len induction treatment. For studies investigating consolidation treatment, results were compared descriptively.
Results: Ten studies, of which 9 non-randomized studies and 1 randomized study, with a total of 571 patients that received len induction treatment were included in the meta-analysis. A subgroup analysis was performed for patients undergoing len monotherapy (Len-mono) and len combination therapy (Len-combo).
The summarized ORR using the random effects model of the two Len-combo in elderly/unfit studies was higher compared to standard treatment with a pooled ORR of 82% [95% CI: 72 - 89%] compared to 65.7% for R-Clb and 77.3% for G-Clb (Fig1A). The summarized ORR of Len-combo in the 5 young/fit studies was 87% [95% CI: 70 – 95%] compared to 90.4% for FCR, however, the chemotherapy regimens differ between the studies (Fig1B). Treatment with Len-mono was not superior compared to standard treatment in both elderly/unfit and young/fit patients (Fig1A+B).
Seven studies, including 2 randomized studies, with a total of 305 patients that received len consolidation treatment were compared descriptively. All studies showed an improvement in response or PFS during consolidation with len. Moreover, one placebo-controlled study showed a significant PFS advantage for patients treated with lenalidomide consolidation, although no difference in overall survival was found.
Toxicity was slightly increased with len therapy. Neutropenia was the most common toxicity but was usually manageable. Tumor lysis syndrome and tumor flare response grade 3/4 occurred rarely when individualized dose escalation of len was performed and thrombo-embolic events occurred in less than 5% when aspirin prophylaxis was given.
Summary/Conclusion: This meta-analysis demonstrates that elderly/unfit CLL patients benefit from treatment with len in combination with rituximab/chlorambucil compared to R-Clb and G-Clb. In young/fit patients, standard FCR treatment remains superior. When len was given as consolidation treatment after induction treatment, responses increased and PFS was prolonged. Toxicity was higher compared to standard treatment, but was manageable when adequate prophylaxis was used.

PF391 INFLUENCE OF ATORVASTATIN THERAPY ON GALECTIN-3, VE-CADHERIN, AND CARDIOVASCULAR RISK IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA

B. Samura [1,*], Y. Kolestik [2], V. Syvolap [1]

[1]Department of Internal Diseases, [2]Department of Pathophysiology, Zaporizhzhya State Medical University, Zaporizhzhya, Ukraine

Background: The vast majority of chronic lymphocytic leukemia survivors experience late effect of treatment including cardiovascular events. These effects contribute most of the substantial effects excess mortality in patients with full or partial response to CLL treatment.
Aims: We aimed to evaluate the impact of atorvastatin on galectin-3 and VE-cadherin, and cardiovascular risk in patients with chronic lymphocytic leukemia in remission.
Methods: One hundred fifty seven out subjects with chronic lymphocytic leukemia in full or partial remission were enrolled in the study. Atorvastatin at doses 20 mg/d and 40 mg/d was prescribed for patients with hypercholesterinemia, dyslipidemia, coronary artery disease risk factors. Blood samples for biomarkers measurements were collected at the visit of inclusion into the study. Plasma levels of galectin-3, and VE-cadherin were measured by ELISA method at baseline and after 1 year of observation period.
Results: Two hundred seventy cumulative clinical events occurred in 68 patients (43.3%) within the follow-up, with their distribution being as follows: 12 deaths for cardiovascular reasons, 17 life-threatening arrhythmias, 36 cardiac ischemic events, 9 strokes, 38 decompensated chronic heart failures, and 58 hospital admissions for cardiovascular reasons. Patients were divided to two groups depending on the atorvastatin treatment. At baseline there were no difference in levels of biomarkers between groups. In one year there were significant differences in levels of galectin-3 (8,86 ± 5,62 ng/ml vs 16,74 ± 8,52 ng/ml; p = 0,035), VE-cadherin (0,76 ± 0,64 ng/ml vs 2,19 ± 1,66 ng/ml; p = 0,046) in the group without atorvastatin treatment. The optimal cut-off point of galectin-3 level for distinguishing high cardiovascular risk patients from low risk ones was 11.75 ng/ml, with a sensitivity of 70.4% and a specificity of 96.8%; for VE-cadherin – 0.53 ng/ml, with a sensitivity of 72.6% and a specificity of 95.2%. Combination of galectin-3 and VE-cadherin had high negative prognostic value (93.4%) for evaluation of cardiovascular events.
Atorvastatin treatment were associated with decreasing of cumulative cardiovascular events with appearance of early differences between groups during 3 year observation time (long-rank test, $\chi2 = 11,775$, p = 0,001). During first year of observation event-free survival were better for patients treated with atorvastatin 40 mg/d in comparing to patients treated with atorvastatin 20 mg/d (long-rank test, $\chi2 = 6,147$, p = 0,013).
Summary/Conclusion: Among patients with chronic lymphocytic leukemia in remission galectin-3 and VE-cadherin are associated with increased risk of cardiovascular events within 3 year observation period. Atorvastatin prevents increasing of galectin-3 and VE-cadherin and reduces risk of cardiovascular events in this group of patients. It was proposed to prescribe atorvastatin to patients with level of galectin-3 11.75 ng/ml or higher, and/or level of VE-cadherin 0.53 mg/ml or higher for prevention of cardiovascular events during 3 year period.

PF392 MONOCLONAL GAMMOPATHY AND HYPOGAMMAGLOBULINEMIA AS INDEPENDENT PROGNOSTIC FACTORS IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA: A RETROSPECTIVE MULTICENTRIC EXPERIENCE

A. Corbingi [1,*], I. Innocenti [2], A. Tomasso [1], R. Pasquale [3], A. Visentin [4], M. Varettoni [5], F. Autore [2], F. Morelli [1], L. Trentin [4], G. Reda [3], L. Laurenti [1,2]

[1]Hematology, Università Cattolica del Sacro Cuore, [2]Hematology, Fondazione policlinico universitario A. Gemelli, Rome, [3]Hematology, Fondazione IRCCS Ca'Granda, Ospedale Maggiore Policlinico, Milan, [4]Hematology, Università degli Studi di Padova, Padova, [5]Hematology, Fondazione IRCCS, Policlinico San Matteo, Pavia, Italy

Background: Chronic Lymphocytic Leukemia (CLL) is an indolent B-cell lymphoproliferative disorder. Several prognostic factors such as IGHV mutation status and chromosomal aberrations as trisomy 12, del11q, del13q or del17p have been detected so far. More recent genetic mutations such as BIRC3, SF3B1, NOTCH1 and TP53 stratifies even further the prognosis and outcome in CLL patients (pts). However all data above reported, because of expensive techniques and experience typical of big laboratories, are not available to all medical centers while data concerning the presence of hypogammaglobulinemia, IgM or IgG monoclonal gammopathy are easily achievable, even though the prevalence and the impact on natural history of CLL pts is controversial and contradictory.

Table 1: Patients' characteristics.

	Total	IgM/CLL	IgG/CLL	Hypogamma	normal gamma level
Patients (n)	1359	68	128	172	991
Sex (M/F)	753/606	34/34	73/55	95/77	553/440
Age (median y.o.) Range	66 (26-96)	68.5 (47-82)	67 (33-89)	68 (35-96)	65 (26-88)
Median IgM level[1] (mg/dL) Range	52 (17-3300)	291 (29-3300)	54.5 (8-1209)	25 (3-300)	53 (0.2-1443)
Median IgG level[2] (mg/dL) Range	893.5 (106-10.000)	864 (302-2700)	1045.5 (247-3939)	568 (120-1290)	929 (106-10.000)
Median TTP[3] (range)	36 (1-3222)	26 (1-210)	28 (1-223)	28 (1-216)	25.5 (1-3222)
Median TTT[3] (range)	36 (1-3222)	30 (1-210)	30 (1-223)	29 (1-216)	25 (1-3222)
Median OS[3] (range)	72 (1-3222)	72 (1-253)	56 (1-258)	73 (1-375)	74 (1-3222)

[1] normal range: 70-400 mg/dL
[2] normal range: 700-1600 mg/dL
[3] months

Aims: The aim of the study is to evaluate the prevalence and the outcome of monoclonal IgM/CLL, IgG/CLL and hypogammaglobulinemia compared with CLL pts with normal immunoglobulin (Ig) levels.
Methods: We collected from four different Italian centers 1359 pts diagnosed with typical CLL from 1987 to 2017 with a baseline assessment of serum Ig, immunofixation, chromosomal aberrations and clinical features; evaluating their impact on time to progression (TTP), time to treatment (TTT) and overall survival (OS).
Results: Once assessment was made, pts included in our study who met eligibility criteria were 1359. Median age was similar in all the groups and data gathered from the four centers showed an overlapping rate about prevalence and time-dependent-parameters in CLL pts and their related subclasses.The overall prevalence of monoclonal gammopathy is 14% of whom 128 pts (9%) with IgG/CLL, 68 pts (5%) with IgM/CLL.