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Abstract : 184

Results of a Phase II Randomizing Intensified Rituximab Pre-Phase Followed By Standard FCR Vs Standard FCR in Previously Untreated Patients with Active B-Chronic Lymphocytic Leukemia (B-CLL). CLL2010FMP (for fit medically patients): A Study of the French Cooperative Intergroup on CLL and WM

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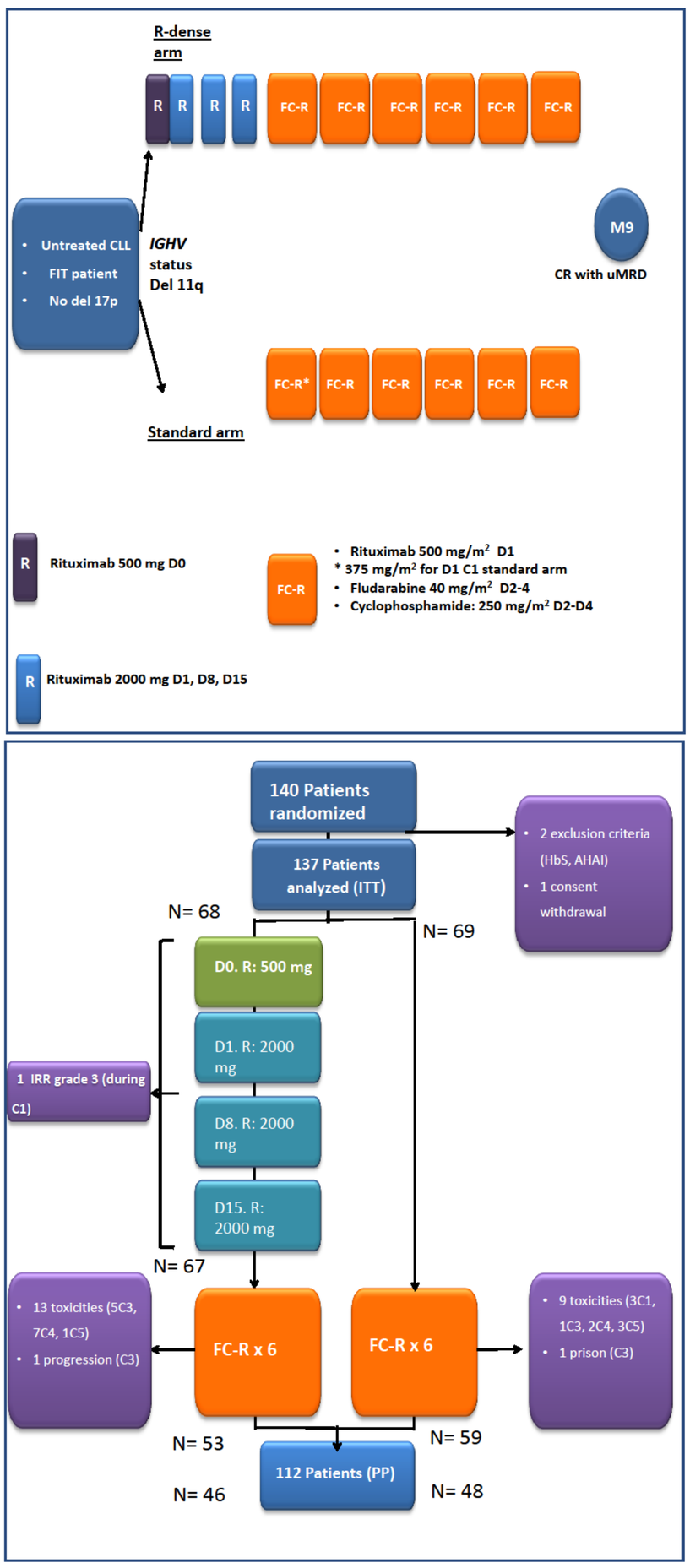
BACKGROUND

- Rituximab dosing regimen is largely empirical in CLL patients and phase I study has suggested a dose response relationship in previously treated CLL patients. Pharmacokinetics data from REACH study, randomising FCR and FC for relapsed/refractory CLL, showed a correlation between rituximab exposure evaluated by AUC and Cthrough and clinical response. Pharmacokinetics analyses showed a faster clearance (CL2) of rituximab in CLL patients compared to non-Hodgkin's lymphoma patients. We purposed to intensify rituximab regimen before the first course of FCR in order to improve rituximab exposure and increase response rate in untreated, medically fit CLL patients.

PATIENTS AND TREATMENT

Figure 1: Study design and patients disposition

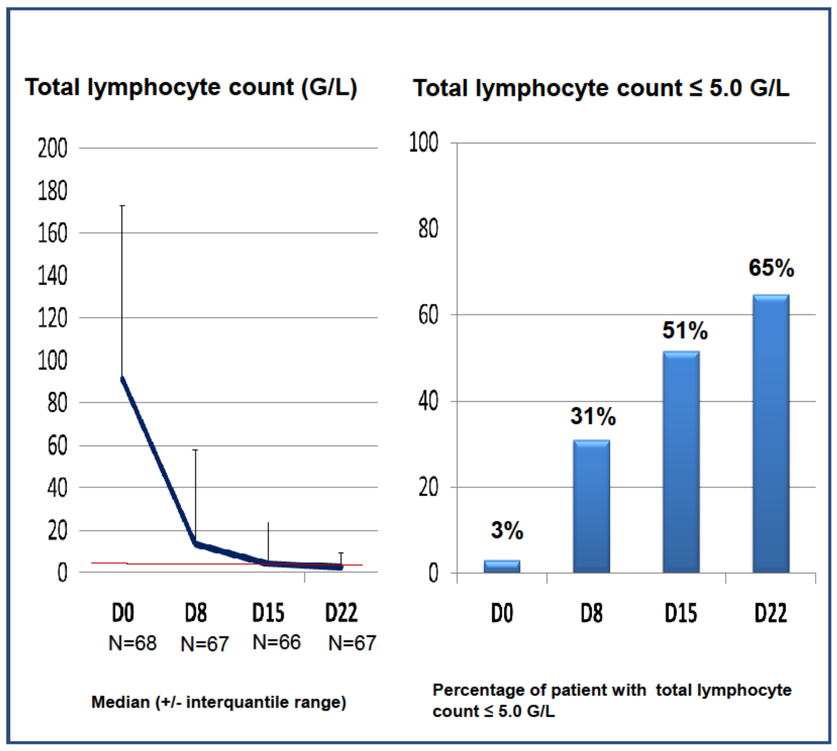


RESULTS

Table 1. Patients characteristics

	R-Dense n = 68 n		Standard n = 69 n		P
Median Age (range)	58.3 (52.9-61.4)	68	54.1 (52.7-62.0)	69	NS
Male, n (%)	49 (72.1)	68	51 (73.9)	69	NS
Median lymphocyte count, 10^9/L (range)	89.6 (42.2-136.0)	68	46.5 (20.7-101.0)	68	NS
β_2-microglobulin > 3.0 mg/L, n (%)	28 (45.2)	62	37 (59.7)	62	NS
Binet stage A active B active C	3 (4.4) 49 (72.1) 16 (23.5)	68	0 49 (71.0) 20 (29.0)	69	NS
Bulky > 5 cm, n (%)	9 (13.24)	68	14 (20.29)	69	NS
IGVH unmutated, n (%)	41 (61.2)	67	41 (62.1)	66	NS
FISH analysis, n (%) Trisomy 12 del(13p) del(11q)	4 (8.3) 27 (50.0) 13(19.7)	48 54 66	5 (11.4) 32 (61.5) 12 (17.6)	44 52 64	NS

Figure 2: Changes in B-cells during rituximab pre-phase



STATISTICS

The primary endpoint was the complete response (CR+CRi) rate according to iwCLL 2008 criteria associated with undetectable minimal residual disease (uMRD; < 10-4 by 8 colors FC assay) in peripheral blood and bone marrow 3 months after the last cycle. To calculate the number of patients, we will use the Simon method in one step with the following hypothesis: in our previous study we observed a complete response rate with uMRD of 35% in patients having received the combination of fludarabine, cyclophosphamide and rituximab at standard dose. We assume an increase of 15% of complete response rate with uMRD by using high dose of rituximab.

ACKNOWLEDGEMENTS

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Figure 3: Response rates

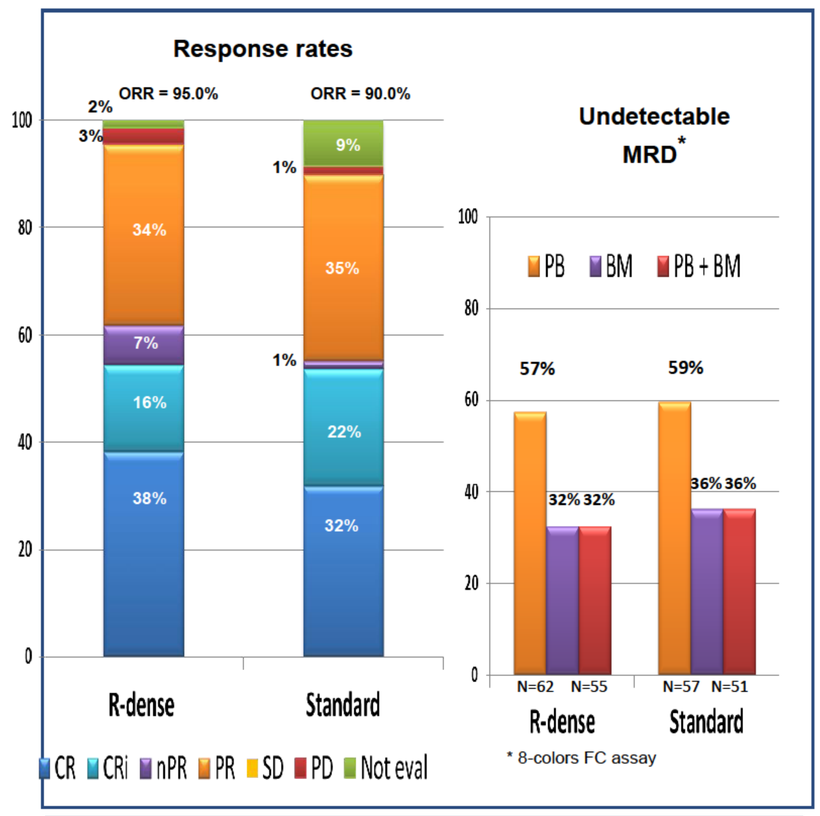
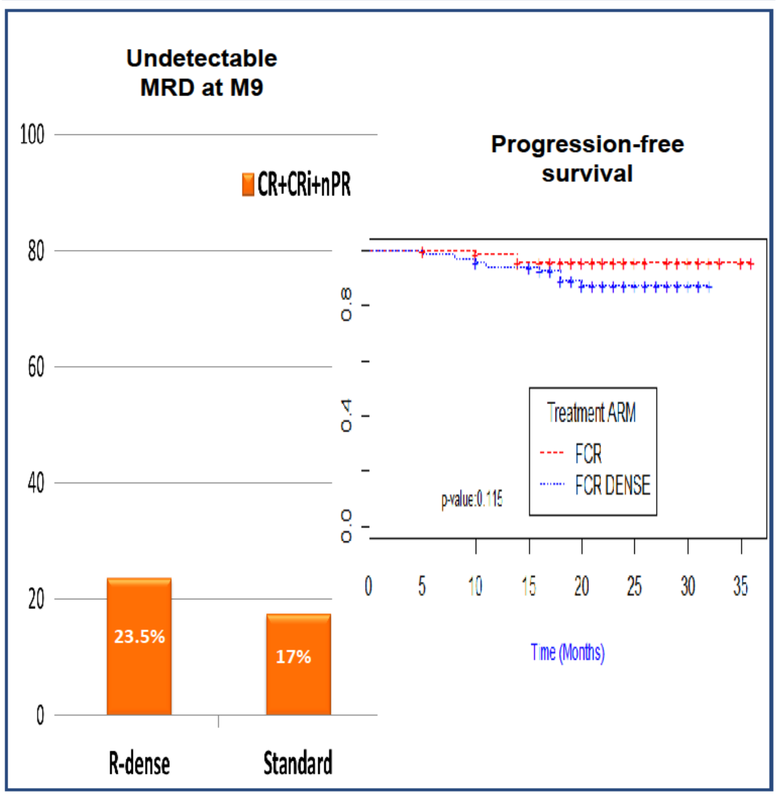


Figure 4: uMRD for patients in response and progresson-free survival



CONCLUSION

Intensified rituximab pre-phase is safe in untreated medically fit CLL patients and most of patients reached normal lymphocyte count at the end of the pre-phase. However, intensified rituximab pre-phase followed by FCR did not allow to significantly increase CR+CRi with uMRD rate compared to standard FCR. Longer follow-up of these patients is warranted

DISCLOSURES

Leprêtre: Honoraria, Roche; Delmer: Honoraria, Roche ; **Feugier:** Honoraria, Roche ; **Cymbalista:** Honoraria, Roche ; **Leblond :** Honoraria, Roche;

Cartron: Consultancy, Honoraria:,Roche

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