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Frequent monitoring in chronic lymphocytic leukemia clinical trials: what is the true value?

Agnes Mattsson[1,2], Jeanette Lundin[1,3], Tom Mulder[1], Sandra Eketorp-Sylvan[1], Marzia Palma[1,3], Lotta Hansson[1,3], Anders Österborg[1,3]

[1]Department of Oncology-Pathology, Karolinska Institutet, Stockholm, [2]Department of Internal Medicine, Södersjukhuset, Stockholm, [3]Department of Hematology, Karolinska University Hospital, Stockholm

Introduction

- Industry-initiated clinical trial protocols require frequent:
  - Admissions
  - Blood analyses
  - Computerized tomography (CT)
- The value of intense monitoring has not been systematically analyzed
- It is in bright contrast to recommendations by iwCLL guidelines

Methods

- Patients who participated in industry-initiated clinical trials were included
- Descriptive analyses were performed on number of admissions, blood tests and CT examinations
- Patients served as their own controls and were analyzed twice; once according to the study protocol and once hypothetically according to iwCLL guidelines
- Time to response (TTR), time to progression (TTP) and objective response rate (ORR) was compared

Results

- 42 patients with CLL from 7 industry-initiated trials at one centre were included
- Treatment start between February 2013 and December 2020
- Median follow-up time was 38 months (range 2-108)
- Median total radiation dose was 100 mSv (range 16-22 to 136-187) in the protocol group
- ORR was 90% per protocol and 93% when analysed according to iwCLL guidelines (ns)
- The median TTR was 5.6 months (per protocol) versus 4.6 months (per iwCLL) (Fig 1)
- TTP was almost identical (Fig 2)

Table 1. Baseline characteristics

		Number (%)
Median age at treatment start (range)		73 (52-87)
Gender		
	Male	25 (60)
	Female	17 (40)
ECOG		
	0	23 (55)
	1	16 (38)
	2	3 (7)
Genetics		
	17p/TP53	12 (29)
Median number of prior treatments		
	First-line	18 (43)
	Second-line	14 (33)
	Later-line	10 (24)
Type of treatment		
	Zanubrutinib	16 (38)
	Ibrutinib	10 (24)
	R-bendamustine	5 (12)
	O-ibrutinib	4 (10)
	R-bendamustine + ibrutinib	3 (7)
	O-idelalisib	2 (5)
	Acalabrutinib	1 (2)
	O-leukeran	1 (2)

Table 2. Treatment follow-up

	Protocol	iwCLL	p-value
Admissions, median (range)	18 (3-34)	10 (1-18)	p<0.001
Blood tests, median (range)	30 (3-73)	18 (1-45)	p<0.001
CT examinations, median (range)	10 (2-17)	0	p<0.001
Number of bone marrow biopsies, median (range)	1 (0-4)	0 (0-0)	ns

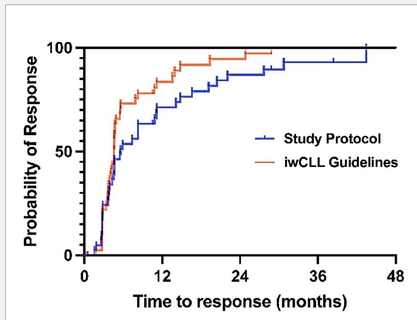

Fig 1. Time to response

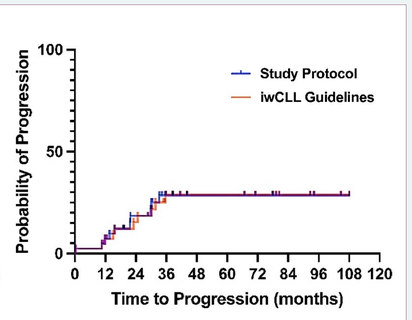

Fig 2. Time to progression

Conclusion

- Clinical trials results in extra admissions, blood tests and CT examinations
- The value of such intense monitoring appears to be limited
- For many patients, the cumulative radiation dose from CT examinations was higher than recommended in recent national protection guidelines
- Harmonization between clinical trial protocols and iwCLL guidelines is warranted
- Extended analyses on more patients and centers are warranted

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Contact information:
Agnes Mattsson, MD
Karolinska Institutet, Department of Oncology-Pathology
SE-17176 Stockholm, Sweden
E-mail: agnes.mattsson@regionstockholm.se

KAROLINSKA University Hospital

Karolinska Institutet