RESEARCH LETTER

Supplementary material

Single-agent rituximab is an effective salvage therapy in pretreated hairy cell leukemia patients.

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Supplementary methods

Patients were judged in complete response (CR) if they stringently met the Consensus Resolution criteria for CR in peripheral blood (hemoglobin at least 12 g/dL, platelet counts higher than 100,000/mmc and neutrophil counts higher than 1,500/mmc, no circulating hairy cells) and in the bone marrow (complete disappearance of hairy cell infiltrates with hematoxylin-eosin staining, along with an immunohistochemical CD20 positivity lower than or equal to 10% of marrow

cellularity) and with no residual organomegaly. PR required the resolution of all peripheral blood cytopenias, with the persistence of at least 5% of circulating hairy cells or the reduction of at least 50% of the bone marrow leukemic infiltrate or of any previously detected organomegaly. Minimal response (MR) indicated a peripheral blood hematological improvement in at least one among hemoglobin concentration, platelet counts, neutrophil counts, without the clearance of circulating hairy cells (yet needed to be less than 50% of the initial circulating burden). Patients were classified as non-responder if failed to achieve at least a minor response.

The main study objectives were the overall response rate (ORR) to rituximab, which indicated the proportion of patients achieving a CR, a PR or a MR; the time-to-next treatment (TTNT), calculated from the date of rituximab start to the moment in which a subsequent treatment was initiated; progression-free survival (PFS) and overall survival (OS). TTNT was calculated on all courses of rituximab received in order to capture the efficacy of the drug even when repeated twice or more times. PFS and OS, instead, were calculated on all patients from the time of rituximab inception to the first documented disease progression, death or last follow-up visit.

Demographics and patients' characteristics were summarized by descriptive statistics and survival functions were estimated by using the Kaplan–Meier method and compared using log-rank test. Statistical analyses were performed with Stata 17 (StataCorp LP, TX).

The study was approved by our institutional board (Ethical Committee AVEC of Bologna, approval id 1043/2021/Oss/AOUBo). All participants gave written informed consent (when applicable) in accordance with the Declaration of Helsinki to

retrospectively collect their data. As for the retrospective design of the study, we received an authorization to analyze data also of patients who were deceased or lost to follow up at the time of data collection.

Supplementary table. Published experiences with single-agent rituximab in pretreated hairy cell leukemia patients

Author, year	Patients	Previous lines	Rituximab schedule	ORR	CR	Median duration of response
Lauria, 2001[12]	10	—	375 mg/m^2 × 4 weeks	50%	10%	—
Hagberg, 2001[14]	8	3	375 mg/m^2 × 4 weeks	75%	62%	14 months
Nieva, 2003[15]	24	1	375 mg/m^2 × 4 weeks	26%	13%	—
Thomas, 2003[16]	15	1	375 mg/m^2 × 8 weeks	80%	67%	42 months
Zenhäusern, 2008[17]	26	1	375 mg/m^2 × 4 weeks	80%	32%	37 months
Leclerc, 2015[18]	24 (*)	—	375 mg/m^2 × 4 or 8 weeks	79%	54%	23 months
This study	33 (**)	2	375 mg/m^2 × 4 weeks	72%	28%	33 months (***)

(*) Only patients treated with single-agent rituximab at relapse. (**) It includes 5 patients treated more than once (39 courses overall).

(***) Time-to-next treatment.

ORR, overall response rate; CR, complete response

References in the table are to the main text.

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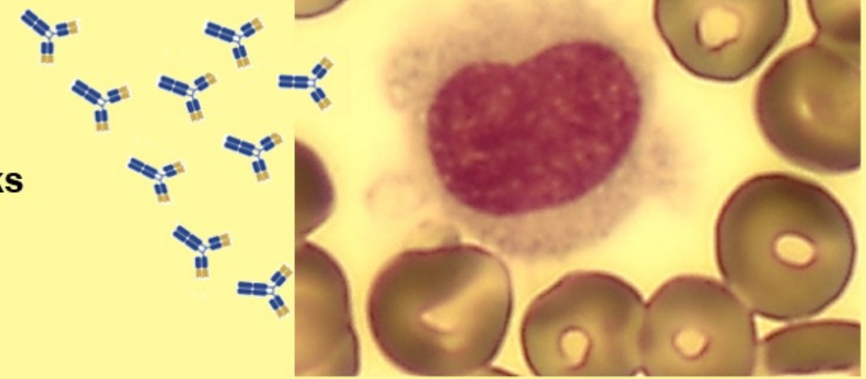
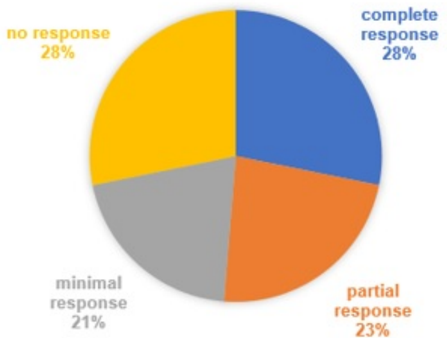
33 patients with relapsed/refractory HCL
39 rituximab courses

Rituximab
375 mg/m^2
Weekly, 4 weeks



- Median third line of therapy in multiply treated patients

- Overall response rate: 71.8%



- Median time-to-next treatment: 33 months ▶
- Median progression-free survival: 24 months
- Median overall survival: 154 months