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Abstract 3686 Obinutuzumab (GA101) in Combination with Cyclophosphamide, Doxorubicin, Vincristine and Prednisone (CHOP) or Bendamustine in Patients with Previously Untreated Follicular Lymphoma (FL): Results of the Phase Ib GAUDI Study (BO21000)

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GA101 is a glycoengineered, humanized type II anti-CD20 monoclonal antibody (mAb) anticipated to have superior B-cell-depleting activity to rituximab *in vivo*on the basis of its enhanced FcR binding and because of the direct cell death induced by type II CD20 mAbs. GA101 has shown significant single-agent activity in Phase I and II studies in patients with FL, and activity in combination with CHOP and fludarabine plus cyclophosphamide in patients with resistant/refractory FL in the first part of this Phase I trial (Radford et al. ASH 2011; abstract 270).

This report describes the safety, toxicity, and efficacy of remission induction of GA101 in combination with CHOP or bendamustine in 81 patients aged > 18 years with treatment-naïve CD20+ grade 1–3b FL with at least one measurable lesion (longest diameter > 1.5 cm by CT scan). All patients received a flat dose of GA101 (1,000 mg on Days 1 and 8 of Cycle 1 and Day 1 of subsequent cycles) combined with either 6–8 cycles of CHOP (every 3 weeks) or 4–6 cycles of bendamustine (90 mg/m^{2}Days 1 and 2 every 4 weeks) on a per center choice basis. Patients achieving complete response (CR) or partial response (PR) were eligible to receive GA101 maintenance therapy (1,000 mg) every 3 months for 2

years or until progression. The primary objective was safety, and secondary objectives included overall response rate (ORR), CR rate, and pharmacokinetics. Response was assessed at the end of induction using International Working Group response criteria; unconfirmed CRs were classified as PRs.

40 patients received G-CHOP and 41 G-bendamustine. Baseline characteristics were similar for both groups: median age 53.5 and 57 years; bone marrow involvement 53% and 49%; bulky disease (≥ 7 cm) 45% and 41%; Median time from diagnosis was only 1.20 months for both groups, high-risk FLIPI status (3–5) 45% and 46%, and intermediate risk (FLIPI 2) 38% and 34%.

38 G-CHOP and 37 G-bendamustine patients completed all cycles of planned induction therapy. Three patients withdrew without any response assessment. In the G-CHOP arm, one withdrawal was due to a GA101-associated infusion-related reaction [IRR] after Cycle 1 and another patient was found to be ineligible and withdrawn after Cycle 1. In the G-bendamustine arm one patient withdrew consent after Cycle 2. Three other patients were withdrawn after interim response assessment, none for safety reasons (insufficient response in the G-bendamustine arm and administrative reasons for two in the G-CHOP arm).

The most frequent adverse events were IRRs (all grades: 58% G-CHOP; 59% G-bendamustine; grade 3/4: 5% G-CHOP; 10% G-bendamustine). No Grade 3/4 IRRs occurred after cycle 3.

Grade 3/4 neutropenia was reported in 43% of patients in the G-CHOP arm and 29% of patients in the G-bendamustine arm during induction, resulting in delayed delivery of 7.0% and 4.8% of chemotherapy cycles. All delays but one were no longer than 2 weeks.

Grade 3/4 infections occurred in 23% of patients receiving G-CHOP and 10% of patients receiving G-bendamustine. Approximately half of these were neutropenic infections or sepsis and all resolved with appropriate management.

ORR at the end of the induction period was 95% (38/40) in the G-CHOP arm (CR rate 35%) and 92.7% (38/41) in the G-bendamustine arm (CR rate 39%) (Table).

Serum GA101 concentrations increased during the induction period and were similar for both regimens. Mean C_{max} was 300–600 µg/mL and C_{min}100–300 µg/mL. Following the final administration, a decline in GA101 serum concentration was seen that was similar for the two treatment combinations.

In conclusion, efficacy and safety data for GA101 combined with CHOP and bendamustine are encouraging for first-line treatment of patients with FL. Based on these promising results GA101 is now being studied in combination with various chemotherapy regimens

in a randomized Phase III study against the standard of care, rituximab-based immunochemotherapy.

	Patients, n (%)	
	G-CHOP (n = 40)	**G-bendamustine (n = 41)**
Efficacy		
Overall response	38 (95.0)	38 (92.7)
Complete response*	14 (35.0)	16 (39.0)
Partial response	24 (60.0)	22 (53.7)
Stable disease	0	1 (2.4)
Progressive disease	0	1 (2.4)
Not assessed	2 (5.0)	1 (2.4)
Safety		
Grade 3/4 IRRs	2 (5.0)	4 (9.8)
Grade 3/4 neutropenia	17 (43)	12 (29)
Grade 3/4 infections	9 (23)	4 (10)

* CRu were classified as PR

Disclosures: Dyer: *Roche:* Consultancy, Research Funding. **Off Label Use:** Obinutuzumab (GA101) in Combination with Cyclophosphamide, Doxorubicin, Vincristine and Prednisone (CHOP) or Bendamustine in Patients with Previously Untreated Follicular Lymphoma (FL). **Grigg:** *Roche:* Membership on an entity's Board of Directors or advisory committees, Research Funding. **Dreyling:** *Roche:* Honoraria, Support of (other) clinical trials and Scientific Advisory Boards Other. **Rule:** *Roche:* Consultancy, Research Funding. **Lei:** *Roche:* Employment. **Wassner-Fritsch:** *Roche:* Employment. **Wenger:** *Roche:* Employment. **Marlton:** *Roche:* Honoraria, Membership on an entity's Board of Directors or advisory committees.