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TOLERABILITY AND OUTCOMES OF BRUTON TYROSINE KINASE INHIBITORS FOR CHRONIC LYMPHOCYTIC LEUKEMIA IN PATIENTS WITH SEVERE RENAL DYSFUNCTION

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INTRODUCTION

- There is limited data on the outcomes and tolerability of Bruton Tyrosine Kinase (BTK) inhibitors for chronic lymphocytic leukemia (CLL) in patients with severe renal dysfunction
- Renal dysfunction is a common comorbidity in CLL, both from pre-existing CKD as well as CLL related kidney injury
- The most common BTK inhibitor, ibrutinib, is thought to be safe for use in patients with severe renal dysfunction – however these patients were excluded from prospective studies, and as such there is no guidance on dosing under the FDA label
- In this multicenter study of patients in the National VA healthcare system, we present a retrospective analysis of the safety and tolerability of BTK inhibitors in severe renal impairment

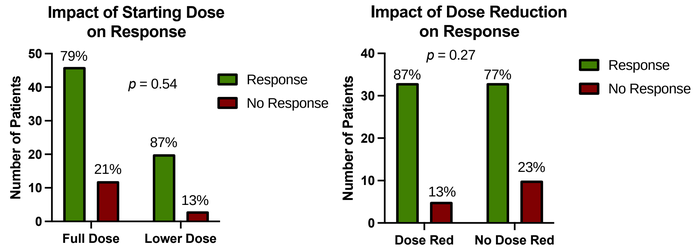
METHODS

- Electronic query of U.S. Veterans Affairs (VA) Corporate Data Warehouse, followed by retrospective review
- **Inclusion Criteria**:
  - Diagnoses of CLL treated with BTK inhibitors between 2013-2022.
  - Severe CKD during treatment period, defined as estimated glomerular filtration rate (eGFR) < 30 ml/min/1.73 m2
- **Exclusion Criteria:**
  - Isolated acute kidney injuries lasting < 1 month
- Only patients who received ibrutinib therapy were included in multivariate analyses
- Fisher's exact test was utilized to evaluate categorical variables, logistic regression for binary outcomes, and log-rank and Cox regression for time-to-event analyses.

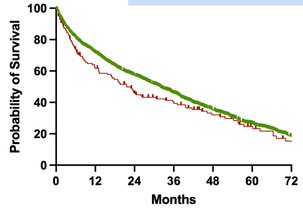
RESULTS

- Electronic query along with subsequent confirmatory chart review identified **115 patients from 68 different VA institutions** who received BTK inhibitors with an eGFR <30 during therapy
- Ibrutinib dose reductions at initiation or during treatment were associated with a longer duration of therapy (mean duration of treatment **41.6 months** with dose reduction vs **19.6 months** without dose reduction)
- Ibrutinib dose reductions did not significantly reduce the response rate to ibrutinib or worsen survival
- No improvement in renal function noted in any patient after BTK inhibitor treatments, including 11 patients with CLL-related kidney dysfunction

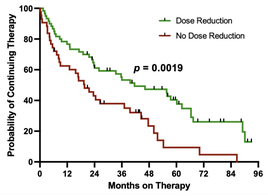
Effect of Ibrutinib Dose on Response



Duration of Therapy



	Without Severe RD	With Severe RD
Median Duration	31.8 months	21.6 months
Hazard Ratio	0.86 (95% CI, 0.69-1.07)	



	Dose Red	No Dose Red
Median Duration	41.6 months	19.6 months
Hazard Ratio	0.50 (95% CI, 0.31-0.82)	

Baseline Characteristics

	BTK (N = 115)
Median age at start of therapy, years (range)	74 (54 – 97)
Male sex, N (%)	113 (98%)
Race, N (%)	
White	79 (69%)
African American	30 (26%)
Asian	1 (1%)
Unknown	5 (4%)
Use of Oral Targeted Agents, N (%)	
Ibrutinib	103 (90%)
Acalabrutinib	18 (16%)
Zanubrutinib	3 (3%)
Renal Dysfunction at start of therapy, N (%)	
eGFR 30-59 ml/min/1.73 m^2	39 (34%)
eGFR 15-29 ml/min/1.73 m^2	51 (44%)
eGFR < 15 ml/min/1.73 m^2	23 (20%)
Unknown eGFR	2 (2%)
Renal Dysfunction during therapy, N (%)	
eGFR 15-29 ml/min/1.73 m^2	68 (59%)
eGFR < 15 ml/min/1.73 m^2	47 (41%)
Dialysis, N (%)	
At start of therapy	21 (18%)
During therapy	35 (30%)
Etiologies of Chronic Kidney Disease, N (%)	
Hypertension and/or diabetes	60 (52%)
Obstructive	12 (10%)
CLL-related	11 (10%)
Other	20 (19%)
Comorbidities, N (%)	
Cirrhosis	5 (4%)
Heart Failure	27 (23%)
Atrial Fibrillation	16 (14%)

CONCLUSIONS

- BTK Inhibitors appear to be a reasonable therapeutic option in severe renal impairment, including in older adults and those on dialysis
- Periodic lab monitoring is needed given the risk of worsening renal function
- Dose modifications may improve tolerability and duration of treatment without reducing efficacy
- Severe renal dysfunction is unlikely to improve with CLL treatment, even in CLL-related kidney failure

ACKNOWLEDGEMENTS

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