Bone Health and Potential Risk Factors for Bone Loss in Patients with Chronic Lymphocytic Leukemia (CLL)

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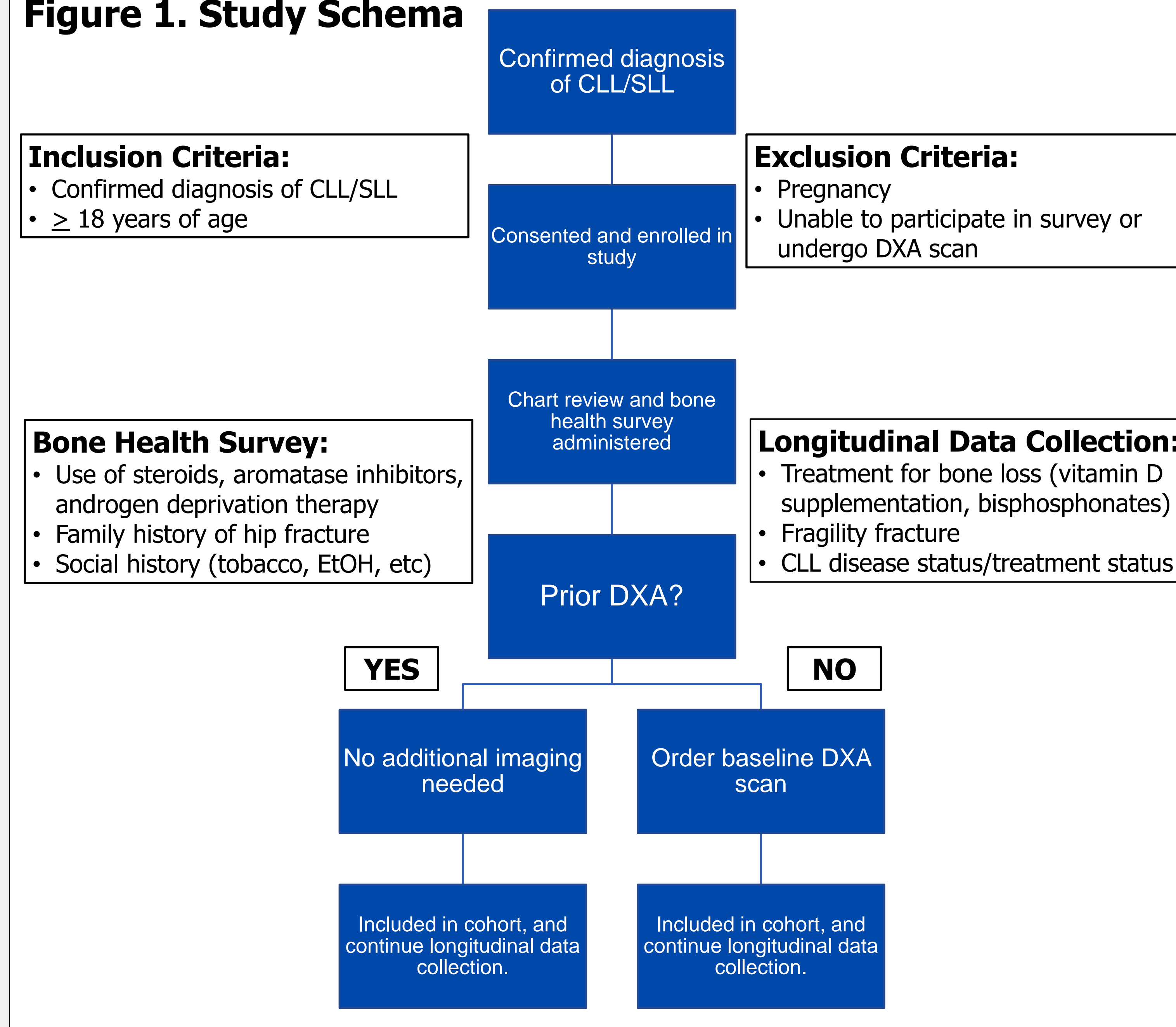[6] Division of Medical Oncology, Department of Medicine, Duke University Medical Center, Durham, NC

Introduction

- Chronic lymphocytic leukemia (CLL) is the most common leukemia in adults with an average age at the time of diagnosis of 72 years.
- Average overall survival in the era of targeted therapies is > 10 years.
- The burden of comorbid conditions significant impacts morbidity and mortality in older patients with CLL [1].
- Olszewki et al published a retrospective case-control study in patients with treatment naïve CLL [2]
    - ↑ risk of axial fractures in patients with CLL compared to controls
- A pilot study published in 2018, aimed to identify hematologic diseases at high risk for bone loss and osteoporosis [3]
    - ↑ bone loss in patients with hematologic malignancies compared to the general population
    - 49% of patients with CLL had bone loss
        - 14% meeting criteria for osteoporosis
        - 39% met criteria for osteopenia
- As osteoporosis is common in the aging population, a fall can lead to significant morbidity, mortality, and cause treatment delays, holds, or discontinuations. Studies have shown inferior EFS and OS in CLL patients following treatment holds [4].

Methods

Figure 1. Study Schema

Confirmed diagnosis of CLL/SLL

Inclusion Criteria:
- Confirmed diagnosis of CLL/SLL
- ≥ 18 years of age

Consented and enrolled in study

Exclusion Criteria:
- Pregnancy
- Unable to participate in survey or undergo DXA scan

Chart review and bone health survey administered

Bone Health Survey:
- Use of steroids, aromatase inhibitors, androgen deprivation therapy
- Family history of hip fracture
- Social history (tobacco, EtOH, etc)

Longitudinal Data Collection:
- Treatment for bone loss (vitamin D supplementation, bisphosphonates)
- Fragility fracture
- CLL disease status/treatment status

Prior DXA?

YES → No additional imaging needed → Included in cohort, and continue longitudinal data collection.

NO → Order baseline DXA scan → Included in cohort, and continue longitudinal data collection.

Preliminary Studies

- Retrospective cohort study aimed at examining the prevalence of osteoporosis, osteopenia, screening of bone mineral density by DXA, use of therapeutics for osteoporosis or osteopenia, and cumulative incidence of fragility fractures.

- **Methods:**
    - Obtained a nationally representative 5% sample of Medicare files from CMS between 2010 – 2015.
    - Defined cohort of beneficiaries with CLL based on diagnosis of CLL
    - Selected non-cancer control cohort (age/sex/race matched)
    - Identified diagnoses based on ICD-9 or 10 codes
    - For DXAs, searched common CPT codes
    - Identified bisphosphonate use using Medicare Part D event records for drug fills and carrier and outpatient facility claims for IV medications.

Table 1. Baseline Characteristics

	CLL cohort (n=10,834)	Comparison cohort (n=54,170)
Age, mean yrs (SD)	78.4 (7.8)	78.4 (7.8)
Sex – Female, n (%)	5,472 (50.5)	27,360 (50.5)
Race – White, n (%)	10,059 (92.8)	50,295 (92.8)
Osteoporosis, n (%)	1,596 (14.7)	7,283 (13.4)
Osteopenia, n (%)	1,108 (10.2)	4,686 (8.7)
Any oral or IV bisphosphonate n/N (%)	161/1,289 (12.5)	938/6,063 (15.5)
Chemotherapy received, n (%)	1,231 (11.4)	1,579 (2.9)

- Patients with CLL had a significantly ↑ incidence of osteoporosis and osteopenia
- However had lower rates of bisphosphonate use

Table 2. Cumulative Incidence of Bone Density Screening

	CLL Cancer Cohort (N=10,834)	Comparison Cohort (N=54,170)	p-value
Bone density screening			
1-year	746 (7.3%) (6.8-7.8%)	3206 (6.4%) (6.2-6.7%)	.001
2-year	1265 (13.1%) (12.4-13.8%)	5265 (11.5%) (11.2,-11.8%)	< .001
3-year	1535 (16.6%) (15.8-17.3%)	6349 (14.7%) (14.4-15.1%)	< .001

- Patients with CLL had a significantly ↑ incidence of BMD screening
- On subgroup analysis, CLL patients who had received chemotherapy had lower rates of screening

Table 3. Cumulative Incidence of Osteoporotic Bone Fractures

	CLL Cancer Cohort (N=10,834)	Comparison Cohort (N=54,170)	p-value
Bone fracture			
1-year	387 (3.7%) (3.4-4.1%)	1600 (3.2%) (3.0-3.4%)	.003
2-year	584 (5.9%) (5.5-6.4%)	2479 (5.4%) (5.1-5.6%)	.009
3-year	744 (8.0%) (7.5-8.6%)	3076 (7.2%) (6.9-7.4%)	.002

- Cumulative incidence of fractures was ↑ in the CLL cohort

Ongoing Study

Patient Demographics
- 17 patients enrolled
- Average Age: 76 years
- 58.8% female
- 41.2% male
- 20% complex karyotype
- 17.6% del17p or TP53 mutations

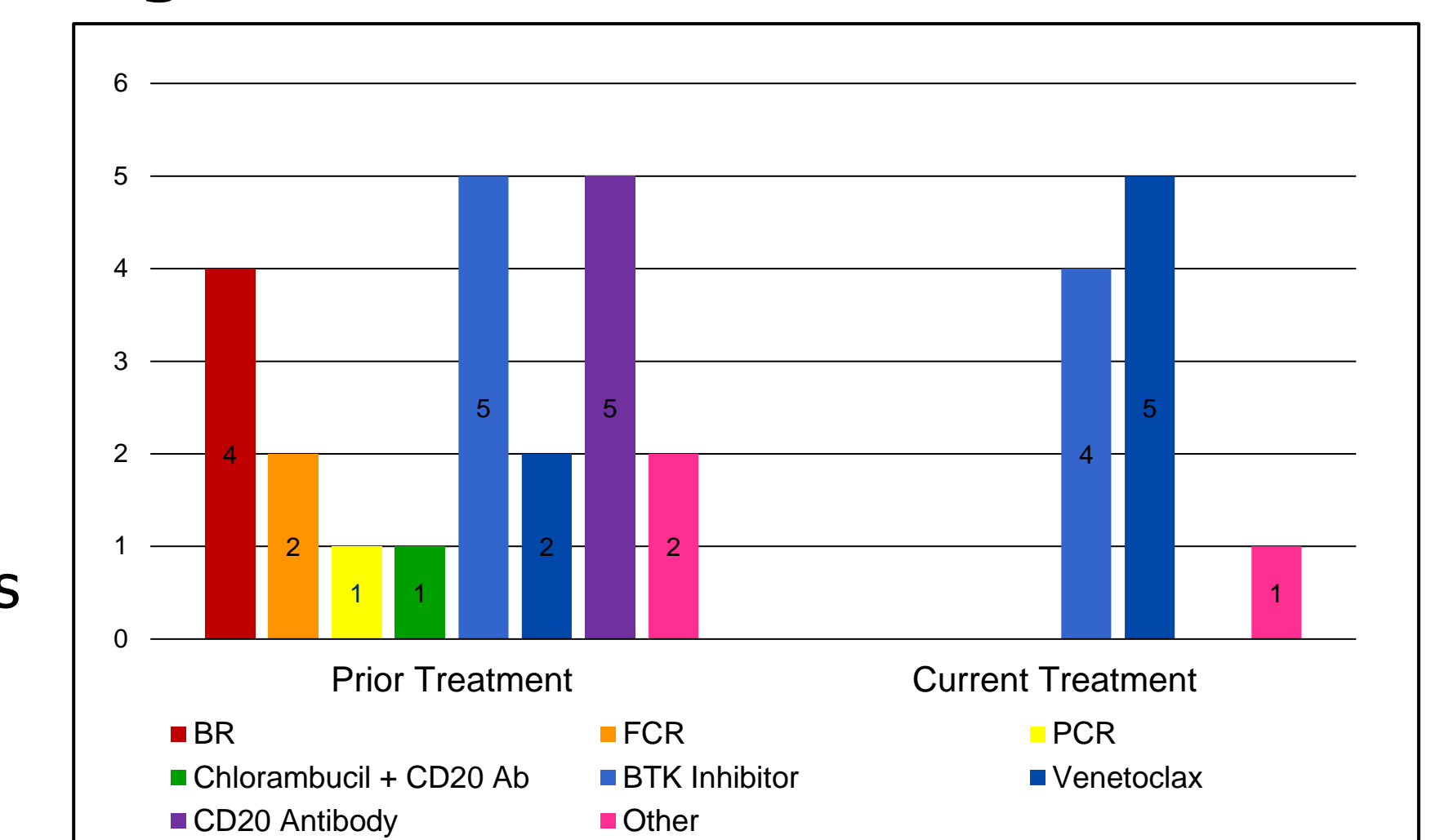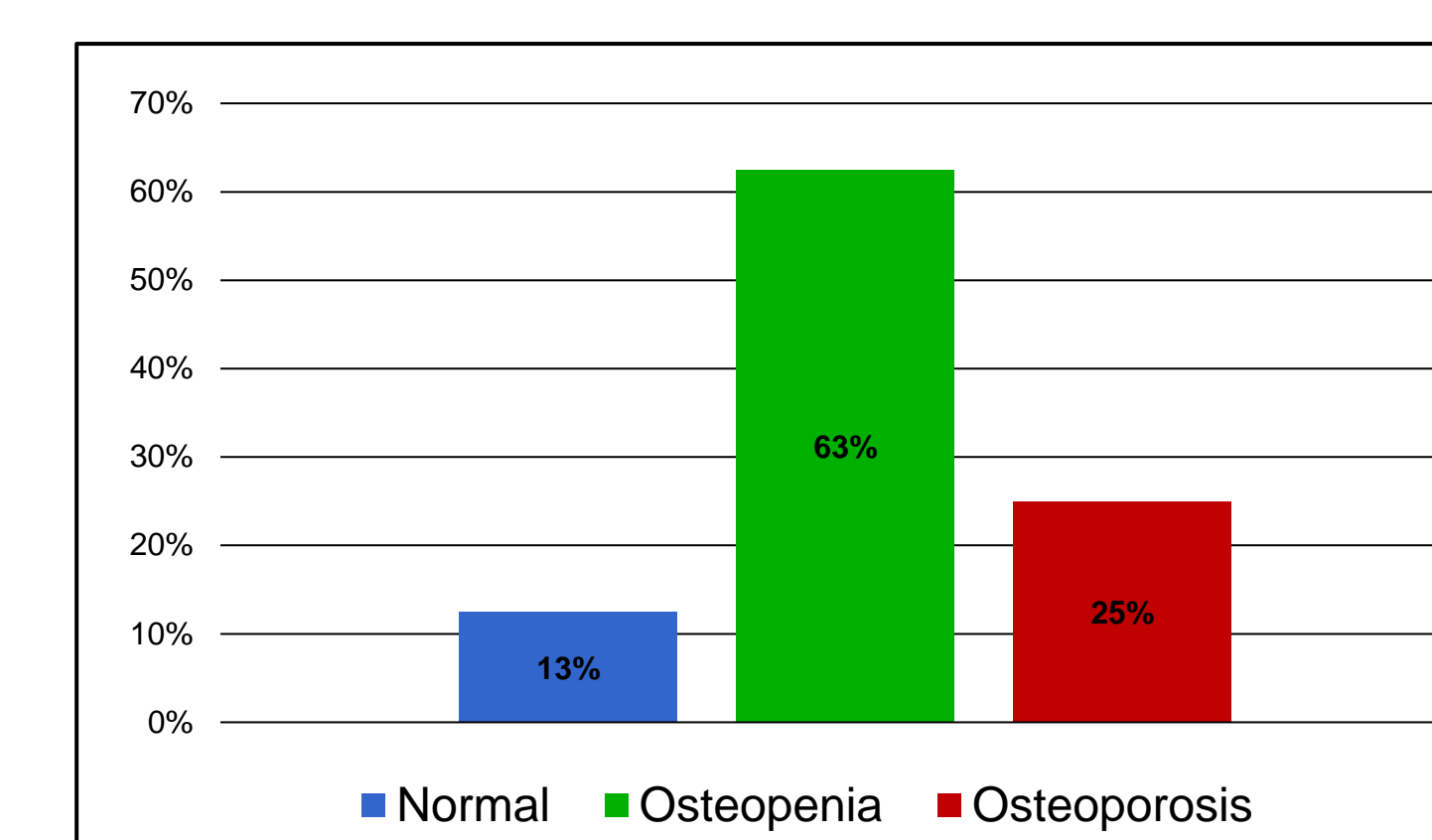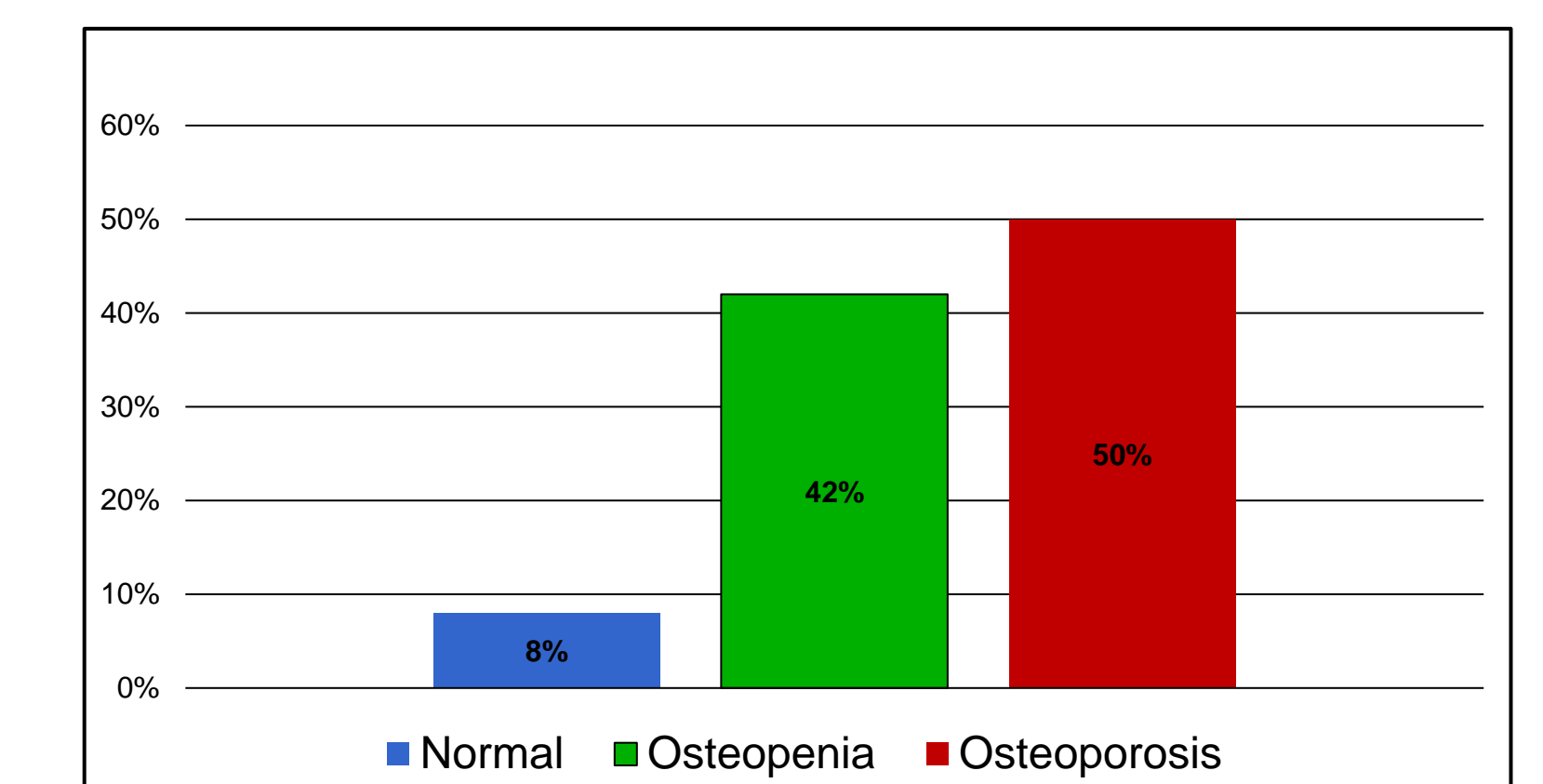Figure 2. Prior and Current Treatment
Legend: BR, Chlorambucil + CD20 Ab, CD20 Antibody, FCR, BTK Inhibitor, Other, PCR, Venetoclax

Figure 3. Results of DXA Scans
Legend: Normal 13%, Osteopenia 63%, Osteoporosis 25%

- **2** with prior hip fractures
- **2** with prior vertebral fractures
- **Risk Factors:**
    - 3 history of steroid use
    - 1 on aromatase inhibitor
    - 2 history of maternal hip fracture
- **Treatment:**
    - 5 Bisphosphonate
    - 8 Ca/Vit D
    - 1 Romosozumab (Evenity)

Clinical Diagnosis for Osteoporosis:
- T-score < -2.5
- History of fragility fracture
- FRAX score = 10-year risk of Major Osteoporotic Fracture > 20% or Hip Fracture > 3%

Figure 4. Clinical Diagnosis
Legend: Normal 8%, Osteopenia 42%, Osteoporosis 50%

References

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2. Olszewski, A.J., R. Gutman, and C.B. Eaton, *Increased risk of axial fractures in patients with untreated chronic lymphocytic leukemia: a population-based analysis.* Haematologica, 2016. **101**(12): p. e488-e491.
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4. Parikh, S.A., et al., *The impact of dose modification and temporary interruption of ibrutinib on outcomes of chronic lymphocytic leukemia patients in routine clinical practice.* Cancer Medicine, 2020. **9**(10): p. 3390-3399.