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# POSTER ABSTRACTS

## 623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

### Serum Soluble Interleukin-2 Receptor Levels in Hairy Cell Leukemia As a Marker of Tumor Burden with Prognostic Value and As a Tool for Disease Monitoring

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**Background**

Neoplastic cells in hairy cell leukemia (HCL) express the $\alpha$ chain of the interleukin-2 receptor on their surface, which is secreted in large amounts in the serum in a soluble form (sIL-2R). High serum levels of sIL-2R have previously been reported in HCL. Thus, we assessed whether serum sIL-2R levels correlated with tumor burden, represented a prognostic factor, and if they could be used as a tool for disease monitoring.

**Methods**

Serum levels of sIL-2R were measured in 59 patients affected by classical HCL followed at the Hematology Unit of Padova University Hospital. To assess whether sIL-2R levels were representative of tumor burden, we evaluated the relationship of pre-therapy sIL-2R levels with other hematologic features such as leukocyte count, the presence of splenomegaly, $\beta$-2 microglobulin levels, lactate dehydrogenase (LDH) levels, CD38 expression, the percentages of circulating hairy cells and bone marrow infiltration. In 50 patients we investigated whether post-therapy sIL-2R levels correlated with clinical response and measurable residual disease (MRD) status evaluated by immunohistochemistry according to consensus guidelines.

To determine the usefulness of serum sIL-2R levels for disease monitoring, yearly serial sIL-2R levels were measured in 59 patients, including 5 (8.4%) cases in watch & wait phase and 54 (91.6%) with disease remission after therapy with purine analogues. sIL-2R kinetics were correlated with time to cytopenia (TTC) (hemoglobin <100g/L, neutrophils < 1000/μL or platelets <100.000/μL) and time to next treatment (TTNT).

Serum sIL-2R levels were measured by enzyme-linked immunosorbent assay. The correlation of sIL-2R levels with other variables was evaluated by linear or logistic regression as appropriate. Medians were compared using the Mann-Whitney U test. Survival and univariate analyses for TTC and TTFT were conducted according to the Kaplan-Meier method and Cox proportional hazards model.

**Results**

The mean age of patients was 60.6 years; 10 were females (17%), and 49 were males (83%). Among treated patients, 47/54 (87%) received cladribine and 7/54 (13%) pentostatin.

Pre-therapy sIL-2R levels significantly correlated with leukocyte count ($r^2 = 0.13$; $p = 0.009$), $\beta$-2 microglobulin levels ($r^2 = 0.44$; $p < 0.001$), CD38 expression ($p = 0.018$), the percentage of circulating hairy cells ($r^2 = 0.17$; $p = 0.017$) and the percentage of bone marrow infiltration ($r^2 = 0.15$; $p = 0.009$), but not splenomegaly ($p = 0.167$) or LDH levels ($r^2 = 0.02$; $p = 0.369$).

We found a significant difference between serum sIL-2R levels measured before and after therapy (median 16.185 vs 599 kU/L respectively; $p < 0.001$), with a median reduction in sIL-2R levels of 15.628 kU/L after treatment with purine analogues. A similar decrease in sIL-2R levels after therapy was observed in 4 relapsed patients treated with rituximab-vemurafenib (median pre-therapy sIL-2R 11.460 vs. 467 kU/L after treatment, $p = 0.03$; median reduction 10.848 kU/L).

Among responding patients, the absolute value of log10(sIL-2R) levels measured 6 months after therapy was a predictor of shorter TTNT in univariate analysis (HR 15.14; 95% CI 1.3 - 176; $p = 0.03$). Furthermore, sIL-2R correlated with the depth of response. Post-therapy median sIL-2R levels were significantly lower in patients achieving a complete remission (CR) versus

those who did not (median 568 kU/L for CR vs. 3.272 kU/L for partial remission/stable disease; p = 0.002). A statistically significant difference was also observed in post-therapy sIL-2R levels between MRD- and MRD+ patients (median 502 vs 724 kU/L; p = 0.003) (Figure 1A).

In the patients that underwent yearly serial sIL-2R measurements during follow-up, a rise from the nadir after therapy in serum sIL-2R levels of ≥ 25% between two samples was associated with both shorter TTC (HR 26.2; 95 % CI 3.44 - 200; p < 0.001) (Figure 1B) and TTNT (HR 8.83; 95 % CI 1.9 - 40.9; p < 0.001).

**Conclusion**

The consistent reduction in sIL-2R levels after therapy and their correlation with other standard disease parameters show how serum sIL-2R levels could be an effective marker of tumor burden in HCL. While more data is required to validate its use in clinical routine, sIL-2R could be used as an effective marker for disease monitoring. Moreover, given the prognostic significance of post-therapy levels, sIL-2R may represent a prognostic factor alongside MRD to identify those patients that are more likely to develop early relapse.

**Disclosures Visentin:** *Takeda:* Speakers Bureau; *CSL behring:* Membership on an entity's Board of Directors or advisory committees; *AstraZeneca:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Abbvie:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Janssen:* Membership on an entity's Board of Directors or advisory committees; *BeiGene:* Membership on an entity's Board of Directors or advisory committees, Research Funding.

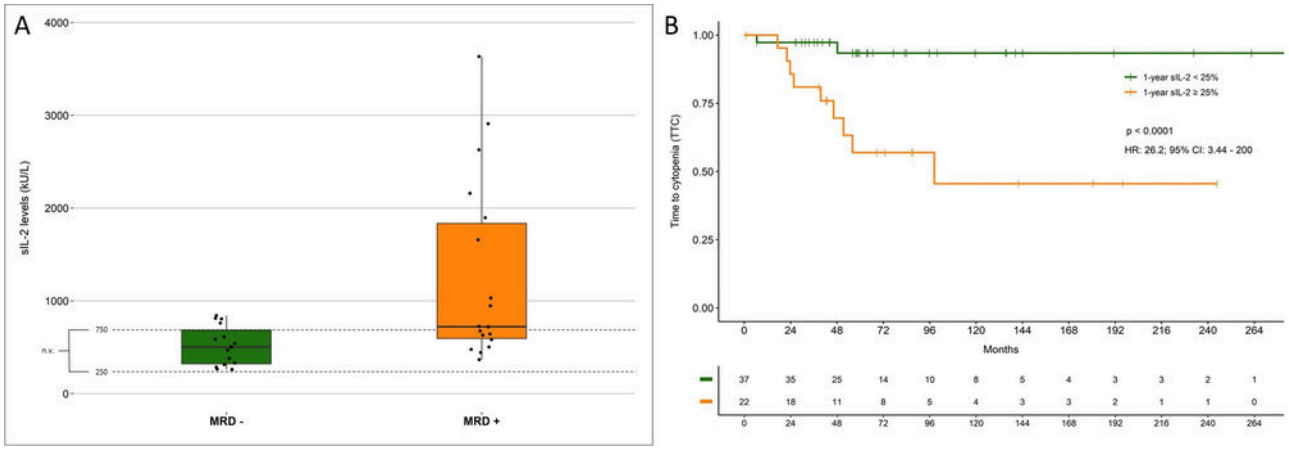


**Figure 1**

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