

# Menin inhibitors: A promising new class of treatment for AML



## KEY TAKEAWAYS

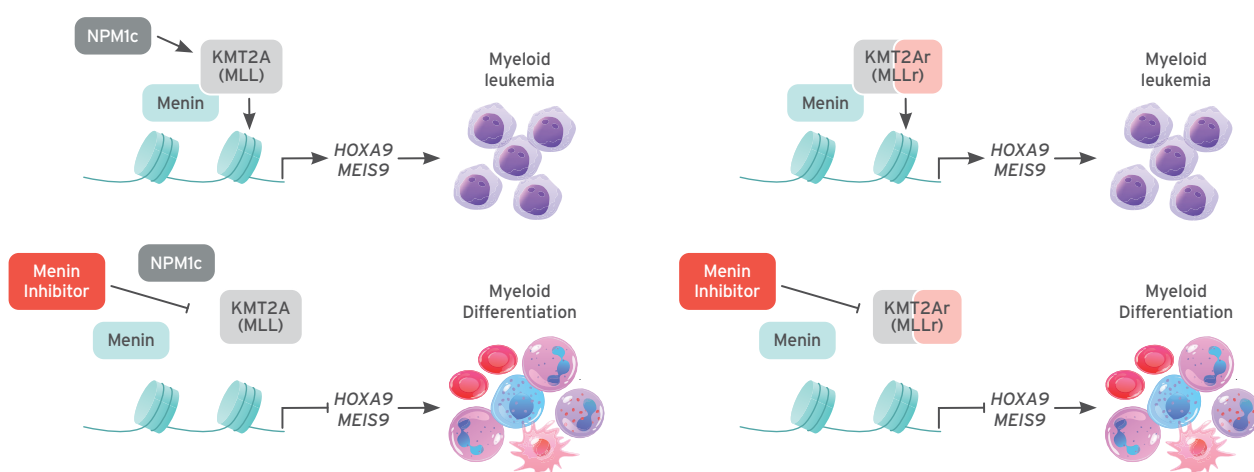
- Overall outcomes in patients with R/R AML remain **very poor** even with the availability of targeted treatments
- **Menin inhibitors** are new treatments currently in clinical development and show promise for R/R AML with *KMT2A* rearrangements or *NPM1* mutations

## Overview of menin inhibitors

Menin inhibitors are a new class of drugs currently being developed to treat acute myeloid leukemia (AML). They **show promise** for patients whose leukemia is associated with specific genetic changes like *KMT2A* rearrangements (*KMT2Ar*) or *NPM1* mutations (*NPM1m*).

## How menin inhibitors work

Certain types of acute leukemia, specifically those with *MLL/KMT2A* rearrangements and *NPM1* mutations, develop and grow because of abnormal activity in certain genes (*HOX* and *MEIS1*). This abnormal activity is linked to a protein interaction involving menin and *KMT2A*. By targeting and blocking the menin-*KMT2A* interaction, menin inhibitors can potentially stop or slow down the growth of these leukemia cells.



## Clinical challenges and common side effects seen in early studies

- **Side effects:** Some menin inhibitors can cause QT interval prolongation (a heart rhythm issue) and differentiation syndrome (a severe reaction to cancer treatment)<sup>1</sup>
- **Drug interactions:** Dose adjustments may be needed when menin inhibitors are taken with certain other medications<sup>1</sup>
- **Resistance mutations:** Some patients may develop mutations that make the treatment less effective over time<sup>2</sup>

## Key findings from recent studies presented at EHA 2024

### 1. DSP-5336<sup>1</sup>

- Phase 1/2 study
- DSP-5336 was tested on **57 patients** with relapsed or refractory (R/R) acute leukemia with *KMT2Ar* and *NPM1m*
- DSP-5336 was well-tolerated and overall, **57% of patients with R/R AML responded to the treatment**
- The study is ongoing to find the best dose for Phase 2

### 2. Bleximenib (JNJ-75276617)<sup>3</sup>

- Phase 1b study
- Bleximenib was tested in combination with other drugs (venetoclax and azacitidine) in **34 patients** with R/R AML with *KMT2Ar* and *NPM1m*
- Bleximenib was well-tolerated and overall, **79% of patients responded to the treatment**
- The study is ongoing to find the best dose for Phase 2

### 3. Balomenib (ZE63-0302)<sup>2</sup>

- Pre-clinical studies
- Balomenib was designed to avoid resistance mutations and severe side effects
- Balomenib showed **promising results** in animal models
- Currently being tested in healthy volunteers to further understand its safety and how it moves through the body



## WHAT DOES THIS MEAN FOR PATIENTS?

Menin inhibitors are promising new drugs for treating AML and are currently being developed. These drugs are particularly effective for patients with specific genetic changes, such as *KMT2A* rearrangement and *NPM1* mutations, which occur in about one-third of patients with AML.

Early clinical trials have shown potential, but have also reported some cases of cardiac toxicity and the development of resistance mutations. Despite these challenges, menin inhibitors have demonstrated encouraging results in terms of response rates, even in heavily pre-treated patients. This progress offers hope for improved treatment outcomes for those with R/R AML and specific genetic changes. Ongoing trials aim to determine the optimal dosage and further ensure the safety of these new menin inhibitors.

**References:** 1. Daver N, et al. Presentation at 29th European Hematology Association (EHA) Congress, Madrid. June 13-16, 2024. Abstract #S132; 2. Hertlein E, et al. Presentation at 29th EHA Congress, Madrid. June 13-16, 2024. Abstract #S130; 3. Wei H, et al. Presentation at 29th EHA Congress, Madrid. June 13-16, 2024. Abstract #S133.