International Journal of Pharmaceutical Research and Development

ISSN Print: 2664-6862
ISSN Online: 2664-6870
Impact Factor: RJIF 8.55
IJPRD 2025; 7(2): 138-148
www.pharmaceuticaljournal.net
Received: 24-05-2025
Accepted: 27-06-2025

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Benzimidazole derivatives in oncology: A review of molecular targets and therapeutic potential in clinical trial

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DOI: https://doi.org/10.33545/26646862.2025.v7.i2b.174

Abstract
Cancer continues to be a leading global health burden, prompting the need for innovative therapeutic strategies that address treatment resistance, toxicity, and specificity. Benzimidazole and its derivatives have emerged as promising pharmacophores in oncology due to their versatile biological activities, including kinase inhibition, microtubule disruption, and modulation of apoptosis pathways. This review explores recent advances in the development of benzimidazole-based compounds targeting various cancers, such as glioblastoma, colorectal cancer, leukaemia, breast, and lung malignancies. Notable examples include inhibitors of the neddylation pathway, tubulin-binding agents, and kinase-targeting molecules, which demonstrate potent *in vitro* and *in vivo* efficacy. Several benzimidazole derivatives, such as compound 12b and 7c, exhibited low nanomolar cytotoxicity and overcame drug resistance mechanisms, particularly in paclitaxel- and EGFR-TKI-resistant models. Additionally, benzimidazole–triazole hybrids have shown dual functionality by serving as both cytotoxic agents and PET imaging probes through Galectin-1 targeting. The integration of computational modelling, cell line assays, molecular docking, and clinical trials underlines the translational relevance of these scaffolds. Collectively, benzimidazoles represent a promising platform for developing next-generation anticancer therapeutics and diagnostic agents, particularly in the context of precision medicine.

Keywords: Cell line, Clinical trial, Docking studies, EGFR, Kinase, Leukaemia

Introduction
Cancer represents one of the most formidable global health challenges, marked by the unregulated growth and spread of abnormal cells. As per recent statistics from the World Health Organization (WHO), cancer was responsible for nearly 10 million deaths in 2020, signifying its status as a leading cause of mortality worldwide [1]. The disease is complex and multifaceted, involving various biological mechanisms and occurring in a broad range of forms, each with unique clinical features and therapeutic implications.

Broadly classified based on the tissue or cell of origin, cancers include carcinomas (arising from epithelial cells), sarcomas (from connective tissues like bone or muscle), leukaemia (blood-forming tissues), lymphomas (immune system components), and melanomas (originating from pigment-producing cells) [2]. Among the most commonly diagnosed malignancies globally are cancers of the lung, breast, colon and rectum, prostate, and stomach [3].

Traditional cancer treatments such as surgical removal, chemotherapy, and radiation therapy have been the mainstays of clinical management for decades. While these approaches have improved survival outcomes in many cancers, they often come with significant limitations, including non-selectivity, adverse effects, and resistance development [4]. This has prompted a shift toward more sophisticated, individualized therapies that leverage molecular and genetic insights into tumour biology.

Recent advances in oncology have introduced a new era of targeted treatments, which are designed to interfere with specific genetic mutations or proteins involved in cancer progression. For instance, therapies targeting mutated EGFR, BRAF, or overexpressed HER2 have shown promising results in selected cancer types [5].

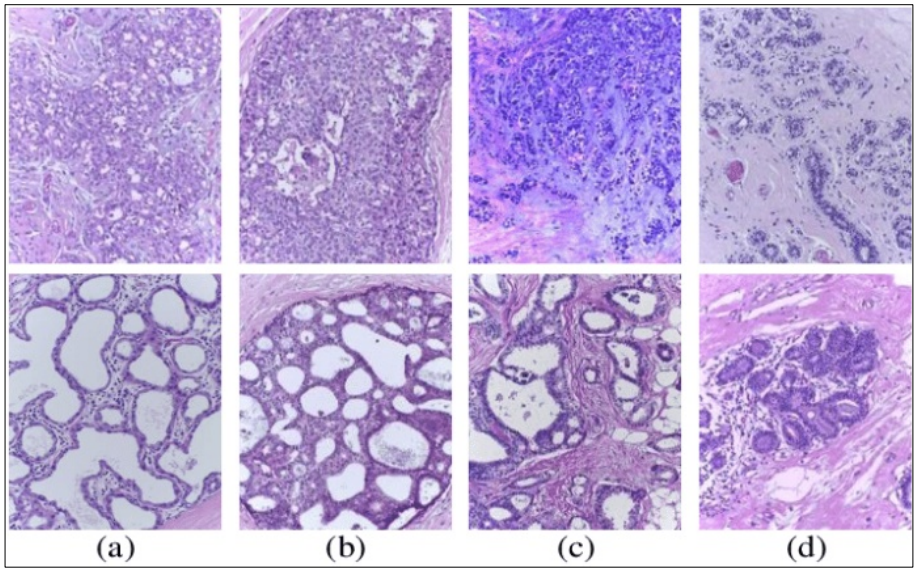

Fig 1: (a) Carcinoma (b): Sarcoma (c) Squamous cell carcinoma (d) Clear cell sarcoma

Similarly, immunotherapies, particularly immune checkpoint inhibitors such as anti-PD-1/PD-L1 and CTLA-4 antibodies, have transformed treatment protocols in cancers like melanoma and non-small cell lung carcinoma, achieving unprecedented survival benefits in certain patient populations [6, 7].

In parallel, technological progress has enhanced early detection and treatment personalization. Tools such as next-generation sequencing (NGS), liquid biopsies, and artificial intelligence (AI)-based diagnostic platforms are improving the precision and speed of cancer diagnosis and monitoring. These innovations, coupled with discoveries in biomarker research and precision medicine, are allowing clinicians to tailor interventions based on the unique molecular profile of a patient's tumour [8].

Targeting Various Enzymes, Receptors, And Signalling Pathways Associated with Benzimidazole Scaffolds

G. R. Oxnard *et.al.*, have reported the TATTON study (NCT02143466). It was a phase I b clinical trial designed to evaluate the safety and tolerability of combining osimertinib, a third-generation EGFR tyrosine kinase inhibitor (TKI), with other targeted therapies in patients with advanced EGFR-mutated non-small-cell lung cancer (NSCLC) who had previously progressed on EGFR-TKI treatment. The study tested three combination regimens: osimertinib with selumetinib (a MEK1/2 inhibitor), savolitinib (a MET inhibitor), and durvalumab (a PD-L1 monoclonal antibody). A total of 77 patients were enrolled and received one of the three combinations: 36 in the selumetinib arm, 18 in the savolitinib arm, and 23 in the durvalumab arm. Common treatment-related side effects included diarrhoea, rash, and nausea with selumetinib; nausea, rash, and vomiting with savolitinib; and rash, vomiting, and diarrhoea with durvalumab. Dose-limiting toxicities (DLTs) were observed at higher doses across all groups, particularly in the continuous selumetinib arm and at the higher savolitinib and durvalumab dose levels. The objective response rates (ORRs) were promising and comparable across all groups—42% with selumetinib, 44% with savolitinib, and 43% with durvalumab. However, the combination with durvalumab raised significant concerns due to a higher incidence of interstitial lung disease (ILD), making it unsuitable for further clinical use. They have concluded that, combining osimertinib with either selumetinib or savolitinib demonstrated potential therapeutic benefit with manageable toxicity, warranting further investigation. In contrast, the osimertinib-durvalumab combination posed safety risks and is not recommended for continued development [9].

Xin Chen *et.al.*, have developed novel benzimidazole derived neddylation inhibitors. Aberrant activation of the ubiquitin-like protein neddylation pathway has been observed in multiple human cancers and is often associated with disease progression, making it a compelling target for therapeutic intervention. In earlier work, the antihypertensive drug candesartan cilexetil (CDC) was identified as a novel inhibitor of the Nedd8-activating enzyme (NAE), demonstrating its potential to inhibit tumour growth through disruption of the neddylation pathway. Building on this discovery, a series of 42 benzimidazole-based derivatives were rationally designed and synthesized, using CDC as the structural lead, with the goal of enhancing both neddylation inhibition and anticancer activity. Among these, compound 35 emerged as the most promising candidate, exhibiting significantly greater inhibitory potency against NAE (IC_{50} = 5.51 μM) compared to CDC (IC_{50} = 16.43 μM). Further *in vitro* evaluations demonstrated that compound 35 selectively inhibited cancer cells while sparing normal cells. Mechanistic studies at the cellular level, coupled with *in vivo* assessments in A549 human lung cancer xenograft models, confirmed its antitumor activity. Additionally, molecular docking simulations supported the strong interaction of compound 35 with the NAE target. These findings suggest that compound 35 holds strong potential as a next-generation neddylation pathway inhibitor, and may serve as a valuable lead compound for the development of novel anticancer therapies [10].

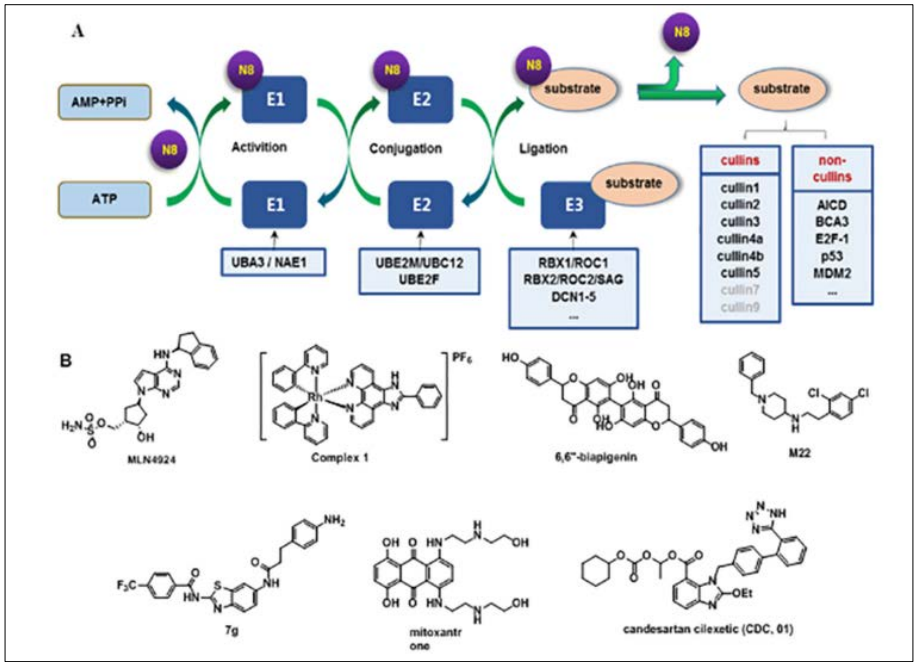

Fig 2: The process of neddylation (A) and reported NAE inhibitors (B)

Kaviarasan Lakshmanan *et al.*, have performed docking studies and reported that MAP kinase plays a critical role in the development and progression of diseases such as osteoarthritis, **i**nflammation, and various forms of cancer, making it a significant molecular target in therapeutic drug discovery. A wide array of p38 MAP kinase inhibitors has been developed, utilizing different chemical scaffolds and targeting either the ATP-binding pocket or allosteric sites of the kinase. In this study, a series of benzimidazole derivatives incorporating 4H-chromen-4-one moieties were computationally designed and structurally optimized to evaluate their potential as MAP kinase inhibitors. Using molecular docking techniques implemented in Auto Dock and Discovery Studio, the interaction profiles of these compounds with the MAP kinase active site were examined. Their docking results revealed that all designed compounds demonstrated favourable binding energies, in comparison to the reference anticancer agent Imatinib. Notably, compounds D1 and D6 exhibited superior binding affinity, suggesting their potential as more effective inhibitors. In addition, molecular descriptors and physicochemical properties of the compounds were assessed using Molinspiration, supporting their drug-likeness and possible biological activity. Based on these promising in silico results, future work will focus on the synthesis of these benzimidazole-based candidates followed by *in vitro* and *in vivo* screening to validate their anticancer efficacy [11].

Taku FUJIMURA *et al.*, have reported the effectiveness of the encorafenib and binimetinib (E + B) combination in treating advanced melanoma with BRAF mutations beyond the first line of therapy remains uncertain. This study examined a group of 22 patients with BRAF-mutated advanced melanoma who received E + B as second-line or later treatment. The observed objective response rate (ORR) across all patients was 68.4%, with an even higher ORR of 73.3% among those treated in the second-line or later settings. These findings suggest that the clinical benefit of E + B in previously treated patients may be on par with its performance as a first-line targeted therapy. However, overall survival (OS) and progression-free survival (PFS) in this real-world cohort were lower than those reported in prior clinical trials. Additionally, while the rate of serious adverse events was somewhat elevated compared to earlier studies, the regimen was generally well tolerated by patients. Overall, this analysis supports the efficacy and manageable safety profile of encorafenib plus binimetinib when used as a subsequent-line therapy for BRAF-mutated melanoma, indicating its potential as a viable option beyond first-line treatment [12].

Kamaraj Karthick *et al.*, have performed molecular docking studies. Kinase enzymes are central to cellular proliferation and survival, making them critical targets in anticancer drug development. Among various chemotypes, benzimidazole derivatives have gained attention for their capacity to inhibit protein kinases and suppress cancer cell growth. These compounds are also known for a broad spectrum of biological activities, including antibacterial, antiviral, and anti-inflammatory effects, as well as for their role in modulating immune responses and reducing viral loads. Their study explored the protein kinase inhibitory potential of several benzimidazole derivatives through in silico molecular docking, along with their pharmacokinetic properties. The focus was on two crucial kinase targets: Cyclin-dependent kinase 4/Cyclin D1 (CDK4/CycD1) and Aurora B kinase. The binding interactions of the compounds were evaluated, and among them, 2-phenylbenzimidazole demonstrated the most potent inhibitory activity, with a binding energy of −8.2 kcal/mol, indicating strong target engagement. Additionally, the pharmacokinetic profiles and drug-likeness of the compounds were assessed using admetSAR and SwissADME tools. The results revealed favourable ADMET properties, aligning with Lipinski's Rule of Five, suggesting these molecules are suitable candidates for further preclinical development. This study supports the potential of benzimidazole-based molecules as promising leads for the design of novel anticancer therapeutics targeting key kinase enzymes [13].

Jian Zhang *et al.*, have performed a randomised phase 1 clinical trial. Abemaciclib, a selective inhibitor of cyclin-dependent kinases 4 and 6 (CDK4/6), has been approved for

use either as monotherapy or in combination with endocrine therapy—for treating hormone receptor-positive, HER2-negative (HR+/HER2−) advanced breast cancer outside of China. This study aimed to assess the safety, tolerability, and pharmacokinetic (PK) profile of abemaciclib in Chinese patients diagnosed with advanced or metastatic cancers. This was a phase I, open-label, multicentre clinical trial, where eligible patients were randomly assigned (1:1) to receive oral abemaciclib at doses of 150 mg or 200 mg every 12 hours over a 28-day treatment cycle. The primary objective was to evaluate safety, while secondary outcomes included PK analysis and preliminary assessment of anticancer activity. Out of 26 randomized participants, 25 patients received treatment (12 at 150 mg and 13 at 200 mg). All treated individuals experienced at least one treatment-emergent adverse event (TEAE). Most adverse events were mild to moderate (CTCAE Grade 1 or 2). The most frequently observed Grade ≥ 3 toxicities were neutropenia (32%) and thrombocytopenia (24%). Four patients (16%) discontinued therapy due to adverse effects. PK evaluation showed that abemaciclib had slow absorption, with peak plasma levels reached around 6 hours post-dose and a half-life of approximately 24 hours. In terms of clinical outcomes, no complete responses were noted; however, two patients (8%) exhibited partial tumour responses, with one being confirmed. The overall disease control rate (DCR) was 68% (17 patients). They concluded that abemaciclib demonstrated a favourable safety profile and pharmacokinetics in Chinese patients, aligning with findings from previous studies in non-chinese populations. Early signs of antitumor activity were also evident, supporting further clinical evaluation in this population [14].

Francesca Aroldi *et al.*, have performed a phase1a/b clinical trial (EudraCT Number: 2014–000463–40). Treating RAS-mutant (RAS^MT) colorectal cancer (CRC) remains highly challenging due to persistent feedback activation of the RAS/MEK signalling pathway. Preclinical investigations have highlighted the MET/STAT3 axis as a key contributor to resistance against KRAS-MEK inhibition in these tumours. This phase I clinical trial was designed to evaluate the safety, tolerability, and initial efficacy of a dual-targeted approach combining binimetinib (a MEK1/2 inhibitor) and crizotinib (a MET inhibitor) in patients with advanced RAS^MT CRC. Their study began with a dose escalation phase, enrolling patients with various advanced solid tumours using a rolling-6 design to determine the maximum tolerated dose (MTD). This was followed by a dose expansion phase involving RAS^MT metastatic CRC patients to assess early clinical outcomes. Patients also underwent pharmacokinetic and biomarker analyses, including circulating tumour DNA (ctDNA), c-MET expression by immunohistochemistry (IHC), and MET gene amplification assessments through in situ hybridization (ISH). In total, 20 patients participated in the dose escalation phase, leading to the identification of the MTD: binimetinib 30 mg twice daily (days 1–21 in a 28-day cycle) and crizotinib 250 mg once daily (continuous dosing). Dose-limiting toxicities included grade ≥3 elevations in liver enzymes (transaminitis), creatine phosphokinase, and fatigue. In the dose expansion phase, 36 patients with RAS^MT CRC were treated. Pharmacokinetic and pharmacodynamic data indicated adequate target inhibition. Across both phases, the most commonly reported treatment-related adverse events (TRAEs) were rash (80.4%), fatigue (53.4%), and diarrhoea (51.8%), with grade ≥3 TRAEs seen in 44.6% of participants. The best observed clinical outcome in the RAS^MT CRC cohort was stable disease in 7 patients (24%), with no objective tumour responses. High MET protein expression (IHC H-score >180 and MET ISH +3) was seen in 7 patients, but only one showed MET amplification, and this patient discontinued therapy during the first cycle due to toxicity. Moreover, patients with a high baseline KRAS^MT allele frequency had shorter median overall survival than those with lower allele levels. They concluded that, the binimetinib and crizotinib combination demonstrated poor tolerability and limited efficacy, with no tumour responses in patients with advanced RAS^MT CRC, indicating the need for alternative strategies in this difficult-to-treat population [15].

Li-wen Ren *et al.*, have reported benzimidazoles induce concurrent apoptosis via arresting cell cycle. Glioblastoma multiforme (GBM) is the most aggressive and deadly form of primary brain tumour in adults, accounting for nearly half of all gliomas. Despite advances in research, the current standard treatment temozolomide faces significant limitations due to frequent development of drug resistance. To identify alternative therapeutic options, weighted gene co-expression network analysis (WGCNA) was applied to The Cancer Genome Atlas (TCGA) dataset to identify key regulatory genes (hub genes) associated with GBM. Further drug repurposing efforts using the Connectivity Map (CMAP) platform suggested several azole compounds with potential anti-GBM properties. Among these, three benzimidazole derivatives—flubendazole, mebendazole, and fenbendazole—were found to exhibit potent, dose-dependent inhibition of U87 and U251 glioblastoma cell proliferation, with IC_{50} values below 0.26 μM. Further investigations revealed that at concentrations ranging from 0.125 to 0.5 μM, benzimidazoles significantly reduced DNA synthesis, cell migration, and invasion, and modulated the expression of key markers involved in epithelial-mesenchymal transition (EMT). Mechanistic studies showed that these compounds induced G2/M cell cycle arrest through the P53/P21/cyclin B1 axis. In addition to their antiproliferative effects, benzimidazoles triggered pyroptos via activation of the NF-kB/NLRP3/GSDMD pathway, and potentially induced mitochondria-mediated apoptosis. *In vivo*, treatment with flubendazole at doses of 12.5, 25, and 50 mg/kg/day (i.e.) for three weeks in a nude mouse xenograft model of U87 cells significantly suppressed tumour growth without apparent toxicity. These findings suggest that benzimidazole compounds, traditionally used as antiparasitic, show strong promise as potential therapeutics for glioblastoma multiforme, warranting further clinical investigation [16].

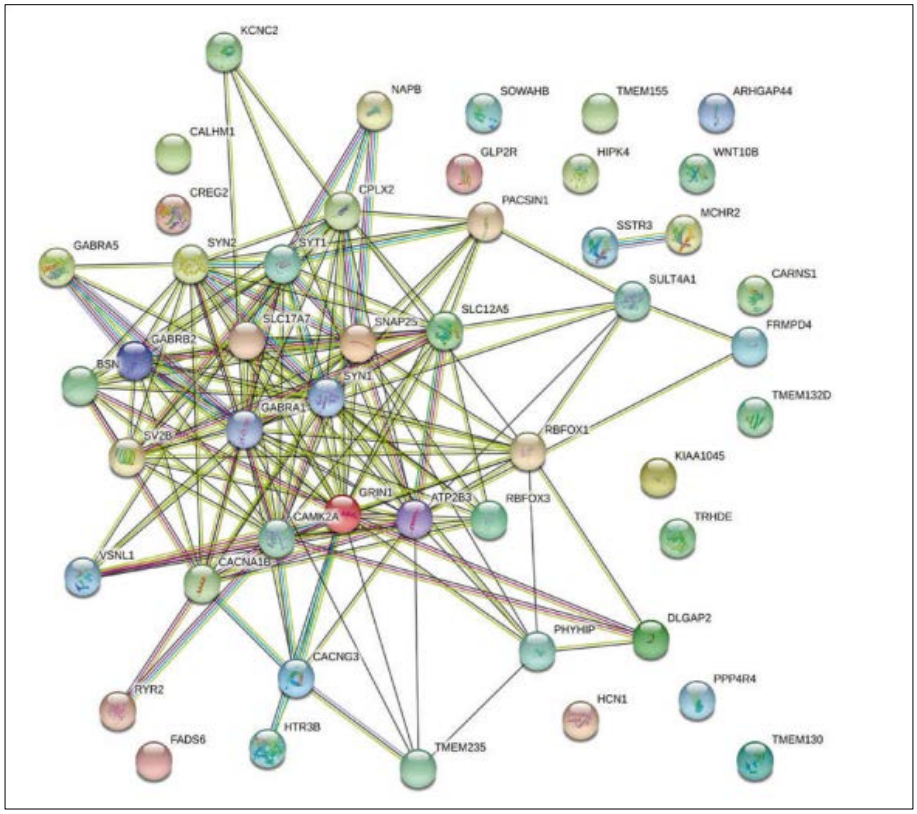

Fig 3: Drug repurposing based on hub gene identification by WGCNA analysis on the CMAP platform.

Sanne C.F.A. Huijberts *et al.*, Combination therapies targeting BRAF and EGFR have been developed for patients with BRAFV600E-mutated metastatic colorectal cancer (CRC), yet many patients experience either intrinsic non-response or acquired resistance, limiting long-term treatment efficacy. This study aimed to identify the genetic alterations that contribute to treatment resistance in patients undergoing MAPK pathway inhibition based on BRAF and EGFR blockade. This cohort study analysed genetic alterations in patients with BRAFV600E-mutated advanced CRC who were treated with inhibitors targeting the MAPK pathway. Tumour samples were collected and assessed at baseline, during treatment, and upon disease progression to detect changes associated with treatment response and resistance. A total of 37 patients were evaluated. Non-responders showed a higher frequency of genetic alterations in genes such as EGFR and PIK3CA, which were associated with poor response to treatment. Moreover, 75% of non-responders harboured mutations in genes other than TP53, APC, or BRAF, compared to 46% of responders, suggesting a broader mutational landscape in non-responders. In patients who developed secondary resistance (n = 16), the most frequent mutations occurred in the PI3K pathway (n = 6) and in receptor tyrosine kinases (n = 4), indicating reactivation of upstream signalling pathways. Their study found that genetic alterations affecting the PI3K pathway and receptor tyrosine kinases were the most common mechanisms underlying both primary resistance and acquired resistance to BRAF/EGFR-targeted therapies. These findings suggest that combination or sequential treatment strategies involving additional targeted agents may help overcome resistance and prolong therapeutic response in patients with BRAFV600E-mutant metastatic CRC [17].

Naoya Kondo *et al.*, have developed 2-(2-Hydroxyphenyl)-1H-benzimidazole based fluorescence sensor targeting boronic acids for versatile application in Boron Neutron Capture Therapy. In boron neutron capture therapy (BNCT), the therapeutic efficacy relies heavily on both the concentration and precise localization of boron-10 (^{10}B) within tumour tissues. To support the analysis of boron-containing compounds used in BNCT, this study introduces a novel fluorescent probe, named BITQ. Upon combining BITQ with BPA, a commonly used ^{10}B-labeled boron agent, a strong and highly specific fluorescent signal was rapidly generated. The fluorescence was quantitative and selective, enabling effective detection of BPA. Using BITQ, researchers successfully visualized BPA distribution in live cells and measured its concentration in mouse blood, with results comparable to those obtained through established analytical techniques. These findings demonstrate that BITQ is a powerful and reliable fluorescence-based tool for studying boronic acid-containing agents, offering great potential for enhancing BNCT research and monitoring [18].

Yuto Hibino *et al.*, Erdheim–Chester disease (ECD) is a rare form of non-Langerhans cell histiocytosis characterized by diverse clinical features and commonly linked to mutations in the MAPK/ERK signalling pathway. Typically, BRAF and KRAS mutations—both known oncogenic drivers—are mutually exclusive, as they activate the same signalling cascade. This report describes a rare case of ECD with concurrent BRAFV600E and KRASG12R mutations, successfully treated with combined BRAF and MEK inhibition. A 70-year-old male presented with a mesenteric nodal mass and symptoms including central diabetes insipidus, raising suspicion of ECD. Histological analysis of the biopsy showed CD68 and CD163 positivity, and negativity for S100, CD1a, and CD21, confirming the diagnosis of ECD. Further molecular analysis using both liquid biopsy and tumour tissue gene panel testing identified the presence of both BRAFV600E and KRASG12R mutations, each with distinct variant allele frequencies.

Immunohistochemistry specific to the BRAFV600E mutation confirmed its expression in a subset of proliferating histiocytes. This suggested the coexistence of two separate clones—one harbouring BRAFV600E and the other KRASG12R. A personalized treatment approach was initiated using encorafenib (100 mg once daily) and binimetinib (15 mg twice daily), aiming to target both clones through dual inhibition of BRAF and MEK. The patient experienced rapid clinical improvement and marked radiological regression following the initiation of combination therapy. The treatment was well tolerated and led to significant symptom resolution. Hence, this case highlights a unique presentation of ECD with dual BRAFV600E and KRASG12R mutations, demonstrating that combined BRAF and MEK inhibition may offer a viable and effective treatment strategy in patients with suspected clonal heterogeneity. To the best of our knowledge, this is the first reported instance of ECD successfully treated with encorafenib and binimetinib, paving the way for future exploration of targeted therapies in genetically complex cases [19].

Patrizia Froesch *et al.,* have performed phase 1 B SAKK 19/16 trial. KRAS mutations occur in approximately 20–25% of non-squamous non-small cell lung cancer (NSCLC) cases, and therapies that target the RAS/MEK/ERK signalling pathway are currently under investigation. This phase 1B, open-label, multicentre clinical trial was conducted to determine the recommended phase 2 dose (RP2D) and evaluate the preliminary anticancer efficacy of binimetinib, a MEK inhibitor, in combination with cisplatin and pemetrexed in patients with advanced KRAS-mutated NSCLC. Eligible participants had stage III or IV NSCLC, were untreatable with curative intent, and carried KRAS mutations in exon 2 or 3 (codons 12, 13, or 61). Patients had not received prior systemic therapy. Treatment involved up to four cycles of cisplatin (75 mg/m²) and pemetrexed (500 mg/m²), combined with oral binimetinib (30 or 45 mg twice daily, days 1–14 of each 21-day cycle). Patients could then continue on maintenance therapy with pemetrexed and binimetinib until disease progression or unacceptable toxicity. Between May 2017 and December 2019, 18 patients were enrolled (13 in dose escalation and 5 in the expansion phase). The median age was 60 years (range: 48–73), and 87.5% of patients harboured KRAS codon 12 mutations. No dose-limiting toxicities (DLTs) were observed during dose escalation. The median number of treatment cycles administered was 2 (range: 1–17). Treatment was discontinued primarily due to disease progression (33%) or patient/physician decision (27%). Among the 16 patients evaluable for safety, the most frequent grade 3 treatment-related adverse events included lung infections (25%), fatigue (19%), and anaemia (19%). In the subgroup of 9 evaluable patients treated at the MTD (45 mg BID), the objective response rate (ORR) was 33% (95% CI: 7–70%). The median progression-free survival (PFS) was 5.7 months (95% CI: 1.1–14.0), and the median overall survival (OS) was 6.5 months (95% CI: 1.8–not reached). The combination of binimetinib with cisplatin and pemetrexed was generally well tolerated, with no unexpected toxicities reported. However, the addition of binimetinib did not demonstrate a clear improvement in early antitumor activity within this patient cohort [20].

Liang- Jun Wang *et al.,* have performed the cell line studies. Albendazole (ABZ), a benzimidazole-based anthelmintic, exhibits microtubule-destabilizing properties and has shown promise as a repurposed agent for cancer treatment. Their study aimed to explore the role of MCL1 in ABZ-induced apoptosis, using human leukaemia K562 cells as a model. Exposure of K562 cells to ABZ for 24 hours led to mitotic arrest, but did not significantly trigger apoptosis or mitochondrial membrane depolarization. Mechanistically, ABZ activated p38 MAPK signalling, which in turn suppressed Sp1-driven MCL1 transcription and concurrently stabilized SIRT3 mRNA, resulting in elevated SIRT3 protein levels. Additionally, ABZ and A-1210477 (a known MCL1 inhibitor) each enhanced the cytotoxic effects of ABT-263, a dual BCL2/BCL-XL inhibitor, likely through their MCL1-suppressing mechanisms. Notably, unlike ABZ, A-1210477 did not influence SIRT3 expression and was more directly cytotoxic to K562 cells. Interestingly, SIRT3 overexpression reduced the cytotoxic effects of A-1210477, suggesting a protective role. In a drug-resistant K562 subline (K562/R) that is unresponsive to ABT-263, ABZ treatment induced apoptosis and mitochondrial loss, although SIRT3 levels remained unchanged. When SIRT3 was overexpressed in these resistant cells, ABZ-induced cytotoxicity was partially reversed. These findings suggest that albendazole upregulates SIRT3, which in turn modulates the timing and extent of apoptosis following MCL1 suppression. The study underscores a complex interplay between MCL1 downregulation, SIRT3 expression, and ABZ-mediated cell death, offering insights for enhancing the effectiveness of combination therapies in leukaemia [21].

Ellen Weisberg *et al.,* have studied the effects of the multi-kinase inhibitor midostaurin in combination with chemotherapy in the models of acute myeloid leukaemia. Recent advancements in Acute Myeloid Leukaemia (AML) therapy have led to the development of targeted agents for genetically defined subgroups. One such agent, midostaurin, became the first FDA-approved FLT3 inhibitor for newly diagnosed AML patients harbouring FLT3 mutations. Interestingly, data from early-phase clinical trials (Phase I/II) revealed that even some patients without FLT3 mutations experienced transient clinical responses to midostaurin. This observation suggests that its broad kinase inhibition profile may offer therapeutic benefits beyond FLT3-mutant AML. In this study, midostaurin demonstrated potent activity at sub micromolar concentrations *in vitro* and showed antileukemic effects *in vivo* in AML cell lines and primary samples expressing wild-type FLT3. When compared with other FLT3 inhibitors under clinical evaluation, midostaurin consistently exhibited superior or comparable efficacy. Furthermore, the compound was found to act synergistically with standard chemotherapeutics and selected targeted therapies in FLT3-wild-type AML models. This synergy may be due to midostaurin's ability to target multiple kinases associated with AML pathogenesis, such as SYK and KIT, and to interfere with pro-survival signalling through the ERK pathway. These results highlight midostaurin's potential utility not only for FLT3-mutant AML but also as a chemo sensitizing agent in broader AML patient populations, including those without FLT3 mutations. Further clinical investigation is warranted to explore its use in combination regimens for improved treatment outcomes [22].

Anna M. schoepf *et al.,* This structure–activity relationship (SAR) study focuses on the development of novel

chemosensitizers designed to target therapy-resistant cancer stem cells (CSCs). Using a compound derived from the angiotensin II type 1 receptor blocker telmisartan, specifically 4′-((2-propyl-1H-benzo[d]imidazole-1-yl) methyl)-[1,1′-biphenyl]-2-carboxylic acid, as a lead structure, researchers identified that the biphenyl unit plays a critical role in exerting chemo sensitizing effects. Chemical modifications, such as replacing the carboxylic acid (COOH) group with methyl carboxylate or carboxamide, substantially increased the compound's ability to sensitize resistant cancer cells. These newly developed compounds were found to be non-cytotoxic yet highly effective against CSCs, helping to overcome resistance by disrupting key survival mechanisms. Specifically, they targeted hyperactivated STAT5 signalling and elevated drug transporter activity, which are commonly associated with CSC-mediated resistance. Among these, the carboxamide derivative of telmisartan (referred to as telmi-amide, compound 7c) significantly inhibited tumour growth in a leukaemia xenograft model resistant to imatinib, both when used alone and in combination with imatinib. This compound also demonstrated favourable oral bioavailability and a good safety profile. These telmisartan-based derivatives represent a promising class of chemosensitizers capable of targeting drug-resistant CSCs across multiple cancer types, including leukaemia, ovarian, and prostate cancers. Their ability to disrupt CSC-associated resistance pathways highlights their potential as part of innovative treatment strategies in challenging malignancies [23].

Sarah H. M. Khairat *et al.*, have synthesized novel benzimidazole compounds and evaluated with target molecule. Sphingosine kinase 1 (SphK1) has emerged as a promising therapeutic target in the treatment of various diseases, particularly in oncology. Although several SphK1 inhibitors have been developed recently, achieving high potency and selectivity remains a major hurdle. In this study, a new series of benzimidazole derivatives was synthesized and evaluated for their ability to inhibit SphK1. The enzyme inhibition activity of all synthesized compounds was assessed, and many demonstrated significant inhibitory effects against SphK1. Fluorescence binding studies and molecular docking simulations confirmed strong binding affinities of several compounds, notably compounds 33, 37, 39, 41, 42, 43, and 45. These selected compounds underwent further evaluation, and their IC_{50} values were determined, indicating high potency. Among them, compound 41 exhibited the lowest IC_{50}, along with strong cytotoxic effects across various cancer cell lines. Molecular docking results showed that these compounds fit well within the ATP-binding site of SphK1 and formed key hydrogen bonds with essential catalytic residues. This investigation highlights the potential of benzimidazole-based inhibitors as effective agents against SphK1, supporting their further development as therapeutic candidates in diseases where SphK1 plays a crucial role, particularly cancer [24].

Tao Liao *et al.*, have developed chitosan/mesoporous silica nanoparticle. To improve the therapeutic effectiveness of anticancer drugs and minimize their side effects, a "tumour-responsive targeting" strategy was employed to develop a dual pH-sensitive drug delivery system (DDS) based on chitosan (CHI) and mesoporous silica nanoparticles (MSN). In this system, doxorubicin hydrochloride (DOX) was used as the model drug and was encapsulated within MSNs that had been functionalized with benzimidazole (Bz) groups. A chitosan-graft-β-cyclodextrin (CHI-g-CD) polymer was used as a gatekeeping layer, anchored via host–guest interactions between the β-cyclodextrin (β-CD) moiety and the Bz-functionalized MSN surface. To achieve tumour-specific targeting, a peptide ligand (Ad-GRGDS) was attached, and the exterior was further modified with methoxy poly (ethylene glycol) benzaldehyde (MPEG-CHO) through a pH-responsive benzoic imine linkage. At physiological pH (7.4), the PEG shell acted as a protective barrier, concealing the targeting moieties and imparting a stealth-like character to the nanoparticles. In the acidic tumour microenvironment, the benzoic imine bond was cleaved, exposing the RGD peptide and the positive surface charge of CHI, thereby facilitating selective tumour targeting. Once internalized by cancer cells, the acid-sensitive interaction between β-CD and Bz was disrupted, triggering controlled DOX release. Experimental results from both *in vitro* and *in vivo* studies confirmed that this DDS system induced apoptosis in cancer cells, significantly inhibited tumour growth, and reduced off-target toxicity of DOX to normal tissues. The developed platform, referred to as DOX@MSN-CHI-RGD-PEG, presents a promising approach for precision cancer therapy [25].

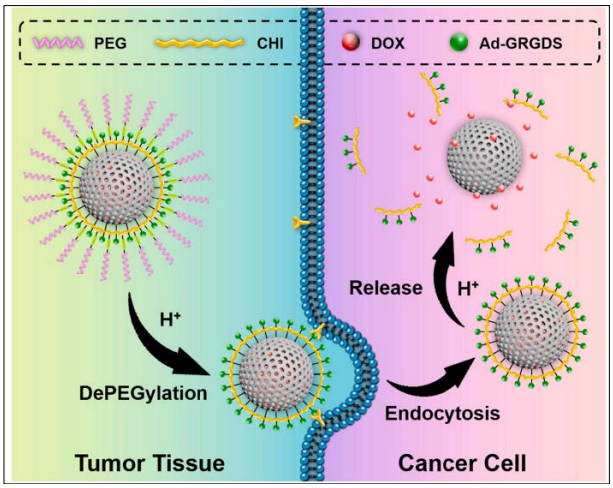

Fig 4: Schematic illustration of dual-pH-sensitive DOX@MSN-CHI-RGD-PEG for "tumour-triggered targeting" cancer therapy

Samira Nashaat *et al.*, have developed new benzimidazoles targeting the breast cancer. In this study, a novel series of benzimidazole derivatives was synthesized, incorporating either six- or five-membered heterocyclic rings, along with pyrazano- and pyrido-benzimidazole linkers, resulting in compounds labelled 5–8 and 10–14, respectively. To assess their anticancer activity, the compounds were evaluated against the MCF-7 breast cancer cell line. The most promising candidates were further tested on WI-38 normal human lung fibroblast cells to determine their selectivity and safety profile. Notably, most compounds exhibited potent cytotoxicity against MCF-7 cells while demonstrating minimal toxicity toward normal cells. Among them, compounds 5, 8, and 12 showed the highest activity and were selected for further mechanistic studies. These lead compounds were subjected to a Pin1 inhibition assay, using tannic acid as a reference standard. Compound 8 underwent additional testing to evaluate its influence on the cell cycle and its role in apoptosis induction. Results revealed that it activated intrinsic apoptotic pathways by promoting reactive

oxygen species (ROS) accumulation, increasing Bax expression, reducing Bcl-2 levels, and activating caspases 6, 7, and 9. Furthermore, NMR-based binding studies using 15N–1H HSQC confirmed that compound 12 interacted directly with the 15N-labeled Pin1 enzyme, as evidenced by noticeable chemical shift perturbations. Molecular docking simulations, performed using Molecular Operating Environment (MOE) software, provided insights into the binding interactions, highlighting the significance of hydrogen bonding in the activity of these compounds. Their work introduces a new set of benzimidazole derivatives with strong potential as anti-breast cancer agents, supported by biological, biochemical, and computational evidence of their mechanism of action and molecular targets [26].

Aditya Bardia *et al.,* have done phase 1b clinical trial. This multicentre, open-label Phase Ib clinical trial evaluated the safety and therapeutic potential of a combination therapy using binimetinib, a MEK inhibitor, and buparlisib, a PI3K inhibitor, in patients diagnosed with advanced solid tumors harbouring RAS or RAF mutations. A total of 89 patients with advanced-stage solid tumors—who had experienced disease progression despite standard treatments or had no available standard therapy—were enrolled. All participants were required to have measurable disease, according to RECIST version 1.1, and an ECOG performance status of 0 to 2. The study assessed various dosing combinations of binimetinib and buparlisib to determine the maximum tolerated dose (MTD) and the recommended phase II dose (RP2D). By the data cut-off point, 32 of the 89 patients had discontinued treatment due to adverse events. The RP2D for continuous treatment was established as buparlisib 80 mg once daily combined with binimetinib 45 mg twice daily. However, the combined regimen led to a lower-than-expected dose intensity, primarily due to toxicity. Notably, 6 patients (12%) with RAS/BRAF-mutant ovarian cancer experienced a partial tumour response. Pharmacokinetic assessments showed that binimetinib exposure was not significantly influenced by buparlisib. Additionally, pharmacodynamic studies indicated suppression of phosphorylated ERK (PERK) and S6 (pS6) in tumour tissue samples. While simultaneous targeting of the MEK and PI3K pathways showed potential anti-tumour activity, particularly in ovarian cancers with RAS or BRAF mutations, continuous dosing regimens were associated with intolerable toxicities outside the defined DLT period. These findings suggest that intermittent or pulsatile dosing strategies may improve the tolerability and effectiveness of this combination therapy [27].

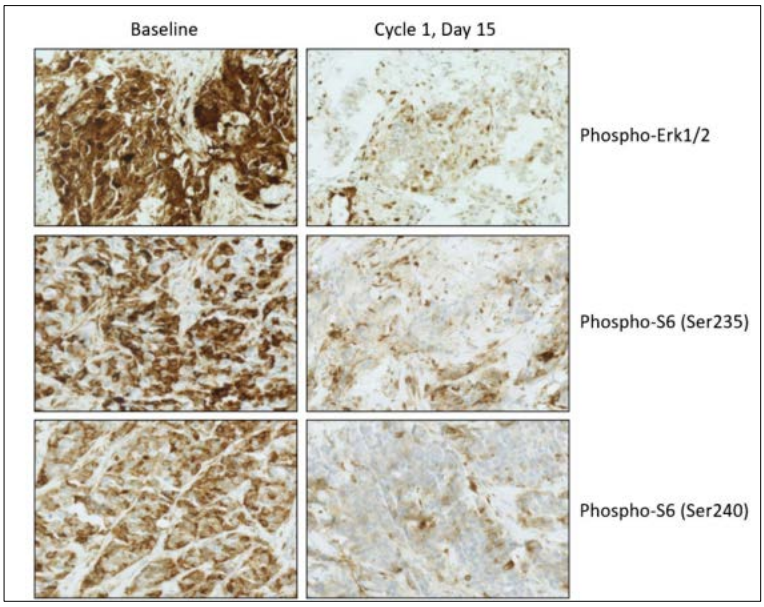

Fig 5: Immunohistochemical staining on pre- and postbaseline tumour biopsies

Rosalba Florio *et al.,* have screened benzimidazole-based anthelmintics. the repurposing of existing non-oncologic drugs offers a cost-effective and promising strategy to expand the arsenal of available anticancer therapies. Among such candidates, benzimidazole-based anthelmintic agents, widely used in both human and veterinary medicine for their antiparasitic properties, have emerged as potential antitumor compounds. In this study, a broad selection of benzimidazole-derived anthelmintics, including enantiomerically pure forms where chiral centres were present, was evaluated for their cytotoxic activity against several cancer cell lines, specifically those derived from paraganglioma, pancreatic cancer, and colorectal cancer. Compounds such as flubendazole, parbendazole, oxibendazole, mebendazole, albendazole, and fenbendazole demonstrated notable antiproliferative effects, with IC_{50} values ranging from low micromolar to nanomolar concentrations. To further assess their drug-like potential, in silico analyses of physicochemical characteristics, pharmacokinetics, and medicinal chemistry profiles were conducted, providing valuable insights into the structural features responsible for their activity. In addition, given the polypharmacological nature of many active pharmaceutical ingredients, a computational target prediction was performed. This revealed novel cancer-relevant molecular targets that may contribute to their observed antitumor effects. These findings support the rationale for repurposing benzimidazole-based anthelmintics as multifunctional anticancer agents and highlight their potential to act through previously unrecognized mechanisms, warranting further preclinical and clinical investigation [28].

Jia-Hong Lei *et al.,* have performed their study by targeting the colchicine binding site by ELR510444 and parbendazole to achieve desire drug design. Microtubules, composed of α-

and β-tubulin heterodimers, are well-established targets in anticancer therapy due to their critical role in cell division. Compounds such as ELR510444 and parbendazole are known to interact with tubulin at the colchicine binding site, thereby disrupting microtubule polymerization and exhibiting antiproliferative effects. Despite their potential, the absence of detailed structural data on tubulin in complex with these molecules has limited efforts to design improved derivatives with enhanced efficacy. In this study, we present the crystal structures of tubulin bound to ELR510444 at a 3.1 Å resolution and to parbendazole at a 2.4 Å resolution. These structures reveal the key molecular interactions between the inhibitors and the colchicine binding site on tubulin. The structural insights provided form a foundation for rational drug design, particularly for developing new benzsulfamide and benzimidazole-based compounds aimed at targeting the colchicine site on tubulin for cancer therapy [29].

Yichang Ren *et al.*, A series of newly synthesized indazole and benzimidazole derivatives were developed and evaluated for their tubulin inhibitory and antiproliferative activities. Among these, compound 12b emerged as the most potent, demonstrating an average IC_{50} of 50 nm. across various cancer cell lines—slightly outperforming the reference compound, colchicine. Notably, 12b exhibited comparable efficacy against both paclitaxel-resistant (A2780/T, IC_{50} = 9.7 nm.) and non-resistant parental (A2780S, IC_{50} = 6.2 nm.) ovarian cancer cells, indicating its ability to overcome paclitaxel resistance *in vitro*. Structural studies using X-ray crystallography confirmed its binding at the colchicine site on tubulin, with a resolved complex structure at 2.45 Å resolution. In their *in vivo* studies using a melanoma tumour model, treatment with 12b resulted in tumour growth inhibition of 78.7% at 15 mg/kg and 84.3% at 30 mg/kg, demonstrating significant anticancer potential. These findings highlight compound 12b as a promising lead candidate for further development in anticancer therapy, especially for overcoming resistance to conventional microtubule-targeting drugs [30].

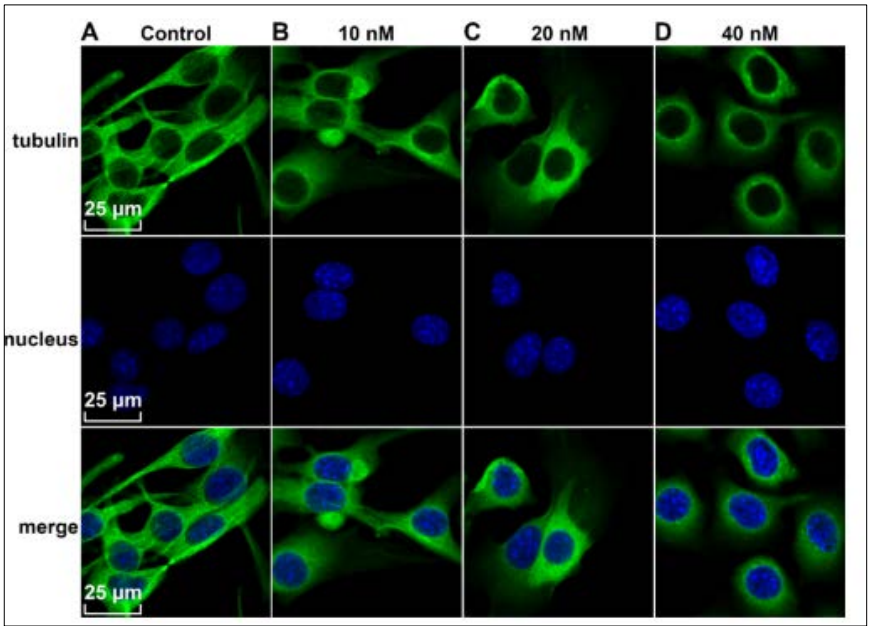

Fig 6: Effects of compound 12b on microtubules. B16-F10 cells were treated with vehicle control 0.1% DM

Nerella Sridhar Goud *et al.*, have developed novel benzimidazole-triazole hybrids for treating lung cancer. Their study introduces a newly synthesized series of benzimidazole–triazole hybrid compounds designed to induce apoptosis mediated by galectin-1 (Gal-1) and evaluated for their anticancer potential. The compounds were tested against various human cancer cell lines, including breast cancer (MCF-7 and MDA-MB-231), lung cancer (A-549 and NCI-H460), and keratinocyte cancer (HaCaT), using the MTT assay. Among the synthesized derivatives, compound 7c demonstrated the most potent growth-inhibitory activity, with IC_{50} values of 0.63 ± 0.21 µM (A-549) and 0.99 ± 0.01 µM (NCI-H460). It also showed significant cytotoxic effects against breast cancer cells, MCF-7 (IC_{50} = 1.3 ± 0.18 µM) and MDA-MB-231 (IC_{50} = 0.94 ± 0.02 µM). To explore its potential for positron emission tomography (PET) imaging, fluorine-18 radiolabelling of compound 7c was successfully performed using a GE Tracerlab FX2N module. The purified [^18F]7c exhibited a radiochemical purity of over 95% and a residual DMF content of 78 ± 3 ppm, confirmed by HPLC and GC analysis, respectively. Mechanistic studies confirmed apoptosis induction in A-549 cells through various assays including JC-1 staining, DAPI staining, Annexin V-FITC/PI, and flow cytometry, indicating a reduction in mitochondrial membrane potential, cell cycle arrest at the sub-G1 phase, and increased apoptotic cell populations. Additionally, ELISA confirmed that 7c significantly reduced Gal-1 expression in a dose-dependent manner. Protein–ligand interaction studies using Surface Plasmon Resonance (SPR) and fluorescence spectroscopy validated the binding of 7c to Gal-1, with a KD of 1.19 µM and a Ka of 9.5 × 10^3 M^{-1}, respectively. Furthermore, in silico ADMET and molecular docking analyses supported its favourable pharmacokinetic properties and effective binding within the Gal-1 domain. These findings suggest that benzimidazole–triazole hybrids, particularly compound 7c, hold significant promise as Gal-1-targeting anticancer agents with the dual potential for cytotoxic activity and use as PET imaging probes, especially in lung cancer therapy [31].

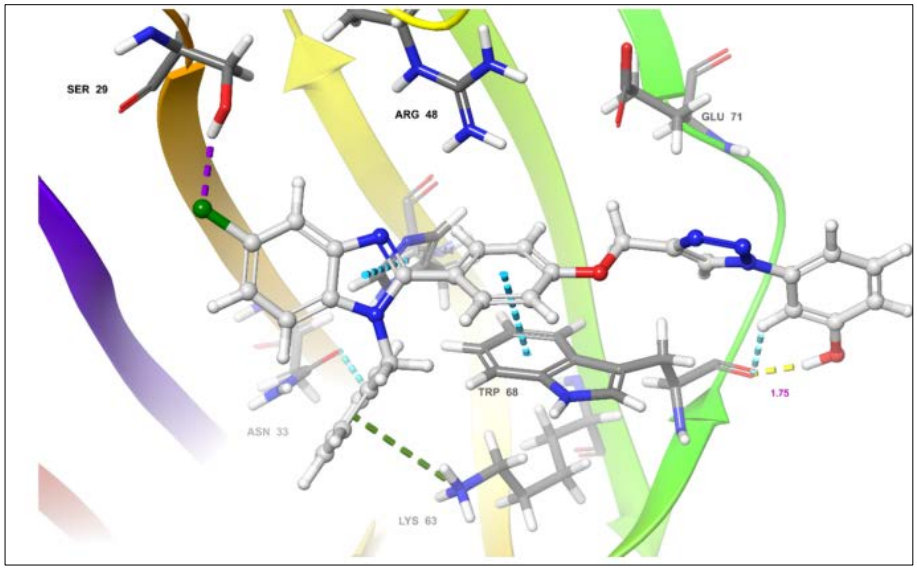

Fig 7: 3D ligand interaction diagram of compound 7c with the active site of Gal-1 protein (PDB ID: 4Y24)

Conclusion

The therapeutic potential of benzimidazole and its derivatives has been significantly expanded through recent discoveries demonstrating their ability to inhibit key oncogenic pathways and overcome resistance in various cancer types. From targeting tubulin and kinases to modulating apoptotic and immune-related pathways, these compounds exhibit strong preclinical efficacy and pharmacological promise. Compounds like 12b and 7c exemplify the clinical relevance of benzimidazole scaffolds, showing potent antitumor effects and the ability to address challenges such as drug resistance and tumour heterogeneity. Moreover, their compatibility with advanced technologies such as radiolabelling and molecular imaging positions benzimidazole derivatives at the forefront of theragnostic applications. As the field moves forward, integrating benzimidazole-based agents into multimodal treatment strategies, including immunotherapy and targeted therapy, could offer more effective and personalized solutions for cancer management. Future research should focus on optimizing selectivity, improving pharmacokinetics, and validating clinical efficacy through well-designed trials to fully realize their potential in modern oncology.

Despite these promising developments, several challenges remain. These include the high cost of novel therapies, unequal access to advanced care, emergence of therapy resistance, and the lack of reliable predictive biomarkers. Therefore, ongoing interdisciplinary research is essential to deepen our understanding of tumour biology and to translate scientific discoveries into effective, accessible treatments.

This review aims to explore the major categories of cancer and highlight the recent therapeutic trends and emerging strategies aimed at improving clinical outcomes and reducing the global burden of cancer.

Acknowledgment

The authors are thankful to the principal, management and department of pharmaceutical chemistry in Nargund College of Pharmacy, Bangalore for their support and guidance.

Conflicts of interest

All authors declare there are no conflicts of interest.

References

1. World Health Organization. Cancer [Internet]. 2022 [cited 2025 Jul 30]. Available from: https://www.who.int/news-room/fact-sheets/detail/cancer
2. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell. 2011;144(5):646–674.
3. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al*. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide. CA Cancer J Clin. 2021;71(3):209–249.
4. Arruebo M, Vilaboa N, Sáez-Gutierrez B, Lambea J, Tres A, Valladares M, *et al*. Assessment of the evolution of cancer treatment therapies. Cancers (Basel). 2011;3(3):3279–3330.
5. Druker BJ. Imatinib as a paradigm of targeted therapies. Adv Cancer Res. 2004;91:1–30.
6. Topalian SL, Hodi FS, Brahmer JR, Gettinger SN, Smith DC, McDermott DF, *et al*. Safety and activity of anti–PD-1 antibody in cancer. N Engl J Med. 2012;366(26):2443–2454.
7. Robert C, Schachter J, Long GV, Arance A, Grob JJ, Mortier L, *et al*. Pembrolizumab versus Ipilimumab in advanced melanoma. N Engl J Med. 2015;372(26):2521–2532.
8. Dienstmann R, Vermeulen L, Guinney J, Kopetz S, Tejpar S, Tabernero J. Consensus molecular subtypes and the evolution of precision medicine in colorectal cancer. Nat Rev Cancer. 2017;17(2):79–92.
9. Oxnard GR, Yang JCH, Yu H, Kim SW, Saka H, Horn L, *et al*. TATTON: a multi-arm, phase Ib trial of osimertinib combined with selumetinib, savolitinib, or durvalumab in EGFR-mutant lung cancer. Ann Oncol. 2020;31(4):507–516.
10. Chen X, Yang X, Mao F, Wei J, Xu Y, Li B, *et al*. Development of novel benzimidazole-derived neddylation inhibitors for suppressing tumor growth *in vitro* and *in vivo*. Eur J Med Chem. 2021;210:112964.
11. Lakshmanan K, Byran G. Identification of benzimidazole containing 4H–chromen–4–one derivative as potential MAP kinase inhibitors by in-

silico approaches. J Recept Signal Transduct. 2020;41(2):153–158.
12. Fujimura T, Yoshino K, Kato H, Fujisawa Y, Nakamura Y, Yamamoto Y, *et al*. Case series of BRAF-mutated advanced melanoma treated with encorafenib plus binimetinib combination therapy. J Dermatol. 2020;48(3):397–400.
13. Karthick K, Abishek K, Angel Jemima E. In silico study, protein kinase inhibition and molecular docking study of benzimidazole derivatives. Bioinform Biol Insights. 2024;18:1–10.
14. Zhang J, Yang N, Ji D, Shen W, Li W, Han R, *et al*. A randomized phase I study of abemaciclib in Chinese patients with advanced and/or metastatic cancers. Target Oncol. 2021;16(2):177–187.
15. Aroldi F, Elez E, André T, Perkins G, Prenen H, Popovici V, *et al*. A Phase Ia/b study of MEK1/2 inhibitor binimetinib with MET inhibitor crizotinib in patients with RAS mutant advanced colorectal cancer (MErCuRIC). BMC Cancer. 2025;25(1).
16. Ren L, Li W, Zheng X, Liu J, Yang Y, Li S, *et al*. Benzimidazoles induce concurrent apoptosis and pyroptosis of human glioblastoma cells via arresting cell cycle. Acta Pharmacol Sin. 2025;43:194–208.
17. Huijberts SCFA, Boelens MC, Bernards R, Opdam FL. Mutational profiles associated with resistance in patients with BRAFV600E mutant colorectal cancer treated with cetuximab and encorafenib ± binimetinib or alpelisib. Br J Cancer. 2020;124(1):176–182.
18. Kondo N, Takada S, Hagimori M, Temma T. Development of a 2-(2-hydroxyphenyl)-1H-benzimidazole-based fluorescence sensor targeting boronic acids for versatile application in boron neutron capture therapy. Cancers (Basel). 2023;15(6):1862.
19. Hibino Y, Sakai R, Takahashi H, Takeda T, Hirose N, Tokunaga M, *et al*. Efficacy of combined encorafenib and binimetinib treatment for Erdheim–Chester disease harboring concurrent BRAFV600E and KRASG12R mutations: A case report. Cancer Rep. 2024;7(12).
20. Froesch P, Mark M, Rothschild SI, Li Q, Godar G, Rusterholz C, *et al*. Binimetinib, pemetrexed and cisplatin, followed by maintenance of binimetinib and pemetrexed in patients with advanced non-small cell lung cancer (NSCLC) and KRAS mutations. Lung Cancer. 2021;156:91–99.
21. Wang LJ, Liou LR, Shi YJ, Chiou JT, Lee YC, Huang CH, *et al*. Albendazole-induced SIRT3 upregulation protects human leukemia K562 cells from the cytotoxicity of MCL1 suppression. Int J Mol Sci. 2020;21(11):3907.
22. Weisberg E, Meng C, Case AE, Tiv HL, Gokhale PC, Buhrlage SJ, *et al*. Effects of the multi-kinase inhibitor midostaurin in combination with chemotherapy in models of acute myeloid leukaemia. J Cell Mol Med. 2020;24(5):2968–2980.
23. Schoepf AM, Gebhart M, Federspiel M, Heidegger I, Puhr M, Hotze M, *et al*. Eradication of therapy-resistant cancer stem cells by novel telmisartan derivatives. J Med Chem. 2024;68(1):287–306.
24. Sarah S, Omar MA, Ragab F, Roy S, Turab AA, Abdelsamie AS, *et al*. Design, synthesis, and biological evaluation of novel benzimidazole derivatives as sphingosine kinase 1 inhibitor. Arch Pharm (Weinheim). 2021;354(9):e2100099.
25. Liao T, Liu C, Ren J, Chen HS, Kuang Y, Jiang B, *et al*. A chitosan/mesoporous silica nanoparticle-based anticancer drug delivery system with a “tumor-triggered targeting” property. Int J Biol Macromol. 2021;183:2017–2029.
26. Nashaat S, Henen MA, El-Messery SM, Eisa H. New benzimidazoles targeting breast cancer: Synthesis, Pin1 inhibition, 2D NMR binding, and computational studies. Molecules. 2022;27(16):5245.
27. Bardia A, Gounder M, Rodon J, Janku F, Lolkema MP, Stephenson JJ, *et al*. Phase Ib study of combination therapy with MEK inhibitor binimetinib and phosphatidylinositol 3-kinase inhibitor buparlisib in patients with advanced solid tumors with RAS/RAF alterations. Oncologist. 2019;25(1):e33–e43.
28. Florio R, Carradori S, Veschi S, Brocco D, Di Genni T, Cirilli R, *et al*. Screening of benzimidazole-based anthelmintics and their enantiomers as repurposed drug candidates in cancer therapy. Pharmaceuticals (Basel). 2021;14(4):372.
29. Lei JH, Ma LL, Xian JH, Chen H, Zhou JJ, Chen H, *et al*. Structural insights into targeting of the colchicine binding site by ELR510444 and parbendazole to achieve rational drug design. RSC Adv. 2021;11(31):18938–18944.
30. Ren Y, Wang Y, Li G, Zhang Z, Ma L, Cheng B, *et al*. Discovery of novel benzimidazole and indazole analogues as tubulin polymerization inhibitors with potent anticancer activities. J Med Chem. 2021;64(8):4498–4515.
31. Goud NS, Pooladanda V, Soukya PS, Alvala R, Kumar P, *et al*. Novel benzimidazole-triazole hybrids as apoptosis inducing agents in lung cancer: Design, synthesis, 18F-radiolabeling & galectin-1 inhibition studies. Bioorg Chem. 2020;102:104125.