Results of a Phase 1 Study of AME-133v (LY2469298), an Fc-Engineered Humanized Monoclonal Anti-CD20 Antibody, in FcγRIIIa-Genotyped Patients with Previously Treated Follicular Lymphoma

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Abstract

Purpose: AME-133v is a humanized monoclonal antibody engineered to have increased affinity to CD20 and mediate antibody-dependent cell-mediated cytotoxicity (ADCC) better than rituximab. Safety, pharmacokinetics, and efficacy were assessed in a phase 1/2 trial in patients with previously treated follicular lymphoma (FL).

Patients and Methods: AME-133v was characterized in vitro by ADCC and cell binding assays. A phase 1 study was conducted in which 23 previously treated patients with FL were assigned sequentially to one of five dose-escalation cohorts of AME-133v at 2, 7.5, 30, 100, or 375 mg/m² weekly/C24 doses.

Results: AME-133v showed a 13- to 20-fold greater binding affinity for CD20 and was 5- to 7-fold more potent than rituximab in ADCC assays. Cell binding assays showed AME-133v and rituximab competed for an overlapping epitope on the CD20 antigen, and AME-133v inhibited binding of biotinylated rituximab to CD20 in a concentration-dependent manner. AME-133v was well tolerated by patients and common related adverse events included chills and fatigue. One patient experienced a dose-limiting toxicity of neutropenia. AME-133v showed nonlinear pharmocokinetics with properties similar to rituximab. Selective reduction of B cells during and after AME-133v treatment was shown by flow cytometry of peripheral blood. A partial or complete response was observed in 5 of 23 (22%) patients and the median progression-free survival was 25.4 weeks.

Conclusions: AME-133v was safe and well tolerated at the doses tested. AME-133v showed encouraging results as an anti-CD20 therapy in heavily pretreated FL patients with the less favorable FcγRIIIa F-carrier genotype. Clin Cancer Res; 18(5); 1395–403. ©2012 AACR.
 NK cells from 158-homozygous-VV donors better than the other 2 antibodies. This suggests that an antibody with enhanced ability to mediate ADCC may be more effective clinically, particularly in patients who are FcRIIIa F-carriers.

Although rituximab monotherapy is effective in patients with FL, several studies suggested that rituximab is less effective in F-carriers. In a clinical trial of rituximab in 49 previously untreated patients with FL, patients with the 158-VV FcRIIIa genotype had a significantly higher response rate at 2 months (100% vs. 67%) and 12 months (90% vs. 51%) compared with F-carriers (7). A retrospective assessment of 87 patients with FL treated with rituximab showed that patients with the 158-VV genotype had significantly higher response rates compared with F-carriers, as well as a significantly longer time to progression (534 days vs. 174 days, respectively; ref. 8). The Swiss Clinical Cancer Research (SACK) group analyzed the effect of FcRIIIa F-carriers. This provides a strong rationale for the development of AME-133v therapy in FL, patients, and in particular, those patients who are FcRIIIa F-carriers.

**Materials and Methods**

**AME-133v engineering**

AME-133v is a humanized IgG1 variant monoclonal antibody engineered to have greater affinity for CD20 and greater ADCC activity compared with rituximab in vitro. The parent murine IgG2a anti-CD20 antibody was humanized with codon-substituted variations of the antibody complementarity determining regions (CDR) inserted into human antibody germ line frameworks. CDR variants were screened for binding to CD20 antigen present on human Ramos B lymphoma cells in an ELISA format. Beneficial CDR mutations were combined and selected Fab clones were expressed as whole IgG1 molecules, purified and characterized further. To directly compare cell binding kinetics in solution, rituximab and AME-133 were tested for their binding to both SKW6.4 B lymphoma cells (intermediate CD20 antigen expression; ref. 10) and primary human CD19-positive peripheral blood B cells (high CD20 antigen expression) with a Sapidyne (Boise, ID) KinElX instrument.

Starting from a humanized high-affinity anti-CD20 IgG1, 2 amino acid changes were introduced into its Fc region and tested for ADCC activity using a single-point ADCC assay format. Variants showing superior activity were confirmed by full titrations using purified mAbs.

**Antibody-dependent cell-mediated cytotoxicity assays**

Standard cytolytic assays were used to measure the ADCC activity of AME-133 Fc region variants. Briefly, immune effector cells were isolated from the blood of healthy donors using Histopaque-1077 (Sigma) separation and plastic adherence. Effector cells were added to CD20 opsonized target cells at a ratio of 20 to 1 and incubated for 3 hours at 37°C. Assay plates were centrifuged and supernatants analyzed for lactate dehydrogenase released from the cytosol of damaged cells using a cytotoxicity detection kit (Roche Applied Science). The plates were read at 490 nm and raw absorbance (A) values were converted to % maximal response using the following equation: % maximal response = experimental A - basal A/maximal A - basal A × 100, with maximal A determined by adding 2% Triton X-100 to the target cells and basal release measured for a mixture of effector and target cells in the absence of sensitizing IgG.

**Cell binding assays**

For competition experiments involving prebound rituximab, titrations of biotinylated rituximab were incubated with SKW6.4 B cells overnight at 37°C. After incubation, nonbiotinylated competitor antibody (AME-133v or a nonspecific IgG1) or PBS was added directly without prior washing. The time-dependent displacement of rituximab from the cells was followed at 37°C by detecting the residual bound biotinylated rituximab with neutravidin alkaline
Phase 1 Study of AME-133v in Patients with Follicular Lymphoma

Phosphatase conjugate and development with AMP/PNP [AMP (2-aminoo-2-methyl-1-propanol; Thermo Scientific) and PNP-phosphatase substrate (p-nitrophenyl phosphate disodium salt; Santa Cruz Biotechnology, Inc.)] substrate. Absorbance was read at 560 nm using a Molecular Devices plate reader. For direct competition experiments titrations of biotinylated rituximab and AME-133v were prepared individually, mixed together, and added to SKW6.4 cells followed by incubation for 2 hours at 37°C. Following incubation, the plates were processed as previously described.

Phase 1 patient selection

Patients were eligible for the study if they were at least 18 years old with diagnosis of CD20+ follicular B cell non-Hodgkin lymphoma, had the FcγRIIIa (with SNP coding for F/F or F/V at position 158) as determined by FcγR genotyping (Beckmann Coulter Genomics), and had measurable disease. Prior treatment with chemotherapy, rituximab, or both for FL was required. Prior rituximab was allowed if the patient had not relapsed or progressed within 120 days of the last infusion of rituximab. In addition, patients had no evidence of hepatitis B or C infection and had discontinued all previous cancer and high-dose corticosteroid therapies at least 30 days prior to study entry. All eligible patients had adequate hematopoietic, renal, and hepatic function, and women of childbearing potential were required to use a medically acceptable contraceptive regimen.

Phase 1 trial design and dose escalation

The trial was an open-label, multicenter, phase 1, dose-escalation study of AME-133v (LY2469298), administered intravenously in 4 weekly doses, in patients with previously treated CD20+ FL. The primary objective of the phase 1 study was to determine the safety and tolerability of repeat administration of AME-133v at 5 dose levels: 2, 7.5, 30, 100, and 375 mg/m2. A standard '3 + 3' enrollment design was employed. After the last patient in a cohort received their fourth dose, a 2-week safety period was observed. The study was conducted in accordance with the principles of the Declaration of Helsinki, Good Clinical Practice ICH Tripartite Guideline (January 1997), and basic principles of Good Clinical Practice as outlined in the current version of 21 Code of Federal Regulations (CFR). The protocol and informed consent for this study was approved by Institutional Review Boards at each participating institution and all patients were required to sign informed consent prior to study entry (ClinTrials registry number NCT00354926).

AME-133v was diluted in normal saline and administered with an infusion or syringe pump. The 2, 7.5, and 30 mg/m2 doses were delivered over fixed infusion times of 30, 60, and 180 minutes, respectively. For the 100 and 375 mg/m2 doses, the first dose was delivered at a rate up to 25 mg/h for the first 30 minutes, which was increased by up to 50 mg/h every 30 minutes. Subsequent infusions were administered at an initial rate of up to 100 mg/h and increased by up to 100 mg/h increments every 30 minutes until a maximum rate of 300 mg/h was reached. All patients were premedicated with acetaminophen 650 mg and diphenhydramine 50 mg. Premedication with steroids was prohibited.

Side effects were assessed according to the National Cancer Institute (NCI) Adult Common Toxicity Criteria (CTCAEv.3.0). A dose-limiting toxicity (DLT) was defined as the occurrence of any grade 3 or higher drug-related adverse event (AE), with the following modifications: grade 3 hematopoietic toxicity was defined as an absolute neutrophil count nadir of 500 to 1,000/µL, or a decrease in platelets or hemoglobin of 50% to 74% from the lower limit of normal or the pretreatment value, whichever is less (11). Grade 3 infusion reactions (e.g., fever, chills, rigors, bronchospasm, urticaria, and hypotension) and tumor lysis syndrome that were transient and resolved without sequelae were not considered DLTs in this study. Any patient who experienced a DLT did not receive additional study medication and was followed until the toxicity resolved to a CTCAEv.3.0 grade 1 severity.

All patients who received at least 1 dose of AME-133v were evaluated for safety, pharmacokinetic, and lymphoma response. SAS procedures (version 8 or higher) were employed for the generation of all tables, graphs, and statistical analyses, except where otherwise specified.

Pharmacokinetic and pharmacodynamic studies

AME-133v concentration and time data were collected from a total of 23 patients enrolled in the 2, 7.5, 30, 100, and 375 mg/m2 dose groups. All pharmacokinetic samples were drawn predose before infusion 1; 3 to 5 days after infusion 1, predose before infusions 2, 3, and 4; and 1, 5, and 9 weeks after infusion 4.

The pharmacokinetic data collected from these patients were analyzed by means of nonlinear mixed effect modeling using NONMEM software (version VI.2) with NM-TRAN and PREDPP. The pharmacokinetic model describing the pharmacokinetic profile of AME-133v was parameterized in terms of CL, V1, Q, and V2, which correspond to the clearance (CL), volume of the central compartment, intercompartmental CL, and volume of the peripheral compartment, respectively. Peripheral blood B cells were quantitated with fluorescence-activated cell sorting on samples collected at baseline and at all subsequent study visits.

Response criteria

Response to treatment was assessed according to the 1999 National Cancer Institute Working Group criteria, 9 weeks after the last dose (12) and subsequently every 3 months until disease progression, death, or another therapy was initiated. Additional endpoints included duration of response and progression-free survival (PFS).

Results

AME-133v characterization

Relative to rituximab, AME-133v showed a 13- to 20-fold increase in binding affinity for CD20 with a Kd of...
approximately 100 pmol/L when tested on SKW6.4 cells and primary B lymphocytes (Supplementary Table S1). The increased binding was due to a large improvement in the antibody off rate although a modest improvement in on-rate was also observed. AME-133v was also approximately 6-fold more potent than rituximab in ADCC assays and showed improved binding affinity to the V/V as well as V/F and F/F forms of the FcR (Supplementary Fig. 1A and B). Competitive binding experiments were carried out to determine whether AME-133v and rituximab bound to the same epitope on the CD20 antigen expressed on SKW6.4 B cells. Direct competition assays, in which AME-133v and rituximab were premixed prior to the addition of the mixture to the cells, showed that AME-133v inhibited the binding of biotinylated rituximab to CD20 in a concentration-dependent manner (Supplementary Fig. S1C and S1D). The ability of AME-133v to displace prebound rituximab from the surface of SKW6.4 cells was assessed as a function of time (Supplementary Fig. S1E). The nonspecific competitor IgG1 at 150 μg/mL had no effect upon the binding of rituximab even after 32-hour incubation; however, in the presence of AME-133v, a time-dependent reduction in rituximab binding signal was observed, with most of the biotinylated rituximab being competed from the cells within 32 hours. Additional prebound rituximab experiments assessing concentrations of 75 and 150 μg/mL of AME-133v yielded similar results to the 25 μg/ml concentration (data not shown). These results further underscore the time rather than dose-dependent nature of rituximab displacement by AME-133v.

Phase 1 dose escalation
Between August 2006 and November 2007, 23 patients with previously treated CD20⁺ FL were enrolled to the phase 1 portion of this study. The median age of the patients was 61 years (range: 37–77) with a slight male predominance (13 of 23). All patients were F-carriers in at least 1 allele of the FcγRIIIa gene. Patient characteristics including genotypes for FcRs II and III are shown in Table 1. At baseline, 16 patients had an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0, and 6 patients had an ECOG PS of 1. All patients received prior systemic therapy, with a median number of 2 prior regimens (range: 1–6). Only 1 patient was rituximab naïve.

Safety
All 23 patients reported one or more AEs (Supplementary Table S2). The most common AEs were chills (13 patients; 57%), nausea (7 patients; 30%), fatigue and dizziness (each 6 patients; 26%), vomiting (5 patients; 22%), and arthralgia, headache, hypotension, and upper respiratory tract infection (each 4 patients; 17%). Nine patients reported

<table>
<thead>
<tr>
<th>Patient</th>
<th>Cohort (mg/m²)</th>
<th>Age (y)</th>
<th>Stage</th>
<th>FcγR2a genotype</th>
<th>FcγR3a genotype</th>
<th>Best response</th>
<th>PFS (days)</th>
<th>PFS censored flag</th>
<th>Prior therapy</th>
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Abbreviations: R, rituximab; C, chemotherapy; RM, rituximab maintenance; RIT, radioimmunotherapy.
infections (including influenza, nasopharyngitis, tinea pedis, upper respiratory tract infection, urinary tract infection, and viral infection), and 6 of these patients were in the 2 highest dose groups. The only grade 3/4 AE that occurred in more than one patient was neutropenia (2 patients). The grades 3 and 4 AEs, regardless of attribution are listed in Table 2. The only grade 3 AE attributed to study therapy was bronchospasm, which was an infusion reaction and was not considered a DLT. Other AEs, including potential infusion reaction-related AEs were of grade 1 or 2 (Table 3). The majority of patients experienced infusion-related reactions, which were most commonly grade 1. There were more events reported at the first infusion (91% of patients) compared with subsequent infusions (14% to 23% of patients), as depicted in Fig. 1. Two patients reported treatment-emergent serious AEs: one with neutropenia as previously described, and one with a small intestinal obstruction due to progression of lymphoma. The latter patient received only 1 dose of study drug, withdrew consent, and received no further study drug.

One DLT was observed during the dose escalation period. In cohort 4 (100 mg/m²), a patient experienced grade 4 neutropenia 1 week after the fourth dose of AME-133v. The event met the criteria for a serious AE and was considered possibly related to the study drug. The patient recovered completely in 11 days. As a result of this DLT, 3 more patients were added to the cohort, and no additional DLTs were observed. The dose was escalated to the highest planned dose level of 375 mg/m², 6 patients were enrolled according to the protocol, and no DLTs were observed. In the 2 mg/m² cohort, 1 additional patient was enrolled to replace a patient who withdrew consent after receipt of 1 dose of study drug. In the 30 mg/m² dose cohort, 2 eligible patients were consented concurrently and both were allowed to enroll. Thus, a maximum tolerated dose was not reached during the dose-escalation period.

Multiple gated acquisition cardiac scans were evaluated for patient eligibility, at baseline and at 1 week and 9 weeks post last infusion. No clinically significant findings were observed for any patient at any visit.

**Pharmacokinetics**

Due to values below the limit of quantitation, the data from the 4 patients enrolled in the 2 mg/m² dose group were excluded from the analysis. In addition, 1 patient from the 375 mg/m² dose group was deemed an outlier and was

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**Table 2.** AEs of toxicity grade 3 or higher

<table>
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<th>Grade 3/4 AEs</th>
<th>Dose (mg/m²)</th>
<th>2 (N = 4)</th>
<th>7.5 (N = 3)</th>
<th>30 (N = 4)</th>
<th>100 (N = 6)</th>
<th>375 (N = 6)</th>
<th>Total (N = 23)</th>
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<tr>
<td></td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>(%)</td>
</tr>
<tr>
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<td>2</td>
<td>3</td>
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*aGrade 4 and a DLT; all others grade 3.

bAttributed to study therapy; all others considered not related to study therapy.

**Table 3.** AEs reported at infusion

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<th>Second infusion</th>
<th>Third infusion</th>
<th>Fourth infusion</th>
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<td>4</td>
<td>4</td>
<td>5</td>
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<tr>
<td>7.5 mg/m²</td>
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<tr>
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excluded from the analysis. Therefore, the analysis was conducted on a total of 216 serum AME-133v observations from 18 patients. Due to nonlinearity in the pharmacokinetics of AME-133v across the dose range tested and the small number of observations, the best fit was obtained with a 2-compartment model with a dose-dependent CL term.

The population pharmacokinetic parameters of AME-133v are summarized in Supplementary Table S3 and are similar to those previously reported for rituximab (13). The typical CL estimates range from 0.75 to 0.24 L/d from 7.5 to 375 mg/m², and the typical volume of the central and peripheral compartments are 2.98 and 2.70 L, respectively. A visual predictive check (VPC) of the AME-133v concentration-time profile is illustrated in Fig. 2A–D. Interindividual variability was moderate to large with 50% and 36% for CL and V1, respectively (Supplementary Table S3).

Response and time to event assessments

All 23 patients were included in the investigator reported response assessment. Twenty-two patients received all 4 doses of study drug and one patient discontinued the study after receiving 1 dose of study drug. The majority of patients experienced a reduction in lymphoma volume (Supplementary Fig. S2). Two patients achieved a complete

Figure 1. Patients reporting an AE on the day of infusion, stratified by infusion number. Ninety-nine percent of events were grade 1 or 2.

Figure 2. VPC of AME-133v concentration-time profile with 5th, 50th, and 95th percentiles shown (o, observed concentrations) at doses of 7.5 mg/m² (A), 30 mg/m² (B), 100 mg/m² (C), and 375 mg/m² (D).
response (CR) and 3 patients achieved a partial response (PR; Supplementary Table S4). Four of the 5 responses were observed in patients treated at 100 and 375 mg/m² doses. The duration of response ranged from 21 to 145.1 weeks.

In all patients the number of B cells, identified using the B-cell antigen CD19, present in the peripheral blood before and after AME-133v were analyzed. There was a dose dependent, rapid and specific depletion of the B cells in all patients receiving at least 7.5 mg/m² of AME-133v (Supplementary Fig. S3). In all dose groups except the 2 mg/m² group, the depletion persisted for at least 3 months post last dose before beginning to recover toward baseline levels.

Discussion

We describe the preclinical and phase 1 clinical trial results of AME-133v, an anti-CD20 monoclonal antibody rationally designed to improve upon the clinical activity of rituximab. Rituximab is effective as a single agent and, when combined with or sequenced after chemotherapy, it increases the response rate and PFS in patients with treatment-naïve or previously treated FL (14, 15, 16). Several studies suggest that the survival of patients with FL has improved over time and at least some of this improvement is likely due to rituximab (17, 18).

Despite the importance of rituximab, the impact of the FcγRIIIa genotype on outcome to rituximab suggests that it is possible to improve outcomes even further by enhancing the activity of the CD20 antibody. The preclinical studies by Bowles and colleagues showed that a CD20 antibody optimized for ADCC is more effective at activating NK cells in vitro than rituximab, and this improvement was more profound in the FcγRIIIa F-carrier effector cells (5, 6). As previously outlined, patients with FL and the high affinity 158-VV FcγRIIIa genotypes have a higher response rate and time to progression after rituximab treatment. Other studies in patients with FL have suggested that chemotherapy negates this effect, although this has not been proven in a well-designed, prospective clinical trial (19–21). To our knowledge, this is the first such trial to select (or stratify) patients on the basis of their FcγRIIIa genotype. Two studies in patients with diffuse large B-cell lymphoma treated with R-CHOP provide conflicting results, and the possibility persists that FcγRIIIa genotype may play a role even in the face of chemotherapy (22, 23).

The impact of the FcγRIIIa genotype on outcome after cancer therapy is not limited to rituximab or lymphoma. In patients with Her-2/neu breast cancer treated with trastuzumab and taxane, those with 158-VV FcγRIIIa genotype had a higher response rate and longer PFS than F-carriers (24). Similarly, FcγRII and FcγRIIIa status combined was predictive of outcome to cetuximab combined with irinotecan even after adjusting for k-ras mutational status in patients with metastatic colorectal cancer (25). Furthermore, the HR was similar to the impact of k-ras mutational status.

AME-133v was developed to improve CD20 affinity and ADCC potency via protein engineering with the goal of achieving enhanced effectiveness in the entire FL patient population (which was not tested in this clinical trial) and particularly in those patients expressing the 158 F/F or F/V FcγRIIIa polymorphism. Preclinical studies of AME-133v showed that it has a higher affinity for CD20 and mediates ADCC better than rituximab in vitro. Furthermore, competitive binding experiments confirmed that AME-133v and rituximab bind to an overlapping epitope on the CD20 antigen expressed on SKW6.4 B cells. The concentration of AME-133v competitor antibody used in the displacement assay (25 μg/mL) was equivalent to the highest concentration used in the rituximab titration and approximately 5.2-fold lower than the clinical levels achieved with 375 mg/m². This amount of AME-133v displaced significant quantities of rituximab from the cell surface after 32 hours, even in the presence of saturating concentrations of prebound rituximab. This is important because further development of this antibody would occur in patients who had been treated with rituximab before and may still have measurable levels of serum rituximab.

In a small phase I study of AME-133v (therein denoted LY2469298) in Japan (26), AME-133v (100 or 375 mg/m² weekly x4) was well tolerated and generated objective responses in 5 of 10 patients (50%) who had previously treated FL and had received rituximab alone or rituximab-containing regimens. Two of 3 complete responders were F-carriers and one complete responder was 158-VV FcγRIIIa genotype. No DLTs were observed.

The safety and clinical impact of AME-133v were also evaluated in phase 1 of this trial. Overall, all doses of AME-133v evaluated were safe and well tolerated. There were no discontinuations due to drug-related AEs and no deaths during the study. During phase 1, there was no detection of human anti-human antibodies in any of the patients in this dose-escalation study either before or up to 5 weeks after the last infusion. Only one patient experienced a DLT, and a maximum tolerated dose was not reached. Of the 4 serious AEs that occurred, only one was considered related to study drug and 2 were considered treatment emergent. AME-133v displayed a safety profile similar to other anti-CD20 antibodies (27). AME-133v showed a nonlinear pharmacokinetics and moderate to large interpatient variability consistent with results observed for rituximab (13). Also, selective reduction in B-cell counts was observed at all doses and particularly at higher doses. The clinical activity observed is encouraging but difficult to interpret without a control arm or a historical control from similarly treated F-carrier patients with relapsed FL. The median duration of response was not estimable due to the large number of censored responses; however, median PFS was 25.4 weeks. Approximately 64% of patients showed at least some decrease in tumor size. Further study will be necessary to establish the response rate not only in FcγRIIIa F-carriers but in patients expressing the homozygous valine receptor polymorphism as well.
Two anti-CD20 monoclonal antibodies are currently marketed and more are in development (2). Veltuzumab (ha20, IgG) has a 3-fold longer off rate than rituximab in Raji cells, whereas AME-133v had an approximately 13-fold longer off rate than rituximab with SKW6.4 lymphoma cells in this study (27). In addition, AME-133v showed a 13- to 20-fold increase in binding affinity for CD20 with a Kd of approximately 100 pmol/L when tested on SKW6.4 cells and primary B lymphocytes. Veltuzumab has a Kd reportedly similar to rituximab at around 8 nmol/L (28, rituximab label), suggesting AME-133v has a nearly 80-fold increase in binding affinity in these cell binding assays compared with rituximab or veltuzumab. Ofatumumab is an IgG1κ monoclonal antibody indicated for the treatment of patients with chronic lymphocytic leukemia refractory to fludarabine and alemtuzumab (29). The response rate after treatment with ofatumumab was 43% in a phase II study of patients with relapsed or refractory FL (30). Another second generation anti-CD20 mAb, GA101, has shown promise in refractory FL (31). This glycoengineered, humanized mAb is primarily cytolytic toward CD20-expressing B cells and binds a different epitope than rituximab or AME-133v. Finally, ocrelizumab another humanized anti-CD20 mAb with increased ADCC activity compared with rituximab has recently shown activity in relapsed/refractory non-Hodgkin lymphoma patients (32, 33). The AEs and infusion reactions seem to be similar among these antibodies suggesting these effects may be relevant to the entire class of monoclonal antibodies to CD20 (2, 27–33).

In conclusion, AME-133v has a greater CD20 binding affinity and ability to mediate ADCC than rituximab and is similar in these activities to several second generation anti-CD20 antibodies in vitro. In this phase 1 study, AME-133v was safe and well tolerated across the dose range tested. The pharmacokinetic profile was similar to rituximab, and B-cell depletion and objective clinical responses were observed. Preliminary efficacy results in this small phase I study in FcγRIIIa F-carriers showed modest activity, and further elucidation of the efficacy and safety profile of AME-133v from phase II studies is forthcoming.

Disclosure of Potential Conflicts of Interest
S.P. Carpenter, B.W. Allan, and J.G. Nelson are employees of Applied Molecular Evolution, a wholly-owned subsidiary of Eli Lilly and Company. The other authors disclosed no potential conflicts of interest.

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Results of a Phase 1 Study of AME-133v (LY2469298), an Fc-Engineered Humanized Monoclonal Anti-CD20 Antibody, in Fc γ RIIIa-Genotyped Patients with Previously Treated Follicular Lymphoma

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