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ORAL ABSTRACTS

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

Validation of POD24 As a Robust Early Clinical End Point of Poor Survival in Mantle Cell Lymphoma from 1280 Patients on Clinical Trials

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Background

The prognosis of mantle cell lymphoma (MCL) has largely improved in the past decade; however, the disease is characterized by a heterogeneous clinical course. Several retrospective studies identified early progression of disease (i.e. within two years, POD24) as a potential overall survival (OS) surrogate, but this has not been validated in cohorts of patients prospectively included in clinical trials in rituximab maintenance era.

Methods

We performed a pooled analysis of French patients with MCL included in six randomized clinical trials (EU-MCL younger NCT00209222, LyMA NCT00921414, LyMA101 NCT02896582, EU-MCL elderly NCT00209209, MCL-R2 NCT01865110 and RiBVD NCT01457144). Survival analysis using Landmark approach evaluated the association of POD24 status with post-event OS for all patients: starting from POD24 event or two years for patients without POD24 event. Logistic regression models were used to evaluate the association between POD24 status and (1) clinico-biological factors at diagnosis; (2) autologous

stem cell transplantation at end-of-induction (ASCT) and anti-CD20 maintenance (RM) in responding patients after induction only.

Results

Among 1386 MCL patients, 106 censored for clinical follow-up before 24 months were excluded from the analysis, leading to 1280 patients evaluable for POD24 status: 299 with a POD24 event and 981 without. The 299 (23%) patients with a POD24 event had a post-event median OS of 9.3 months (95% CI 8.4-11.8) versus not reached in patients without POD24 event (95% CI 97.8-NR). Within the 981 non-POD24 patients, 314 presented a late relapse with a post-relapse median OS of 49.4 months (95% CI 30.4-56.8), significantly longer than OS of POD24 patients (HR=0.39; 95%CI 0.31-0.48; p<0.001). Compared to patients without a POD24 event, POD24 patients were older, had more frequently a performance status >1, elevated LDH and higher leucocytes leading to higher MIPI scores (high-risk MIPI 61% *vs.* 29%; p<0.001), more frequent blastoid variant (24% *vs.* 9%; p<0.001) and Ki67 > 30% (45% *vs.* 23%, p<0.001). Regarding treatment, POD24 patients had less frequently received high-dose cytarabine (21% *vs.* 39%, p<0.001) as well as ASCT (26% *vs.* 47%, p<0.001). In a final model, including baseline factors and treatment strategies, induction was not associated with risk of POD24, and only baseline variables (age, performance status, LDH, leucocytes and Ki67>30%) remained significantly associated with POD24 status. Within responding patients only (CR/CRu/PR at end-of-induction, n=1000), 150 had a POD24 event, and ASCT or RM were not significantly associated with POD24 status whereas age, LDH and Ki67>30% remained significant.

Conclusion

Using this large dataset of patients included in clinical trials, we confirm that POD24 can be used as a surrogate for OS in MCL. ASCT as well as RM have not a clear benefit to prevent early relapse within two years after the diagnosis in responding patients at end-of-induction.

Disclosures Sarkozy: *Incyte Bioscience:* Consultancy, Other: Travel, Accommodations, Expenses; *BMS:* Consultancy; *Janssen:* Consultancy; *GSK:* Consultancy; *AbbVie:* Honoraria; *Gilead:* Other: Congress fees; *Roche:* Other: Travel, Accommodations, Expenses, Research Funding; *Prelude Therapeutics:* Consultancy; *Beigene:* Consultancy; *Lilly:* Honoraria; *Gilead:* Other: Travel, Accommodations, Expenses; *Takeda:* Other: Travel, Accommodations, Expenses. **Thieblemont:** *Bayer:* Honoraria; *Kite:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses; *Cellectis:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses; *Gilead Sciences:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses; *AbbVie:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses; *Takeda:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Roche:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses, Research Funding; *Incyte:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Janssen:* Honoraria, Other: Travel Expenses; *Amgen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses; *Hospira:* Research Funding; *Novartis:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses; *BMS/Celgene:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses, Research Funding; *Paris University, Assistance Publique, hopitaux de Paris (APHP):* Current Employment; *Kyte, Gilead, Novartis, BMS, Abbvie, F. Hoffmann-La Roche Ltd, Amgen:* Honoraria. **Morschhauser:** *F. Hoffmann-La Roche Ltd, AbbVie, BMS, Genmab, Gilead, Novartis:* Consultancy; *F. Hoffmann-La Roche Ltd, Gilead, AbbVie:* Membership on an entity's Board of Directors or advisory committees. **Safar:** *janssen:* Honoraria. **Ghesquieres:** *Gilead, Roche:* Consultancy; *Gilead, Roche, Bristol Myers Squibb, AbbVie, Novartis:* Honoraria. **Dreyling:** *Astra Zeneca, Beigene, Gilead/Kite, Janssen, Lilly, Novartis, Roche:* Honoraria; *Abbvie, Bayer, BMS/Celgene, Gilead/Kite, Janssen, Roche:* Research Funding; *Abbvie, Astra Zeneca, Beigene, BMS/Celgene, Gilead/Kite, Janssen, Lilly/Loxo, Novartis, Roche:* Other: Scientific advisory boards. **Cheminant:** *Innate Pharma:* Research Funding; *AstraZeneca:* Other: Travel accomodations and Meeting inscription; *Amgen:* Honoraria; *Abbvie:* Research Funding.

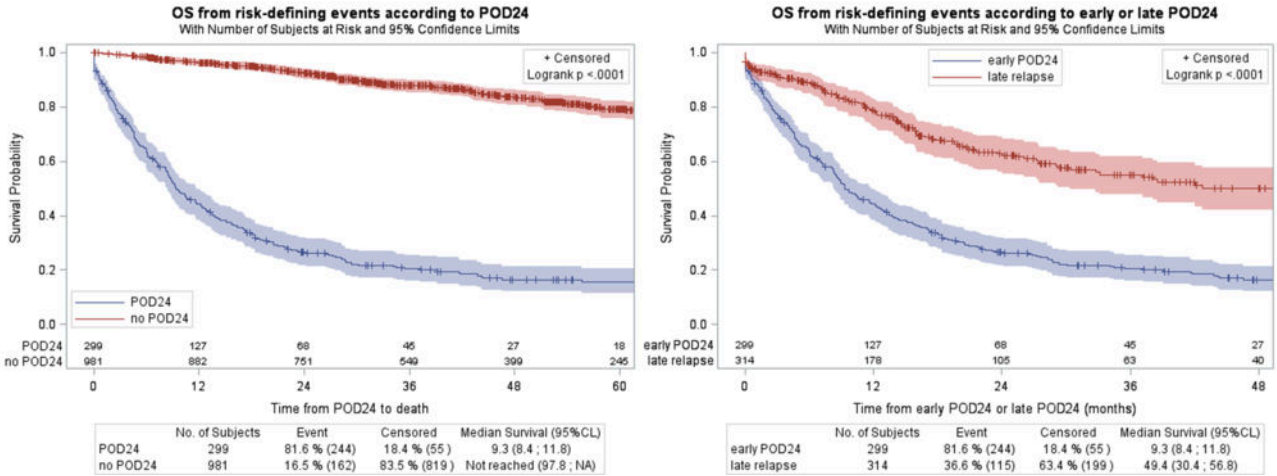

Figure 1

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