

OTHER MALIGNANCIES IN THE HISTORY OF CLL– A RETROSPECTIVE, MULTICENTER STUDY BY ERIC, IN HARMONY

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Background

- Other malignancies occurring in patients with CLL are a well-known, but insufficiently investigated area
- The purpose of the present project is to determine the incidence and prevalence of other malignancies both preceding or following CLL diagnosis and their impact on the disease course and overall survival (OS).

Study design

- Multicentric retrospective analysis on real-world evidence (RWE) patient data
- Analysis of other malignancy incidence in a population of patients with CLL in relation to the disease itself and CLL therapy

Endpoints of the study

Primary

Descriptive statistics of other malignancies in patients with CLL

Secondary

- Patient characteristics (gender, age, CLL prognostic factors)
- CLL therapy duration and sequence of therapies in patients with CLL with other malignancies
- Overall survival of CLL with other malignancies

Inclusion criteria

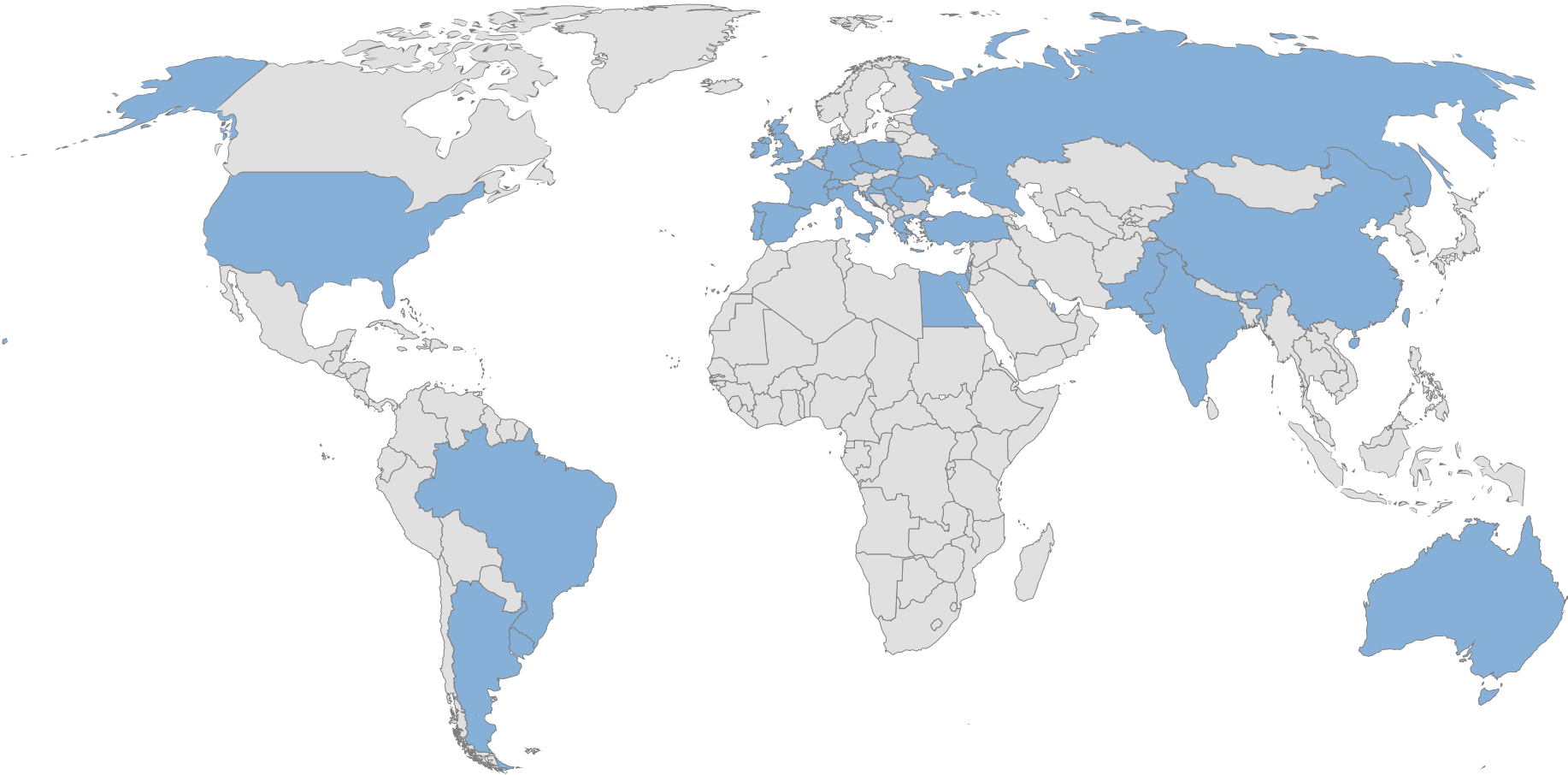
- Data from consecutive set of patients with CLL
- Clinical and laboratory data available
- Patients diagnosed with CLL between years **2000 and 2016**

Data collection

Variables:

- Diagnosis CLL/SLL/MBL
- Demographics (age, gender)
- CLL data (date of diagnosis, staging, FISH, IGHV, treatment, treatment response, death, reason of death)
- Other malignancy (type, date of diagnosis)

Participating countries - 33



Participating sites

Number of sites	64
Number of countries	33
Total number of patients diagnosed 2000-2016	13,808
Median age at diagnosis (range)	66 years (range, 27-92)
Median months to follow-up (range)	77 months (range, 49-199)

Patient Characteristics

Patient characteristics (n=13,808)		
Sex	Male/ Female	61.7%/38.3%
Binet stage at diagnosis	A	74%
	B	16%
	C	10%
del(11q)	Positive/ Negative	14.1%/85.9%
del(17p) and/or TP53 mutation	Positive/ Negative	10.8%/89.2%
IGHV gene status	Mutated/ Unmutated	52%/48%
Treatment status	Treated/ Untreated	53.6%/46.4%
Total lines of treatment	1	59.3%
	2	19.3%
	3	11%
	≥4	10.3%
Therapies received (at any line)	CIT	71.5%
	CIT +novel agents	21.3%
	Only novel agents	7.2%

Results

Other malignant neoplasms in the history of CLL

All other malignancies besides CLL (excluding Richter's transformation)	2919	21,1%
Richter's transformation	390	3,8%

Timing of other malignancy in relation to CLL diagnosis

Before CLL diagnosis	980	7,1%
After CLL diagnosis	1939	14%

Other hematological neoplasms diagnosed after CLL

MDS/AML	98	31%
Other lymphoid malignancies	155	49%
Other	64	20%

Non- hematological neoplasms diagnosed after CLL

Non-melanoma skin cancer	502	31%
Prostate cancer	211	13%
Colon cancer	176	10,9%
Breast cancer	96	5,9%
Bronchus/lung cancer	139	8,6%
Melanoma	94	5,8%

Non-hematological neoplasms diagnosed after CLL

- Breast, prostate, colon were significantly more prevalent in untreated patients ($p < 0.01$)
- The follow-up of treated vs untreated patients did not differ significantly
- Only NMSC was significantly more prevalent ($p = 0.007$) in treated patients

MDS/AML in patients with CLL

Subgroups with increased incidence of MDS/AML	p value
Unmutated IGHV	0.05
del(11q)	0.009
Treated patients	<0.001
≥3 treatment lines	<0.01
Treated with FCR	<0.001

*On multivariate analysis, treatment with FCR was the only significant predisposing factor

Conclusions

- The development of other hematological malignancies, especially MDS/AML, was associated certain biological features as well as treatment for CLL.
- A highly relevant risk was identified for patients treated with CIT, particularly the FCR regimen.
- Solid tumors appeared unaffected by treatment administration, indicating that solid tumor occurrence in patients with CLL is mainly an age-related phenomenon.

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