

## The 65th ASH Annual Meeting Abstracts

## 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; *Collectis:* 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:** *AstraZeneca, Beigene, Gilead/Kite, Janssen, Lilly, Novartis, Roche:* Honoraria; *Abbvie, Bayer, BMS/Celgene, Gilead/Kite, Janssen, Roche:* Research Funding; *Abbvie, AstraZeneca, Beigene, BMS/Celgene, Gilead/Kite, Janssen, Lilly/Loxo, Novartis, Roche:* Other: Scientific advisory boards. **Cheminant:** *Innate Pharma:* Research Funding; *AstraZeneca:* Other: Travel accommodations and Meeting inscription; *Amgen:* Honoraria; *Abbvie:* Research Funding.

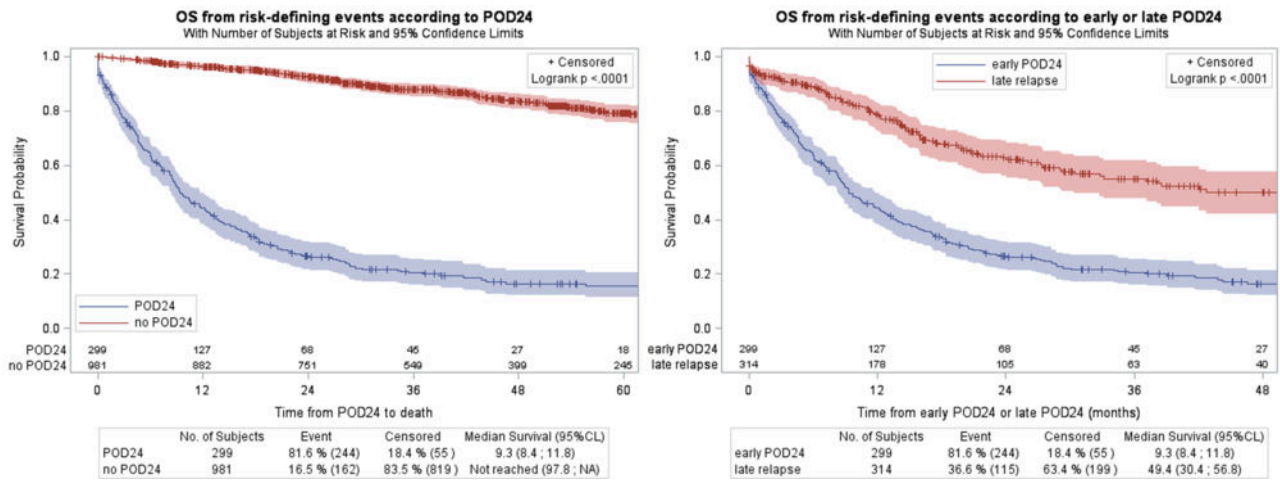


Figure 1

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