

















A Snapshot of Innovative Therapies in AML

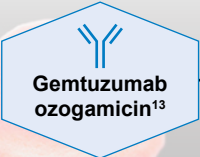



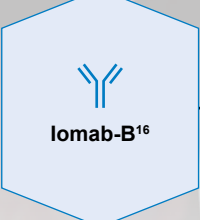
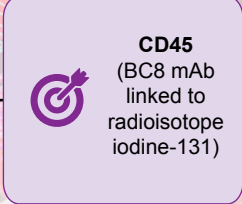

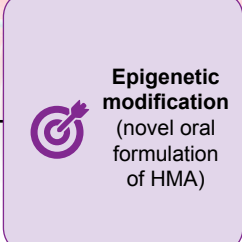
Current Status, Dosing, and Other Considerations

| DRUG | STATUS | TARGET | DOSE | CONSIDERATIONS |
|---|---|--|---|---|
|  CPX-351¹⁻³ | Approved Adults with newly diagnosed t-AML or AML-MRC | Cytotoxic therapy (liposomal cytarabine + daunorubicin 5:1 molar ratio)  | Induction: daunorubicin 44 mg/m ² and cytarabine 100 mg/m ² liposome IV over 90 min on d 1, 3, and 5 ^a | <input type="checkbox"/> Can cause prolongation of blood count suppression; monitor blood counts regularly until recovery <input type="checkbox"/> Not recommended in patients with decreased cardiac function |
|  Midostaurin⁴ | Approved Plus chemotherapy in adults with newly diagnosed <i>FLT3</i> -mutation-positive AML |  FLT3 | 50 mg orally twice daily with food on d 8-21 of each induction cycle with cytarabine and daunorubicin and on d 8-21 of each consolidation cycle with high-dose cytarabine | <input type="checkbox"/> GI events most common <input type="checkbox"/> Promote therapy adherence <input type="checkbox"/> Be mindful of potential drug-drug interactions |
|  Gilteritinib⁵ | Approved Adults with <i>FLT3</i> -mutation-positive R/R AML |  FLT3 | 120 mg orally daily | <input type="checkbox"/> Most common AEs include myalgia/arthralgia, transaminase increase, fatigue/malaise, noninfectious diarrhea, dyspnea, edema, rash, pneumonia, nausea, stomatitis, cough, headache, hypotension, dizziness, and vomiting |
|  Quizartinib⁶⁻⁹ | Phase 3 testing Adults with newly diagnosed and R/R <i>FLT3</i> -ITD-positive AML |  FLT3 | 60 mg used in phase 3 QuANTUM-R study (30-mg lead-in) | <input type="checkbox"/> Most common AEs in early studies included nausea, prolonged QT interval, vomiting, and dysgeusia |
|  Enasidenib¹⁰ | Approved Adults with R/R <i>IDH2</i> -mutation-positive AML |  IDH2 | 100 mg orally daily | Monitor for: <input type="checkbox"/> <i>IDH</i> -differentiation syndrome <input type="checkbox"/> Elevated bilirubin <input type="checkbox"/> GI events <input type="checkbox"/> Leukocytosis |
|  Ivosidenib¹¹ | Approved Adults with <i>IDH1</i> -mutation-positive newly diagnosed AML who are ≥75 years or who have comorbidities that preclude the use of intensive induction chemotherapy or R/R AML |  IDH1 | 500 mg orally daily | Monitor for: <input type="checkbox"/> <i>IDH</i> -differentiation syndrome <input type="checkbox"/> QT prolongation <input type="checkbox"/> Guillain-Barré syndrome <input type="checkbox"/> GI events, nausea, leukocytosis |
|  Venetoclax¹² | Approved In combination with azacitidine or decitabine or low-dose cytarabine for newly diagnosed AML in adults ≥75 years or who have comorbidities that preclude use of intensive induction chemotherapy |  BCL-2 | Ramp-up phase: 100 mg orally on d 1, 200 mg on d 2, 400 mg on d 3; d 4 and beyond: 400 mg (with HMA) or 600 mg (with low-dose cytarabine) | <input type="checkbox"/> Most common AEs as part of combination therapy in AML include nausea, diarrhea, thrombocytopenia, constipation, neutropenia, febrile neutropenia, and fatigue (among others) ^p <input type="checkbox"/> Standard monitoring and prophylaxis measures for TLS are recommended |



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|  <p>Gemtuzumab ozogamicin¹³</p> | <p>Approved Newly diagnosed CD33+ AML in adults, R/R CD33+ AML in adults, and in pediatric patients aged ≥ 2 years</p> |  <p>CD33</p> | <p>Induction: 3 mg/m² (up to one 4.5-mg vial) on d 1, 4, and 7 in combination with daunorubicin and cytarabine</p> | <ul style="list-style-type: none"> <input type="checkbox"/> Infusion-related reactions <input type="checkbox"/> Premedicate with corticosteroid, antihistamine, and acetaminophen <input type="checkbox"/> Monitor platelet counts frequently (hemorrhage) and signs/symptoms of liver toxicity (VOD) |
|  <p>Glasdegib^{14,15}</p> | <p>Approved In combination with low-dose cytarabine for newly diagnosed AML in adults ≥ 75 years or who have comorbidities that preclude use of intensive induction chemotherapy</p> |  <p>Hhp</p> | <p>100 mg orally daily</p> | <ul style="list-style-type: none"> <input type="checkbox"/> Most common AEs include anemia, fatigue, hemorrhage, FN, musculoskeletal pain, nausea, edema, thrombocytopenia, and dyspnea <input type="checkbox"/> See label for other common AEs and for information on the potential for embryo-fetal toxicity and appropriate management approaches |
|  <p>Iomab-B¹⁶</p> | <p>Phase 3 SIERRA study Adults aged ≥ 55 years with active, R/R AML, adequate organ function, and related/unrelated matched donor</p> |  <p>CD45 (BC8 mAb linked to radioisotope iodine-131)</p> | <p>Dosimetry directed (SIERRA study)</p> | <ul style="list-style-type: none"> <input type="checkbox"/> Preliminary data from the ongoing phase 3 SIERRA trial confirm the feasibility of targeted conditioning with Iomab-B with near-universal and rapid engraftment of older patients with active AML and high BM blast burden <input type="checkbox"/> No nonrelapse mortality reported in the Iomab-B arm; select nonhematologic AEs included stomatitis, malnutrition, and epistaxis, among others |
|  <p>Oral azacitidine^{17,18}</p> | <p>Phase 2 data as maintenance therapy post-HCT in AML Phase 3 QUAZAR study Maintenance with oral azacitidine in adults aged ≥ 55 years with AML in first complete remission induced substantial improvements in OS and RFS following induction chemotherapy +/- consolidation (non-HCT candidates)</p> |  <p>Epigenetic modification (novel oral formulation of HMA)</p> | <p>300 mg orally daily for 14 d of 28-d treatment cycles (QUAZAR study)</p> | <ul style="list-style-type: none"> <input type="checkbox"/> In phase 3 testing, most common grade 3/4 AEs included neutropenia, thrombocytopenia, and anemia |

^a For additional induction, use d 1 and 3 for subsequent cycles, if needed; for consolidation: daunorubicin 29 mg/m² and cytarabine 65 mg/m² liposome IV over 90 min on d 1 and 3. ^b See prescribing information for a complete list of common AEs with venetoclax combinations in AML.¹²

AML: acute myeloid leukemia; AML-MRC: AML with myelodysplasia-related changes; BCL-2: B cell lymphoma 2; BM: bone marrow; CD: cluster of differentiation; FLT3: fms-like tyrosine kinase 3; FN: febrile neutropenia; HCT: hematopoietic cell transplantation; Hhp: hedgehog pathway; HMA: hypomethylating agent; IDH: isocitrate dehydrogenase; ITD: internal tandem duplication; mAb: monoclonal antibody; RFS: relapse-free survival; R/R: relapsed or refractory; t-AML: therapy-related acute myeloid leukemia; TLS: tumor lysis syndrome; VOD: veno-occlusive disease.

1. Lancet JE et al. 52nd Annual Meeting of the American Society of Clinical Oncology (ASCO 2016). Abstract 7000. 2. Lancet JE et al. 2017 Annual BMT Tandem Meetings (BMT Tandem 2017). Abstract 19.3. Vyxeos (daunorubicin and cytarabine) Prescribing Information. <http://pp.jazzpharma.com/pi/vyxeos.en.USPI.pdf>. 4. Rydapt (midostaurin) Prescribing Information. <https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/rydapt.pdf>. 5. Xospata (gilteritinib) Prescribing Information. <https://astellas.us/docs/xospata.pdf>. 6. <https://clinicaltrials.gov/ct2/show/NCT02668653>. 7. <https://clinicaltrials.gov/ct2/show/NCT02039726>. 8. Cortez J et al. 23rd Congress of the European Hematology Association (EHA 2018). Abstract LB2600. 9. <https://pharmaphorum.com/market-access-2/fda-grants-leukaemia-drug-breakthrough-status/>. 10. Idhifa (enasidenib) Prescribing Information. <https://media.celgene.com/content/uploads/idhifa-pi.pdf>. 11. Tibsovo (ivosidenib) Prescribing Information. <https://www.tibsovo.com/pdf/prescribinginformation.pdf>. 12. Venclaxta (venetoclax) Prescribing Information. <https://www.rxabbvie.com/pdf/venclaxta.pdf>. 13. Mylotarg (gemtuzumab ozogamicin) Prescribing Information. <http://labeling.pfizer.com/ShowLabeling.aspx?id=9548>. 14. <https://www.fda.gov/drugs/fda-approves-glasdegib-aml-adults-age-75-or-older-or-who-have-comorbidities>. 15. Daurismo (glasdegib) Prescribing Information. <http://labeling.pfizer.com/ShowLabeling.aspx?id=11336>. 16. Agura E et al. 60th American Society of Hematology Annual Meeting and Exposition (ASH 2018). Abstract 1017. 17. Roboz GJ et al. *Future Oncol*. 2016;12:293-302. 18. Wei AH et al. 61st Annual Meeting and Exposition of the American Society of Hematology (ASH 2019). Abstract LBA-3.

Access the activity, "Advances in AML Care: Highlights From Recent Science," at [PeerView.com/VKE40](https://www.peerview.com/VKE40)