# Budget Impact Analysis of Venetoclax Combination Therapies for the Treatment of Newly Diagnosed Acute Myeloid Leukemia Patients Who Are Aged 75 Years or Older, or Who Have Comorbidities That Preclude Use of Intensive Induction Chemotherapy

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## OBJECTIVE

Based on the evolving treatment landscape, a budget impact analysis (BIA) was conducted to assess the adoption of venetoclax + HMAs for newly diagnosed AML patients who are aged 75 or older or who have comorbidities precluding use of intensive chemotherapy, from a US third-party payer perspective. The BIA incorporated the latest market projections and the final analysis of VIALE-A trial data, ensuring that the clinical inputs for venetoclax + azacitidine reflected the most up-to-date evidence.

## CONCLUSIONS

The adoption of venetoclax provides the potential to avoid subsequent AML management costs for patients with newly diagnosed AML who are aged 75 years or older, or who have comorbidities that preclude use of intensive chemotherapy. The cost saving offsets the increased drug cost, leading to a reduced overall budget impact.

There were larger budget savings associated with venetoclax entry from 100% Medicare perspective because of the increased target population size.

Adding venetoclax to the formulary for this indication could reduce the budget impact on a US payer, while providing a robust alternative to address the unmet needs in this patient population.

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## Disclosures

AbbVie and Genentech sponsored, designed, and interpreted the data, and reviewed the final version. Y. Xu, J. Nguyen and K. Miu are employees of and have equity ownership on AbbVie. C.W. Lin and M. Montez are employees of and have equity ownership on Genentech. X. Chai and X. Chen are employees of Analysis Group, Inc., which has received funding from AbbVie and Genentech for the conduct of this research. T.W. LeBlanc has received honoraria for consulting/advisory boards from AbbVie, Aglilx, Agios/Servier, Apellis, Astellas, BMS/Celgene, Genentech, Gilead, GSK, Lilly, Menarini/Stemline, Novartis, and Pfizer; speaking related honoraria from AbbVie, Agios, Astellas, BMS/Celgene, GSK, Incyte, and Rigel; equity interest in Dosentrx and ThymeCare (stock options in privately held companies); royalties from UpToDate; research funding from AbbVie, AstraZeneca, BMS, Deverra Therapeutics/Coeptis, GSK, Jazz Pharmaceuticals, and Seattle Genetics.

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AbbVie and Genentech

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## INTRODUCTION

- While intensive induction chemotherapy is the standard of care for patients with newly diagnosed acute myeloid leukemia (AML), many patients—especially those who are older or have severe comorbidities, organ dysfunction, or poor performance status—face an unacceptably high risk of complications and treatment-related mortality.[1-4]
- These patients were routinely treated with low-intensive treatments such as hypomethylating agents (HMAs), including azacitidine or decitabine, and low dose cytarabine (LDAC).[1,3] Over the past decade, the US Food and Drug Administration (FDA) has approved several novel drugs for patients who are 75 years or older, or who have comorbidities that preclude the use of intensive induction chemotherapy, including venetoclax + HMAs/LDAC, glasdegib + LDAC, and ivosidenib with or without azacitidine (with IDH1 mutation). Gemtuzumab ozogamicin is another treatment used in clinical practice.
- Venetoclax, an orally bioavailable BCL-2 inhibitor, has demonstrated high efficacy and safety in this population, and the combination with azacitidine or decitabine was approved by FDA in 2020.
  - Initial phase 1b trials (NCT02203773) confirmed efficacy and tolerability, and these findings were validated in the phase 3 VIALE-A trial (NCT02993523), where venetoclax plus azacitidine significantly improved overall survival (OS), remission rates, duration of remission, and transfusion independence (TI) compared to azacitidine alone.[5-8]
  - The 2025 National Comprehensive Cancer Network (NCCN) guidelines recommend venetoclax plus azacitidine as a category 1 preferred option for patients ineligible for intensive chemotherapy regardless of mutation, and venetoclax plus decitabine as a category 2 option.[9]

## METHODS

### MODEL OVERVIEW

- The model was developed to estimate the 3-year budget impact of adopting venetoclax combinations in a hypothetical US health plan with 1 million members (base-case: 60% commercial, 40% Medicare; scenario analysis: 100% Medicare).
- The interventions are venetoclax in combination with azacitidine or decitabine. Although venetoclax + LDAC is also an approved combination use in the US product insert (USPI), it was not included in the current model due to its limited use in the US clinical setting. Comparators were chosen based on FDA approval in similar indication, NCCN guidelines, and current clinical practice, including azacitidine, LDAC, decitabine, ivosidenib, gemtuzumab ozogamicin, glasdegib + LDAC, and ivosidenib + azacitidine.
- Total healthcare costs were estimated under two scenarios: before and after venetoclax's market penetration, and included costs for drug acquisition and administration, adverse events (AE), hospitalization, disease monitoring, blood transfusions, and subsequent AML management. All costs were adjusted to 2024 USD (**Figure 1**).
- The cost calculation also incorporated clinical inputs, including treatment duration, rates of complete remission (CR) and CR with incomplete hematologic recovery (CRi), time to CR+CRi, ≥56 days TI rate and TI duration, and OS.

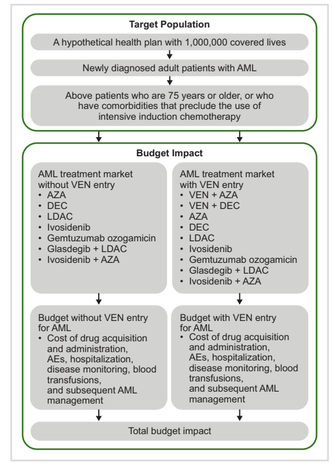
### MODEL ASSUMPTIONS

- The model assumed a constant covered population, incidence rate, and size of the eligible population.
- Drug wastage was considered in the drug cost estimation.
- Patients on posaconazole or strong or moderate CYP3A4 inhibitors were assumed to receive a reduced dosage of venetoclax as indicated in the USPI.[10]
- No mandatory hospitalization was required for patients receiving venetoclax during the treatment initiation period. Hospitalization and monitoring costs during the active treatment period were estimated based on the proportion of patients who achieved CR and CRi, and time to CR+CRi. CR with partial hematologic recovery (CRh) or CR with incomplete platelet recovery were used as proxy of CRi when CRi was not reported in literature.
- Patients who discontinued active first-line treatments received subsequent AML management until the end of the year or death, whichever occurred first.

### MODEL INPUTS

- Target Population: The target population size was estimated using data from the US Census Bureau, the Surveillance, Epidemiology, and End Results (SEER) registries, and published literature.[11-14]
- Market Shares: Based on the latest market projections, venetoclax + azacitidine and venetoclax + decitabine were projected to capture 53% and 15% of the market share, respectively, from all comparators, primarily from azacitidine, ivosidenib, decitabine, and gemtuzumab ozogamicin.
- Costs:
  - Drug costs were calculated using IBM Red Book wholesale acquisition cost, dosing schedules, and treatment duration.[15]
  - Drug administration costs were derived from the Centers for Medicare and Medicaid Services (CMS) physician fee schedule.[16]
  - Grade 3 or 4 AEs that occurred in at least 5% of subjects were included, with AE rates from clinical trials or USPIs and unit costs from Healthcare Cost and Utilization Project Hospital National Inpatient Sample.[10, 17-25]
  - Hospitalization costs were estimated based on the average number of inpatient days per cycle (ie, 28 days), percent of patients achieving CR+CRi, and mean time to CR+CRi reported in the clinical trials.[17-23,26-28] The number of inpatient days and cost per inpatient day were obtained from literature.[29, 30]
  - Monitoring costs were calculated based on monitoring frequency, CR+CRi rates, and mean time to CR+CRi, with monitoring frequency and unit costs from publicly available sources.[16,30]
  - Blood transfusion costs were calculated based on the proportion of patients achieving ≥56-day TI for red blood cell or platelets, TI duration, and transfusion frequencies, with data from literature and CMS Physician Fee Schedule.[16]
  - Subsequent AML management included subsequent treatments, hospitalization, monitoring, transfusion, office visits, emergency department visits, and hospice occurring beyond the active treatment period. Total subsequent AML management costs were estimated from the duration of subsequent AML management (calculated as the difference between mean OS and active treatment duration within 1 year) and the cost per cycle from literature.[31]

**Figure 1. Model framework**




### MODEL OUTPUTS

- The budget impact was presented as total plan costs and per member per month (PMPM) costs and was estimated as the difference between the scenarios with and without the adoption of venetoclax combination therapies.
- Deterministic sensitivity analyses (DSA) and scenario analyses were conducted to assess the sensitivity of the model results to variations in model assumptions and inputs.

## RESULTS

- Target Population: For a hypothetical health plan of 1 million members, the model estimated 48 patients with newly diagnosed AML who are aged 75 or older or who had comorbidities precluding use of intensive chemotherapy.
- Per Patient Costs: The estimated total cost per patient per year was $258,498 for venetoclax + azacitidine, $259,921 for venetoclax + decitabine. The total cost per patient per year for comparators are presented in **Table 1**.

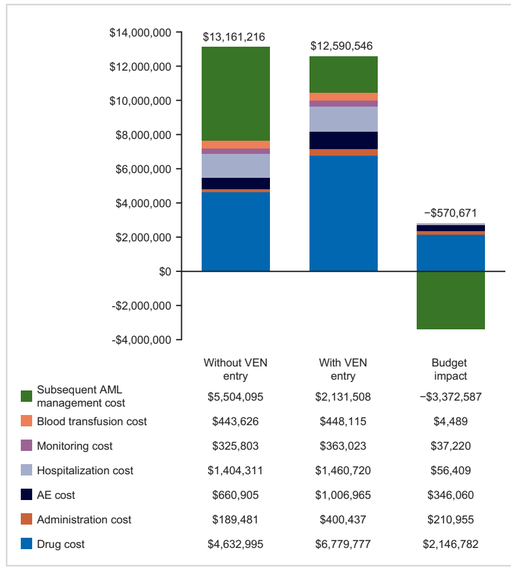
**Table 1. Per patient per year total cost by treatment, 2024 USD**

| Treatment | Drug Cost | Administration Cost | AE Cost | Hospitalization Cost | Monitoring Cost | Blood Transfusion Cost | Subsequent AML Management Cost | Total Cost |
|---|---|---|---|---|---|---|---|---|
| VEN + AZA | $171,096 | $11,152 | $25,211 | $32,548 | $8,330 | $10,161 | $0 | $258,498 |
| VEN + DEC | $141,195 | $8,553 | $22,975 | $26,760 | $6,878 | $6,973 | $46,587 | $259,921 |
| AZA | $22,129 | $7,063 | $18,534 | $35,668 | $8,302 | $9,781 | $105,839 | $207,316 |
| LDAC | $187 | $2,343 | $16,947 | $13,228 | $3,024 | $4,111 | $83,287 | $123,128 |
| DEC | $17,090 | $5,395 | $18,142 | $34,054 | $7,790 | $11,285 | $114,520 | $208,277 |
| Ivosidenib | $218,381 | $0 | $6,346 | $29,848 | $6,967 | $10,840 | $132,488 | $404,869 |
| Gemtuzumab ozogamicin | $67,135 | $738 | $10,868 | $13,091 | $3,027 | $3,416 | $106,197 | $204,472 |
| Glasdegib + LDAC | $82,371 | $7,167 | $14,985 | $19,010 | $4,380 | $5,352 | $197,807 | $331,072 |
| Ivosidenib + AZA | $309,830 | $8,044 | $16,567 | $38,925 | $9,114 | $14,607 | $80,434 | $477,520 |

AE, adverse event; AML, acute myeloid leukemia; AZA, azacitidine; DEC, decitabine; LDAC, low-dose cytarabine; USD, United States Dollar; VEN, venetoclax.

- Total Plan Costs: The adoption of venetoclax combinations was estimated to result in a total plan budget saving of $570,671 per year, for years 1-3 (**Figure 2**).
- PMPM Costs: The adoption of venetoclax combinations was estimated to result in a PMPM cost saving of $0.0476 per year, for years 1-3 (**Figure 3**).
- Cost Attributions: The adoption of venetoclax combinations led to an increase in drug costs (PMPM for drug cost: $0.1789); these were offset by their lower subsequent AML management costs (PMPM for subsequent AML management cost: -$0.2810), resulting in a PMPM cost saving (**Figure 3**).

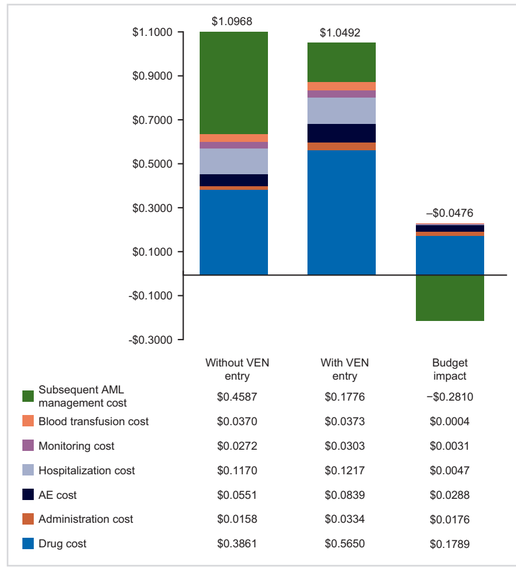
**Figure 2. Budget impact analysis results per year – total plan costs, 2024 USD**




AE, adverse event; AML, acute myeloid leukemia; USD, United States dollars; VEN, venetoclax.

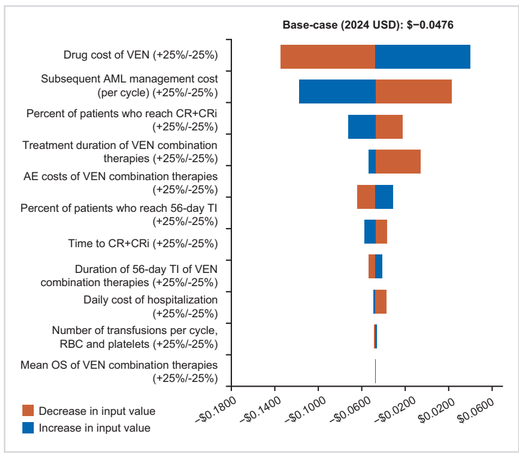
- DSA Results: The results in year 1 (same for year 2 and 3) are presented in **Figure 4**. The model results remained robust in sensitivity analyses, and the model was most sensitive to the unit cost of venetoclax, the subsequent AML management cost, and the percent of patients who reach CR+CRi for venetoclax combinations.
- Medicare Scenario: In a hypothetical health plan with 1 million members and 100% of the population covered by Medicare, the model estimated that 117 patients had newly diagnosed AML who are aged 75 or older or who had comorbidities precluding use of intensive chemotherapy. The budget impact of total plan and PMPM costs was estimated to show a greater magnitude of cost savings, with total plan savings of $1,364,982 and PMPM savings of $0.1137, respectively, per year in years 1-3.

**Figure 3. Budget impact analysis results per year – PMPM costs, 2024 USD**




AE, adverse event; AML, acute myeloid leukemia; USD, United States dollars; VEN, venetoclax.

**Figure 4. DSA – PMPM budget impact, 2024 USD**




AE, adverse event; AML, acute myeloid leukemia; CR, complete response; CRi, complete response with incomplete hematologic recovery; DSA, deterministic sensitivity analysis; RBC, red blood cell; TI, transfusion independence; USD, United States Dollar; VEN, venetoclax.

## LIMITATIONS

- The model factored in mortality up to 1 year, and each year was treated as an independent cohort.
- Efficacy and safety inputs (eg, CR+CRi and AE rates) were based on clinical trials and may not reflect real-world outcomes. For some comparators, inputs came from different trials, limiting comparability.
- While the venetoclax PI reports CR+CRh, CR+CRi was used since it was historically reported in trials for the comparators included in the model. We would expect the impact of these limitations to be minimal because the main driver of the model was drug costs.
- Treatment with venetoclax often involves dose modification and interruptions due to cytopenia as noted in both clinical trials and real-world use. Thus, the drug cost of venetoclax-based therapies may be overestimated in the annual budget estimations.
- Finally, the market share data were based on internal projections from AbbVie and Genentech and are subject to a degree of uncertainty.