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 II 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 evaluable patients (median follow-up 3.3 months), ORR (investigator assessed) was 58% (15 patients), with 7 (27%) complete responses. 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-FL. Median time to response was 1.8 months.

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.

The most common AEs (>20% of pts) during induction included: nausea (50.6/10%), constipation (40.5/5%); 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.
PHASE IB STUDY OF CC-122 IN COMBINATION WITH OBINUTUZUMAB (GA101): RELAPSED OR REFRACTORY (R/R) PATIENTS WITH B-CELL NON-HODGKIN LYMPHOMAS (NHL)


1 Hematology, Institut Gustave Roussy, Villejuif, France; 2 Department of Hematology, Institut Paoli-Calmettes, Marseilles, France; 3 Hematology, Erasmus MC Cancer Institute, Rotterdam, Netherlands; 4 Dipartimento di Oncologia ed Ematologia, Azienda Ospedaliera Universitaria Città della Salute e della Scienza di Torino, Torino, Italy; 5 Hematology, Academic Medical Center, Amsterdam, Netherlands; 6 Institute of Hematology “Seràgnoli”, University of Bologna, Bologna, Italy; 7 Translational Development, Celgene Institute for Translational Research Europe, Seville, Spain; 8 Translational Medicine, Celgene Corporation, San Francisco, California, USA; 9 BioStats, Celgene Corporation, Berkeley Heights, New Jersey, USA; 10 Executive Research, Celgene Institute for Translational Research Europe, Seville, Spain

Introduction: CC-122 is a cereblon modulating agent with promising clinical activity in FL and DLBCL. Preclinically, CC-122 with obinutuzumab has improved activity vs either single agent.

Methods: This phase Ib study (EUDRACT 2014-003333-26; NCT02417285) evaluates CC-122 plus obinutuzumab in patients with CD20+ R/R B-cell NHL. Patients with FL/MZL had ≥1 prior regimens, or ≥2 regimens ± ASCT for DLBCL. Oral CC-122 was given (5 of 7d for 28-d cycles in escalating doses until PD or unacceptable toxicity) plus IV obinutuzumab (1000 mg, d2, 8, 15 of c1 and d1 of c2-8). CC-122 active ingredient in capsule formulation (AIC) 1, 2, 3, and 4 mg and formulated capsules (F6) of 3 and 4 mg were evaluated in separate cohorts. Primary endpoints included safety/tolerability, non-tolerated dose (NTD), and maximum tolerated dose. Response was assessed per Cheson 2007 criteria every 2 cycles to c6, every 3 cycles to c12, and every 6 cycles thereafter.

Results: As of January 12, 2017, 34 R/R B-cell NHL patients (18 DLBCL [8 transformed FL], 15 FL, 1 MZL) were enrolled. At study entry, patients had a median age of 60 y (range, 26-81), 68% were male, and 76% had stage III/IV disease. Of the 16 FL/MZL patients, 44% relapsed <12 months following first-line treatment. The median number of prior regimens was 4 (range, 1-11), and 13 (38%) patients had received prior SCT. One patient experienced a dose-limiting toxicity of grade 4 neutropenia (CC-122 AIC 3 mg); no dose was yet an NTD. Median CC-122 duration was 22 wks (range, 3-71), equivalent to 6 cycles (range, 1-18). CC-122 dose reduction occurred in 10 (29%) patients and temporary interruption in 26 (76%), mainly due to AEs. Interruption due to AEs was <1 wk in 56% of patients. The most common grade 3/4 treatment-emergent AEs (TEAEs) were neutropenia (50%) and thrombocytopenia (21%). Fifteen patients (44%) had ≥1 serious TEAE, including 2 each of febrile neutropenia (related to obinutuzumab), cytokine release syndrome (related to obinutuzumab), and pneumonia. There were 3 deaths during the study (2 PD; 1 AE). ORR was 59% (26% CR; Table 1). Median time to best response was 57 d (median DOR not reached). In evaluable patients, 6-mo PFS was 63%.

Conclusions: CC-122 plus obinutuzumab was well tolerated with favorable response rates and durable remissions in R/R B-cell NHL. CC-122 ≥ 3 mg with obinutuzumab shows the best response rates to date, with deepened response upon prolonged treatment. Study is ongoing to identify the phase II recommended dose.

Data cutoff was 10Feb2017. *3 patients were not evaluable for efficacy.

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

<table>
<thead>
<tr>
<th>Response Status, n (%)</th>
<th>R/R DLBCL *n=18</th>
<th>R/R FL/MZL *n=16</th>
<th>All Patients *n=34</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>8 (44)</td>
<td>12 (75)</td>
<td>20 (59)</td>
</tr>
<tr>
<td>CR</td>
<td>3 (17)</td>
<td>6 (38)</td>
<td>9 (26)</td>
</tr>
<tr>
<td>PR</td>
<td>5 (28)</td>
<td>6 (38)</td>
<td>11 (32)</td>
</tr>
<tr>
<td>SD</td>
<td>4 (22)</td>
<td>3 (19)</td>
<td>7 (21)</td>
</tr>
<tr>
<td>PD</td>
<td>3 (17)</td>
<td>1 (6)</td>
<td>4 (12)</td>
</tr>
</tbody>
</table>

TABLE 1: Best responses with CC-122 and obinutuzumab in evaluable patients.