14	Bortezomib Velcade	MILLENNIUM PHARMS, 2003	4.0	Antineoplastic Agent	Prescription/ intravenous injection or subcutaneou s use	Target: proteasome subunit beta type-1 and type-5 inhibitor Mechanism of action: Inhibits the mammalian 26S proteasome which prevents targeted proteolysis, that can affect multiple signaling cascades within the cell. This disruption of normal homeostatic mechanisms leads to cell death.	Hematologic: thrombocytopenia, neutropenia, anemia. Other: peripheral neuropathy.	[290]
15	Rituximab Rituxan Mabthera	GENENTECH, 1997 IDEC PHARMACEUTIC ALS CORP, 1997		Antineoplastic [microtubule inhibitor], Monoclonal antibody	Prescription / Intravenous, Injection	Target: CD20 Mechanism of action: Binds to the antigen CD20 and mediates B-cell lysis. Mechanisms of cell lysis include complement dependent cytotoxicity (CDC) and antibody dependent cell mediated cytotoxicity (ADCC).	Other: Tumor Lysis Syndrome, infections, renal toxicity, cardiac arrhythmias, bowel obstruction.	[291]
16	Vorinostat Zolinza	MERCK, 2006),,i.	histone deacetylase inhibitor	Prescription / Oral	Target: histone deacetylase 1, 2, 3 and 6 (HDAC1, HDAC2, HDAC3, HDAC6) inhibitor Mechanism of action: 1. Binds to the active site of histone deacetylases and act as a chelator for Zinc ions on the site. 2. Inhibition of histone deacetylases results in the accumulation of acetylated histones and acetylated proteins, including transcription factors crucial for the expression of genes needed to induce cell differentiation.	Hematologic: deep vein thrombosis, thrombocytopenia, anemia. Gastrointestinal: nausea, vomiting, diarrhea, taste disorders. Other: pulmonary embolism, hyperglycemia, chills.	[292]
17	Alisertib MLN8237	Takeda Pharmaceutical C ompany Limited N/A Millennium Pharmaceuticals, Inc. N/A Selleck Chemicals, N/A	.46pg)	Aurora Kinase inhibitor	Prescription/ Oral	Target: aurora A kinase inhibitor Mechanism of action: It is selective and potent inhibitor of AAK. Aurora A directly binds to and regulates the tumover of N-myc, and is essential in N-myc amplified neuroblastomas. Also, Aurora A phosphorylate and regulate p53 function.	Hematologic: neutropenia, thrombocytopenia. Gastrointestinal: diarrhea, nausea. Dermatologic: alopecia. Other: stomatitis, fatigue, somnolence.	[293]
				DRUGS U	NDER TRIAL			
17	Idelalisib Zydelig	GILEAD SCIENCES INC, 2014		Antineoplastic agent, Enzyme inhibitor	Prescription / Oral	Target: phosphatidylinositol 3 kinase inhibitor Mechanism of action: 1. Promotes apoptosis in B-cell lines and primary cells from patients with different B-cell malignancies. 2. Inhibits constitutive and CD40-, TNF-0-, fibronectin-, and BCR-derived PI3K signaling leading to suppression of Akt activation.	Gastrointestinal: diarrhea, nausea, decreased appetite. Dermatologic: rash. Other: pyrexia, fatigue, upper respiratory infection and pneumonia.	[294]
18	Everolimus Afinitor Votubia Zortress	NOVARTIS, 2009 N/A NOVARTIS, 2010		Kinase Inhibitor	Prescription / Oral	Target: mammalian target of rapamycin (mTOR) inhibitor Mechanism of action: Dual inhibition of the ER and P13K/Akt/mTOR signaling pathways, providing synergistic inhibition of tumor.	Gastrointestinal: diarrhea, nausea, decreased appetite. Dermatologic: rash. Other: stomatitis, infections, fatigue, edema, abdominal pain, fever, asthenia, cough, headache.	[295]

19	Ofatumumab Arzerra	GLAXO GRP LTD, 2009		Antineoplastic agent, Monoclonal antibody	Prescription / Injection	Target: CD20 Mechanism of action: 1. Binds to both small and large extracellular loops of the CD20 .The CD20 molecule is not shed from cell surface and is not internalized following antibody binding, 2. Fab domain of ofatumumab binds to CD20 molecule & Fc domain mediates immune effector functions to result in B-cell lysis.	Hematologic: neutropenia, anemia. Gastrointestinal: diarrhea, nausea. Dermatologic: rash. Other: pneumonia, pyrexia, cough, fatigue, dyspnea, bronchitis, upper respiratory tract infections.	[296]
20	Panobinostat Farydak	NOVARTIS PHARMS CORP, 2015	of j	Antineoplastic, Histone Deacetylase Inhibitors	Prescription / Oral	Target: histone deacetylases (HDACs) inhibitor Mechanism of action: Inhibits multiple histone deacetylase enzymes that leads to apoptosis of malignant cells via multiple pathways like Notch signaling pathway	Constitutional symptoms: Hematologic: myelosuppression. Gastrointestinal: gastrointestinal symptoms. Other: fatigue.	[297]
21	Romidepsin Istodax	CELGENE, 2009		Antibiotics, Antineoplastic	Prescription / Infusion	Target: histone deacetylases (HDACs) inhibitor Mechanism of action: 1.Inhibits removal of acetyl groups from lysine residues of N-terminal, maintaining transcriptionally active chromatin state. 2. Altered acetylation of nuclear and cytoplasmic proteins, although precise pathways by which it affects the cell cycle, apoptosis & angiogenesis have not been defined.	Hematologic: neutropenia, thrombocytopenia.	[298]
22	Obatoclax GX15-070	PFIZER, N/A	44	Immunomodulator, BCL-2 inhibitor, Antineoplastic	Under Trial/ Intravenous	Target: pan-BCL-2 inhibitor Mechanism of action: Disrupts survival of cancer cells by inhibiting the Bd-2 pro- survival protein Mcl-1.	Hematologic: thrombocytopenia. Gastrointestinal: diarrhea, nausea, constipation. Dermatologic: rash. Other: abdominal distension, abdominal pain, fatigue, weight loss, dehydration, neuropathy, somnolence, euphoric mood,	[299]
23	Navitoclax 923564-51-6 ABT 263 ABT-737 CS-0013	N/A	The same	Antineoplastic, BCL-2 inhibitor	Under Trial/ Orally Bioavailable	Target: anti-apoptotic protein Bcl-2 inhibitor Mechanism of action: Antagonist of a subset of the B-cell leukemia 2 (Bcl-2) family of proteins with potential antineoplastic activity. Binds to apoptosis suppressor proteins Bcl-2, Bcl-XL, and Bcl-w, frequently overexpressed in a wide variety of cancers and are linked to tumor drug resistance. Inhibition of these apoptosis suppressors prevents their binding to the apoptotic effectors Bax and Bak proteins, thereby triggering apoptotic processes in cells overexpressing Bcl-2, Bcl-XL, and Bcl-w. This eventually reduces tumor cell proliferation.	Hematologic: thrombocytopenia.	[300]
24	Dasiprotimut-T BiovaxID Lympreva	Biovest International, Phase III Clinical Trials (US)	DasiprotimutT is an autologous lymphoma derived Ig idiotype-KLH (keyhole limpet haemocyanin) conjugate active immunotherapy product	Immunostimulant	Phase 3 Trial/ Vaccine	Mechanism of action: Induces a tumour-specific cytotoxic T lymphocyte response	Nearly toxicity- free.	[301]

26	Norcantharidin Aberela Renova Retin-A Avita	Sigma-Aldrich, N/A		serine/threonine- protein phosphatase PP1- alpha catalytic subunit isoform 3	Pre clinical phase	Target: 1. Serine/threonine protein phosphatase 2A, catalytic subunit, alpha isoform. 2. Serine/threonine protein phosphatase PP1-alpha catalytic subunit. Mechanism of action: Inhibits serine/threonine protein phosphatase 2A and PP1-alpha. Causes apoptosis, inhibition of angiogenesis, and metastasis for many cell lines, and can affect multiple pathways controlling cell proliferation. Also, NCTD was found able to inhibit P-glycoprotein (P-gp) and overcome Multi drug resistance.	Other: Reduced cardiac and renal toxicity as compared to cantharidin.	[302]
27	Puerarin Kakonein Ciybio Kudzu	Shannxi Ciyuan Biotech Ltd, N/A Sigma-Aldrich, N/A Thomson Pharma, N/A		Isoflavone Antiallergic Antithrombotic	Pre clinical/ Supplement/ White powder(Avail able from china)	Target: The nuclear factor kappaB pathway. Mechanism of action: 1. Inhibition of phosphorylation and degradation of inhibitor kappaB (I-kappaB), resulting in a reduction of p65NF-kappaB nuclear translocation. 2. Inhibits iNOS, COX-2 and CRP expression via suppression of NF-kB activation	Not available	[303]
28	Atiprimod SK&F106615-A2 Azaspirane	Angene Chemical, N/A Callisto Pharmaceuticals Inc, N/A) } }	Anti-arthritic Anti-inflammatory Immunomodulator	Phase 2 trial /orally bioavailable	Target: JAK-STAT signaling pathway. Mechanism of action: Inhibits the phosphorylation of signal transducer and activator of transcription 3 (STAT3), blocking the signaling pathways of interleukin-6 and vascular endothelial growth factor (VEGF) and downregulating the antiapoptotic proteins Bc1-2, Bcl-XL, and Mc1-1 inhibiting cell proliferation, inducing cell cycle arrest, and inducing apoptosis.	Hematologic: neutropenia. Gastrointestinal: diarrhea, dyspepsia. Other: liver enzyme elevation.	[304, 305]
29	Dinaciclib SCH 727965	Merck &Co, N/A Caymen chemicals, N/A Selleck chemicals, N/A	94. J	CDK inhibitor Antineoplastic	Phase 2 trial /orally bioavailable	Target: p53 signaling pathway. Mechanism of action: Selectively inhibits cyclin dependent kinases CDK1, CDK2, CDK5, and CDK9; Inhibition of the unfolded protein response (UPR) through a CDK1 and CDK5-dependent mechanism. The inhibition of CDK1 and CDK2 may result in cell cycle repression and tumor cell apoptosis.	Hematologic: leukopenia, thrombocytopenia. Gastrointestinal: gastrointestinal symptoms. Dermatologic: alopecia. Other: fatigue.	[306, 307]
30	Alvocidib Flavopiridol	Sanofi-Aventis, N/A Selleck Chemicals, N/A		Flavonoid alkaloid CDK9 kinase inhibitor	Phase 2 trial	Target: cyclin-dependent kinase (CDK) inhibitor Mechanism of action: 1. Induces cell cycle arrest by preventing phosphorylation of cyclin-dependent kinases (CDKs) and by down-regulating cyclin D1 and D3 expression, resulting in G1 cell cycle arrest and apoptosis. 2. Inhibition of P-TEFb: suppressed transcription and decreased phosphorylation of RNA Pol II leading to a decrease in levels of proteins; cyclin D1, VEGF and Mcl-1.	Hematologic: granulocytopenia, anaemia. Gastrointestinal: diarrhea. Other: infection, fatigue.	[308, 309]

31	Fostamatinib disodium Fostamatinib	Rigel Pharmaceuticals, N/A	man	Spleen tyrosine kinase (Syk) inhibitors Immunosuppressa nt Antirheumatic Antineoplastic	Phase3 trial/orally bioavailable	Target: NF-kappa B and B cell receptor signaling pathways. Mechanism of action: 1. Inhibits Syk kinase-mediated IgG Fc gamma receptor signaling, resulting in inhibition of the activation of mast cells, macrophages, and B-cells and related inflammatory responses and tissue damage. 2. Syk kinase mediate diverse cellular responses, including proliferation, differentiation, and phagocytosis.	Hematologic: neutropenia, anemia. Gastrointestinal: nausea, diarrhea. Other: fatigue, increased AST, hypertension.	[310]
32	Enzastaurin LY317615	Denovo Biopharma, N/A	1900 1900	Antineoplastics / Indoles, Piperidines, Pyridines, Pyrrolidinones, serine threonine kinase inhibitor	Phase 3 Trial	Target: Protein kinase C beta (PKC-beta) inhibitor. Mechanism of action: Suppresses signaling through PKC-β and the phosphatidylinositol 3-kinase/AKT pathway to induce tumor cell appoptosis, reduce proliferation, and suppress tumor-induced angiogenesis.	Hematologic: anemia. Gastrointestinal: diarrhea, vomiting. Other: fatigue, dyspnea, hypotension, syncope.	[311]
33	Palbociclib PD-0332991 Ibrance	Pfizer, 2015	- fatoa	CDK4 and CDK6 inhibitor	Phase 3 Trial (Approved)/ Oral	Target: Cyclin-dependent kinase 4/6 (CDK4/6) inhibitor. Mechanism of action: CDK4, CDK6 and cyclin D1 regulate the G1- to 5-phase cell-cycle transition via regulation of phosphorylation of the retinoblastoma (Rb) protein. Inhibition of these proteins leads to reduced phosphorylation of Rb, inhibition of downstream signalling, and increased tumor growth arrest.	Hematologic: leukopenia, anemia, thrombocytopenia. Gastrointestinal: diarrhea, decreased appetite. Dermatologic: alopecia. Other: fatigue, upper respiratory tract infection, stomattis, peripheral neuropathy, asthenia, epistaxis.	[312]
34	Perifosine KRX-0401	Keryx Biopharmaceutica Is/ Aeterna Zentaris, N/A		PI3K inhibitor, Akt inhibitor	Phase 3 Trial	Target: Protein kinase Akt (protein kinase B) Mechanism of action: 1. Modulates membrane permeability, membrane lipid composition, phospholipid metabolism, and mitogenic signal transduction, resulting in cell differentiation and inhibition of cell growth. 2. Inhibits the anti-apoptotic mitogen-activated protein kinase (MAPK) pattiway and modulates the balance between the MAPK and pro-apoptotic stress-activated protein kinase (SAPK/JMK) pathways inducing apoptosis.	Gastrointestinal: Moderate toxicity	[313, 314]
35	MK2206	Merck &Co, N/A	90% -po	AKT Allosteric Inhibitor	Orally Bioavailable	Target: Protein kinase Akt (protein kinase B) Mechanism of action: Inhibits phosphorylation of Thr308 and Ser473 of Akt. Suppresses Akt signalling pathway and promotes cancer cell death as a single agent as well as in combination with other chemotherapeutic agents.	Gastrointestinal: nausea, vomiting, diarrhea. Dermatologic: rash. Other: fatigue, hyperglycemia.	[315]
36	Uprosertib GSK2141795	GlaxoSmithKline, N/A		\KT Inhibitor, \ntineoplastc	Phase 2 trial/orally bioavailable	Target: Protein kinase Akt (protein kinase B) Mechanism of action: It binds to and inhibits Akt activity. Inhibition of the PI3K/Akt signaling pathway, tumor cell proliferation and induction of tumor cell apoptosis.	Dermatologic: rash. Other: hyperglycemia.	[316]

37	SF1126/LY29400 2 SF1126	Semafore Pharmaceuticals, N/A SignalRx Pharmaceuticals, N/A	& July	pan-PI3K inhibitor designed by conjugating RGD peptide to LY294002, Antineoplastics, Drug conjugates	Phase1 Trial	Target: PI3K and mTOR. DNA protein kinase, PIM1, and PLK1. Mechanism of action: 1. Shuts down PI3K-Akt-mTOR signaling. 2. Decreases proliferation and has antiangiogenic and proapoptotic effect.	Hematologic: anaemia. Gastrointestinal: nausea, diarrhoea. Dermatologic: pruritus. Other: fatigue, pyrexia, chills, anorexia, headache.	[317, 318]
38	Tanespimycin 17-AAG	Bristol-Myers Squibb, N/A	XXX	Hsp90 inhibitor	Phase 3 Trial	Target: HSP90 Mechanism of action: Interferes with ATP-dependent chaperones activity, and degrades the client proteins by the proteasome.	Hematologic: anaemia. Gastrointestinal: diarrhoea, vomiting. Other: fatigue, muscle pain, transaminases elevation.	[319, 320]
39	Ganetespib STA-9090	Synta Pharmaceutical, N/A		HSP90 inhibitor	Phase 3 Trial	Target: HSP90 Mechanism of action: Competitive binding with the N- domain ATP-binding pocket of HSP90 disrupting the chaperone cycle. Degrades the client proteins by the proteasome.	Gastrointestinal: diarrhoea, nausea, decreased appetite. Other: fatigue, insomnia.	[321]
40	Pevonedistat MLN4924	Millennium Pharmaceuticals Inc, N/A		Small-molecule Inhibitor Nedd8 Activating Enzyme (NAE)	Phase1 Trial	Target: NEDD activating enzyme (NAE) Mechanism of action: Inhibits NAE resulting in inhibition of CRL neddylation and an increase in levels of CRL substrate proteins, causing induction of DNA replication by blocking degradation of Cdt-1. Novel approach to inhibit NF- B.	Hematologic: neutropenia, thrombocytopenia. Gastrointestinal: nausea, diarrhea.	[322]
41	SNX-5422 SNX-2112.	Pfizer, N/A	\$\$ \$\$\$\rightarrow\tau\$	HSP90 inhibitor	Phase1 Trial	Target: HSP90 Mechanism of action: Disruption of Hsp90 function has been shown to cause degradation of multiple Hsp90 client proteins, leading to inhibition of several key signaling pathways. This in turn results in inhibition of cellular proliferation.	Gastrointestinal: nausea, emesis, diarrhea. Other: fatigue.	[323]
42	Oprozomib PR047	Onyx Pharmaceuticals, N/A	min of	proteasome inhibitor	Phase 1 trial/ Oral	Target: Proteasome subunit beta type-5 Mechanism of action: Inhibits the activity of the proteasome, this may result in an accumulation of unwanted or misfolded proteins. Disruption of various cell signaling pathways may follow, eventually leading to the induction of apoptosis and inhibition of tumor growth.	Hematologic: anemia, neutropenia. Gastrointestinal: diarrhea, nausea. Dermatologic: rash.	[324]

43	Marizomib NPI-0052, Salinosporamide A	Nereus Pharmaceuticals Inc, N/A	H H CH	proteasome inhibitor	Phase 1 trial/	Target: proteasome subunit beta type-1, 2 and 5 Mechanism of action: Marizomib binds and inhibits the 20S catalytic core subunit of the proteasome resulting in an accumulation of polyubiquitinated proteins that causes disruption of cellular processes, cell cycle arrest, the induction of tumor growth and angiogenesis.	Gastrointestinal: nausea, vomiting. Other: fatigue, headache, dizziness, fever.	[325]
44	Cerdulatinib PRT062070	Portola Pharmaceuticals Inc, N/A	NO NO	Syk-JAK inhibitor,antineopla stic, anti inflammatory	Phase 1 trial/ Oral	Target: Syk, JAK1, and JAK3 Mechanism of action: Binds to and inhibits the activity of Syk, JAK1, and JAK3 with preferental inhibition of JAK1 and JAK3-dependent cytokine- mediated signaling and functional responses.	Hematologic: anemia, neutropenia, hematochezia. Other: fatigue, hypotension, increased AST.	[326]
45	Sorafenib tosylate Nexavar	BAYER HLTHCARE, 2005		Multi-kinase inhibitor	Prescription/ Oral	Target: Simultaneous targeting of the Raf/Mek/Erk pathway. Mechanism of action: Sorafenib interacts with multiple intracellular (CRAF, BRAF and mutant BRAF) and cell surface kinases (KIT, FLT-3, VEGFR-2, VEGFR-3, and PDGFR-8). Several of these kinases are thought to be involved in angiogenesis, thus sorafenib reduces blood flow to the tumor. Sorafenib is unique in targeting the Raf/Mek/Erk pathway. By inhibiting these kinases, genetic transcription involving cell proliferation and angiogenesis is inhibited. Interferes with BCR signaling, protein translation and modulates the microenvironment prosurvival signals in MCL.	Hematologic: thrombocytopenia, neutropenia. Gastrointestinal: diarrhea. Dermatologic: hand/foot reactions.	[327]
46	Piceatannol	N/A		protein-tyrosine kinase	Phase 1 trial	Target: Different protein tyrosine kinases Mechanism of action: Inhibits the purified thymocyte protein-tyrosine kinase, p40 and competes for peptide or protein substrate binding site. It also inhibits the activity of the p56lck protein-tyrosine kinase. Inhibits protein tyrosine kinase Syk and induces apoptosis.	N/A	[328]
47	Belinostat PXD-101 Beleodaq	Spectrum pharmaceutical , 2014	X S	HDAC inhibitor, antineoplastic	Phase 2 trial/IV, infusion, oral	Target: HDACs Mechanism of action: Targets HDAC enzymes, inhibiting tumor cell proliferation, inducing apoptosis, promoting cellular differentiation, and inhibiting angiogenesis. This agent may sensitize drug- resistant tumor cells to other antineoplastic agents, possibly through a mechanism involving the down-regulation of thymidylate synthase.	Hematologic: neutropenia, thrombocytopenia. Gastrointestinal: adynamic ileus. Dermatologic: pruritis, rash/erythema, edema.	[329]

48	Entinostat MS-275	Syndax, N/A Merck, N/A	200.50	HDAC inhibitor, antineoplastic	Phase 3 trial	Target: HDAC1 and 3 Mechanism of action: Entinostat binds to and inhibits histone deacetylase. This agent appears to exert dose-dependent effects in human leukemia cells including cyclin-dependent kinase inhibitor 1A (p21/CIP1/WAF1)-dependent growth arrest and differentiation at low drug concentrations; a marked induction of reactive oxygen species (ROS); mitochondrial damage; caspase activation; and, at higher concentrations, apoptosis.	Gastrointestinal: diarrhea. Dermatologic: rash. Other: muscular weakness, fatigue.	[330]
49	Veliparib ABT-888	AbbVie, N/A		PARP inhibitor	Phase 2 trial/ Oral	Target: NF-kappa B signaling pathway. Mechanism of action: A poly(ADP-ribose) polymerase (PARP) -1 and -2 inhibitor. It inhibits PARPs, inhibiting DNA repair and potentiating the cytotoxicity of DNA-damaging agents. Hinders efficient DNA repair and survival of proliferating cells exposed to mild genotoxic stresses.	Hematologic: leukopenia, neutropenia, anemia. Gastrointestinal: nausea, vomiting. Other: dehydration, elevated alanine transaminase level, fatigue.	331
50	Pacritinib SB1518	Baxter, N/A Cell therapeutics, N/A		Janus kinase inhibitor	Phase 2/oral	Target: JAK-STAT signaling pathway Mechanism of action: Competes with JAK2 for ATP binding, it might result in inhibition of JAK2 activation, inhibition of the JAK-STAT signaling pathway, and so caspase-dependent apoptosis.	Hematologic: anemia, thrombocytopenia. Gastrointestinal: diarrhea, nausea, vomiting, constipation, abdominal pain, edema peripheral, abdominal distension. Other: fatigue, cough, dizziness, insomnia, anorexia.	332
51	Carfilzomib PR171 Kyprolis	Onyx pharmaceutical, 2012		Proteasome inhibitor	Prescription/	Target: Proteasome subunit beta type-5. Mechanism of action: Inhibition of the proteasome leads to a decreased cellular proliferation, ultimately resulting in cell cycle arrest and apoptosis of cancerous cells. Induces apoptosis of MCL cells mediated by the activation of JNK, Bcl-2, and mitochondria-related pathways. In addition, carfilzomib inhibits the growth and survival signaling pathways NF-xB and STAT3.	Hematologic: thrombocythemia, anaemia, thrombocytopenia, lymphopenia. Gastrointestinal: nausea. Other: fatigue, hypophosphatemia, hyponatremia.	333

Supplementary Table 4: The pharmacological details of the drugs currently in use or being developed for MCL