Hematology Drugs in the Pipeline

HemOnc Today presents the most recent information about hematology drugs in the pipeline. Drugs listed here are in phase 2 or phase 3 development for a variety of indications. Clinicians can use this chart as a quick reference to learn about the status of those drugs that may be clinically significant to their practice.

Generic name (Brand name, Manufacturer)	Indication(s)	Development status
abexinostat hydrochloride (Pharmacyclics)	B-cell lymphoma	phase 2
ABT-888 (Veliparib, Abbott Laboratories)	non-Hodgkin's lymphoma	phase 2
ACY-1215 (Acetylon Pharmaceuticals)	multiple myeloma	phase 2
AEG35156 (Aegera Therapeutics)	acute myeloid leukemia, chronic lymphocytic leukemia, B-cell lymphoma	phase 2
AGS-005 (Argos Therapeutics)	chronic lymphocytic leukemia	phase 2
AKB-6548 (Akebia Therapeutics)	anemia	phase 2
alisertib (Millennium Pharmaceuticals)	peripheral T-cell lymphoma	phase 3
AlloStim (Immunovative Therapies)	hematological malignancies	phase 2
Alvocidib (Sanofi-Aventis)	B-cell chronic lymphocytic leukemia, prolymphocytic leukemia	phase 2
aminopterin (Syntrix Biosystems)	acute lymphoblastic leukemia	phase 2
anemia protein therapy (Medgenics)	anemia	phase 2
angiotensin 1-7 (Tarix Pharmaceuticals)	acceleration of engraftment of hematopoietic cells post-transplant	phase 2
anti-thymocyte globulin (Thymoglobulin, Genzyme Transplant)	acute myeloid leukemia, myelodysplastic syndrome	phase 2
apixaban (Eliquis; Pfizer, Bristol-Myers Squibb)	prevention and treatment of venous thromboembolism	phase 3
AR-42 (Arno Therapeutics)	chronic lymphocytic leukemia, B-cell lymphoma, multiple myeloma	phase 2
AR-67 (Arno Therapeutics)	myelodysplastic syndrome	phase 2
ARC1779 (Archemix)	thrombotic thrombocytopenic purpura	phase 2
ARO-002 (Arog Pharmaceuticals)	enhancement of stem cell engraftment	phase 2
ARRY-520 (Array BioPharma)	acute myeloid leukemia, multiple myeloma	phase 2
arsenic trioxide (Trisenox, Cephalon) **READ PERSPECTIVE** on this drug from Eytan M. Stein, MD, and Martin S. Tallman, MD, on page 61.	multiple myeloma, myelodysplastic syndrome/acute myeloid leukemia	phase 2/phase 3
ART-123 (Artisan Pharma)	disseminated intravascular coagulation	phase 2
AS-1411 (Antisoma)	acute myeloid leukemia	phase 2
AS-1413 (Antisoma)	acute myeloid leukemia	phase 3
AT-101 (Ascenta Therapeutics)	chronic lymphocytic leukemia, non-Hodgkin's lymphoma	phase 2
AT7519 (Astex Pharmaceuticals)	chronic lymphocytic leukemia, mantle cell lymphoma, multiple myeloma	phase 2
AT9283 (Astex Pharmaceuticals)	acute myeloid leukemia, multiple myeloma	phase 2
ATIR (Kiadis Pharma)	graft-versus-host disease, bone marrow transplantation-related infections	phase 3
AUY922 (Novartis)	multiple myeloma	phase 2
azacitidine (Vidaza, Celgene)	acute myeloid leukemia, lymphoma	phase 3
AZD1152 (AstraZeneca)	acute myeloid leukemia	phase 2
bafetinib (CytRx)	chronic myeloid leukemia	phase 2
B-cell lymphoma vaccine (BiovaxID, Biovest)	follicular lymphoma/mantle cell lymphoma	phase 3/phase 2
belinostat (Spectrum Pharmaceuticals)	acute myeloid leukemia, peripheral T-cell lymphoma	phase 2

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bendamustine (Treanda, Cephalon)	pediatric acute lymphoblastic leukemia, pediatric acute myeloid leukemia, mantle cell lymphoma, multiple myeloma	phase 2
betrixaban (Portola Pharmaceuticals)	prevention of thromboembolism	phase 3
BHQ880 (Novartis)	multiple myeloma	phase 2
BI-811283 (Boehringer Ingelheim)	chronic myeloid leukemia	phase 2
Birinapant (TetraLogic Pharmaceuticals)	acute myeloid leukemia	phase 2
BIW-8962 (Kyowa Hakko Kirin Pharma)	multiple myeloma	phase 2
blinatumomab (Amgen) **READ PERSPECTIVE** on this drug from Nelson Chao, MD, MBA, and David Rizzieri, MD, on page 62.	acute lymphoblastic leukemia	phase 2
bortezomib (Velcade, Millennium Pharmaceuticals)	T-cell prolymphocytic leukemia, diffuse large B-cell lymphoma, graft-versus-host disease / mantle cell lymphoma, non-Hodgkin's B-cell lymphoma, follicular non-Hodgkin's lymphoma	phase 2/phase 3
brentuximab vedotin (Adcetris, Seattle Genetics/Millennium)	non-Hodgkin's lymphoma, anaplastic large-cell lymphoma / Hodgkin's lymphoma	phase 2/phase 3
BT-062 (Biotest AG)	multiple myeloma	phase 2
cancer vaccine (GVAX Leukemia, BioSante Pharmaceuticals)	acute myeloid leukemia, chronic myeloid leukemia, multiple myeloma	phase 2
cancer vaccine (PR1, The Vaccine Company)	myelodysplastic syndrome, chronic myeloid leukemia / acute myeloid leukemia	phase 2/phase 3
canfosfamide (Telcyta, Telik)	diffuse large B-cell lymphoma, mantle cell lymphoma, non-Hodgkin's lymphoma	phase 2
carfilzomib (Onyx)	multiple myeloma	phase 3
carlecortemcel-L (StemEx, Gamida Cell)	hematopoietic support for patients with chronic myeloid leukemia, myelodysplastic syndrome, and relapsed or refractory hematologic malignancies	phase 3
CAT-8015 (MedImmune)	CD22+ chronic lymphocytic leukemia	phase 2
CB3304 (Cougar Biotechnology)	multiple myeloma	phase 2
cenersen (Eleos)	acute myeloid leukemia, chronic lymphocytic leukemia	phase 2
CEP-18770 (Cephalon)	multiple myeloma	phase 2
certoparin (Novartis)	prevention of thromboembolism	phase 3
CLL immunotherapeutic vaccine (MaxCyte)	chronic lymphocytic leukemia	phase 2
clofarabine injection (Clolar, Genzyme)	acute myeloid leukemia	phase 3
CPX-351 (Celator Pharmaceuticals)	acute myeloid leukemia	phase 2
CT-011 (CureTech)	acute myeloid leukemia, diffuse large B-cell lymphoma, follicular lymphoma	phase 2
CYT387 (YM Biosciences)	myelofibrosis	phase 2
dabigatran etexilate (Pradaxa, Boehringer Ingelheim)	prevention, treatment of venous thromboembolism	phase 3
dacetuzumab (Seattle Genetics)	chronic lymphocytic leukemia	phase 2
danusertib (Nerviano Medical Sciences)	chronic myeloid leukemia	phase 2
daratumumab (Genmab)	multiple myeloma	phase 2
darexaban maleate (Astellas)	prevention of venous thrombosis after surgery	phase 3
darinaparsin (Ziopharm Oncology)	peripheral T-cell lymphoma, multiple myeloma	phase 2
DCC-2036 (Deciphera Pharmaceuticals)	chronic myeloid leukemia	phase 2

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decitabine (Dacogen, Eisai) **READ PERSPECTIVE** on this drug from Yogen Saunthararajah, MD, on page 61.	pediatric acute myeloid leukemia / acute myeloid leukemia	phase 2/phase 3
deferiprone (Ferriprox, ApoPharma)	iron overload in patients with hematologic disorders that require chronic transfusion therapy	phase 3
denosumab (Xgeva, Amgen)	multiple myeloma	phase 2
dinaciclib (Merck)	chronic lymphocytic leukemia	phase 3
dovitinib (Novartis)	multiple myeloma	phase 2
edoxaban tosylate (Daiichi Sankyo)	prevention of venous thromboembolism	phase 3
egaptivon pegol (Archemix)	prevention of thrombosis	phase 2
elacytarabine (Elacyt, Clavis Pharma)	acute myeloid leukemia	phase 3
elotuzumab (Bristol-Myers Squibb) **READ PERSPECTIVES** on this drug from Don M. Benson Jr., MD, PhD, on page 61, and Jason Valent, MD, on page 62.	multiple myeloma	phase 3
eltrombopag (Promacta, GlaxoSmithKline)	chemotherapy-induced thrombocytopenia	phase 2
entinostat (Syndax Pharmaceuticals)	Hodgkin's lymphoma	phase 2
enzastaurin (Eli Lilly)	diffuse large B-cell lymphoma	phase 3
epratuzumab (Immunomedics)	pediatric acute lymphoblastic leukemia, diffuse large B-cell lymphoma, follicular lymphoma	phase 2
epratuzumab Y-90 (Immunomedics)	acute lymphoblastic lymphoma, diffuse large B-cell lymphoma, recurrent non-Hodgkin's lymphoma	phase 2
eptacog alfa (Novo Nordisk)	bleeding episodes in Glanzmann thrombasthenia	phase 3
erlotinib (Tarceva, Genentech)	myelodysplastic syndrome	phase 2
everolimus (Afinitor, Novartis)	mantle cell lymphoma, Waldenström's macroglobulinemia	phase 2
Factor XIII concentrate (Fibrogammin P, CSL Behring)	congenital Factor XIII deficiency	phase 3
ferric carboxymaltose (Injectafer, Luitpold Pharmaceuticals)	anemia	phase 3
ferric pyrophosphate-supplemented dialysate (Rockwell Medical Technologies)	anemia	phase 3
FG-2216 (FibroGen)	anemia	phase 2
FG-4592 (FibroGen)	anemia	phase 2
forodesine (BioCryst Pharmaceuticals)	chronic lymphocytic leukemia, cutaneous T-cell lymphoma	phase 2
fostamatinib (AstraZeneca)	hematological malignancies	phase 2
galiximab (Biogen Idec)	non-Hodgkin's lymphoma	phase 2
ganetespib (Synta Pharmaceuticals)	acute lymphoblastic leukemia, acute myeloid leukemia, chronic myeloid leukemia	phase 2
GL-0817 (Gliknik)	multiple myeloma	phase 2
GMI-1070 (Pfizer, GlycoMimetics)	vaso-occlusive crisis in patients with sickle cell disease	phase 2
GRNVAC1 (Argos Therapeutics)	acute myeloid leukemia	phase 2
GS-1101 (Gilead Sciences) **READ PERSPECTIVE** on this drug from Kanti R. Rai, MD, on page 62.	chronic lymphocytic leukemia/indolent non-Hodgkin's lymphoma	phase 3/phase 2
GSK2110183 (GlaxoSmithKline)	leukemia, multiple myeloma	phase 2

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GSK2130579A (GlaxoSmithKline)	acute myeloid leukemia	phase 2
GVAX Leukemia (BioSante Pharmaceuticals)	acute myeloid leukemia, chronic myeloid leukemia	phase 2
GVAX Myeloma (BioSante Pharmaceuticals)	multiple myeloma	phase 2
HQK-1001 (HemaQuest Pharmaceuticals)	sickle cell disease	phase 2
HuM195-Bi-213 (Actinium Pharmaceuticals)	acute myeloid leukemia	phase 2
human mesenchymal stem cell therapy (Prochymal, Osiris Therapeutics)	graft-versus-host disease	phase 3
human prothrombin complex (Octaplex, Octapharma)	reversal of anticoagulation therapy	phase 3
ibritumomab tiuxetan (Zevalin, Spectrum Pharmaceuticals)	diffuse large B-cell lymphoma	phase 2
ibrutinib (Janssen Biotech and Pharmacyclics) **READ PERSPECTIVE** on this drug from Kanti R. Rai, MD, on page 62.	chronic lymphocytic leukemia, diffuse large B-cell lymphoma, mantle cell lymphoma, multiple myeloma	phase 2
imetelstat (Geron)	chronic lymphocytic leukemia, multiple myeloma	phase 2
imexon (Amplimexon, AmpliMed)	non-Hodgkin's lymphoma, multiple myeloma	phase 2
Imprime PGG (Biothera)	chronic lymphocytic leukemia	phase 2
indatuximab ravtansine (Biotest)	relapsed or refractory multiple myeloma	phase 2
inolimomab (Leukotac, EUSA Pharma)	graft-versus-host disease	phase 3
inotuzumab ozogamicin (Pfizer)	non-Hodgkin's lymphoma/diffuse large B-cell lymphoma	phase 3/phase 2
interferon alpha (Veldona, Amarillo Biosciences)	polycythemia vera	phase 2
interleukin-12 gene therapy (OncoSec Medical)	cutaneous T-cell lymphoma	phase 2
IPH-2101 (Innate Pharma)	multiple myeloma	phase 2
ISF35 (Memgen)	chronic lymphocytic leukemia, chronic myeloid leukemia, follicular lymphoma, diffuse large cell lymphoma, mantle cell lymphoma, small lymphocytic lymphoma	phase 2
ixazomib (Millennium Pharmaceuticals)	multiple myeloma	phase 2
KW-2478 (Kyowa Hakko Kirin Pharma)	multiple myeloma	phase 2
KW-0761 (Kyowa Hakko Kirin Pharma)	cutaneous T-cell lymphoma, peripheral T-cell lymphoma	phase 2
L-annamycin (Callisto Pharmaceuticals)	acute myeloid leukemia, acute lymphoblastic leukemia	phase 2
L-asparaginase (ERYtech Pharma)	acute lymphoblastic leukemia	phase 3
L-glutamine (Emmaus Medical)	sickle cell disease	phase 2
lenalidomide (Revlimid, Celgene)	chronic lymphocytic leukemia, mantle cell lymphoma, non-Hodgkin's lymphoma	phase 3
lestaurtinib (Cephalon)	acute myeloid leukemia, Philadelphia-negative classic myeloproliferative disorders	phase 2
leukemia DNA vaccine (Inovio Pharmaceuticals)	acute myeloid leukemia, chronic myeloid leukemia	phase 2
LOR-2040 (Lorus Therapeutics)	acute myeloid leukemia	phase 2
lorvotuzumab mertansine (ImmunoGen)	multiple myeloma	phase 2
lucatumumab (Novartis)	lymphoma	phase 2
mapatumumab (Human Genome Sciences)	multiple myeloma	phase 2
melphalan intravenous (CyDex Pharmaceuticals)	multiple myeloma	phase 2

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Generic name (Brand name, Manufacturer)	Indication(s)	Development status
mesenchymal stem cell therapy (Mesoblast)	bone marrow regeneration after transplantation	phase 3
midostaurin (Novartis)	acute myeloid leukemia	phase 3
milatuzumab (Immunomedics)	chronic lymphocytic leukemia, non-Hodgkin's lymphoma, recurrent multiple myeloma	phase 2
MK-7956 (Merck)	mantle cell lymphoma	phase 2
mocetinostat (MethylGene)	chronic lymphocytic leukemia, diffuse large B-cell lymphoma, follicular lymphoma	phase 2
mogamulizumab (Poteligeo, Kyowa Hakko Kirin)	T-cell leukemia-lymphoma	phase 2
MSC1936369B (EMD Serono)	hematological malignancies	phase 2
naloxone lotion (Elorac)	pruritus accompanying cutaneous T-cell lymphoma	phase 2
navitoclax (Abbott Laboratories)	chronic lymphocytic leukemia, non-Hodgkin's lymphoma	phase 2
nelarabine (Arranon, GlaxoSmithKline)	acute lymphoblastic leukemia, T-cell lymphoma	phase 3
NiCord (Gamida Cell)	hematological malignancies, umbilical cord blood stem cell therapy	phase 2
nilotinib (Tasigna, Novartis)	chronic myeloid leukemia, acute lymphoblastic leukemia	phase 2
NN1731 (Novo Nordisk)	hemophilia	phase 3
NN7008 (Novo Nordisk)	hemophilia A	phase 3
NN7088 (Novo Nordisk)	hemophilia A	phase 3
NN7999 (Novo Nordisk)	hemophilia B	phase 3
obatoclax (Cephalon)	chronic lymphocytic leukemia, follicular lymphoma, mantle cell lymphoma	phase 2
OBI-1 (Inspiration Biopharmaceuticals)	episodic bleeding in patients with inhibitor antibodies to human coagulation Factor VIII	phase 3
obinutuzumab (Biogen Idec)	chronic lymphocytic leukemia, non-Hodgkin's lymphoma, B-cell lymphoma	phase 3
oblimersen (Genasense, Genta)	acute myeloid leukemia	phase 3
ocaratuzumab (Mentrik Biotech)	non-Hodgkin's lymphoma	phase 2
ofatumumab (Arzerra, GlaxoSmithKline)	chronic lymphocytic leukemia, diffuse large B-cell lymphoma, follicular lymphoma, Waldenström's macroglobulinemia	phase 2
omacetaxine (Omapro, Cephalon)	acute myeloid leukemia, myelodysplastic syndrome	phase 2
ON 01910.NA (Estybon, Onconova Therapeutics)	myelodysplastic syndrome	phase 3
oral azacitidine (Celgene)	myelodysplastic syndrome	phase 2
P 27600 (Piramal Life Sciences)	mantle cell lymphoma	phase 2
pacritinib (S*BIO)	myelodysplastic syndrome, myeloid leukemia	phase 2
panobinostat (Novartis)	acute lymphoblastic leukemia, acute myeloid leukemia, myelodysplastic syndrome/multiple myeloma, Hodgkin's lymphoma	phase 2/phase 3
PEG-PAL (BioMarin Pharmaceutical)	hyperphenylalaninemia	phase 2
pegylated rFVIII (Baxter)	hemophilia	phase 2
peg rFVIII (Bayer)	hemophilia A	phase 3
peginesatide (Hematide, Affymax)	anemia	phase 3
pentostatin (Nipent, Hospira)	chronic lymphocytic leukemia	phase 3
perifosine (Aeterna Zentaris)	chronic lymphocytic leukemia, lymphoma, Waldenström's macroglobulinemia/multiple myeloma	phase 2/phase 3
pixantrone (Cell Therapeutics)	diffuse large B-cell lymphoma	phase 3

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plitidepsin (Aplidin, PharmaMar)	multiple myeloma	phase 3
PLX3397 (Plexxikon)	acute myeloid leukemia, recurrent or refractory Hodgkin's lymphoma	phase 2
pomalidomide (Celgene)	multiple myeloma, myelofibrosis, anemia	phase 3
ponatinib (Ariad Pharmaceuticals)	acute lymphoblastic leukemia, chronic myeloid leukemia	phase 2
PR104 (Proacta)	acute myeloid leukemia	phase 2
pralatrexate (Folotyn, Allos Therapeutics)	B-cell non-Hodgkin's lymphoma/peripheral T-cell lymphoma	phase 2/phase 3
quisinostat (Johnson & Johnson)	cutaneous T-cell lymphoma	phase 2
quizartinib (Ambit Biosciences, Astellas)	acute myeloid leukemia	phase 2
recombinant Factor VIII Fc fusion protein (Biogen Idec)	hemophilia A	phase 3
recombinant Factor IX (Baxter)	hemophilia	phase 3
recombinant human antithrombin III (Atryn, GTC Biotherapeutics)	antithrombin III-dependent heparin resistance requiring anticoagulation	phase 3
remestemcel-L (Prochymal, Osiris Therapeutics)	graft-versus-host disease	phase 3
reslizumab (Cinquil, Cephalon)	hypereosinophilic syndrome	phase 3
rFIXFc (Biogen Idec)	hemorrhagic episodes in patients with hemophilia B	phase 3
rFXIII (Novo Nordisk)	congenital FXIII deficiency, bleeding associated with congenital FXIII deficiency	phase 3
RGI-2001 (REGiMMUNE)	graft-versus-host disease	phase 2
Rhitol (Kiadis Pharma)	graft-verus-host disease	
rigosertib (Onconova Therapeutics)	myelodysplastic syndrome, lymphoma	phase 3
romiplostim (Nplate, Amgen)	chemotherapy-induced thrombocytopenia	phase 2
ruxolitinib (Jakafi, Incyte)	hematologic tumors, essential thrombocythemia/polycythemia vera	phase 2/phase 3
samalizumab (ALXN6000, Alexion)	chronic lymphocytic leukemia, multiple myeloma	phase 2
samarium SM-153 lexidronam injection (Quadramet, Jazz and EUSA Pharma)	multiple myeloma	phase 2
sapacitabine (Cyclacel Pharmaceuticals)	chronic lymphocytic leukemia, myelodysplastic syndrome/acute myeloid leukemia	phase 2/phase 3
saratin (BioVascular)	thrombosis	phase 2
SAR245409 (Sanofi)	non-Hodgkin's lymphoma	phase 2
SAR3419 (Sanofi)	B-cell malignancies	phase 2
SB1518 (S*BIO)	myeloproliferative disorders	phase 2
semuloparin (Sanofi-Aventis)	prevention of venous thromboembolism	phase 3
sepantronium bromide (Astellas)	non-Hodgkin's lymphoma	phase 2
SGI110 (Astex Pharmaceuticals)	acute myelodysplastic syndrome	phase 2
siltuximab (Janssen Biotech)	multiple myeloma	phase 2
SL-401 (Stemline Therapeutics)	acute myeloid leukemia, myelodysplastic syndrome	phase 2
SNS01-T (Senesco Technologies)	multiple myeloma	phase 2
sorafenib (Nexavar, Bayer HealthCare)	acute myeloid leukemia, myelodysplastic syndrome, multiple myeloma	phase 2
sotatercept (Celgene)	chemotherapy-induced anemia	phase2/phase 3

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TAK-442 (Takeda Pharmaceuticals)	thromboembolism	phase 2
TALL-104 (Abiogen Pharma)	chronic myeloid leukemia	phase 2
tamibarotene (CytRx)	acute promyelocytic leukemia	phase 2
tecarfarin (ARYx Therapeutics)	prevention of thromboembolism	phase 3
temozolomide (Temodar, Merck)	acute myeloid leukemia	phase 2
terutroban sodium (Servier)	prevention of thromboembolism	phase 3
TG-101348 (TargeGen)	myelofibrosis	phase 2
TH-302 (Threshold Pharmaceuticals)	multiple myeloma	phase 2
TH9402 (Kiadis Pharma)	graft-versus-host disease	phase 2
thiarabine (Access Pharmaceuticals)	leukemia/lymphoma	phase 2
tissue repair stem cell therapy (Aastrom Biosciences)	osteonecrosis	phase 3
TKI258 (Novartis)	multiple myeloma	phase 2
tosedostat (Chroma Therapeutics)	acute myeloid leukemia	phase 2
tositumomab and iodine I-131 tositumomab (Bexxar, GlaxoSmith-Kline)	mantle cell lymphoma	phase 2
trametinib (GlaxoSmithKline)	acute myeloid leukemia/multiple myeloma	phase 3/phase 2
treosulfan (Medac)	acute lymphoblastic leukemia, acute myeloid leukemia, myelodysplastic syndrome	phase 2
TRU-016 (Emergent BioSolutions)	chronic lymphocytic leukemia, non-Hodgkin's lymphoma	phase 2
TXA127 (Tarix Pharmaceuticals)	chemotherapy-induced thrombocytopenia	phase 2
varespladib (Anthera Pharmaceuticals)	prevention of acute chest syndrome in patients with sickle cell disease	phase 2
veltuzumab (Immunomedics) **READ PERSPECTIVE** on this drug from Matt Kalaycio, MD, on page 62.	chronic lymphocytic leukemia, non-Hodgkin's lymphoma	phase 2
vincristine sulfate liposomal injection (Marqibo, Talon Therapeutics)	non-Hodgkin's lymphoma/acute lymphoblastic leukemia	phase 2/phase 3
vorapaxar (Merck)	arterial thrombosis	phase 3
vorinostat (Zolinza, Merck)	acute myeloid leukemia, myelodysplastic syndrome, B-cell lymphoma/multiple myeloma	phase 2/phase 3
vosaroxin (Sunesis Pharmaceuticals)	acute myeloid leukemia	phase 3
VTX-2337 (VentiRx Pharmaceuticals)	B-cell lymphoma	phase 2
WT1 (GlaxoSmithKline)	acute myeloid leukemia	phase 2
zanolimumab (Emergent BioSolutions)	cutaneous T-cell lymphoma	phase 2
zosuquidar trihydrochloride (Kanisa Pharmaceuticals)	acute myeloid leukemia	phase 3

Information in this chart was compiled from the Pharmaceutical Research and Manufacturers of America, NIH (www.clinicaltrials.gov), corporate websites and the databases of HEMONC TODAY. The publisher or editors do not assume responsibility for any errors or omissions.

Hematology Drugs in the Pipeline

HEMONC TODAY asked key opinion leaders to offer perspective about hematology drugs in the pipeline they believe have the potential to change practice.

PERSPECTIVE: ARSENIC TRIOXIDE

Eytan M. Stein

Martin S. Tallman

On Sept. 25, 2000, the FDA approved arsenic trioxide [ATO (Trisenox, Cephalon)] for patients with acute promyelocytic leukemia (APL) who have relapsed or are refractory to all-trans retinoic acid (ATRA) and an anthracycline. Given the remarkable efficacy of ATO in relapsed and refractory disease, phase 2 studies have attempted to move ATO — in combination with ATRA — to the front-line setting. Recent data from a phase 2 clinical trial conducted by the Australasian Leukaemia and Lymphoma Study Group using idarubicin in combination with ATRA and ATO for only three total cycles of therapy (one induction and two cycles of consolidation) followed by maintenance with ATRA plus low-dose chemotherapy for newly diagnosed APL demonstrated an enviable 2-year freedom from relapse rate of 97.5% and OS of 93.2%. Exciting data from a randomized phase 3 trial of newly diagnosed APL patients that compares arsenic and ATRA induction with ATRA plus anthracycline induction and consolidation are eagerly awaited and will be reported at the American Society of Hematology Annual Meeting in December in Atlanta.

The evolution of treatments for patients with newly diagnosed APL from chemotherapy alone to chemotherapy with ATRA — and, in the 21st century, ATRA with ATO — mirrors the development of effective targeted agents in solid tumors and other hematologic malignancies. In addition, early studies with oral arsenic raise the possibility that APL may become curable with oral drug therapy alone, which will drastically improve patient quality of life during treatment. This should be viewed as a positive development for both patients and their physicians and will make APL the only leukemia that is potentially curable without any chemotherapy.

— Eytan M. Stein, MD

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Disclosure: Stein and Tallman report no relevant financial disclosures.

PERSPECTIVE: ELOTUZUMAB

Don M. Benson Jr.

Monoclonal antibody (mAb) therapy has revolutionized treatment options for many solid and liquid cancers and yet, to date, no mAb-based therapy has been approved for the treatment of multiple myeloma, the second most common hematologic malignancy. Despite the recent advent of a number of novel therapies, multiple myeloma remains incurable and new options are desperately required. Elotuzumab (Bristol-Myers Squibb) is a humanized IgG1 mAb-targeting CS1, a cell surface glycoprotein expressed nearly universally by multiple myeloma tumor cells but not on most healthy cells. Elotuzumab primarily exerts anti-multiple myeloma efficacy via antibody-dependent cellular cytotoxicity (ADCC). A single-agent, phase 1 trial of elotuzumab showed the mAb to be safe and well tolerated (Zonder JA. *Blood*. 2012;120:552-559).

Early phase, single-arm trials of elotuzumab in combination with lenalidomide/dexamethasone (Lonial S. *J Clin Oncol*. 2012;30:1953-1959) and with bortezomib/dexamethasone (Jakubowiak AJ. *J Clin Oncol*. 2012;30:1960-1965) demonstrated superior response rates and improvement in PFS endpoints compared with historical control data. Currently, elotuzumab is being evaluated in two large phase 3 trials in combination with lenalidomide/dexamethasone in the newly diagnosed and relapsed/refractory settings. Elotuzumab holds great promise as the first mAb therapy for patients with multiple myeloma.

— Don M. Benson Jr., MD, PhD

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Disclosure: Benson reports no relevant financial disclosures.

PERSPECTIVE: DECITABINE

Yogen Saunthararajah

Of the hundreds of conventional and molecular targeted oncotherapeutics, the vast majority have a final common goal to induce irreversible cell cycle exit by apoptosis. In the test tube, all cancers are curable by this approach. In the clinic, however, this approach is undermined by therapeutic index: master regulators of apoptosis (eg, TP53 and p16/CDKN2A) are very commonly inactivated or deleted in cancers, while they remain intact in normal stem cells, so apoptosis-based therapy — though often initially efficacious — selects against normal cells while selecting for apoptosis-resistant malignant subclones.

Second- or third-line drugs may appear different, targeting different proximal molecular targets, but since the final common pathway is apoptosis, responses tend to be desultory. Furthermore, the destruction of normal stem cells causes toxicity that constrains the intensity and duration of therapy, and that compromises quality of life in its few remaining months. In fact, the few disseminated cancers which we cure are the few in which key apoptosis genes are intact (germ cell cancers, etc). Of these, those that are relapsed/refractory are characterized by a high prevalence of TP53 or CDKN2A abnormalities. Apoptosis-based therapy is fundamentally unsound in the latter cases and in most other disseminated cancers. Thus there is a need for therapy that is not just different with regard to the proximal molecular target, but also in the downstream pathway utilized for irreversible cell cycle exit.

Decitabine (Dacogen, Eisai) is an exciting drug because it can potentially fit this bill. Decitabine has two interesting characteristics. First, the deoxyribose sugar moiety of decitabine is unmodified. Hence, at relatively low concentrations, decitabine can incorporate into DNA without terminating DNA chain elongation and without cytotoxicity. Second, DNA-incorporated decitabine depletes DNA methyltransferase 1 (DNMT1), a central member of the network of chromatin-modifying enzymes that mediates transcription repression.

Leukemia and cancer cells express strikingly high levels of master drivers of lineage-differentiation (this is also a feature of cancer 'stem' cells). The disruption to transcription repression by decitabine-induced depletion of DNMT1 renews expression of the late-differentiation target genes of these master regulators of differentiation, producing irreversible cell cycle exit in cancer and leukemia cells by p53/p16-independent maturation pathways. The same non-cytotoxic treatment maintains the self-renewal of normal stem cells, which do not express high levels of lineage-specifying transcription factors. Thus, decitabine is potentially a true alternative to existing apoptosis-based therapies.

However, there are major pharmacologic barriers that need to be surmounted if this agent is to fulfill its clinical potential. The epigenetic therapeutic effect of DNMT1-depletion is S-phase dependent, and exposure time and distribution are crucial determinants of activity, but decitabine is rapidly inactivated by the ubiquitously expressed enzyme cytidine deaminase, producing a plasma half-life of minutes in vivo. Furthermore, its intracellular half-life depends on the activity of the enzyme deoxycytidine kinase, which is expressed to different extents in different malignancies. With careful attention to these pharmacologic issues via alternative dosages, schedules, routes of administration and formulation, perhaps decitabine could offer a true complement or alternative to multiple existing drugs, via its p53/p16-independent, and normal stem cell-sparing mechanism of action.

— Yogen Saunthararajah, MD

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Disclosure: Saunthararajah has a patent application for oral-THU decitabine and a patent for the use of decitabine for ex vivo expansion of normal stem cells, but he does not receive any royalties, licensing or consulting fees.

Alcazar O. *Int J. Cancer*. 2012;131:18-29.
Hu Z. *Mol Cancer Ther*. 2010;9:1536-43.
Milhem M. *Blood*. 2004;103:4102-4110.
Negrotto S. *Cancer Res*. 2011;71:1431-1441.
Negrotto S. *Leukemia*. 2012;26:244-254.
Ng KP. *Leukemia*. 2011;25:1739-1750.
Saunthararajah Y. *Semin Oncol*. 2012;39:97-108.

Hematology Drugs in the Pipeline

PERSPECTIVE: ELOTUZUMAB

Jason Valent

Elotuzumab (Bristol-Myers Squibb) is an anti-CS1 humanized IgG monoclonal antibody. The publications of Tai and colleagues and Hsi and colleagues highlight that CS1 is a cell surface glycoprotein with high level of gene expression in multiple myeloma cells but not detected in significant levels in normal tissues or cancer cell lines from other tumor types. CS1 functions in adhesion of plasma cells to bone marrow stromal cells, and elotuzumab is able to inhibit adhesion of multiple myeloma cells to bone marrow stromal cells. In addition, and perhaps more importantly, elotuzumab induces antibody dependent cellular cytotoxicity of myeloma cells through an NK cell mechanism.

Phase 1 study of single-agent elotuzumab in relapsed/refractory multiple myeloma patients demonstrated good tolerability. Adverse reactions were primarily limited to infusion reactions during the first dose and were common. Chills, flushing, pyrexia, rigors, dyspnea and fatigue were reported and graded 1 or 2. Doses of more than 5 mg/kg led to a serum half life of 10 to 11 days, with maximum serum concentrations of drug increasing with higher elotuzumab dose levels. Subsequent phase 1 studies have examined the combination of elotuzumab with lenalidomide and dexamethasone in 28 patients, and elotuzumab with bortezomib in 29 patients. Both studies achieved the maximum proposed elotuzumab dose of 20 mg/kg basically given weekly. Infusion reactions again were very common. They were mostly grade 1 or 2, and they were manageable with corticosteroid, antihistamine and acetaminophen. Response to therapy in the relapsed or refractory setting seemed to be enhanced by the elotuzumab-containing combinations. Partial response or better was achieved in 82% of patients in the lenalidomide and dexamethasone study. In the bortezomib study, partial response or better was achieved in 48% of patients. Most interestingly, two of six patients with prior lenalidomide exposure responded to the combination of elotuzumab and lenalidomide (1 PR, 1 VGPR), and two of three patients refractory to bortezomib achieved a partial response with the combination of elotuzumab and bortezomib.

Ongoing randomized phase 3 trials are evaluating lenalidomide and/or bortezomib and dexamethasone with or without elotuzumab in relapsed/refractory and newly diagnosed multiple myeloma. A biomarker study also is examining the use of elotuzumab in high-risk, smoldering multiple myeloma. These investigations ultimately will determine if the addition of elotuzumab to anti-plasma cell therapy increases response rates over standard therapy alone. One concern about the long-term use of this agent may be hypogammaglobulinemia, but reports of infections in the phase 1 studies were mostly mild.

Further evaluation of elotuzumab in other plasma cell disorders is warranted due to the high-level gene expression of CS1 in plasma cells and seeming synergistic effect of this monoclonal antibody with other anti-plasma cell therapies. The finding of elotuzumab-treated patients refractory to either lenalidomide or bortezomib who then responded to these agents when combined with elotuzumab is particularly promising. In addition, the 82% objective response rate in the relapsed/refractory setting with combination lenalidomide and elotuzumab is encouraging and leads to optimism that the inclusion of elotuzumab with standard anti-plasma cell therapy will increase OS of multiple myeloma patients.

For further review of elotuzumab, I would suggest articles by Blade and Benson.

— Jason Valent, MD

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Disclosure: Valent reports no relevant financial disclosures.

Benson Jr DM. *J Clin Oncol*. 2012;30:2013-2015.

Blade J. *J Clin Oncol*. 2012;30:1904-1906.

Hsi ED. *Clin Cancer Res*. 2008;14:2775-2784.

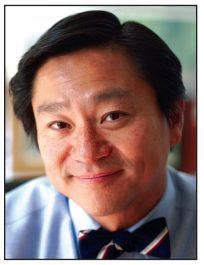
Jakubowiak AJ. *J Clin Oncol*. 2012;30:1960-1965.

Lonial S. *J Clin Oncol*. 2012;30:1953-1959.

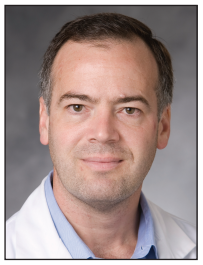
Tai YT. *Blood*. 2008;112:1329-1337.

Zonder JA. Abstract #2773. Presented at: 50th ASH Annual Meeting and Exposition; December 6-9, 2008; San Francisco.

PERSPECTIVE: BLINATUMOMAB



Nelson Chao



David Rizzieri

It is understandable if viewing the long list of agents in clinical development provides the reader a sense of optimism. Blinatumomab (Amgen) is a nice example of a novel approach meeting success. This agent is a bispecific, single-chain antibody derivative against CD3 and 19. It is designed to link T and B cells, thus causing T-cell activation and a cytotoxic T-cell response against CD19-expressing cells, which leads to apoptosis. Clinical evidence is encouraging in multiple lymphoid diseases, with a recent study in relapsed/refractory ALL resulting in 12 of 18 patients attaining a remission (Topp MS. *Blood*. 2011;118:252). Infusional side effects and reversible central nervous system toxicities were the most common toxicities noted. This agent is the first successful exploitation this technology in this field. Its success should lead to future expansion of this approach.

— Nelson Chao, MD, MBA

HEMONC TODAY Editorial Board member

— David Rizzieri, MD

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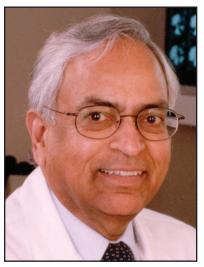
Disclosure: Chao and Rizzieri are co-investigators on a study involving this drug as a treatment for acute lymphoblastic leukemia.

PERSPECTIVE: GS-1101 AND IBRUTINIB



Kanti R. Rai

In the areas in which I am most interested, I am very happy to see two drugs included in the listing of new drugs in the pipeline that are on a rapid course of development, and each one of these are likely to be very effective in improving the natural history of some of the most vexing chronic B-cell malignancies. I am referring to GS-1101 (Gilead Sciences) and ibrutinib (Janssen Biotech, Pharmacyclics). These drugs offer us a path of radical departure from the empirical therapies of the past for chronic lymphocytic leukemia (CLL), indolent lymphoma, diffuse large cell lymphoma and mantle cell lymphoma. The mechanism of activity of both these drugs is by inhibiting certain enzymes (both are kinases), which, in turn, induce trafficking of lymphocytes from the enlarged lymph nodes and bone marrow into the blood. This step removes the cells from the sanctuaries where they enjoyed protection from apoptosis and where they were able to proliferate.

GS-1101 is an inhibitor of PI3 kinase, while ibrutinib inhibits Bruton tyrosine kinase. They both are available in oral formulation as tablets or capsules. They both, as single agents, result in dramatic shrinkage in the size of even massively enlarged lymphoid masses while, transiently, increasing the number of lymphocytes in the circulating blood. Phase 2 and phase 3 trials are currently ongoing with each of the two drugs.

In my opinion, the best results are likely to be seen when each is given in combination with an anti-B cell monoclonal antibody and/or a chemotherapy drug. Initial reports presented at various national and international congresses have been extremely promising and, therefore, there is an understandable level of excitement among treating physicians, as well as the patient communities.

— Kanti R. Rai, MD

HEMONC TODAY Editorial Board member

Disclosure: Rai reports no relevant financial disclosures.

PERSPECTIVE: VELTUZUMAB

Matt Kalaycio

The remarkable efficacy of rituximab (Rituxan, Genentech) against CD20-positive lymphomas has led to the subsequent development of other anti-CD20 targeted agents such as ofatumumab (Arzerra, GlaxoSmithKline). Both of these agents also are effective against chronic lymphocytic leukemia (CLL), but the higher doses of these agents required because of the low CD20 density of CLL cells recently have been shown to be potentially disadvantageous due to "shaving" of the CD20 antigen from complement activation. Veltuzumab (Immunomedics) is another anti-CD20 monoclonal antibody that is active against CD20-positive lymphomas at lower doses. In fact, the doses are so low that it can be concentrated into a formulation that can be given subcutaneously. Thus, veltuzumab may avoid both the shaving phenomenon in CLL and the infusion reactions incurred by rituximab. This intriguing agent is currently being studied in clinical trials in patients with lymphoma and CLL.

— Matt Kalaycio, MD

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