

COMORBIDITIES, POLY THERAPY AND DRUG-DRUG INTERACTIONS IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA TREATED WITH TARGETED THERAPY



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Background and importance:

The use of Bruton's tyrosine kinase inhibitors (BTKi) and BCL2 inhibitors (BCL2i) has revolutionized chronic lymphocytic leukemia (CLL) treatment. CLL typically occurs in older patients, who have comorbidities and multiple medications in therapy and consequently potential clinically significant drug-drug interactions (DDI), which may have adverse effects on outcomes.

Aim and objectives:

The aim of the study is to assess comorbidity and polytherapy in CLL patients treated with BTKi and BCL2i. Another aim is to determine potential clinically significant DDIs of these drugs.

Materials and methods:

- single-center study in Clinical Hospital Merkur, Zagreb, Croatia
- two-month period
- pharmacist-obtained medication history + medical records
- Cumulative Illness Rating Scale (CIRS)
- medication use categories:
 - low drug use (< 5 medications),
 - polytherapy (5 - 9 medications),
 - excessive polytherapy (≥ 10 medications)
- UpToDate® Lexidrug™

Results:

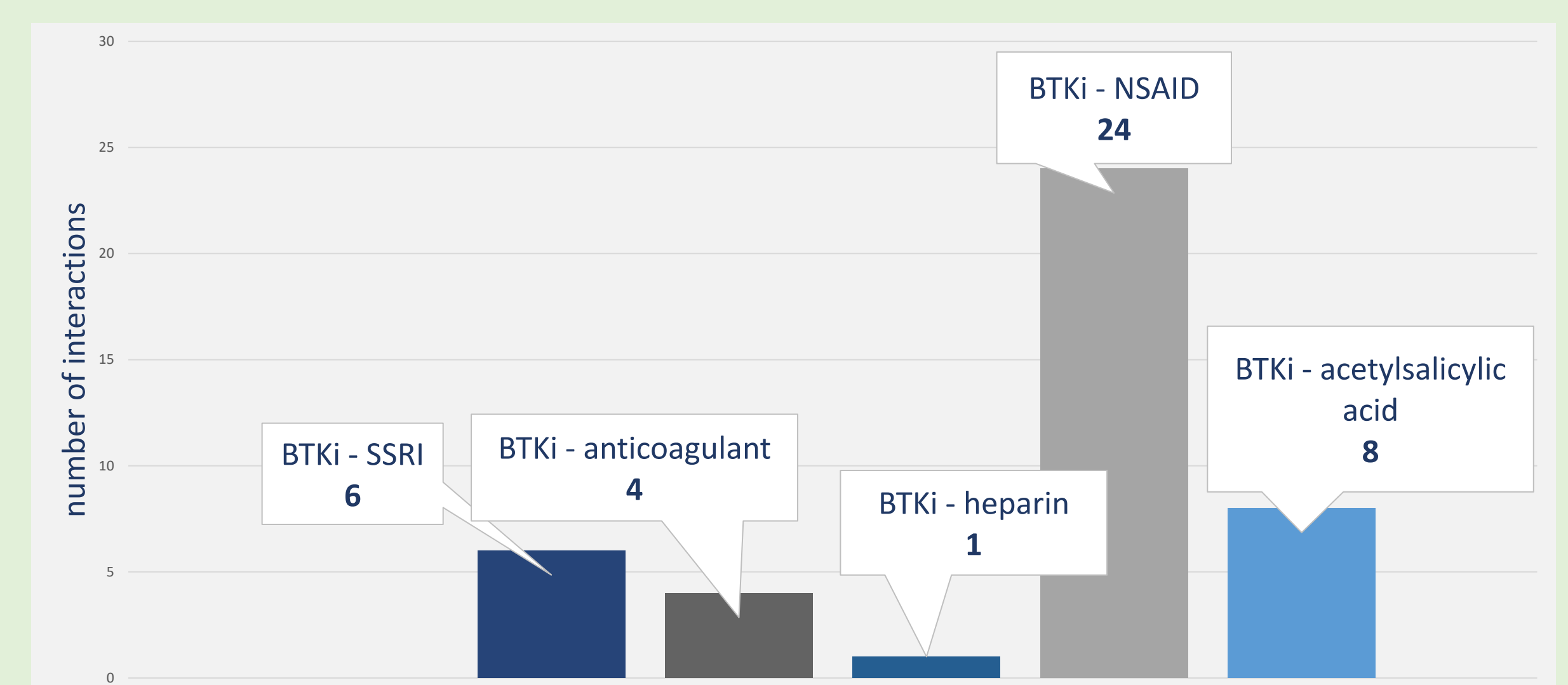
- 59 subjects
 - 24 (40.7%) treated with ibrutinib
 - 18 (30.5%) treated with acalabrutinib
 - 2 (3.4%) treated with zanubrutinib
 - 15 (25.4%) treated with venetoclax (monotherapy or combination with CD20 antibody)

age, years, median (IQR)	69 (61,5 – 74,5)
≥ 65 years, N (%)	39 (66,1)
sex, male, N (%)	42 (71,2)
ECOG score 0, N (%)	50 (84,8)
ECOG score 1, N (%)	9 (15,3)

number of comorbidities, median (IQR)	3 (2 – 4,5)
patients with at least one comorbidity, N (%)	54 (91,5)
CIRS score, median (IQR)	6 (3,5 – 10)
CIRS ≤ 6, N (%)	32 (54,2)
CIRS 7 – 12, N (%)	19 (32,2)
CIRS 13 – 18, N (%)	8 (13,6)

number of medications per patient, median (IQR)	7 (5 – 11)
medication use categories, N of patients (%)	
low drug use	12 (20,3)
polytherapy	27 (45,8)
excessive polytherapy	20 (33,9)

patients receiving BTKi, N	44
patients with ≥ 1 potential clinically significant DDI involving BTKi, N (%)	31 (70,5)
total number of DDI involving BTKi	46
- significance level C	44
- significance level D	2



The most common consequence of BTKi DDIs was an **increased risk of bleeding**, recorded in 65.9% of patients taking BTKi.

patients receiving venetoclax, N	15
patients with ≥ 1 potential clinically significant DDI involving venetoclax, N (%)	4 (26,7)
total number of DDI involving venetoclax	7
- significance level C	5
- significance level D	2

Conclusion and relevance:

The incidence of polytherapy and DDIs is significant and should be regularly analyzed in prescribed pharmacotherapy of CLL patients treated with targeted therapy.

