Keywords: CD19; diffuse large B-cell lymphoma (DLBCL); non-Hodgkin lymphoma (NHL).

“FOCUS ON…” SESSION: CHEMOTHERAPY-FREE COMBINATIONS

35 FINAL RESULTS OF CALGB 50803 (ALLIANCE): A PHASE 2 TRIAL OF LENALIDOMIDE PLUS RITUXIMAB IN PATIENTS WITH PREVIOUSLY UNTREATED FOLLICULAR LYMPHOMA

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Background: In 2008 we initiated a multicenter phase 2 trial of lenalidomide and rituximab in patients (pts) with previously untreated follicular lymphoma (FL) and evaluated whether FcR polymorphisms and changes in circulating pro-angiogenic cell populations were associated with outcomes.

Methods: Pts with untreated FL, grade 1-3a, stage 3-4 or bulky stage 2, FLIPI 0-2, were eligible. Treatment consisted of lenalidomide 20 mg/day on days 1-21 of a 28-day cycle for 12 cycles plus rituximab administered weekly x 4 on cycle 1 and day 1 of cycle 4, 6, 8, and 10. Polymorphisms in FcgR2A and FcgR3A were evaluated. Circulating endothelial cells (CEC), endothelial progenitor cells (EPC), and hematopoietic progenitor cells (HPC) were evaluated pre-treatment and at completion of therapy. The primary endpoint was complete response (CR).

Results: Sixty-five pts started treatment and are included in this analysis. The median age was 53 y (range 32-79); 68% were FLIPI 0-1. Fifty-one pts (78.5%) completed 12 cycles of lenalidomide. Reasons for early termination included adverse events (n = 6) and patient refusal (n = 6) and disease progression (n = 2). Grade 3-4 neutropenia occurred in 21%. Infections occurred in 40%, including grade 3 infections in 7% and one pt (2%) grade 3 febrile neutropenia. Grade 1-2 and grade 3 fatigue were reported in 51 and 4 pts, respectively. Grade 1-2 and grade 3 rash were noted in 32% and 8% of pts, respectively. Other common adverse events included grade 1-2 diarrhea (38%), grade 1-2 constipation (25%), grade 1-2 nausea (25%), grade 1-2 arthralgia (22%). Grade 1-2 thromboembolic events were reported in 3 pts (5%). Notably, grade 3 tumor lysis syndrome was reported in two patients (3%) and grade 3 serum sickness was reported in one pt (2%).

Overall, 62/65 (95%) of patients responded, including 72% CR (95% CI 60-83%). Mean CECs and HPCs decreased significantly compared to baseline (p < 0.01 in both), while EPCs remained stable (p = 0.88). There was no association between decrease in CEC/HPC or FcgR2A/FcgR3A polymorphism and CR. Sixteen pts have progressed, including 7 pts with a best response of CR, 8 of 9 patients with a best response of PR, and one with SD. With a median follow-up of 5 years, the 2-year, 3-year, and 4-year PFS were 86%, 81%, and 73%. There was no association between FLIPI and CR rate or PFS. Overall survival is 100%.

Conclusion: In this multicenter phase 2 trial, lenalidomide plus rituximab yielded complete responses in 72% of pts with previously untreated FL, meeting the predefined criteria for a positive study. Seventy percent of all patients remain free from progression at 5 years.

Keywords: follicular lymphoma (FL); lenalidomide; rituximab.

36 L-MIND: MOR208 COMBINED WITH LENALIDOMIDE (LEN) IN PATIENTS WITH RELAPSED OR REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA (R-R DLBCL) – A SINGLE-ARM PHASE II STUDY

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Introduction: The Fc-enhanced CD19 antibody MOR208 and the immunomodulatory drug LEN have demonstrated single agent activity in patients with R-R DLBCL. MOR208 and LEN have shown synergy in vitro and in vivo in preclinical lymphoma models. This ongoing phase II study was designed to assess the safety and efficacy of MOR208 plus LEN in patients with R-R DLBCL.

Methods: Patients >18 years of age with R-R DLBCL, ECOG performance status 0-2, adequate organ function, having previously received at least 1 but not more than 3 prior therapies, including at
least 1 CD20-targeting regimen and who are not candidates for autologous stem cell transplant (ASCT), are eligible. Treatment comprises up to 12, 28-day cycles of MOR208 12 mg/kg IV, administered weekly during cycles 1–3 (loading dose day 4 of cycle 1) and every second week during cycles 4–12 plus LEN 25 mg administered po days 1–21 of each cycle. Patients progression-free after 12 cycles receive up to 12 additional cycles of MOR208 12 mg/kg IV, administered every second week. The primary endpoint is the overall response rate (ORR) by central radiology assessment. Secondary endpoints include disease control, duration of response, progression-free and overall survival, safety, and response by cell of origin and other biomarkers. A preplanned safety evaluation was undertaken.

Results: 31 of 80 planned patients were enrolled prior to data cutoff (3 January 2017). Median age was 74 years (range 47–82); 45% of patients received ≥2 prior lines of therapy; 23% had rituximab refractory disease; 74% had Ann Arbor stage ≥III disease; 65% had elevated lactate dehydrogenase level, and 52% had a poor revised International Prognostic Index (3–5). The most common treatment-emergent adverse events (any grade/grade ≥ 3 [% patients]) were neutropenia (39/26), anemia (23/0), thrombocytopenia (16/6), infections (26/10) diarrhea (13/0), pyrexia (13/0), and rashes (13/6). Of 26 response assessable patients (median follow-up 3.3 months), ORR (investigator assessed) was 58% (15 patients), with 7 (27%) complete responses. The median time to response was 1.8 months.

Conclusions: The combination of MOR208 plus LEN is well tolerated and shows promising activity in patients with R DLBCL. Accrual and follow-up of patients is ongoing, as are cell of origin and other biomarker analyses.

Keywords: CD19; diffuse large B-cell lymphoma (DLBCL); lenalidomide.

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A PHASE II LYSA STUDY OF OBINUTUZUMAB COMBINED WITH LENALIDOMIDE FOR RELAPSED OR REFRACTORY FOLLICULAR B-CELL LYMPHOMA


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Background: The combination of rituximab (RTX) and lenalidomide (LEN) has been shown to be synergistic in patients (pts) with previously untreated and relapsed follicular lymphoma (FL). A combination of obinutuzumab (GA), a glycoengineered type II anti-CD20 antibody, with LEN (GALEN) might be even more efficient while retaining a similarly manageable safety profile. We determined the recommended GA + LEN dosing in part IB of this study. Here, we report the results of the Phase II part assessing efficacy and safety of GALEN therapy in a cohort of relapsed/refractory (R/R) FL pts (NCT01582776).

Methods: Eligible pts had a ECOG PS ≤ 2 and previously received at least 1 RTX-containing prior regimen. Induction treatment consisted of LEN 20 mg on d 1-21 of a 28-d cycle for the first cycle and on d 2-22 of a 28-d cycle from cycles 2 to 6. GA 1000 mg was given i.V. on d 8, 15, and 22 of cycle 1 and at D1 of cycles 2 to 6. Responding pts then received maintenance with 12 cycles of LEN at 10 mg on d 2-22 every 28 d for 18 cycles and GA 1000 mg every 8 wk for 12 cycles until progression or unacceptable toxicity. The primary study endpoint was overall response rate (ORR) by investigator assessment at the end of induction according to 1999 IWG criteria. Secondary endpoints included ORR and complete response (CR) according to IWG 2007, progression-free survival (PFS), overall survival (OS) and safety.

Results: 89 pts with WHO FL gr 1-2 (73.2%), 3a (15.5%) or unspecified (11.3%) were enrolled between Jun 2014 and Dec 2015. Median age was 64 y, 62.8% men, 83.7% Ann Arbor stage III-IV, 34.9% with bulky lesions (≥ 5 cm) and 31.0% with elevated LDH. Median time from initial diagnosis was 73.7 mo (range, 12-254) and 27.9% had progressed within 2 years of first-line treatment. Median number of prior regimens was 2 (range, 1–7): 26.7% were refractory to a RTX-containing regimen or last prior therapy. 88 pts were assessable for safety and 86 for efficacy. With a median follow-up of 18.1 mo, 75 pts (87.2%) completed induction and 67 (78%) went on maintenance (ongoing in 45 pts). At the time of cut-off, 19 (22.1%) pts progressed and 10 (11.6%) had died mainly due to FL (6 pts). Response at the end of induction, PFS and OS are summarized in the table.

Most common AEs (>20% of pts) during induction (≤ Gr 3/4) were gastrointestinal disorders (76.1/2.3), infections (62.5/6.8), asthenia (52.3/2.3), neutropenia (30.7/28.4), muscle spasms (30.7/0), and cough (20.7/0). Febrile neutropenia occurred in 3.4% pts. AEs of special interest were rash (19.3/0), peripheral neuropathy (17.0/1.1), IRR (14.8, 3.4), venous thrombosis (1.1/0). 6 second primary malignancies were reported in 3 pts (5 basal carcinoma and 1 myelodysplastic syndrome).

Conclusion: Oral LEN plus GA infusion is highly effective in relapsed or refractory FL pts with no unexpected toxicity.

Keywords: follicular lymphoma (FL); lenalidomide; obinutuzumab.