

# Venetoclax plus hypomethylating agents for the treatment of patients with acute myeloid leukemia

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## Introduction

Venetoclax (VEN) is a selective BCL-2 inhibitor that has been shown to be effective when used in combination with hypomethylating agents (HMAs) or, at less extent, low-dose cytarabine (LDAC) for the treatment of elderly patients with acute myeloid leukemia (AML), who are unfit for intensive chemotherapy (IC). In particular, complete remission rates (CR) and median survival in selected molecular subgroups approximate or also exceed those currently achievable with conventional IC, raising the question of the possible use of VEN-HMA in patients potentially eligible to IC, including young adult ones. However, while enthusiasm and excitement for these results seem to be fully justified, a number of questions still remain unresolved: (1) will data of phase 1-2 studies and registration studies be reproduced in the real world? (2) which unfit criteria would be adopted for the definition of the ideal candidates to receive the combination? (3) Should all patients with unfavorable molecular findings at presentation, mostly those with concomitant TP53 mutation and complex karyotype, independently from age, receive Ven/HMA? (4) How to elect between azacitidine (AZA) or decitabine (DEC) in combination with Ven? (5) Is Ven/HMA therapy an ideal bridge to allogeneic transplantation? (6) which treatment for refractory or relapsing patients after therapy with VEN/HMA