VENTURA · ACUTE MYELOID LEUKEMIA

Ventura

Ranked FDA-approved drug combinations for refractory disease.

PATIENT ID	INDICATION	AGE / SEX	REPORT DATE
CW-2026-002311	R/R AML	59 / F	Jun 18, 2026

TOP COMBINATION (FDA-APPROVED INGREDIENTS)

Glasdegib + Decitabine + Venetoclax

Hedgehog inhibition restores ven sensitivity in BCL-2 escape; HMA primes the response.

78

VENTURA SCORE / 100

TOP 10 COMBINATIONS · RANKED BY PREDICTED RESPONSE

Mechanism-grounded combinations of FDA-approved drugs; off-label use to be reviewed by ordering MD.

#	Combination	Rationale	Score
1	**Glasdegib + Decitabine + Venetoclax**	Hedgehog + HMA + BCL-2 re-sensitization	78
2	**Selinexor + Venetoclax + Azacitidine**	XPO1 + BCL-2 + HMA epigenetic priming	73
3	**Quizartinib + Azacitidine + Venetoclax**	FLT3-i (subclonal) + HMA + BCL-2	68
4	**Gemtuzumab Ozogamicin + Decitabine**	CD33 ADC + HMA	64
5	**Ivosidenib + Venetoclax**	IDH1 inhibition (low-VAF) + BCL-2	61
6	**Mitoxantrone + Etoposide + Cytarabine (MEC)**	Cytotoxic salvage	55
7	**Vyxeos (CPX-351)**	Liposomal cyto/dauno	52
8	**Magrolimab + Azacitidine**	CD47 + HMA (clinical-trial only)	48
9	**Pevonedistat + Azacitidine**	NEDD8 + HMA	44
10	**Allogeneic HSCT prep**	Cellular therapy bridge	—

WHY THIS COMBINATION · MECHANISTIC RATIONALE

Glasdegib + Decitabine + Venetoclax

Patient escape mechanism: BCL-2 family rebalancing toward MCL-1.

After three prior lines (HMA → ven+aza → CAR-T), CBM modeling indicates BCL-2 dependency loss and MCL-1 upregulation drive resistance. Pure BCL-2 re-challenge predicted at TRI 24.

Why Hedgehog: leukemic-stem-cell self-renewal axis.

Glasdegib inhibits SMO in the Hedgehog pathway, depleting the LSC pool that fuels MCL-1 expression. CBM predicts 38% LSC depletion at standard glasdegib dosing.

Why HMA: epigenetic re-priming.

Decitabine resensitizes TP53-WT clones to apoptosis and reopens the BCL-2 dependency window lost during prior venetoclax exposure.

Why venetoclax (re-challenge): now with restored sensitivity.

With LSC depleted and BCL-2 dependency restored, predicted ORR climbs from 11% (ven alone) to 56% (combination).

VALIDATION

78% blinded accuracy

Takeda TAK-659 cell-line study · 70 lines · independently blinded

METHODS

Mechanistic biosimulation across the Cellworks Computational Biology Model (CBM):

- Evaluates infinite combinations of FDA-approved drugs against the patient-specific tumor state
- Each combination scored on mechanism alignment + predicted response (Ventura Score 0–100)
- Only combinations using FDA-approved ingredients reported; off-label use noted

Reference: 350+ drug library · CBM v26.2 · 100K+ patient-history priors · CLIA-certified delivery.

DISCLAIMER

This is an example report demonstrating Cellworks Ventura deliverable format.
Actual patient reports are derived from real molecular data and reviewed by ordering physicians.
Off-label combinations require informed consent and IRB review where applicable. Sources cited inline.