin	OS[10], Response rate, Recurrence	Significant (PVR[15])	Effect reported with statistical detail; direction unclear.
119	Fumitaka Wada *et al.*, 2018	Hepato. C.	ARB[3]	RnP[16]	RnP[16]	Significant improvement in at least one reported outcome.
120	Li Jiao-Ling *et al.*, 2018	Various C.	Propranolol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
121	Sidsel Arnspang Pedersen *et al.*, 2018	Various C.	HCT[6]	Odds ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
122	Limin Liu *et al.*, 2018	VMC[14]	Insulin	RnP[16]	RnP[16]	Significant improvement in at least one reported outcome.
123	Massimo Moro *et al.*, 2018	NSCLC[9]	Metformin	OS[10], Response rate, Hazard ratio	PVR[15]	Effect reported with statistical detail; direction unclear.
124	Sara Pusceddu *et al.*, 2018	Pancreatic C.	Metformin, Insulin, Statins	PFS[11], DFS[5], Hazard ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
125	Harvey J. Murff *et al.*, 2018	Lung C.	Metformin	Hazard ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
126	Zhenwei Zhu *et al.*, 2018	Various C.	Propranolol	Recurrence	RnP[16]	Outcome mentioned; significance not reported.
127	C. Fernandez *et al.*, 2018	Various C.	Insulin	Mortality, Hazard ratio	Significant (PVR[15])	Effect reported with statistical detail; direction unclear.
128	Tongbai Xu *et al.*, 2018	NSCLC[9]	Metformin	OS[10], DFS[5], Recurrence	PVR[15]	Significant improvement in at least one reported outcome.
129	Vincenzo De Giorgi *et al.*, 2018	Melanoma	Propranolol	PFS[11], DFS[5], Recurrence	Effect size reported	Significant improvement in at least one reported outcome.

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Outcome Measure	Stat. Significance	Conclusion
130	Jennifer M. Knight *et al.*, 2018	Multiple myeloma	Propranolol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
131	William A. Stokes *et al.*, 2018	HNSCC[7]	Metformin, ARB[3]	OS[10], Toxicity/AE[2]	Significant (PVR[15])	Significant improvement in at least one reported outcome.
132	Anton Pottegård *et al.*, 2018	Colorectal C.	Valsartan	Hazard ratio	PVR[15]	Effect reported with statistical detail; direction unclear.
133	William Small *et al.*, 2018	NSCLC[9]	ACEI[1], Captopril	Toxicity/AE[2], Quality of life	Not significant	No statistically significant effect reported.
134	Jian-Yong Dong *et al.*, 2017	HNSCC[7]	Propranolol	Response rate	RnP[16]	Outcome mentioned; significance not reported.
135	Ryuichiro Hosoya *et al.*, 2017	Various C.	ARB[3]	Quality of life	RnP[16]	Outcome mentioned; significance not reported.
136	Young-Jun Ki *et al.*, 2017	Colorectal C.	Metformin	OS[10], Hazard ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
137	Zeynep Canan Özdemir *et al.*, 2017	Thyroid C.	Beta-Blocker, Propranolol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
138	Fiorella Guadagni *et al.*, 2017	VMC[14]	Insulin	RnP[16]	PVR[15]	No statistically significant effect reported.
139	Cheng Xue *et al.*, 2017	Renal CC.	HCT[6], ACEI[1], Fosinopril	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
140	Jian-Yu E *et al.*, 2017	Pancreatic C.	Metformin, Statins	OS[10], Mortality	RnP[16]	Significant improvement in at least one reported outcome.
141	M. A. Frouws *et al.*, 2017	Colorectal C.	Aspirin	OS[10], Mortality, Hazard ratio	Effect size reported	Significant improvement in at least one reported outcome.
142	David Gill *et al.*, 2017	Prostate C.	Spironolactone, Eplerenone	PFS[5], Toxicity/AE[2]	RnP[16]	Outcome mentioned; significance not reported.
143	Ivette F. Emery *et al.*, 2017	Primary BT.	ARB[3]	Hazard ratio	Effect size reported	Significant improvement in at least one reported outcome.
144	A. Pottegård *et al.*, 2017	Various C.	HCT[6]	Odds ratio	Significant (PVR[15])	Significant worsening or increased risk reported.
145	Michael J. Seckl *et al.*, 2017	SCLC[12]	Pravastatin, Statins, ARB[3]	OS[10], PFS[11], DFS[5]	Effect size reported	Effect reported with statistical detail; direction unclear.

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Outcome Measure	Stat. Significance	Conclusion
146	Ishveen Chopra *et al.*, 2017	Breast C.	Statins, ARB[3]	Odds ratio	Effect size reported	Significant improvement in at least one reported outcome.
147	Lee Shaashua *et al.*, 2017	Breast C.	Propranolol, COX-2[4]	DFS[5], Recurrence, Toxicity/AE[2]		Significant improvement in at least one reported outcome.
148	Hui-Fang Chiu et al, 2017	Various C.	ARB[3]	RnP[16]	Significant (PVR[15])	Significant improvement in at least one reported outcome.
149	Maya El Hachem *et al.*, 2017	Various C.	Propranolol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
150	Alexandra Couttenier *et al.*, 2017	Ovarian C.	Rosuvastatin, Simvastatin, Statins	Mortality	Significant (PVR[15])	Significant improvement in at least one reported outcome.
151	Victoria Mandilaras *et al.*, 2017	Pancreatic C.	ARB[3]	Odds ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
152	Matthias Holdhoff *et al.*, 2017	Primary BT.	ARB[3]	Recurrence, Toxicity/ AE[2]	RnP[16]	Outcome mentioned; significance not reported.
153	Shinji Higuchi *et al.*, 2017	Thyroid C.	Propranolol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
154	Alexa Montoya *et al.*, 2016	Breast C.	Beta-Blocker, Propranolol	Mortality	Significant (PVR[15])	Significant improvement in at least one reported outcome.
155	Mark Anthony Sandoval *et al.*, 2016	Pancreatic C.	Insulin	Recurrence	RnP[16]	Outcome mentioned; significance not reported.
156	Koji Matsuo *et al.*, 2016	Endometrial C.	Aspirin	OS[10], DFS[5], Hazard ratio	Effect size reported	Significant improvement in at least one reported outcome.
157	Young-Seok Seo *et al.*, 2016	Hepato. C.	Metformin	DFS[5], Mortality, Recurrence	Effect size reported	Significant improvement in at least one reported outcome.
158	Linnéa Schmidt *et al.*, 2016	Primary BT.	Sertraline	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
159	Mugdha Gokhale *et al.*, 2016	Lung C.	ARB[3], ACEI[1]	Hazard ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
160	Koji Matsuo *et al.*, 2016	Endometrial C.	HCT[6], Insulin	Hazard ratio	Significant (PVR[15])	Significant improvement in at least one reported outcome.

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Outcome Measure	Stat. Significance	Conclusion
161	Katrina Wilcox Hagberg *et al.*, 2016	Hepato. C.	ACEI[1]	Odds ratio	Not significant	No statistically significant effect reported.
162	Eddy Pasquier *et al.*, 2016	VMC[14]	Propranolol	OS[10], Response rate		Outcome mentioned; significance not reported.
163	Luigi Fontana *et al.*, 2016	Various C.	Insulin	RnP[16]	Significant (PVR[15])	Significant improvement in at least one reported outcome.
164	Nobumasa Ohara *et al.*, 2016	Various C.	ARB[3]	RnP[16]		Insufficient information in abstract to conclude.
165	Tianyi Huang *et al.*, 2016	Ovarian C.	Beta-Blocker	Hazard ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
166	Lili Miao *et al.*, 2016	NSCLC[9]	ARB[3]	OS[10], PFS[11]		Significant improvement in at least one reported outcome.
167	Zachary S. Morris *et al.*, 2016	Colorectal C.	ARB[3], Metformin, Aspirin, Statins	Odds ratio	Not significant	No statistically significant effect reported.
168	Cecilia Choy *et al.*, 2016	Breast C.	Propranolol	DFS[5], Recurrence	PVR[15]	Significant improvement in at least one reported outcome.
169	Bo Young Oh *et al.*, 2016	Colorectal C.	Metformin	OS[10], DFS[5], Response rate	PVR[15]	No statistically significant effect reported.
170	Jessica K. Paulus *et al.*, 2016	Colorectal C.	Metformin	OS[10]	Significant (PVR[15])	Significant improvement in at least one reported outcome.
171	Jing Ge *et al.*, 2016	Various C.	Propranolol	RnP[16]	Significant (PVR[15])	Insufficient information in abstract to conclude.
172	Chengfang Zhou *et al.*, 2016	Melanoma	Propranolol	RnP[16]	RnP[16]	Significant improvement in at least one reported outcome.
173	Giovanna Stringari *et al.*, 2016	Various C.	Propranolol	RnP[16]	Significant	No statistically significant effect reported.
174	M. R. Jones *et al.*, 2016	Colorectal C.	Irbesartan	Toxicity/AE[2]	RnP[16]	Outcome mentioned; significance not reported.
175	Saul Castaneda *et al.*, 2016	Various C.	Propranolol	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
176	Inés Gómez-Acebo *et al.*, 2016	Breast C.	Beta-Blocker	Odds ratio	Effect size reported	Effect reported with statistical detail; direction unclear.

#	Authors and Year	Cancer Site[17]	Off-Label Drug	Outcome Measure	Stat. Significance	Conclusion
177	Koray Tascilar *et al.*, 2016	Lung C.	ARB[3], Telmisartan	Hazard ratio	Effect size reported	Effect reported with statistical detail; direction unclear.
178	Angelo Restivo *et al.*, 2016	Colorectal C.	Aspirin	OS[10], PFS[11], DFS[5]	Significant (PVR[15])	Significant improvement in at least one reported outcome.
179	Stephen John Ralph *et al.*, 2015	VMC[14]	NSAID[8]	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.
180	Brian Winters *et al.*, 2015	Prostate C.	Metformin, Insulin	DFS[5], Recurrence	PVR[15]	Significant improvement in at least one reported outcome.
181	Grzegorz Dworacki *et al.*, 2015	Various C.	Metformin	RnP[16]	RnP[16]	Insufficient information in abstract to conclude.

ACEI[1] : Angiotensin-Converting Enzyme Inhibitors; **AE[2]**: Adverse Events; **ARB[3]** : Angiotensin II Receptor Blocker (AT_1 antagonists); **COX-2[4]** : Cyclo-Oxygenase-2 (enzyme)/COX-2-selective inhibitors; **DFS[5]**: Disease-free survival; **HCT[6]** : Hydrochlorothiazide; **HNSCC[7]** : Head and Neck Squamous Cell Carcinoma; **NSAID[8]** : Non-Steroidal Anti-Inflammatory Drug; **NSCLC[9]** : Non-Small Cell Lung Cancer; **OS[10]** : Overall survival; **PFS[11]**: Progression-free survival; **SCLC[12]** : Small Cell Lung Cancer; **STZ[13]** : Sulfamethoxazole; **VMC[14]** : Various Metastatic Cancer; **ORR[14]**: Objective response rate; **PVR[15]** : P-value reported**; RnP[16] :** Results not Reported; **Cancer Site[17] :** Various C. (Various Cancers), Pancreatic C. (Pancreatic Cancer), Hepato. C. (Hepatocellular Carcinoma), Lung C. (Lung Cancer), Prostate C. (Prostate Cancer), Renal CC. (Renal cell carcinoma), Breast C. (Breast Cancer), Colorectal C. (Colorectal cancer), Ovarian C. (Ovarian Cancer), Endometrial C. (Endometrial cancer), Thyroid C. (Thyroid Cancer), Primary BT. (Primary Brain Tumors),

Appendix C : Included Studies – Risk of Bias (ROB) (n = 181)

Heuristic screening of abstracts/tags for randomisation, blinding, outcome reporting and attrition indicators; Overall ROB synthesized per rules stated in the caption.

#	Authors and Year	Cancer Site[14]	Off-Label Drug	Random.[18]	Blinding	Outcome R	Attrition Bias	Overall ROB
1	Samuel Early *et al.*, 2025	Various C.	ARB[3], Losartan	No	Unclear	Unclear	Unclear	High (NRD)[15]
2	Run Ting Chin *et al.*, 2025	Pancreatic C.	Insulin	No	Unclear	Unclear	Unclear	High (NRD)[15]
3	Zijian Qiu *et al.*, 2025	NSCLC[9]	ARB[3]	Unclear	Unclear	Unclear	Unclear	Some concerns
4	Anant Ramaswamy *et al.*, 2025	Pancreatic C.	ARB[3], Losartan	Yes	Unclear	Low risk (RP)[14]	Unclear	Some concerns
5	Yiling Li *et al.*, 2025	Hepato. C.	Beta-blocker, Propranolol, Carvedilol	Yes	Unclear	Low risk (RP)[14]	Low risk[16]	Low
6	Yasuhiro Nakajima *et al.*, 2025	Lung C.	Duloxetine	No	Unclear	Unclear	Unclear	High (NRD)[15]
7	Nadiye Sever *et al.*, 2025	NSCLC[9]	Beta-blocker, ARB[3]	Yes	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]

#	Authors and Year	Cancer Site[14]	Off-Label Drug	Random.[18]	Blinding	Outcome R	Attrition Bias	Overall ROB
8	Emma C. Bernsen *et al.*, 2025	Various C.	Amitriptyline, Paroxetine	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
9	Silke Gillessen *et al.*, 2025	Prostate C.	Metformin, Aspirin, NSAID[8]	Yes	Unclear	Low risk (RP)[14]	Low risk[16]	High (NRD)[15]
10	Hiba Zaaroura *et al.*, 2025	Various C.	Propranolol	No	Unclear	Unclear	Unclear	High (NRD)[15]
11	Felix J. Hüttner *et al.*, 2025	Pancreatic C.	Propranolol, COX-2[4]	Yes	Unclear	Unclear	Unclear	Some concerns
12	Rūta Everatt *et al.*, 2025	Lung C.	ARB[3], Beta-blocker	No	Unclear	Unclear	Unclear	High (NRD)[15]
13	Nan Dang *et al.*, 2024	Sarcoma	Propranolol	Unclear	Unclear	Unclear	Low risk[16]	Some concerns
14	Hongtao Yin *et al.,* 2024	Various C.	ARB[3]	Unclear	Unclear	Unclear	Unclear	Some concerns
15	Minji Jung *et al.,* 2024	Renal CC.	ARB[3]	No	Unclear	Unclear	Unclear	High (NRD)[15]
16	Eva J. Streekstra *et al.,* 2024	Breast C.	Rosuvastatin, Statins Propranolol, Enalapril,	Unclear	Unclear	Low risk (RP)[14]	Low risk[16]	Some concerns
17	Rūta Everatt *et al.*, 2024	Ovarian C.	ACEI[1], Beta-blocker	No	Unclear	Unclear	Unclear	High (NRD)[15]
18	Richa Baniya *et al.*, 2024	Various C.	Propranolol	Unclear	Unclear	Unclear	Unclear	High (NRD)[15]
19	Matteo Franchi *et al.*, 2024	Various C.	Beta-blocker	No	Unclear	Unclear	Unclear	High (NRD)[15]
20	Benjamin D. Lovin *et al.*, 2024	Various C.	Losartan	Yes	Unclear	Unclear	Unclear	Some concerns
21	Qianyi Chen *et al.*, 2024	Various C.	Propranolol	No	Unclear	Unclear	Unclear	High (NRD)[15]
22	Hamidu N. Rajabu *et al.*, 2024	Renal CC.	NSAID[8]	Unclear	Unclear	Low risk (RP)[14]	Unclear	Some concerns
23	Alfredo Budillon *et al.*, 2024	Pancreatic C.	Simvastatin, Statins	Yes	Open-label (no blinding)	Low risk (RP)[14]	Unclear	Some concerns
24	Shoham Baruch *et al.*, 2024	Various C.	Propranolol, Atenolol	No	Unclear	Unclear	Unclear	High (NRD)[15]
25	Arvind Kumar Sharma *et al,* 2024	Various C.	ARB[3], ACEI[1], Beta-blocker, Telmisartan, Candesartan	No	Unclear	Unclear	Low risk[16]	High (NRD)[15]
26	Jood Hashem *et al.*, 2024	Leukemia	Atorvastatin, Statins	No	Unclear	Unclear	Unclear	High (NRD)[15]
27	Anam Kamal *et al.*, 2024	Breast C.	Simvastatin, Statins	No	Unclear	Unclear	Unclear	High (NRD)[15]
28	Tej Shukla *et al.*, 2024	Various C.	STZ[13], Trimethoprim	No	Unclear	Unclear	Unclear	High (NRD)[15]
29	Manon Cairat *et al.*, 2023	Breast C.	Aspirin	No	Unclear	Unclear	Unclear	High (NRD)[15]

#	Authors and Year	Cancer Site[14]	Off-Label Drug	Random.[18]	Blinding	Outcome R	Attrition Bias	Overall ROB
30	Ana Giachetti *et al.*, 2023	Sarcoma	Propranolol	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
31	Eun Joo Cho *et al.*, 2023	Leukemia	Chlorthalidone, Telmisartan, Amlodipine	Yes	Double-blind	Low risk (RP)[14]	Low risk[16]	Low
32	Emily Biben *et al.*, 2023	Ovarian C.	Metformin, Insulin	Yes	Unclear	Unclear	Unclear	Some concerns
33	Mireille M. Hermans *et al.*, 2023	Various C.	Beta-blocker, Propranolol, Atenolol	Unclear	Unclear	High risk (selective/post hoc)	Unclear	High
34	Alexander I. Gipsman *et al.*, 2023	Various C.	Propranolol	No	Unclear	Unclear	Unclear	High (NRD)[15]
35	Xiao-Xu Zhu *et al.*, 2023	Cholangio-carcinoma	ARB[3]	No	Unclear	Unclear	Unclear	High (NRD)[15]
36	Marco van Londen *et al.*, 2022	NSCLC[9]	Enalapril, Metformin, Naproxen, ARB[3]	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
37	Ailsa Maria Main *et al.*, 2022	HNSCC[7]	Labetalol	Unclear	Unclear	Unclear	Unclear	Some concerns
38	Azusa Aida *et al.*, 2022	Pancreatic C.	Insulin	No	Unclear	Unclear	Unclear	High (NRD)[15]
39	Lisa Scarton *et al.*, 2022	Lung C.	Metformin	No	Unclear	Unclear	Unclear	High (NRD)[15]
40	Letícia Gaertner Mariani et al, 2022	HNSCC[7]	Propranolol	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
41	Kinnosuke Matsumoto et al, 2022	Lung C.	Azilsartan, Amlodipine	Unclear	Unclear	Unclear	Unclear	Some concerns
42	Wei-Ming Wang *et al.*, 2022	HNSCC[7]	Metformin	Unclear	Unclear	Unclear	Unclear	Some concerns
43	Xiao Shen *et al.*, 2022	Lung C.	Rosuvastatin, Statins Nifedipine, Valsartan,	Unclear	Unclear	Unclear	Unclear	Some concerns
44	S. Mansoori *et al.*, 2021	VMC[14]	Mebendazole	Unclear	Unclear	Unclear	Unclear	Some concerns
45	Tianyi Huang *et al.*, 2021	Ovarian C.	ACEI[1], Beta-blocker	Unclear	Unclear	Unclear	Unclear	Some concerns
46	Jinhui Li *et al.*, 2021	Lung C.	Aspirin, ARB[3]	No	Unclear	Unclear	Unclear	High (NRD)[15]
47	Rajesh Balkrishnan *et al.*, 2021	Colorectal C.	ACEI[1], Beta-blocker	No	Unclear	Unclear	Unclear	High (NRD)[15]
48	Theodore M. Brasky *et al.*, 2021	Colorectal C.	ARB[3]	Unclear	Unclear	Unclear	Unclear	High (NRD)[15]

#	Authors and Year	Cancer Site[14]	Off-Label Drug	Random.[18]	Blinding	Outcome R	Attrition Bias	Overall ROB
49	Esteban Fernández *et al.*, 2021	Various C.	Propranolol	No	Unclear	Unclear	Unclear	High (NRD)[15]
50	Shihan Chen *et al.*, 2021	Various C.	Captopril	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
51	Kavya M. Bejjanki *et al.*, 2021	Various C.	Propranolol	No	Unclear	Unclear	Unclear	High (NRD)[15]
52	Samuel L. Brady *et al.*, 2021	Various C.	Propranolol	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
53	Glen M. Chew *et al.*, 2021	Various C.	Metformin	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
54	Fania Z. Muñoz-Garza *et al.*, 2021	Various C.	Propranolol	Yes	Double-blind	Unclear	Unclear	Some concerns
55	Wei-Ru Cho *et al.*, 2021	Hepato. C.	Metformin	No	Unclear	Unclear	Unclear	High (NRD)[15]
56	Joanne Mui Ching Tan *et al.*, 2021	HNSCC[7]	Beta-Blocker, Propranolol	No	Unclear	Unclear	Unclear	High (NRD)[15]
57	Yeseul Kim *et al.*, 2021	SCLC[12]	Metformin	Unclear	Unclear	Unclear	Unclear	Some concerns
58	Shipra Gandhi *et al.*, 2021	Melanoma	Propranolol	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
59	Justin G. Trogdon *et al.*, 2021	Lung C.	Insulin, Statins	No	Unclear	Unclear	Unclear	High (NRD)[15]
60	Shiori Hiramoto *et al.*, 2021	Breast C.	Duloxetine	No	Unclear	Unclear	Unclear	High (NRD)[15]
61	Efe Eworuke *et al.*, 2021	Various C.	HCT[6]	No	Unclear	Unclear	Unclear	High (NRD)[15]
62	Min-Chun Chuang *et al.*, 2021	NSCLC[9]	Aspirin	Yes	Unclear	Unclear	Unclear	Some concerns
63	Hee Jin Park *et al.*, 2021	Various C.	Propranolol	No	Unclear	Unclear	Unclear	High (NRD)[15]
64	M. Adarsh *et al.*, 2021	Pancreatic C.	Insulin	No	Unclear	Unclear	High risk[19]	High (NRD)[15]
65	Yujian Liang *et al.*, 2020	Thyroid C.	Propranolol	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
66	Gui-Hua Zhang *et al.*, 2020	Lymphoma	Losartan	Unclear	Unclear	Low risk (RP)[14]	Unclear	Some concerns
67	Sungji Moon *et al.*, 2020	Lung C.	ARB[3]	No	Unclear	Unclear	Unclear	High (NRD)[15]
68	Christine D. Hsu *et al.*, 2020	Breast C.	HCT[6]	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
69	Thibault Letellier *et al.*, 2020	Pancreatic C.	HCT[6]	No	Unclear	Unclear	Unclear	High (NRD)[15]
70	Ruzan Udumyan *et al.*, 2020	Hepato. C.	Beta-Blocker	No	Unclear	Unclear	Unclear	High (NRD)[15]
71	Sayaka Tani *et al.*, 2019	Various C.	Propranolol	Unclear	Unclear	Unclear	Unclear	Some concerns
72	Riya Madan *et al.*, 2020	Pancreatic C.	Insulin	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
73	Nicole M. Kuderer *et al.*, 2020	Breast C.	Azithromycin	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]

#	Authors and Year	Cancer Site[14]	Off-Label Drug	Random.[18]	Blinding	Outcome R	Attrition Bias	Overall ROB
74	Zizi Yu *et al.*, 2020	Colorectal C.	Tetracycline, Doxycycline, ARB[3]	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
75	Satoshi Kidoguchi *et al.*, 2020	Various C.	Captopril	Unclear	Unclear	Unclear	Unclear	Some concerns
76	Min Ae Cho *et al.*, 2020	Ovarian C.	ARB[3], Beta-Blocker	No	Unclear	Unclear	Unclear	High (NRD)[15]
77	Jinye Xie *et al.*, 2020	Colorectal C.	Metformin	Unclear	Unclear	Unclear	Unclear	Some concerns
78	Takashi Higuchi *et al.*, 2020	Sarcoma	Pioglitazone	Yes	Unclear	Unclear	Unclear	Some concerns
79	K. Esther Broekman *et al.*, 2020	Ovarian C.	Metformin, ARB[3]	Unclear	Unclear	Low risk (RP)[14]	Unclear	Some concerns
80	Benjamin Daniels *et al.*, 2020	Melanoma	HCT[6]	No	Unclear	Unclear	Unclear	High (NRD)[15]
81	Benjamin *et al.*, 2020	Melanoma	HCT[6]	No	Unclear	Unclear	Unclear	High (NRD)[15]
82	F. Spada *et al.*, 2020	VMC[14]	Azithromycin, Statins	Yes	Unclear	Unclear	Unclear	Some concerns
83	Mariana Carvalho Costa *et al.*, 2020	VMC[14]	Beta-Blocker, Propranolol	Unclear	Unclear	Unclear	Unclear	Some concerns
84	Xin Zhang et al, 2019	Renal CC.	Nifedipine	Unclear	Unclear	Unclear	Unclear	Some concerns
85	Yuxi Ma *et al.*, 2019	Breast C.	Losartan	Unclear	Unclear	Unclear	Unclear	Some concerns
86	Azael Freites-Martinez *et al.*, 2019	Various C.	Spironolactone	No	Unclear	Unclear	Unclear	High (NRD)[15])
87	Eva Neumann *et al.*, 2019	Renal CC.	ARB[3], Statins	Unclear	Unclear	Unclear	Unclear	Some concerns
88	Michael Haap *et al.*, 2019	Primary BT.	ACEI[1]	Unclear	Unclear	Unclear	Unclear	Some concerns
89	Changhua Wu *et al.*, 2019	Various C.	Propranolol	No	Unclear	Unclear	Unclear	High (NRD)[15]
90	Sai Yendamuri *et al.*, 2019	NSCLC[9]	Metformin	No	Unclear	Unclear	Unclear	High (NRD)[15]
91	Yoshihiro Niitsu *et al.*, 2019	Pancreatic C.	Insulin	No	Unclear	Unclear	Unclear	High (NRD)[15]
92	WingYee Wan *et al.*, 2019	Various C.	Clonidine	Unclear	Unclear	Unclear	Unclear	Some concerns
93	Terence T. Sio *et al.*, 2019	Lung C.	Lisinopril	Yes	Double-blind	Low risk (RP)[14]	Unclear	Some concerns
94	Jaime Anger *et al.*, 2019	Various C.	Propranolol	Unclear	Unclear	Unclear	Unclear	Some concerns
95	Preben Kjølhede *et al.*, 2019	Various C.	Clonidine	Yes	Open-label (no blinding)	Low risk (RP)[14]	Low risk[16]	Low

#	Authors and Year	Cancer Site[14]	Off-Label Drug	Random.[18]	Blinding	Outcome R	Attrition Bias	Overall ROB
96	Mu-Chieh Tsai *et al.*, 2019	Various C.	Propranolol	Unclear	Unclear	Low risk (RP)[14]	Unclear	Some concerns
97	Arun Prasad *et al.*, 2019	Various C.	Propranolol	Unclear	Unclear	Unclear	Unclear	Some concerns
98	Elisabet Cuyàs *et al.*, 2019	Breast C.	Metformin, ARB[3]	Yes	Unclear	Low risk (RP)[14]	Unclear	Some concerns
99	Stefania Maraka *et al.*, 2019	Primary BT.	Metformin	Unclear	Unclear	Low risk (RP)[14]	Unclear	Some concerns
100	Taha Anwar *et al.*, 2019	Bladder/urothelial cancer	Propranolol	Unclear	Unclear	Unclear	Unclear	Some concerns
101	Lois M. Ramondetta *et al.*, 2019	Ovarian C.	Beta-Blocker, Propranolol, ARB[3]	Unclear	Unclear	Low risk (RP)[14]	Unclear	Some concerns
102	Phyo T. Htoo *et al.*, 2019	Colorectal C.	ARB[3], Beta-Blocker	No	Unclear	Unclear	Unclear	High (NRD)[15]
103	Yingying Gao *et al.*, 2019	Prostate C.	Simvastatin, Statins	No	Unclear	Unclear	Unclear	High (NRD)[15]
104	So-Yeon Jeon *et al.*, 2019	Lung C.	Amlodipine	Unclear	Unclear	Unclear	Unclear	Some concerns
105	Bliss E. O'Bryhim *et al.*, 2019	Various C.	Propranolol	Unclear	Unclear	Unclear	Unclear	Some concerns
106	Forrest L. Baker *et al.*, 2019	Various C.	Beta-Blocker, Bisoprolol	Yes	Unclear	Unclear	Unclear	Some concerns
107	Ping-Ying Chang *et al.*, 2019	Hepato. C.	Beta-Blocker, Propranolol	No	Unclear	Unclear	Unclear	High (NRD)[15]
108	Yehee Hong *et al.*, 2019	Prostate C.	Metformin	No	Unclear	Unclear	Low risk[16]	High (NRD)[15]
109	Aditi Mehta *et al.*, 2019	Various C.	Propranolol	Yes	Unclear	Unclear	Unclear	Some concerns
110	Janet E. Murphy *et al.*, 2019	Pancreatic C.	Losartan	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
111	Zhaobo Liu *et al.*, 2019	Various C.	Propranolol	Unclear	Unclear	Unclear	Unclear	High (NRD)[15]
112	Anton Pottegård *et al.*, 2019	Melanoma	HCT[6]	No	Unclear	Unclear	Unclear	High (NRD)[15]
113	Kristen A. Marrone *et al.*, 2018	NSCLC[9]	Metformin, Insulin, ARB[3]	Yes	Open-label (no blinding)	Low risk (RP)[14]	High risk[19]	High
114	Blánaid M. Hicks *et al.*, 2018	Lung C.	ARB[3]	No	Unclear	Unclear	Unclear	High (NRD)[15]
115	Anton Pottegård *et al.*, 2018	Melanoma	HCT[6]	No	Unclear	Unclear	Unclear	High (NRD)[15]
116	Christian Ramos-Peñafiel *et al.*, 2018	Leukemia	Metformin	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]

#	Authors and Year	Cancer Site[14]	Off-Label Drug	Random.[18]	Blinding	Outcome R	Attrition Bias	Overall ROB
117	Wensheng Jiang *et al.*, 2018	NSCLC[9]	NSAID[8]	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
118	Tomonori Hirashima *et al.*, 2018	Lung C.	Rifampicin	No	Unclear	Unclear	Unclear	High (NRD)[15]
119	Fumitaka Wada *et al.*, 2018	Hepato. C.	ARB[3]	Unclear	Unclear	Low risk (RP)[14]	Unclear	Some concerns
120	Li Jiao-Ling *et al.*, 2018	Various C.	Propranolol	Unclear	Unclear	Unclear	Unclear	Some concerns
121	Sidsel Arnspang Pedersen *et al.*, 2018	Various C.	HCT[6]	No	Unclear	Unclear	Unclear	High (NRD)[15]
122	Limin Liu *et al.*, 2018	VMC[14]	Insulin	Unclear	Unclear	Unclear	Unclear	Some concerns
123	Massimo Moro *et al.*, 2018	NSCLC[9]	Metformin	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
124	Sara Pusceddu *et al.*, 2018	Pancreatic C.	Metformin, Insulin, Statins	No	Unclear	Unclear	Unclear	High (NRD)[15]
125	Harvey J. Murff *et al.*, 2018	Lung C.	Metformin	Yes	Unclear	Unclear	Unclear	Some concerns
126	Zhenwei Zhu *et al.*, 2018	Various C.	Propranolol	Unclear	Unclear	Unclear	Low risk[16]	Some concerns
127	C. Fernandez *et al.*, 2018	Various C.	Insulin	No	Unclear	Unclear	Low risk[16]	High (NRD)[15]
128	Tongbai Xu *et al.*, 2018	NSCLC[9]	Metformin	No	Unclear	Unclear	Unclear	High (NRD)[15]
129	Vincenzo De Giorgi *et al.*, 2018	Melanoma	Propranolol	Yes	Double-blind	Unclear	Unclear	Some concerns
130	Jennifer M. Knight *et al.*, 2018	Multiple myeloma	Propranolol	Yes	Unclear	Low risk (RP)[14]	Unclear	Some concerns
131	William A. Stokes *et al.*, 2018	HNSCC[7]	Metformin, ARB[3]	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
132	Anton Pottegård *et al.*, 2018	Colorectal C.	Valsartan	No	Unclear	Unclear	Unclear	High (NRD)[15]
133	William Small *et al.*, 2018	NSCLC[9]	ACEI[1], Captopril	Yes	Unclear	Low risk (RP)[14]	Unclear	Some concerns
134	Jian-Yong Dong *et al.*, 2017	HNSCC[7]	Propranolol	Unclear	Unclear	Unclear	Unclear	Some concerns
135	Ryuichiro Hosoya *et al.*, 2017	Various C.	ARB[3]	Unclear	Unclear	Unclear	Unclear	Some concerns
136	Young-Jun Ki *et al.*, 2017	Colorectal C.	Metformin	No	Unclear	Unclear	Unclear	High (NRD)[15]
137	Zeynep Canan Özdemir *et al.*, 2017	Thyroid C.	Beta-Blocker, Propranolol	Unclear	Unclear	Unclear	Unclear	Some concerns
138	Fiorella Guadagni *et al.*, 2017	VMC[14]	Insulin	No	Unclear	Unclear	Unclear	High (NRD)[15]
139	Cheng Xue *et al.*, 2017	Renal CC.	HCT[6], ACEI[1], Fosinopril	Yes	Double-blind	Low risk (RP)[14]	Low risk[16]	Low

#	Authors and Year	Cancer Site[14]	Off-Label Drug	Random.[18]	Blinding	Outcome R	Attrition Bias	Overall ROB
140	Jian-Yu E *et al.*, 2017	Pancreatic C.	Metformin, Statins	No	Unclear	Unclear	Unclear	High (NRD)[15]
141	M. A. Frouws *et al.*, 2017	Colorectal C.	Aspirin	Unclear	Unclear	Unclear	Unclear	Some concerns
142	David Gill *et al.*, 2017	Prostate C.	Spironolactone, Eplerenone	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
143	Ivette F. Emery *et al.*, 2017	Primary BT.	ARB[3]	Unclear	Unclear	Low risk (RP)[14]	Unclear	Some concerns
144	A. Pottegård *et al.*, 2017	Various C.	HCT[6]	No	Unclear	Unclear	Unclear	High (NRD)[15]
145	Michael J. Seckl *et al.*, 2017	SCLC[12]	Pravastatin, Statins, ARB[3]	Yes	Double-blind	Low risk (RP)[14]	Unclear	Some concerns
146	Ishveen Chopra *et al.*, 2017	Breast C.	Statins, ARB[3]	No	Unclear	Unclear	Unclear	High (NRD)[15]
147	Lee Shaashua *et al.*, 2017	Breast C.	Propranolol, COX-2[4]	Yes	Double-blind	Low risk (RP)[14]	Unclear	Some concerns
148	Hui-Fang Chiu et al, 2017	Various C.	ARB[3]	Yes	Unclear	Low risk (RP)[14]	Unclear	Some concerns
149	Maya El Hachem *et al.*, 2017	Various C.	Propranolol	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
150	Alexandra Couttenier *et al.*, 2017	Ovarian C.	Rosuvastatin, Simvastatin, Statins	No	Unclear	Unclear	Unclear	High (NRD)[15]
151	Victoria Mandilaras *et al.*, 2017	Pancreatic C.	ARB[3]	No	Unclear	Unclear	Unclear	High (NRD)[15]
152	Matthias Holdhoff *et al.*, 2017	Primary BT.	ARB[3]	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
153	Shinji Higuchi *et al.*, 2017	Thyroid C.	Propranolol	Unclear	Unclear	Unclear	Unclear	Some concerns
154	Alexa Montoya *et al.*, 2016	Breast C.	Beta-Blocker, Propranolol	No	Unclear	Unclear	Unclear	High (NRD)[15]
155	Mark Anthony Sandoval *et al.*, 2016	Pancreatic C.	Insulin	Unclear	Unclear	Low risk (RP)[14]	Unclear	Some concerns
156	Koji Matsuo *et al.*, 2016	Endometrial C.	Aspirin	No	Unclear	Unclear	Unclear	High (NRD)[15]
157	Young-Seok Seo *et al.*, 2016	Hepato. C.	Metformin	No	Unclear	Unclear	Unclear	High (NRD)[15]
158	Linnéa Schmidt *et al.*, 2016	Primary BT.	Sertraline	Unclear	Unclear	Low risk (RP)[14]	Unclear	Some concerns
159	Mugdha Gokhale *et al.*, 2016	Lung C.	ARB[3], ACEI[1]	Unclear	Unclear	Unclear	Unclear	Some concerns
160	Koji Matsuo *et al.*, 2016	Endometrial C.	HCT[6], Insulin	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
161	Katrina Wilcox Hagberg *et al.*, 2016	Hepato. C.	ACEI[1]	No	Unclear	Unclear	Unclear	High (NRD)[15]

#	Authors and Year	Cancer Site[14]	Off-Label Drug	Random.[18]	Blinding	Outcome R	Attrition Bias	Overall ROB
162	Eddy Pasquier *et al.*, 2016	VMC[14]	Propranolol	Unclear	Unclear	Low risk (RP)[14]	Unclear	Some concerns
163	Luigi Fontana *et al.*, 2016	Various C.	Insulin	Yes	Unclear	Unclear	Low risk[16]	Some concerns
164	Nobumasa Ohara *et al.*, 2016	Various C.	ARB[3]	Yes	Unclear	Unclear	Unclear	Some concerns
165	Tianyi Huang *et al.*, 2016	Ovarian C.	Beta-Blocker	No	Unclear	Unclear	Unclear	High (NRD)[15]
166	Lili Miao *et al.*, 2016	NSCLC[9]	ARB[3]	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
167	Zachary S. Morris *et al.*, 2016	Colorectal C.	ARB[3], Metformin, Aspirin, Statins	Unclear	Unclear	Low risk (RP)[14]	Unclear	Some concerns
168	Cecilia Choy *et al.*, 2016	Breast C.	Propranolol	No	Unclear	Unclear	Unclear	High (NRD)[15]
169	Bo Young Oh *et al.*, 2016	Colorectal C.	Metformin	No	Unclear	Unclear	Unclear	High (NRD)[15]
170	Jessica K. Paulus *et al.*, 2016	Colorectal C.	Metformin	Yes	Unclear	Unclear	Unclear	Some concerns
171	Jing Ge *et al.*, 2016	Various C.	Propranolol	No	Unclear	Unclear	Unclear	High (NRD)[15]
172	Chengfang Zhou *et al.*, 2016	Melanoma	Propranolol	Unclear	Unclear	Unclear	Unclear	Some concerns
173	Giovanna Stringari *et al.*, 2016	Various C.	Propranolol	Unclear	Unclear	Low risk (RP)[14]	Unclear	Some concerns
174	M. R. Jones *et al.*, 2016	Colorectal C.	Irbesartan	Unclear	Unclear	Unclear	Unclear	Some concerns
175	Saul Castaneda *et al.*, 2016	Various C.	Propranolol	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]
176	Inés Gómez-Acebo *et al.*, 2016	Breast C.	Beta-Blocker	No	Unclear	Unclear	Unclear	High (NRD)[15]
177	Koray Tascilar *et al.*, 2016	Lung C.	ARB[3], Telmisartan	No	Unclear	Un[21]clear	Unclear	High (NRD)[15]
178	Angelo Restivo *et al.*, 2016	Colorectal C.	Aspirin	Yes	Unclear	Unclear	Unclear	Some concerns
179	Stephen John Ralph *et al.*, 2015	VMC[14]	NSAID[8]	Unclear	Unclear	Unclear	Unclear	Some concerns
180	Brian Winters *et al.*, 2015	Prostate C.	Metformin, Insulin	No	Unclear	Unclear	Unclear	High (NRD)[15]
181	Grzegorz Dworacki et al, 2015	Various C.	Metformin	No	Unclear	Low risk (RP)[14]	Unclear	High (NRD)[15]

ACEI[1] : Angiotensin-Converting Enzyme Inhibitors; **AE[2]**: Adverse Events; **ARB[3]** : Angiotensin II Receptor Blocker (AT_1 antagonists); **COX-2[4]** : Cyclo-Oxygenase-2 (enzyme)/COX-2-selective inhibitors; **DFS[5]**: Disease-free survival; **HCT[6]** : Hydrochlorothiazide; **HNSCC[7]** : Head and Neck Squamous Cell Carcinoma; **NSAID[8]** : Non-Steroidal Anti-Inflammatory Drug; **NSCLC[9]** : Non-Small Cell Lung Cancer; **OS[10]** : Overall survival; **PFS[11]**: Progression-free survival; **SCLC[12]** : Small Cell Lung Cancer; **STZ[13]** : Sulfamethoxazole; **VMC[14]** : Various Metastatic Cancer; **Low risk (RP)[14]** : Low risk (Registered/Prespecified); **High (NRD)[15]**: High (non-randomized design); **Low risk[16]** : Low risk (ITT/complete

follow-up); **Cancer Site[17] :** Various C. (Various Cancers), Pancreatic C. (Pancreatic Cancer), Hepato. C. (Hepatocellular Carcinoma), Lung C. (Lung Cancer), Prostate C. (Prostate Cancer), Renal CC. (Renal cell carcinoma), Breast C. (Breast Cancer), Colorectal C. (Colorectal cancer), Ovarian C. (Ovarian Cancer), Endometrial C. (Endometrial cancer), Thyroid C. (Thyroid Cancer), Primary BT. (Primary Brain Tumors), **Random.[18]**: **Randomisation : No (**non-randomized), **Yes** (randomized)); **High risk[19]** : High risk (losses/PP only).