HYPERTENSION AS AN ADVERSE EFFECT OF IBRUTINIB: DOES AGE MATTER?

Anahid A. Hamparsumian, Colette A. Whitney, Dan V. Blalock, Andrea L. Sitlinger, Mohammad Shahsahebi, Kevin C. Oeffinger, Leah L. Zullig, and Danielle M. Brander

Department of Medicine at Duke University, the Center for Onco-Primary Care, Duke Cancer Institute, and the Center of Innovation to Accelerate Discovery and Practice Transformation (ADAPT) at the Durham Veterans Affairs Health Care System

Background

- Ibrutinib and other Bruton-tyrosine kinase inhibitors (BTKi) are the mainstays of treatment of chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL).
- Adverse events (AE) due to therapy account for a major cause of treatment discontinuation.[1,2]
- **Hypertension (HTN) is a well-recognized AE of ibrutinib treatment.**[1,2] Hypertension is also associated with age.
- It is important to more fully understand and optimize management of cardiometabolic risk factors such as HTN in patients with CLL/SLL.

Objective

Determine the prevalence of new-onset or uncontrolled HTN following initiation of ibrutinib and whether age is associated with this outcome.

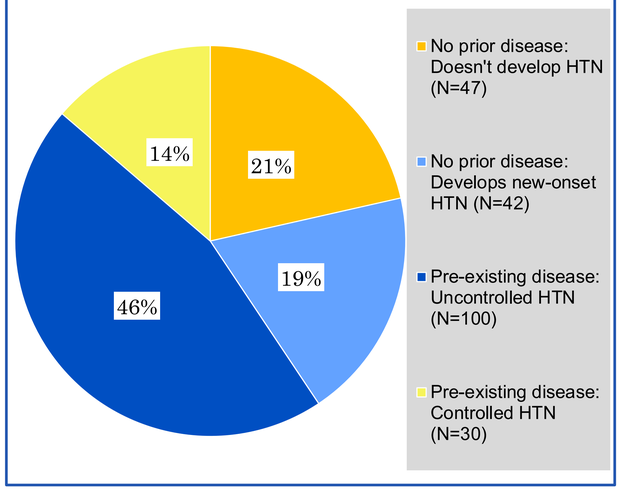
TABLE 1: BASELINE CHARACTERISTICS

	Age < 65yo (N=81)	**Age 65-74yo** (N=81)	**Age ≥ 75yo** (N=57)
Female (%)	33.3	38.3	35.1
BMI (M, SD)	30.0 (7.2)	27.2 (4.4)	26.0 (4.2)
Smoking Status			
Never Smoker (%)	51.9	50.6	45.6
Former Smoker (%)	40.7	45.7	50.9
Current Smoker (%)	7.4	3.7	3.5
Diabetes (%)	28.4	25.0	19.3
Dyslipidemia (%)	48.1	66.7	71.9
CAD (%)	9.9	19.8	31.6

Methods

- Single-center retrospective chart review
- 219 consecutive CLL/SLL patients treated with ibrutinib at Duke University Medical Center from April 2011 through October 2019
- Pre- and post-ibrutinib blood pressures (BP) were reviewed
  - HTN defined as BP ≥ 140/90 mmHg on two consecutive measurements
- Logistic regressions used to predict HTN status using "<65 yo" group as reference

FIGURE 1: DEVELOPMENT OF HTN AFTER INITIATION OF IBRUTINIB



Results

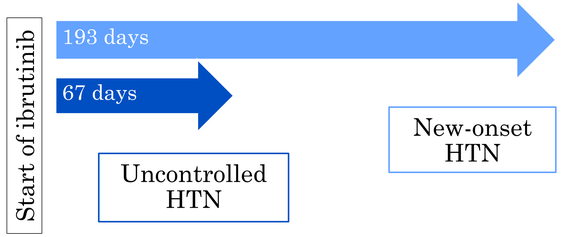
Prior to initiation of ibrutinib:

- 130/219 (59.4%) patients had pre-existing HTN

After initiation of ibrutinib:

- Overall, **142 of 219 (64.8%) patients developed incident or worsened HTN**
- Of the 130 patients with pre-existing HTN: **76.9% developed uncontrolled HTN**
  - Risk was significantly lower in patients ages 65-74yo (p=0.03), compared to those < 65yo
- Of the 89 patients without pre-existing HTN: **47.2% developed new-onset HTN**
  - No significant difference in incidence by age

FIGURE 2: MEDIAN TIME TO DEVELOPMENT OF HTN



Summary

Over two-thirds (65%) of CLL/SLL patients developed new-onset or uncontrolled HTN after starting ibrutinib. Younger adults with pre-existing HTN were at equal or greater risk of developing uncontrolled disease compared to older patients. On average, uncontrolled HTN developed 2 months after initiation of ibrutinib.

Discussion

After initiation of ibrutinib for treatment of CLL/SLL:

- Almost half of patients with no prior diagnosis developed new-onset HTN
  - Younger patients have risk equal to that of older patients for new-onset HTN
- 77% of those with pre-existing disease developed uncontrolled HTN
  - Younger patients are at equal or greater risk of developing uncontrolled HTN
- New-onset HTN developed in 6 months, uncontrolled HTN took only 2 months to develop

These findings highlight the need for close BP monitoring and management of cardiometabolic risk factors in patients being treated for CLL/SLL, including younger patients.

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1. Barr, P.M., Robak, T., Owen, C., et al. Sustained efficacy and detailed clinical follow-up of first-line ibrutinib treatment in older patients with chronic lymphocytic leukemia: extended phase 3 results from RESONATE-2. Haematologica. 2018;103(9):1502-1510.
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