Supporting Online Material for "Recent Advances in the Cellular and Molecular Understanding of Myelodysplastic Syndromes: Implications for New Therapeutic Approaches"

This eTable accompanies a review article by Andrew M. Brunner, MD, and David P. Steensma, MD, in the January 2018 issue of *Clinical Advances in Hematology & Oncology.*

eTable. Emerging Therapies in Myelodysplastic Syndromes[a]

Drug Classes and Drugs	Mechanism of Action	Identifier
Kinase inhibitors		
LGH447	Pim kinase inhibitor	NCT02078609
Quizartinib (AC220)	FLT3 inhibitor	NCT02272478
Rigosertib (SyB C-1101, SyB L-1101, ON 01910.Na)	Inhibits PLK1, RAS mimetic that inhibits PI3K family, RAS/MEK/ERK signaling	NCT01926587 NCT02562443
Ruxolitinib (INCB18424)	JAK inhibitor	NCT01787487
Sorafenib	Inhibition of Raf, VEGFR, PDGFR, FLT3, and other kinases	NCT02196857 NCT02728050 NCT02530476
Tipifarnib	Nonpeptidomimetic quinolinone that binds to and inhibits the enzyme farnesyl protein transferase, preventing the activation of *RAS* genes	NCT02779777
TEW-7197	ALK5 inhibitor that inhibits the activity of TGFBR1 and prevents TGF-ß/TGFBR1-mediated signaling	NCT03074006
ONC201	Akt/ERK inhibitor, blocks PI3K/MAPK/ERK signaling	NCT02392572
Ibrutinib	Small molecular inhibitor of BTK	NCT02553941
sEphB4-HAS	sEphB4 fused to HSA	NCT03146871
OTS167	Inhibitor of MELK, a serine/threonine kinase involved in survival	NCT02795520
BGB324	Inhibitor of AXL receptor tyrosine kinase, enhances chemosensitivity	NCT02488408
Regorafenib	Inhibits VEGFR2/3, Ret, Kit, PDGFR, Raf kinase	NCT03042689
DCC-3014	Inhibitor of the tyrosine kinase receptor CSF1R	NCT03069469
INCB053914	Pim kinase inhibitor	NCT02587598
Deacetylase inhibitors and DNA methyltransferase inhibitors		
Oral azacitidine (CC-486)	DNA methyltransferase inhibitor	NCT02281084 NCT02223052
Guadecitabine (SGI-110)	Nucleoside analogue with DNA methyltransferase inhibitory activity	NCT02907359 NCT02935361
Panobinostat (LBH-589)	Deacetylase inhibitor	NCT02676323
Pracinostat (SB939)	Deacetylase inhibitor	NCT03151304
Entinostat (SNDX-275)	Deacetylase inhibitor	NCT02936752
GSK2879552	LSD1 inhibitor, enhances H3K4 methylation	NCT02929498
Tranylcypromine sulfate	LSD1 inhibitor, enhances H3K4 methylation	NCT02717884 NCT02273102
IMG-7289	LSD1 inhibitor, enhances H3K4 methylation	NCT02842827
ASTX727	DNA methyltransferase inhibitor (decitabine) combined with cytidine deaminase inhibitor (E7727)	NCT02103478
Drugs that alter cell metabolism		
Enasidenib (AG-221) and ivosidenib (AG-120)	Small-molecule inhibitors of mutant *IDH1* (AG-120) and *IDH2* (AG-221)	NCT02577406 NCT03173248

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eTable. *(Continued)* Emerging Therapies in Myelodysplastic Syndromes[a]

Drug Classes and Drugs	Mechanism of Action	Identifier
Drugs that alter cell metabolism *(Continued)*		
CPI-613 (6, 8-bis[benzylthio] octanoic acid)	Inhibitor of pyruvate dehydrogenase and ketoglutarate dehydrogenase	NCT01902381
CB-839	Glutaminase inhibitor	NCT03047993
AEB1102	Co-Argl-PEG–modified human arginase 1; degrades arginine levels	NCT02732184
Tosedostat (CHR-2797)	Inhibits M1 family of aminopeptidases, resulting in amino acid deprivation	NCT02452346
Cytotoxic agents/cell cycle inhibitors		
Cladribine (2-CDA)	Nucleoside analogue	NCT02115295 NCT01515527 NCT02044796 NCT02921061 NCT02728050 NCT02272478
Cytarabine/daunorubicin liposome injection (CPX-351)	Liposomal daunorubicin and cytarabine in a fixed 1:5 ratio	NCT02533115
Vosaroxin (SNS-595)	Quinolone derivative; replication-dependent DNA damage agent	NCT02658487
CFI-400945 fumarate	PLK4 inhibitor, disrupts mitosis and cell division	NCT03187288
AZD2811	AURKB inhibitor; disrupts mitosis and cell division	NCT03217838
OXi4503 (combretastatin A1 diphosphate)	Promotes microtubule depolymerization, mitotic arrest; disrupts tumor blood flow	NCT02576301
FF-10501-01 (inosine 5'-monophosphate dehydrogenase inhibitor)	Inhibits synthesis of guanine nucleotides and GTP, disrupts DNA and RNA synthesis	NCT02193958
AZD4573	CDK9 inhibitor	NCT03263637
Cell surface marker–directed therapies		
Daratumumab	Anti-CD38 human monoclonal antibody	NCT03067571 NCT03011034
BI 836858	Anti-CD33 human monoclonal antibody	NCT02240706
OPN-305	Anti-TLR2 humanized IgG4 monoclonal antibody	NCT02363491
Talacotuzumab (CSL362)	Anti-CD123 (IL3RA) antibody	NCT03011034
SL-401	Recombinant protein consisting of human IL3 fused to diphtheria toxin, binds to IL3RA (CD123)	NCT03113643
CC-90002	Anti-CD47 monoclonal antibody	NCT02641002 NCT02367196
Hu5F9-G4	Anti-CD47 monoclonal antibody	NCT03248479 NCT02678338
Hu8F4	Antibody against PR1/HLA-A2 (epitope expressed on leukemic blasts)	NCT02530034
TTI-621	Antibody fusion protein of the CD47 binding domain linked to human IgG1	NCT02663518
Gemtuzumab ozogamicin	Anti-CD33 antibody conjugated to a cytotoxin	NCT02221310 NCT02117297 NCT02272478
Immunosuppressive and immunomodulatory agents		
ALT-803	IL-15 superagonist mutant and a dimeric IL-15 receptor αSu/Fc fusion protein	NCT02989844 NCT01898793 NCT01885897

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eTable. *(Continued)* Emerging Therapies in Myelodysplastic Syndromes[a]

Drug Classes and Drugs	Mechanism of Action	Identifier
Immunosuppressive and immunomodulatory agents *(Continued)*		
Equine anti-thymocyte globulin	T-cell inhibition by polyclonal antibodies raised in animals	NCT01624805 NCT02462252
Ipilimumab (MDX-101)	CTLA-4 inhibitor	NCT02530463 NCT02890329 NCT01822509
Pembrolizumab (MK-3475)	Anti–PD-1 antibody	NCT03094637 NCT02936752
Durvalumab (MEDI4736)	Anti–PD-L1 antibody	NCT02775903 NCT02117219 NCT02281084
Atezolizumab (MPDL3280A)	Anti–PD-L1 antibody	NCT02508870 NCT02935361
Nivolumab (BMS-936558)	Anti–PD-1 antibody	NCT02530463 NCT02599649 NCT02464657 NCT03259516 NCT03092674 NCT01822509
Pomalidomide (CC4047)	Immunomodulatory agent; modulates cereblon E3 ubiquitin ligase activity	NCT02029950
Sirolimus	mTOR inhibitor	NCT01869114
Lirilumab (BMS-986015)	Antibody against KIRs, activating NK cells	NCT02599649 NCT02399917
PDR001	Anti–PD-1 antibody	NCT03066648
MBG453	Anti–TIM-3 antibody	NCT03066648
ARGX-110	Antibody against CD70, which is the ligand for the costimulatory receptor CD27	NCT03030612
Apoptosis modulation		
Luspatercept (ACE-536)	Modified activin receptor IIB-IgG Fc fusion protein that targets TGF-β signaling via Smad2/3 and GDF-11	NCT02268383 NCT01749514
Venetoclax (ABT-199)	BH3 mimetic that inhibits Bcl-2	NCT02942290 NCT02966782
LY2606368	CHK1 inhibitor; interferes with DNA repair and cell cycle checkpoint control	NCT02649764
ALRN-6924	MDM2/MDMX inhibitor; restores p53 activity	NCT02909972
AZD1775	WEE1 inhibitor; impairs G2 DNA damage checkpoint	NCT02666950
S 64315 (MIK665)	Inhibitor of Mcl-1	NCT02979366
S 055746	Inhibitor of Bcl-2	NCT02920541
DS-3032b	MDM2 antagonist; inhibits p53 degradation	NCT02319369
APR-246	PRIMA-1 analogue; restores wild-type function to mutant p53	
Vaccines and cellular therapies (excluding transplant)		
Cellular immunotherapy	Autologous dendritic cells that have undergone electroporation with WT1 mRNA	NCT03083054
DSP-7888	WT1 protein–derived peptide vaccine	NCT02498665 NCT02436252
BPX-701	Autologous T cells genetically modified to express α/β T-cell receptor reacting with PRAME peptide/HLA*A2.01 and containing the suicide switch	NCT02743611

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eTable. *(Continued)* Emerging Therapies in Myelodysplastic Syndromes[a]

Drug Classes and Drugs	Mechanism of Action	Identifier
Vaccines and cellular therapies (excluding transplant) *(Continued)*		
CD16/IL-15/CD33 tri-specific killer engagers (TriKes)	Cellular therapy directed toward CD33+ malignancies	NCT03214666
CAR-T cells	CAR T cells directed toward several targets, including CD33, CD39, CD56, CD117, CD123, CD34, and MUC1	NCT03291444 NCT03018405
Growth factors		
Eltrombopag	Small molecule agonist of TPO receptor c-Mpl (ie, thrombopoiesis-stimulating agent)	NCT02912208 NCT02928419 NCT01772420 NCT02446145
Romiplostim	Recombinant mimetic of TPO	NCT02335268
Epoetin beta	Recombinant protein similar to human EPO	NCT02145026
Pegol sihematide	Synthetic EPO peptide linked to PEG to increase circulation time	NCT02619097
Drugs that regulate transcription		
GSK525762	BET family inhibitor	NCT01943851
TEN-010 (RO6870810)	BET family inhibitor	NCT02308761
FT-1101	BET family inhibitor	NCT02543879
INCB057643	BET family inhibitor	NCT02711137
CPI-0610	BET family inhibitor	NCT02158858
PLX51107	BRD4 inhibitor, part of the BET family	NCT02683395
Miscellaneous		
H3B-8800	Orally bioavailable splicing factor modulator targeting SF3B1	NCT02841540
Bortezomib	Proteasome inhibition	NCT02312102 NCT02211755
Ganetespib (STA-9090)	Hsp90 inhibitor	NCT02272478
Omacetaxine mepesuccinate (homoharringtonine)	Protein translation inhibitor	NCT02159872
BL-8040	Inhibition of CXCR4	NCT02462252
CX-01 (2-0, 3-0 desulfated heparin)	Binds SDF-1 and CXCR4, as well as platelet factor 4	NCT02995655
Sertraline	Selective serotonin reuptake inhibitor, inflammatory cytokine modulator	NCT02452983
Selinexor (SINE KPT-330)	SINE that restores tumor-suppressing processes	
KPT-8602	Inhibitor of XPO-1 (SINE) that restores tumor-suppressing processes	NCT02228525 NCT02485535
Tamibarotene (SY-1425)	Orally active synthetic retinoid, approximately 10 times more potent than ATRA	NCT02807558
IRX5183	Retinoic acid receptor alpha agonist	NCT02749708
765IGF-MTX	IGF-1 conjugated to methotrexate	NCT03175978
Pevonedistat (MLN4924)	Small-molecule inhibitor of Nedd8-activating enzyme	NCT03268954 NCT03238248
Roxadustat (FG-4592)	HIF prolyl hydroxylase inhibitor	NCT03263091 NCT03303066
Nerofe	Novel tumor cell apoptosis factor, binds T1/ST2 receptor and activates apoptosis	NCT03059615
VSV-hIFNbeta-NIS	Vesicular stomatitis virus carrying the human *NIS* and *IFNB* genes (VSV-hIFN-beta-NIS), which may preferentially target cancer cells	NCT03017820

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eTable. *(Continued)* Emerging Therapies in Myelodysplastic Syndromes[a]

Drug Classes and Drugs	Mechanism of Action	Identifier
Miscellaneous *(Continued)*		
Veliparib (ABT-888)	PARP-1/2 inhibitor	NCT03289910
Imetelstat (JNJ-63935937)	Competitive enzyme inhibitor of telomerase	NCT02598661
Nandrolone decanoate	Androgen therapy for telomeropathies	NCT02055456

Note: The trials in this table include those identified on the clinicaltrials.gov website on September 27, 2017, with the search term "myelodysplastic syndrome"; the search was restricted to "Open" trials. Agents have been included if the study in which they were being tested was in either "Recruiting" or "Not Yet Recruiting" status and excluded if the study was "Completed," "Unknown," or "Terminated." Agents also have been included if they were not already approved by the US Food and Drug Administration for myelodysplastic syndromes (lenalidomide, azacitidine, and decitabine), for acute myeloid leukemia, or for an iron chelation indication. Excluded agents are those for stem cell transplant conditioning, cellular product manipulation, and graft-versus-host disease prevention or treatment.

ATRA, all-trans-retinoic acid; AURKB, Aurora B kinase; BET, bromodomain and extraterminal; BTK, Bruton tyrosine kinase; CAR, chimeric antigen receptor; CDK9, cyclin-dependent kinase 9; CHK1, checkpoint kinase 1; CSF1R, colony-stimulating factor 1 receptor; CTLA-4, cytotoxic T-lymphocyte–associated antigen 4; CXCR4, C-X-C chemokine receptor type 4; EPO, erythropoietin; ERK, extracellular signal–regulated protein; FLT3, Fms-like tyrosine kinase 3; GDF, growth and differentiation factor; GTP, guanosine triphosphate; HSA, human serum albumin; HIF, hypoxia-inducible factor; Hsp90, heat shock protein 90; IDH, isocitrate dehydrogenase; IFN, interferon; IGF-1, insulin-like growth factor 1; IgG, immunoglobulin G; IL, interleukin; IL3RA, interleukin 3 receptor subunit alpha; JAK, Janus-associated kinase; KIRs, killer cell immunoglobulin-like receptors; LSD1, lysine-specific histone demethylase 1; MAPK, mitogen-activated protein; MELK, maternal embryonic leucine zipper kinase; mTOR, mammalian target of rapamycin; NIS, sodium iodide symporter; NK, natural killer; PARP, poly(ADP-ribose) polymerase; PD-1, programmed death 1; PD-L1, programmed death 1–ligand 1; PDGFR, platelet-derived growth factor receptor; PEG, polyethylene glycol; PI3K, phosphoinositide-3 kinase; PLK4, polo-like kinase 4; sEphB4, soluble extracellular domain of EphB4; SINE, selective inhibitor of nuclear export; TGFBR1, transforming growth factor beta receptor 1; TIM-3, T-cell immunoglobulin and mucin domain–containing protein 3; TPO, thrombopoietin; VEGFR, vascular endothelial growth factor receptor.

[a] Updated and based in part on Bejar R, Steensma DP. Recent developments in myelodysplastic syndromes. *Blood*. 2014;124(18):2793-2803.