OUTCOMES AFTER TKI DISCONTINUATION IN PATIENTS WITH PH+ ALL TREATED WITH BLINATUMOMAB AND PONATINIB

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INTRODUCTION

- Ph+ ALL is the most common genetic subgroup of ALL in adults
- Historically associated with worse prognosis prior to invention of TKIs
- Chemotherapy-free regimen with blinatumomab and ponatinib has demonstrated improved overall and event-free survival
- Current guidelines recommend maintenance therapy with tyrosine kinase inhibitor (TKI) monotherapy after remission

OBJECTIVE

- Evaluate long-term clinical outcomes following TKI discontinuation in patients with Ph+ ALL treated with B+P.

METHODS

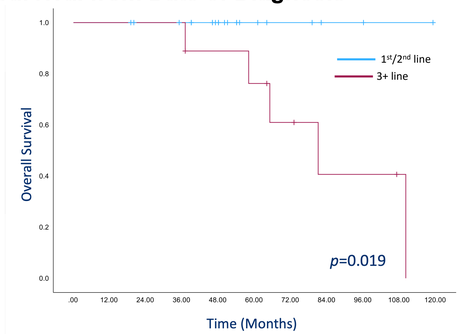
- Retrospective, observational, single-center (Moffitt Cancer Center)
- Inclusion: Adults ≥18 with Ph+ ALL treated with B+P between Jan 2017–Oct 2025 who subsequently discontinued TKI.
  - Includes patients in frontline and relapsed setting
- Primary outcomes: OS and EFS after TKI discontinuation
- Event definition: rising MRD (requiring treatment change), relapse, or death from any cause

BASELINE CHARACTERISTICS

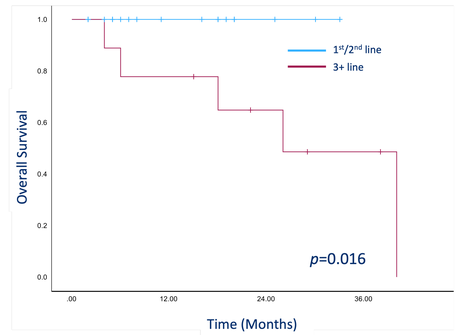
Characteristic	Value
Demographics & Baseline Labs	
Age at diagnosis Median (range), years	**49** 19 – 75
WBC at diagnosis Mean (range), ×10⁹/L · n = 28	**71.2** 2.94 – 454.0
LDH at diagnosis Mean (range), ×ULN · n = 26	**3.86** 0.89 – 13.16
CNS disease prior to blinatumomab n (%)	**6** 19.4%
IKZF1 mutation n (%)	**8** 25.8%
Prior Therapy	
Relapsed/refractory disease n (%)	**16** 51.6%
Prior TKI therapy n (%)	**15** 48.4%
Median number of prior TKIs Median (range), among patients with prior TKI	**1** 1 – 3
Prior ponatinib n (%)	**7** 22.6%
Treatment	
Ponatinib starting dose n (%)	30 mg: 23 (74.2%) 45 mg: 6 (19.4%) 15 mg: 2 (6.5%)
Blinatumomab cycles Median (range)	**3** 1 – 9
Duration of therapy Median (range), months — blinatumomab start to ponatinib end	**30.3** 0.9 – 60.1
CAR-T cell therapy n (%)	**5** 16.1%
Allogeneic stem cell transplant n (%)	**10** 32.3%
MRD Response After Final Blinatumomab Cycle (by clonoSEQ)	
MRD negative n (%)	**20** 64.5%
MRD positive n (%)	**6** 19.4%
No clonoSEQ data available n (%)	**5** 16.1%

RESULTS

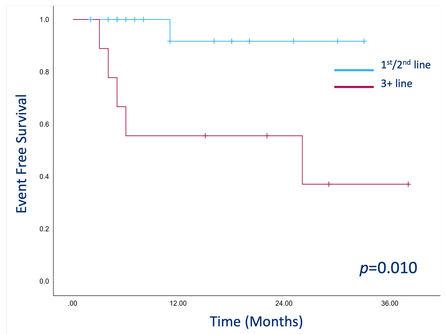
Overall Survival from Date of Diagnosis



Overall Survival from TKI discontinuation



Event Free Survival by Line of Therapy



CONCLUSIONS

- TKI discontinuation after B+P may be safe and feasible in the 1st/2nd line setting after a median of 31 months from the start of B+P (two years of maintenance).
- 3+ Line patients reflect a very high-risk patient population. While TKI discontinuation was feasible for a small number of patients, the risk vs benefit needs to be carefully weighed.

FUTURE DIRECTIONS

- Identify clinical and molecular risk factors that determine TKI discontinuation success

REFERENCES

Kantarjian H, Short NJ, Haddad FG, et al. Results of the Simultaneous Combination of Ponatinib and Blinatumomab in Philadelphia Chromosome-Positive ALL. J Clin Oncol. 2024;42(36):4246-4251. doi:10.1200/JCO.24.00272