

lenalidomide and rituximab are highly active in both frontline and relapsed disease. Obinutuzumab has increased antibody dependent cellular cytotoxicity (ADCC) compared to rituximab in preclinical models and is approved for FL. We hypothesized that the immunologic properties of obinutuzumab and lenalidomide would be synergistic in relapsed FL. The study's objectives were to determine the MTD of lenalidomide with obinutuzumab and describe the efficacy of the combination.

**Methods:** This open label phase I/II study enrolled relapsed/refractory Gr 1–3a FL. Exclusions included transformation, prior malignancy, and infection. Lenalidomide was given on D 2–22 with 1000 mg obinutuzumab on D1, 8, 15, and 22 of cycle 1 and monthly on D 1 for up to 12 cycles. Extended dosing with obinutuzumab was given every 2 months thereafter for up to 30 months total in patients (pts) who responded following doublet therapy. During phase I, three escalating dose levels were planned with 10, 15, and 20 mg of lenalidomide. Phase II planned to enroll 30 pts at MTD with efficacy and safety as primary endpoints.

**Results:** All 36 pts with FL enrolled (6 in dose escalation and 30 at MTD), and all are eligible for efficacy and safety analysis. The median age was 65 with a median of 2 prior therapies. No DLTs were observed in phase I, and 20 mg of lenalidomide was used for the phase II dose. To date, the most common all grade non-hematologic toxicities included fatigue (83%), diarrhea (67%), and rash (53%). Grade 3+ toxicities included neutropenia (23%), infection (11%), and fatigue (8%). The overall response rate was 100% with 78% (95% CI: 60.85–89.88%), of pts attaining complete remission (CR/Cru). At a median follow up of 14 months, 10 pts progressed. The estimated 24 month PFS is 61% (95% CI: 43–87%).

**Conclusions:** Lenalidomide and obinutuzumab is highly active with durable remissions in relapsed FL, with all pts responding and 78% achieving CR. The majority of pts remain on therapy and the combination appeared safe. Correlatives are ongoing to identify biomarkers of response and frontline studies of the combination are currently enrolling.

**Keywords:** follicular lymphoma (FL); immunomodulators (IMiDs); monoclonal antibodies (MoAb).

## 281 INTEGRATED SAFETY DATA WITH COPANLISIB MONOTHERAPY FROM PHASE I AND II TRIALS IN PATIENTS WITH RELAPSED INDOLENT NON-HODGKIN'S LYMPHOMA

P. Zinzani<sup>1\*</sup> | M. Dreyling<sup>2</sup> | A. Patnaik<sup>3</sup> | F. Morschhauser<sup>4</sup> | A. Benson<sup>5</sup> | I. Genvresse<sup>6</sup> | A. Miriyala<sup>7</sup> | J. Garcia-Vargas<sup>7</sup> | B.H. Childs<sup>7</sup>

<sup>1</sup>Department of Hematology, Institute of Hematology "L. e A. Seràgnoli"-University of Bologna, Bologna, Italy; <sup>2</sup>Medizinische Klinik und Poliklinik III, Klinikum der Universität München-Grosshadern, Munich, Germany; <sup>3</sup>Medical Oncology, South Texas Accelerated Research Therapeutics (START) Center for Cancer Care, San Antonio, TX, USA; <sup>4</sup>Department of Hematology, CHRU - Hôpital Claude Huriez, Lille, France; <sup>5</sup>Clinical

Statistics, Bayer HealthCare Pharmaceuticals Inc, Whippany-NJ, USA;

<sup>6</sup>Pharmaceutical Division, Bayer AG, Berlin, Germany; <sup>7</sup>Clinical

Development, Bayer HealthCare Pharmaceuticals Inc, Whippany-NJ, USA

**Introduction:** Phosphatidylinositol 3-kinase (PI3K) is a therapeutic target for patients (pts) with indolent non-Hodgkin's lymphoma (iNHL). Copanlisib is a pan-Class I PI3K inhibitor with predominant activity against PI3K- $\alpha$  and PI3K- $\delta$  isoforms. In contrast to oral PI3K inhibitors that are dosed continuously, intermittent IV administration of copanlisib has demonstrated a different safety profile. We report results here from a pooled safety analysis.

**Methods:** Safety data from 4 studies (NCT00962611, NCT01660451 parts A and B, and NCT02155582) including iNHL pts were pooled for analysis. All pts had received IV copanlisib on days 1, 8, and 15 of a 28-day cycle at either 0.8 mg/kg or an equivalent fixed dose of 60 mg. Treatment emergent adverse events (TEAE) were reported using MedDRA terms and worst NCI CTCAE grading.

**Results:** A total of 168 pts with iNHL were available for safety analysis, including follicular (75%) and marginal zone lymphoma (15%) pts. Median prior lines of therapy was 3 (range 1–10); including rituximab ( $n = 168$ ) and alkylating agents ( $n = 167$ ). The mean duration of treatment was 30.2 weeks ( $\pm 30.4$ ) and mean number of cycles 7.5 ( $\pm 7.6$ ). The most common TEAEs (occurring in  $\geq 20\%$  of the pts) were transient hyperglycemia (51%), diarrhea (36%), transient hypertension (35%), fatigue (29%), nausea (26%), neutropenia (25%), and pyrexia (24%). The most common grade 3 TEAEs ( $\geq 5\%$ ) were hyperglycemia (32%), hypertension (27%), neutropenia (8%), and pneumonia (8%); hyperglycemia and hypertension were transient and largely asymptomatic. Grade 4 TEAEs ( $\geq 5\%$ ) were neutropenia (12%) and hyperglycemia (6%). Serious TEAEs ( $\geq 2\%$ ) were pneumonia (10%), pyrexia, hyperglycemia and pneumonitis (5% each), neutropenia, diarrhea and lung infection (2% each). There were six grade 5 TEAEs, with 3 reported as drug-related: lung infection, respiratory failure, and embolism. Infections ( $\geq 5\%$ ) included upper respiratory (14%), pneumonia (11%), bronchitis (9%), urinary (7%), oral herpes (6%), and rhinitis (5.4%). Opportunistic fungal infections occurred in 3 pts; two *Pneumocystis jirovecii* pneumonia and one bronchopulmonary aspergillosis. GI toxicity included grade 3 diarrhea (5%) and one case of colitis (grade 4) was reported. Suspected non-infectious pneumonitis was reported in 9% (3% grade 3 and no grade 4/5). Treatment discontinuations due to TEAEs (24%) included pneumonitis (2%), neutropenia, thrombocytopenia, fatigue, pneumonia, platelet count decreased, and hyperglycemia (1.8% each).

**Conclusions:** Integrated safety analysis demonstrates that copanlisib had a tolerable and manageable safety profile with a low rate of severe gastrointestinal toxicities, hepatotoxicities, pneumonitis, and opportunistic infections. The most common grade 3 AEs were transient hyperglycemia and transient hypertension, both of which were predictable and manageable and did not lead to significant discontinuation.

**Keywords:** non-Hodgkin lymphoma (NHL); PI3K/AKT/mTOR.

## 282 LYMRIT 37-01: UPDATED RESULTS OF A PHASE I/II STUDY OF <sup>177</sup>LU-LILOTOMAB SATETRAXETAN, A NOVEL CD37-

## TARGETED ANTIBODY- RADIONUCLIDE-CONJUGATE IN RELAPSED NHL PATIENTS

A. Kolstad<sup>1\*</sup> | U. Madsbu<sup>2</sup> | M. Beasley<sup>3</sup> | M. Bayne<sup>4</sup> | T. Illidge<sup>5</sup> | N. O'Rourke<sup>6</sup> | I. Lagerlöf<sup>7</sup> | R. Hájek<sup>8</sup> | W. Jurczak<sup>9</sup> | E. Willenbacher<sup>10</sup> | J. Blakkisrud<sup>11</sup> | A. Muftuler Løndalen<sup>2</sup> | L. Rojkjaer<sup>12</sup> | L. Baylor Curtis<sup>12</sup> | M. Bloma<sup>12</sup> | S. Turner<sup>12</sup> | N. Bolstad<sup>13</sup> | S. Spetalen<sup>14</sup> | M. Erlanson<sup>15</sup> | S. Nygaard<sup>1</sup> | H. Holte<sup>1</sup>

<sup>1</sup>Department of Oncology, Oslo University Hospital, Oslo, Norway; <sup>2</sup>Dept of Radiology and Nuclear Medicine, Oslo University Hospital, Oslo, Norway; <sup>3</sup>Bristol Hospitals NHS Foundation Trust, Bristol Haematology and Oncology Centre, Bristol, UK; <sup>4</sup>Poole General Hospital, Dorset Cancer Centre, Poole, UK; <sup>5</sup>Manchester Academic Health Science Centre, The Christie NHS Foundation Trust, Manchester, UK; <sup>6</sup>Beatson West of Scotland Cancer Centre, Gartnavel General Hospital, Glasgow, Norway; <sup>7</sup>Hematologic Clinic, University Hospital Linköping, Linköping, Sweden; <sup>8</sup>Klinika hematookologie, FNŠP Ostrava, Ostrava, Czech Republic; <sup>9</sup>Oncology, Małopolskie Centrum Medyczne, Kraków, Poland; <sup>10</sup>Innere Medizin V (Hämatologie/Onkologie), Universitätsklinikum Innsbruck, Innsbruck, Austria; <sup>11</sup>The Intervention Centre, Oslo University Hospital, Oslo, Norway; <sup>12</sup>Clinical Department, Nordic Nanovector, Oslo, Norway; <sup>13</sup>Department of Medical Biochemistry, Oslo University Hospital, Oslo, Norway; <sup>14</sup>Department of Pathology, Oslo University Hospital, Oslo, Norway; <sup>15</sup>Dept of Oncology, Norrland University Hospital, Umeå, Sweden

**Introduction:** Lutetium (<sup>177</sup>Lu) lilotomab satetraxetan (Betalutin®) is a novel beta-emitting anti-CD37 ARC in a ready-to-use formulation. CD37 is highly expressed (>90%) in B-cell NHL, providing an alternative target to CD20. LYMRIT 37-01 is a phase I/II, open-label, dose-escalation study to evaluate the safety and preliminary efficacy of Betalutin® monotherapy in patients (pts) with relapsed non-Hodgkin's lymphoma (NHL). We present updated safety and efficacy data for all pts as of February 13, 2017.

**Methods:** Pts with histologically confirmed NHL (follicular (FL) grade I–IIIA, mantle cell (MCL) and marginal zone (MZL)) relapsing after ≥1 prior therapy with <25% bone marrow involvement, platelets (plt) >150 × 10<sup>9</sup>/L, no prior SCT/RIT, and a life expectancy of ≥3 months were enrolled into 1 of 4 dose-escalation arms (part 1) to determine the optimal lilotomab pre-dose and Betalutin® regimen for further evaluation in an expanded cohort (part 2). All pts received pre-treatment with rituximab. Responses were assessed using Cheson IWG response criteria (including CT and PET-CT scans) beginning at week 12.

**Results:** A total of 56 patients have been enrolled; 43 are evaluable for safety and 38 for efficacy. Patients who had reached their platelet/neutrophil nadir were included in the safety assessment. NHL subtypes were FL (n = 31), MCL (n = 4), and MZL (n = 8). The number of prior therapies ranged from 1 to 8. A total of 38 pts received lilotomab 40 mg pre-dose (Arm 1). A total of 10 pts received lilotomab 100 mg/m<sup>2</sup> pre-dose (Arm 4). Arms 2 and 3 without lilotomab pre-dosing were discontinued. Treatment-emergent grade 3/4 AEs in ≥2 pts were neutropenia (42/19%), thrombocytopenia

(28/23%), leukopenia (44/7%) and lymphocytopenia (35/2%); all were reversible. Treatment emergent SAEs in ≥2 pts were thrombocytopenia (n = 2) and atrial fibrillation (n = 2). For patients receiving 15 MBq/kg Betalutin®, mean platelet and neutrophil nadirs were 62 and 1.0 × 10<sup>9</sup>/L with 40 mg lilotomab pre-dose (n = 25) compared to 124 and 2.1 × 10<sup>9</sup>/L with 100 mg/m<sup>2</sup> (n = 3) lilotomab pre-dose, respectively.

The ORR for all pts was 63% (CR 29%) and 65% (CR 27%) for FL pts. Tumor reductions were seen in 84%. The ORR for 22 pts receiving lilotomab 40 mg/15 MBq/kg Betalutin® (Arm 1 MTD) was 64% (CR 36%).

Best Response	All (N=38)	FL (N=26)
Overall response rate (CR+PR)	24 (63%)	17 (65%)
CR	11 (29%)	7 (27%)
PR	13 (34%)	10 (38%)
SD	6 (16%)	3 (12%)
PD	8 (21%)	6 (23%)
Not evaluable	1	1

**Conclusions:** Betalutin® has promising single agent activity in relapsed NHL and was generally well tolerated. A higher lilotomab pre-dose may allow administration of a higher and potentially more efficacious dose of Betalutin®—evaluation is ongoing and updated safety/efficacy results will be reported at the meeting.

**Keywords:** indolent lymphoma; non-Hodgkin lymphoma (NHL); radioimmunotherapy (RIT).

## 283 INTERIM DATA FROM THE FIRST CLINICAL STUDY OF ADCT-301, A NOVEL PYRROLOBENZODIAZAPINE-BASED ANTIBODY DRUG CONJUGATE, IN RELAPSED/REFRACTORY HODGKIN/NON-HODGKIN LYMPHOMA

S.M. Horwitz<sup>1\*</sup> | M.A. Fanale<sup>2</sup> | A.I. Spira<sup>3</sup> | K. Havenith<sup>4</sup> | S. He<sup>5</sup> | J.M. Feingold<sup>5</sup> | M. Hamadani<sup>6</sup>

<sup>1</sup>Department of Medical Oncology, Memorial Sloan-Kettering Cancer Center, New York, USA; <sup>2</sup>Department of Lymphoma/Myeloma, The University of Texas MD Anderson Cancer Center, Houston, USA;

<sup>3</sup>Department of Medical Oncology, US Oncology Research, The Woodlands, USA; <sup>4</sup>R&D Laboratories, ADC Therapeutics, London, UK;

<sup>5</sup>Clinical Development, ADC Therapeutics, Murray Hill, USA; <sup>6</sup>Division of Hematology and Oncology, Medical College of Wisconsin, Milwaukee, USA

**Introduction:** Expression of CD25 occurs in many lymphomas, including Hodgkin (HL), peripheral T cell, cutaneous T cell, and diffuse large B cell. ADCT-301 is an antibody drug conjugate comprising a human monoclonal antibody against CD25 conjugated to a potent pyrrolobenzodiazepine dimer toxin. ADCT-301 has demonstrated potent anti-tumor activity in pre-clinical studies against CD25-expressing hematological malignancies. This first in human clinical trial