# (PS1638) ODYSSEY: A FIRST-IN-HUMAN STUDY OF THE ALDEHYDE DEHYDROGENASE (ALDH) INHIBITOR ABD-3001 IN PATIENTS WITH REFRACTORY/RELAPSED ACUTE MYELOID LEUKEMIA (AML) OR HIGH-RISK MYELODYSPLASTIC SYNDROME (MDS)

**Topic:** 04. Acute myeloid leukemia - Clinical

Mael Heiblig*[1], Lina Benajiba[2], Julien Colle[3], Sandrine Loron[1], Juliette Soret-Dulphy[2], Rafael Daltro de Oliveira[2], Geoffroy Venton[2], Marie-Virginie Larcher[1], Laure Farnault/De Lassus[3], Charlotte Gandillon[4], Muhube Yazir[4], Mileidys Perez[4], Ismail Ceylan[4], Guillaume Martin[4], Annick Pelletier[3], Jean-Jacques Kiladjian[2], Régis Costello[3]

*[1]Centre Hospitalier Lyon Sud, Service Hématologie, Centre d'Investigation des thérapeutiques en oncologie et hématologie de Lyon (CITHOL), Lyon, France; [2]Hôpital Saint-Louis, Service d'Hématologie seniors, Centre d'Investigation Clinique, 14-27 Saint-Louis, Paris, France; [3]Hôpital de la Timone, Service Hématologie et Thérapie Cellulaire, Centre d'Essais Précoces en Cancérologie de Marseille (CEPCM), Marseille, France; [4]Advanced BioDesign, Saint-Priest, France;*

## Background

Despite recent therapeutic progress in acute myeloid leukemia (AML) and high-risk myelodysplastic syndromes (HR-MDS), outcomes for patients with relapsed/refractory (R/R) disease remain poor, underscoring the need for novel targeted approaches. Aldehyde dehydrogenase 1 (ALDH1) is emerging as a promising therapeutic target, as its overexpression is associated with leukemic stemness, chemoresistance, and adverse prognosis. ABD-3001 is a first-in-class, selective ALDH1 inhibitor currently under investigation as monotherapy in R/R AML and HR-MDS (NCT05601726).

## Aims

We report results from the Dose Ranging Study (DRS) of this ongoing multicenter Phase 1 trial. The primary objective is to determine the recommended Phase 2 dose (RP2D) and evaluate safety. Secondary objectives include pharmacokinetics (PK), pharmacodynamics (PD), and preliminary clinical activity.

## Methods

Patients (pts) enrolled in the DRS received intravenous ABD-3001 on 28-day cycles for up to 3 cycles. Three regimens were assessed: 270 mg/m² once weekly (QW), 270 mg/m² twice weekly (BIW) and 405 mg/m² BIW. Adverse events (AEs) were graded by NCI CTCAE v5.0. The safety population included all pts receiving ≥1 dose. Efficacy per ELN 2017 criteria was evaluated in pts completing ≥1 cycle. Target engagement was assessed by ALDH1 activity inhibition and JNK phosphorylation (pJNK) as a molecular PD biomarker.

## Results

As of February 25, 2026, 24 pts (19 AML; 3 HR-MDS) were treated. Median age was 74 years (range 29–89); 62.5% were female; 62.5% had ECOG PS 1. ELN 2022 risk was adverse in 78.9% and intermediate in 26.3%. Pts received a median of 6 prior lines (range 2–69); 62.9% were previously exposed to venetoclax + azacitidine; 12.5% were post-HCT. Key mutations included TP53 (17%), N/KRAS (21%), and FLT3-ITD (4%).
Treatment-related AEs (TRAEs) occurred in 18/24 pts (75%). The most frequent TRAEs were fever (29.1%), infusion-related reactions (IRRs, 20.8%), catheter infection (16.6%), and diarrhea (12.5%). Grade ≥3 TRAEs occurred in 12 pts (50%), mainly IRR (8.3%), interstitial pneumonitis (8.3%), dyspnea (8.3%), and febrile neutropenia (8.3%). ABD-3001-related dose interruptions occurred in 3 pts (12.5%), one per dosing level.
Among 15 evaluable pts, 1 achieved complete remission (CR) and 1 CR with incomplete recovery (CRi). Six pts (40%) exhibited a reduction in bone marrow blasts, including three with ≥50% decrease.
PK analyses showed systemic exposure at all doses with non–dose-proportional increases and no accumulation over 3 cycles. PD data demonstrated consistent ALDH1 inhibition and pJNK activation, with 270 mg/m² showing stronger biological activity than 405 mg/m², supporting a non-linear dose–response relationship.

## Summary/Conclusion

ABD-3001 demonstrated an acceptable and manageable safety profile across all dosing regimens in this first-in-human setting. Early signals of anti-leukemic activity were observed, with 40% of evaluable pts achieving a reduction in marrow blasts, including one CR and one CRi. PD data confirmed on-target ALDH1 inhibition and downstream pathway activation.
These findings support ongoing evaluation of ABD-3001 to determine the RP2D and guide further clinical development in R/R AML and HR-MDS.