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Blood 142 (2023) 4389–4391

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

622.LYMPHOMAS: TRANSLATIONAL-NON-GENETIC

High IL1-RA Plasma Levels at Baseline Allow to Identify Hodgkin Lymphoma Patients with High Risk of Treatment Failure

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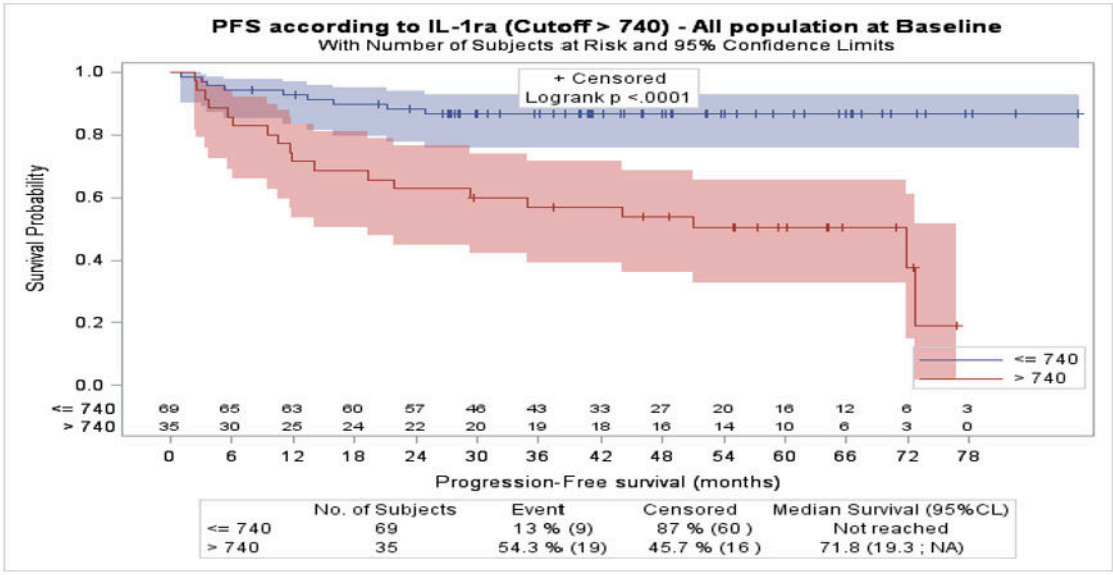
Introduction: About 10% of localized stages and 20-30% of advanced stages patients (pts) with classical Hodgkin lymphoma (cHL) progress or relapse after the first line of treatment. Therapeutic failures prediction at diagnosis is a major challenge to modulate treatments to minimize acute and long-term toxicities, while having optimal efficacy. The development of prognostic tools is crucial to help therapeutic decision. In 2007, *Casasnovas et al. JCO 2007*, demonstrated that a plasma cytokine signature composed of IL1-RA, IL-6 and sCD30 could predict pts outcomes and identify pts with high risk of treatment failure. However, it was unusable in routine practice as the ELISA technique used had extensive delay. Since interim PET during induction chemotherapy became the standard approach to guide the therapeutic strategy, and therefore the use of new pre-therapeutic biomarkers deserves to be investigated in the context of PET-guided treatment. As PD-L1, and thymus and activation-related chemokine (TARC) have an important role in cHL physiopathology we analyzed the prognostic impact on progression-free, and overall survival (PFS and OS) of pretherapeutic plasma levels of PD-L1 and TARC in addition to IL1-RA, IL-6, sCD30, in pts treated with a PET-guided strategy.
Method: The dosage of IL1-RA, IL-6, PD-L1 and TARC was performed using the ELLA automated immunoassay system (Biotechne) while sCD30 was performed in triplicate using ELISA assay. Samples were prospectively collected (period 2016-2020) within the biocollection BIO-LYMPH (NCT04417803) in the pts treated in the department of Hematology at Dijon Hospital. X tile analysis was used to define the optimal cutoff for survival prediction for each cytokine. Survival functions of pts' subgroups defined by the cytokine circulating levels were estimated using the Kaplan-Meier product limit method and compared using the log rank test. The Cox proportional hazard regression model was used to estimate HRs and associated 95% CI in univariate and multivariate analyses.
Results: Among the 105 pts enrolled in this study (Median age: 36 years, range: 17 - 85), 60% were under 45 years, 61% had advanced stage disease, 58% B symptoms, and 39% an IPS >2. 63% of pts had nodular sclerosis HL subtype and 22% had EBV associated HL. Response was assessed at the end of treatment: 89 pts (84 %) achieved a complete response, 4 pts (4%) a partial response, and 9 pts (9%) had progressive disease. With a median follow-up time of 40 months (1-78 months), 13 pts (12 %) relapsed with a median time to relapse of 16 months (range, 4 to 65 months), 14 pts (13 %) died (11 due to cHL progression; 1 due to septic shock; 1 from SARS covid infection; and 1 after a traumatism).
While pretherapeutic plasmatic levels of IL-6, sCD30, TARC and PD-L1 did not impact pts survival, IL1-RA was an independent predictor of both PFS and OS. Indeed, 31% of pts harbored high IL1-RA plasma level (≥ 740 pg/ml) and had an unfavorable PFS (5y-PFS: 50.2% vs 86.7%; HR=4.2, CI=2.1-10.3, p=0.0001, figure 1A) and OS (5y-OS 71.4% vs 95%, HR=4.49, CI=1.3-14.2, p=0.006). PET2 positivity (17% of pts) had an unfavorable prognosis value on PFS (5y-PFS 58% vs 86.6%, HR 4.3, CI= 1.4-12.8, p=0.014) but not on OS (5y-OS 91.8% vs 74.1%; HR=3.2 CI=0.7-14.4, p=0.15) independent from pretherapeutic IL1-RA plasma level (PFS multivariate analysis: PET2 positivity HR=2.43, CI=1-6, p= 0.05; High level IL1-RA HR= 3.4, CI=1.5-8.3, p= 0.005).

The combination of both PET2 results and pretherapeutic IL1-RA plasma levels allow to stratify pts' outcome into 3 groups (figure 1B): - Pts (57%) with low levels of IL1-RA and negative PET2 had a 5y-PFS of 89.3% and 5y-OS of 95.8%, - Pts with high levels of IL1-RA or positive PET2 (35%) had a 5y-PFS of 57% and 5y-OS of 74.8% whereas - Pts with both (8%) had a 5y-PFS of 42.9% and 5y-OS of 71.4%. The groups with one or 2 prognostic factors (PET2+ or high IL1RA and PET2+ & high IL1RA) had a significantly different PFS compared to the double negative group (1 factor: HR=4.7, CI=1.8-12.2, p=0.0011 and 2 factors: HR= 8.57, CI=2.5-28.3, p=0.0004 respectively). The group with 1 prognosis factor had a significantly different OS (HR=4.1, CI=1.1-15.3, p=0.03) compared to double negative group but not the 2 factors group (HR= 4.9, CI=0.8-30, p=0.08).
Conclusion: Pretherapeutic IL1-RA plasma levels allow to stratify the prognosis of pts with cHL treated with first line PET-guided strategies and add prognosis information to PET2 response.

Disclosures Casasnovas: *MSD:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Astra Zeneca:* Consultancy, Honoraria; *GILEAD/KITE:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *BEIGENE:* Consultancy, Honoraria; *BMS:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Abbvie:* Consultancy, Honoraria; *ADC Therapeutics:* Consultancy, Honoraria; *AMGEN:* Consultancy, Honoraria; *ROCHE:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *TAKEDA:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding.

Figures:

Prognosis value of baseline IL1-RA plasma level (A)



Prognosis value of baseline IL1-RA plasma level and PET2 result (B)

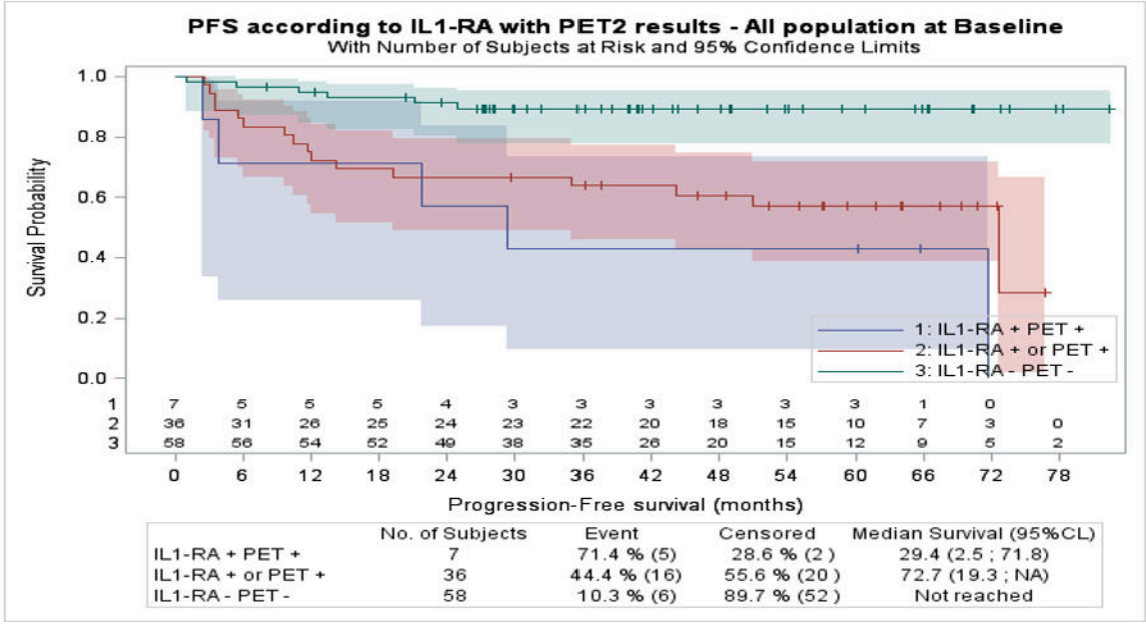


Figure 1

https://doi.org/10.1182/blood-2023-180802