

PHASE 2 STUDY OF ASTX727 (DECITABINE/CEDAZURIDINE) PLUS VENETOCLAX IN PATIENTS WITH RELAPSED/REFRACTORY ACUTE MYELOID LEUKEMIA OR PREVIOUSLY UNTREATED, ELDERLY PATIENTS UNFIT FOR CHEMOTHERAPY

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Background

- ASTX727 is an oral formulation of the fixed dose combination of decitabine and cytidine deaminase inhibitor cedazuridine (35 mg/100 mg).
- Combination of hypomethylating agents with venetoclax (ven) is the standard of care for treating patients (pts) with AML unfit for intensive induction chemotherapy based on age and/or comorbidity.
- We investigated whether a total oral therapy regimen of ASTX727 + ven is feasible and safe.

Methods

Eligibility:

- Pts aged ≥18 years with relapsed/refractory (R/R) AML
- Pts with AML aged ≥ 75 or 18 -74 with comorbid conditions prohibiting intensive chemotherapy (frontline-FL).
- Adequate organ function

Regimen:

- ASTX727 PO daily on days 1-5
- Venetoclax PO on days 1-28 of the first cycle after a dose ramp up of 100-200-400 mg over 3 days.
- Bone marrow exam on day 21±3 days and ven held if blasts < 5% to allow count recovery.
- Cycles are repeated every 4-8 weeks and ven is administered for 21 days in subsequent cycles
- Reductions in dose and duration of both drugs permitted depending on count recovery
- Use of growth factors to enhance count recovery was permitted

Patients Characteristics

Patient characteristics and outcomes	Overall N=37 (%)	Front-line Cohort N=28 (%)	Relapsed / Refractory N=9 (%)
Gender			
Male, No. (%)	20 (54)	18 (64)	2 (22)
Female, No. (%)	17 (46)	10 (36)	7 (78)
Age			
Median [Range] years	75 [46-92]	76.5 [50-92]	70 [46-73]
>80 years	12 (32)	12 (43)	0 (0)
PS, Median [Range]	1 [0-3]	2 [0-3]	1 [1-2]
Bone marrow Blast (%) Median, [Range]	30 [8-81]	29 [8-81]	40 [11-63]
Type of AML, No. (%)			
Secondary	14 (38)	12 (43)	2 (22)
Cytogenetics, No. (%)			
Diploid	11 (30)	9 (32)	2 (22)
Complex	15 (41)	11 (39)	4 (44)
Others	9 (24)	7 (25)	2 (22)
Mutations, No. (%)			
ASXL1	11 (30)	9 (32)	2 (22)
DNMT3A	4 (11)	2 (7)	2 (22)
RUNX1	9 (24)	8 (29)	1 (11)
TET2	13 (35)	13 (46)	0 (0)
TP53	6 (16)	4 (14)	2 (22)
Overall Response, No. (%)		16 (57)	5 (56)
CR	10 (27)	7 (25)	3 (33)
CRi	9 (24)	8 (29)	1 (11)
MLFS	2 (5)	1 (4)	1 (11)
Non responders, No. (%)	14 (38)	10 (36)	4 (44)
Overall survival, No. [Range]		NR [0.6-13]	10.1 [3.2-13]

Results

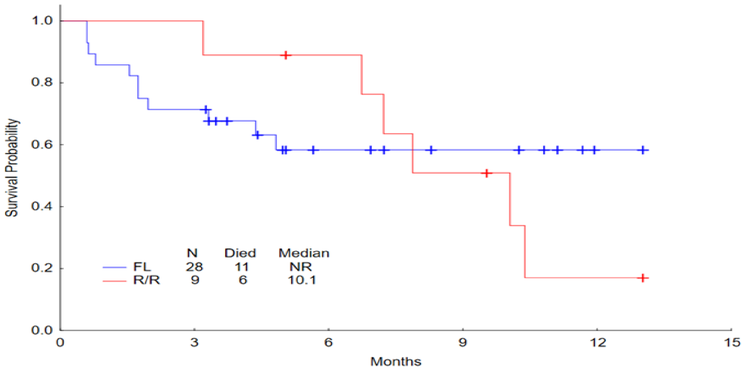
Overall Response Rate:

- FL cohort - **57%** (7 CR, 8 CRi, 1 MLFS and 10 non-responders and 2 not evaluable)
- R/R cohort - **56%** (3 CR, 1 CRi, 1 MLFS with 4 non-responders)

Results

Survival and Toxicity:

- Median follow-up - 7 months
- Median survival – **FL: NR** (range, 0.6-13) months
- Median Survival – **R/R: 10.1** (range, 3.2-13) months
- Adverse event (grade 3 or higher) were mainly **myelosuppression-related**
  - Neutropenic infections in **4 (11%)**
  - Elevation of liver enzymes in 1 (3%) pt.



Conclusion

Total oral therapy of ASTX727 + Venetoclax is safe and feasible, in the advanced elderly population, and demonstrates significant efficacy in pts unfit for chemotherapy in both FL and R/R settings

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