



The 65th ASH Annual Meeting Abstracts

ORAL ABSTRACTS

623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL**Obinutuzumab Versus Rituximab in Transplant Eligible Untreated MCL Patients, a Matching Comparison between the Lyma and Lyma-101 Trials**

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Aim: Obinutuzumab (O) and Rituximab (R) have never been compared in a prospective randomized trial in mantle cell lymphoma (MCL). The LYMA-101 trial (NCT02896582) investigated the Obinutuzumab-DHAP (O-DHAP) regimen followed by autologous stem cell transplant (O-BEAM, ASCT) plus O maintenance (OM) in transplant eligible patients <66y with untreated MCL (Le Gouill et al, Lancet Hem 2020). The LYMA trial (NCT00921414) used the same regimen with Rituximab instead of Obinutuzumab (Le Gouill et al, NEJM 2017). Herein, we report the long-term outcome of patients enrolled in the LYMA-101 trial and used a propensity score matching (PSM) approach to allow a comparison with patients treated in the LYMA trial (i.e. O versus R group matched comparison).

Method:

LYMA (n=299 pts, of whom 120 received R Maintenance, RM) is a phase III prospective trial with a median follow-up of 7.5 years (7.4-7.7) from inclusion (Sarkozy et al, ASCO 2023) that randomized, after ASCT, 240 pts between observation and RM. LYMA-101 (n=86) is a prospective single arm phase 2 trial with a median FU of 5.1y (5-5.25) at the time of the present analysis. We first compared minimal residual disease (MRD) at end of induction (EOI), assessed in both trial with quantitative PCR of clonal immunoglobulin gene and used PSM based on clinical characteristics at inclusion (Sex, Ann Arbor stage, MIPI score, B symptoms, blastoid variant, bulky disease) to balance patients' discrepancies between LYMA-101 and LYMA. To compare PFS and OS from inclusion of patients treated with R versus O based regimen, half of the non-randomized LYMA patients (29 out of 58) were randomly reattributed to the RM arm to create an intention to treat RM (RM-ITT) arm including 149 pts (29

non-randomized and 120 randomized) subsequently matched with the 86 LYMA-101 pts. Balance between populations was checked using standardized mean differences (SMD).

Results:

Eighty-five LYMA-101 pts received the first course of O-DHAP (1 withdrew consent before treatment), 81 (95.3%) completed the 4 cycles and 73 (85.9%) underwent ASCT followed by OM in 69 (81.2%). The estimated 5y PFS and OS since inclusion were 83.4% (95%CI: 73.5-89.8%) and 86.9% (95%CI: 77.6-92.5%) respectively. At EOI, ORR were similar in both studies (89.6% versus 91.8% in LYMA versus LYMA-101 respectively), but within responders, pts treated in LYMA-101 (O-DHAP) had a more frequent MRD negativity than pts treated in LYMA (R-DHAP) both in bone marrow (BM, 82.1% versus 65.3% MRD negativity in O vs R group, Chi2 p=0.011) and blood (95.5% versus 79.2% of MRD negativity in O vs R group, Chi2 p=0.002). These results were confirmed using the propensity score matched populations, with a more frequent MRD negativity in the O versus R group in BM (82.1% vs 63.4%, Chi-2, p=0.01) and blood (95.5% vs 72.9%, Chi-2, p<0.001). To compare PFS and OS since induction, a PSM was performed using the 149 patients treated in the R-group with an RM-ITT and the 85 patients in the O group, resulting in 2 sets of 82 patients with comparable characteristics at inclusion. From treatment initiation, patients treated with O presented a prolonged PFS (p=0.029, figure 1A) and OS (p=0.039, figure 1B) compared to those treated with R, with an estimated 5-year PFS of 82.8% versus 66.6% (HR 1.99, IC95 1.05-3.76) and OS of 86.4% versus 71.4% (HR 2.08, IC95 1.01-4.16) with O and R based regimen respectively.

Finally, 37/120 (30.8%) patients in LYMA and 23/69 (33.3%) in LYMA-101 prematurely stopped R and OM respectively (with a similar mean maintenance duration of 29 and 29.4m with R and OM respectively). Reason for maintenance discontinuation were adverse events in 15 cases in R group (12.5% of the population) versus 14 cases in O group (20% of the population), progression or death in 10 (8.3%) versus 3 (4.3%) cases in the R versus O group respectively. Causes of death were comparable in O and R groups, the most common being lymphoma (42% in O and 53% in R group). Infectious deaths in the O group (N=3) were all COVID related (3/12 deaths, 25%), whereas in the R group (LYMA being conducted before the pandemic), 8 deaths were related to infection (8/97 deaths, 8%, including 1 infectious death out of 22 deaths during RM, 5%).

Conclusion: O-DHAP followed by OM post ASCT provide prolonged PFS and OS in young patients with MCL. O-based therapy in MCL induce deeper response with increased MRD negativity and seems to outperform R-based therapy in term of PFS and OS, without any significant excess of toxicity.

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:** *Paris University, Assistance Publique, hopitaux de Paris (APHP):* Current Employment; *BMS/Celgene:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses, Research Funding; *Kyte, Gilead, Novartis, BMS, Abbvie, F. Hoffmann-La Roche Ltd, Amgen:* Honoraria; *Bayer:* Honoraria; *Incyte:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Takeda:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Collectis:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses; *Kite:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses; *Amgen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses; *Hospira:* Research Funding; *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; *Roche:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses, Research Funding; *Novartis:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses; *Janssen:* Honoraria, Other: Travel Expenses. **Oberic:** *incyte:* Honoraria; *gilead:* Honoraria; *roche:* Honoraria; *AZD:* Honoraria; *BMS:* Honoraria. **Damaj:** *Takeda, Blueprint Medicines Corporation, and Thermo Fisher:* Consultancy, Other: Advisory Role; *Takeda, AbbVie and Pfizer:* Other: Travel and Accommodation Expenses. **Tessoulin:** *Gilead:* Honoraria; *Incyte:* Honoraria; *Abbvie:* Honoraria; *Kite:* Honoraria. **Ribrag:** *Incyte:* Consultancy; *NanoString:* Consultancy; *Roche:* Consultancy; *Argenx:* Research Funding; *Astex Pharmaceuticals:* Research Funding; *GSK:* Research Funding; *Gilead:* Consultancy; *AstraZeneca:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees. **Houot:** *Kite/Gilead, Novartis, Incyte, Janssen, MSD, Takeda, F. Hoffmann-La Roche Ltd:* Honoraria; *Kite/Gilead, Novartis, Bristol-Myers Squibb/Celgene, ADC Therapeutics, Incyte, Miltenyi:* Consultancy. **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. **Cheminant:** *AstraZeneca:* Other: Travel accommodations and Meeting inscription; *Innate Pharma:* Research Funding; *Amgen:* Honoraria; *Abbvie:* Research Funding. **Hermine:** *AB science:* Consultancy, Current equity holder in publicly-traded company, Current holder of stock options in a privately-held company, Research Funding; *Inatherys:* Consultancy, Current equity holder in private company, Research Funding; *BMS, Roche, Blueprint, Alexion:* Research Funding.

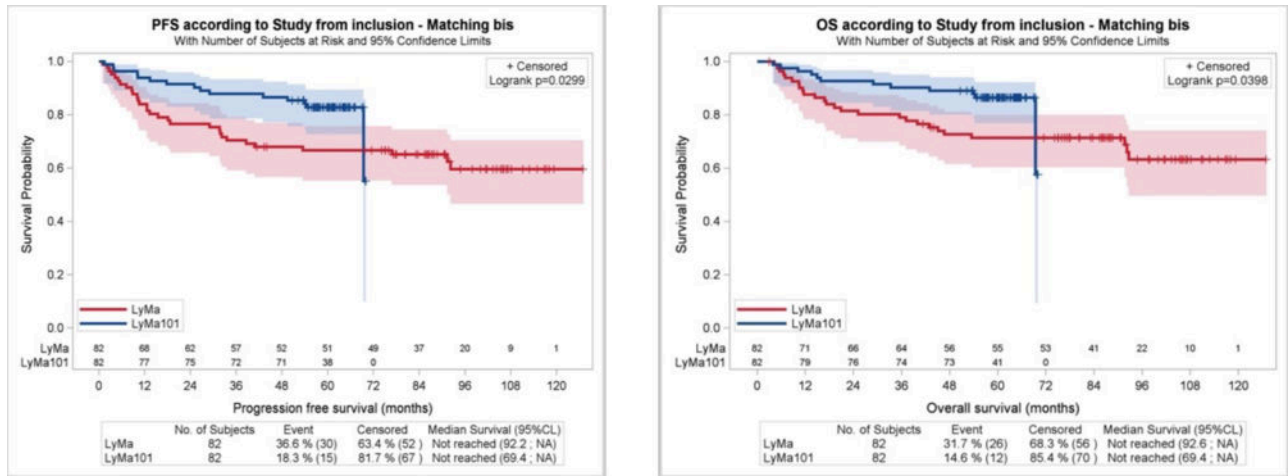


Figure 1

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