

The logo features a white stopwatch icon with the number '5' inside the circular face. To the right of the icon, the word 'Minute' is written in a large, bold, white sans-serif font, and 'Journal Club' is written below it in a smaller, white sans-serif font.

5 Minute Journal Club

Key ASH Presentations
Issue 9, 2012

Obinutuzumab (GA101) in Relapsed/Refractory Non-Hodgkin Lymphoma

CME INFORMATION

OVERVIEW OF ACTIVITY

The annual American Society of Hematology (ASH) meeting is unmatched in its importance with regard to advancements in hematologic cancer and related disorders. It is targeted by many members of the clinical research community as the optimal forum in which to unveil new clinical data. This creates an environment each year in which published results and new information lead to the emergence of many new therapeutic agents and changes in the indications for existing treatments across virtually all malignant and benign hematologic disorders. As online access to posters and plenary presentations is not currently available, a need exists for additional resources to distill the information presented at the ASH annual meeting for those clinicians unable to attend but desiring to remain up to date on the new data released there. To bridge the gap between research and patient care, this CME activity will deliver a serial review of the most important emerging data sets from the latest ASH meeting, including expert perspectives on how these new evidence-based concepts can be applied to routine clinical care. This activity will assist medical oncologists, hematologists and hematology-oncology fellows in the formulation of optimal clinical management strategies and the timely application of new research findings to best-practice patient care.

LEARNING OBJECTIVES

- Develop evidence-based treatment algorithms for patients presenting with high tumor mass follicular lymphoma (FL).
- Optimize outcomes for patients with relapsed or refractory FL through the application of emerging clinical research data.
- Evaluate the benefits and risks of therapy with different monoclonal antibodies as mono- or combination therapy in the treatment of relapsed or refractory FL or other indolent non-Hodgkin lymphomas or previously untreated chronic lymphocytic leukemia.
- Compare and contrast the benefits and risks of radioimmunotherapy and standard immunochemotherapy in the management of newly diagnosed FL.

ACCREDITATION STATEMENT

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

Research To Practice designates this enduring material for a maximum of 1.5 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

HOW TO USE THIS CME ACTIVITY

This CME activity contains slides and edited commentary. To receive credit, the participant should review the slide presentations, read the commentary, complete the Post-test with a score of 75% or better and fill out the Educational Assessment and Credit Form located at ResearchToPractice.com/5MJCASH2012/9/CME.

CONTENT VALIDATION AND DISCLOSURES

Research To Practice (RTP) is committed to providing its participants with high-quality, unbiased and state-of-the-art education. We assess potential conflicts of interest with faculty, planners and managers of CME activities. Real or apparent conflicts of interest are identified and resolved through a conflict of interest resolution process. In addition, all activity content is reviewed by both a member of the RTP scientific staff and an external, independent physician reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

FACULTY — The following faculty (and their spouses/partners) reported real or apparent conflicts of interest, which have been resolved through a conflict of interest resolution process:

Jonathan W Friedberg, MD, MMSc
Professor of Medicine and Oncology
Chief, Hematology/Oncology Division
James P Wilmot Cancer Center
University of Rochester
Rochester, New York

Advisory Committee: Cephalon Inc, Genentech BioOncology;
Consulting Agreement: Mundipharma International Limited;
Data and Safety Monitoring Board: Lilly USA LLC; Paid
Research: Millennium: The Takeda Oncology Company, Onyx
Pharmaceuticals Inc.

Stephanie A Gregory, MD
The Elodia Kehm Chair of Hematology
Professor of Medicine
Director, Section of Hematology
Rush University Medical Center
Chicago, Illinois

Paid Research: Celgene Corporation, MedImmune Inc, Novartis
Pharmaceuticals Corporation, Onyx Pharmaceuticals Inc;
Scientific Advisory Board: Amgen Inc, Genentech BioOncology,
Spectrum Pharmaceuticals Inc, Teva.

Brad S Kahl, MD
Associate Professor
Director, Lymphoma Service
University of Wisconsin School of Medicine and Public Health
Associate Director for Clinical Research
UW Carbone Cancer Center
Madison, Wisconsin

Advisory Committee: Celgene Corporation, Cephalon Inc,
Genentech BioOncology, GlaxoSmithKline, Millennium: The Takeda
Oncology Company.

John P Leonard, MD
Richard T Silver Distinguished Professor of Hematology and
Medical Oncology
Professor of Medicine, Weill Cornell Medical College
New York, New York

Consulting Agreements: Celgene Corporation, Cephalon Inc,
Genentech BioOncology, GlaxoSmithKline, Millennium: The Takeda
Oncology Company.

EDITOR — Dr Love is president and CEO of Research To Practice,
which receives funds in the form of educational grants to develop
CME activities from the following commercial interests: Abbott
Laboratories, Allos Therapeutics, Amgen Inc, ArQule Inc, Astellas,
Bayer HealthCare Pharmaceuticals/Onyx Pharmaceuticals Inc,
Biodesix Inc, Biogen Idec, Boehringer Ingelheim Pharmaceuticals
Inc, Bristol-Myers Squibb Company, Celgene Corporation,
Cephalon Inc, Daiichi Sankyo Inc, Dendreon Corporation, Eisai
Inc, EMD Serono Inc, Genentech BioOncology, Genomic Health
Inc, ImClone Systems, a wholly owned subsidiary of Eli Lilly
and Company, Incyte Corporation, Lilly USA LLC, Medivation
Inc, Millennium: The Takeda Oncology Company, Mundipharma
International Limited, Novartis Pharmaceuticals Corporation,
Regeneron Pharmaceuticals, Sanofi, Seattle Genetics, Spectrum
Pharmaceuticals Inc and Teva.

RESEARCH TO PRACTICE STAFF AND EXTERNAL REVIEWERS

— The scientific staff and reviewers for Research To Practice have
no real or apparent conflicts of interest to disclose.

This educational activity contains discussion of published
and/or investigational uses of agents that are not indicated by
the Food and Drug Administration. Research To Practice does
not recommend the use of any agent outside of the labeled
indications. Please refer to the official prescribing information
for each product for discussion of approved indications,
contraindications and warnings. The opinions expressed are those
of the presenters and are not to be construed as those of the
publisher or grantors.

This activity is supported by educational grants from Allos
Therapeutics, Celgene Corporation, Genentech BioOncology/
Biogen Idec, Incyte Corporation, Millennium: The Takeda
Oncology Company, Onyx Pharmaceuticals Inc, Sanofi and Seattle
Genetics.

Last review date: April 2012
Expiration date: April 2013

To go directly to slides and commentary for this issue, [click here](#).

For this concluding post-ASH summary we focus on a smattering of data sets that shed additional light on a number of relevant clinical questions and therapeutic strategies in the management of indolent NHL, including follicular lymphoma (FL) and CLL:

1. Rituximab (R)/lenalidomide (len) in CLL

Previous preclinical work suggested that the effect of len on natural killer cell expansion enhanced the cytotoxic impact of R, and on that basis several trials evaluating the “R squared” combination were launched, including 3 studies reported at ASH. The first was a Phase II effort evaluating R/len in 59 patients with relapsed/refractory CLL, and the combination produced an impressive overall response rate of 66% with a median time to treatment failure of 24 months. A second Phase II study attempted to assess the combination in patients with previously untreated disease, and more than 75% of patients responded. Finally, an encouraging Phase I-II study evaluating fludarabine/R and escalating doses of len as induction therapy followed by R/len maintenance in 45 previously untreated patients resulted in a 49% CR rate, but dose-limiting toxicity (mainly dermatologic) was observed in more than a third of participants. Len is currently only used by most investigators in very advanced refractory CLL.

2. Alemtuzumab/fludarabine/cyclophosphamide (AFC) in patients with high-risk CLL requiring treatment

At ASH, our understanding of how to integrate alemtuzumab into the treatment algorithm for CLL once again hit a bump in the road with the report from a Phase III trial evaluating low-dose subcutaneous A in combination with FC versus FC alone. Although the addition of the anti-CD52 antibody resulted in slightly better cancer outcomes, substantial toxicity was observed, including flulike symptoms and infection related to immune suppression, and as such this approach remains investigational.

3. Obinutuzumab (GA101)

ASH provided a vivid reminder of the impressive activity of anti-CD20 antibody treatment in B-cell lymphomas with the first results of the landmark ECOG RESORT trial commented on earlier in this series, in which the control arm of 4 weekly doses of R resulted in a 70% response rate, and without further treatment, 86% of patients who responded were progression free at 3 years.

The activity of this bellwether biologic agent is the reason there was great interest in 3 ASH data sets evaluating obinutuzumab (O) — a novel glycoengineered type 2 anti-CD20 MAB with a different functional profile than rituximab (more direct cytotoxicity and cell death but slightly less complement-dependent cytotoxicity). The first, a Phase I-II trial, reported objective responses in patients considered resistant to R, while the second, a randomized Phase II study with 175 patients comparing O to R as single agents in the relapsed setting, showed response rates modestly favoring O. Finally, a Phase I study looked at the agent in combination with CHOP or FC and provided confidence that a large Phase III trial comparing R-CHOP to O-CHOP is feasible.

4. Two data sets on up-front radioimmunotherapy (RIT) in FL

A much anticipated and somewhat disappointing SWOG trial of R-CHOP versus CHOP followed by ¹³¹I-tositumomab consolidation demonstrated similar efficacy and tolerability with a few more cases of AML/MDS in the RIT arm (7 versus 3). The study raises natural questions about a more comprehensive strategy of R/chemo followed by RIT consolidation and R maintenance, which is the approach used in a subsequent Phase II SWOG study that has completed accrual but has not yet reported. Another ASH Phase II report focused on RIT alone up front — this time with 2 fractions of ⁹⁰Y ibritumomab. Thirteen of 76 patients received pretreatment with R in an attempt to clear bone marrow involvement greater than 20%, and 11 of the 13 were able to receive RIT. A median PFS of 36 months was observed, with manageable hematologic toxicity. However, RIT monotherapy up front is rarely utilized in clinical practice pending more definitive trial data.

5. [18F]fluorodeoxyglucose-positron emission tomography (FDG-PET) scans in FL

At ASH we saw the results of a study of interim and end-of-treatment FDG-PET scans in 121 patients with FL receiving R-CHOP. Approximately one quarter had positive end-of-treatment scans, and not surprisingly 2-year PFS and OS were worse in this group. (About half of all patients with positive scans at the end of treatment had disease progression at 2 years.) The challenge of managing these patients remains unanswered and, hopefully, more guidance will come from future clinical research.

6. Bortezomib in FL

A prior report from the 676-patient randomized Phase III LYM3001 study of R alone or with bortezomib in relapsed/refractory disease demonstrated a modest advantage to the combination, and at ASH an impressive translational data set was presented looking at prespecified sera and tissue endpoints that identified a subset of approximately a third of patients in the trial who achieved a greater benefit with the addition of bortezomib. These markers are not “ready for prime time” but are sure to be looked at in studies like ECOG-E2408, evaluating bendamustine/rituximab (BR) followed by R versus bortezomib/BR followed by R versus BR followed by R/len in high-risk FL.

Next we return to our recent breast cancer Patterns of Care survey, this time focusing on management of HER2-positive tumors in the early and advanced disease setting.

Neil Love, MD

Research To Practice

Miami, Florida

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Research To Practice designates this enduring material for a maximum of 1.5 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

This activity is supported by educational grants from Allos Therapeutics, Celgene Corporation, Genentech BioOncology/Biogen Idec, Incyte Corporation, Millennium: The Takeda Oncology Company, Onyx Pharmaceuticals Inc, Sanofi and Seattle Genetics.

Research To Practice
One Biscayne Tower
2 South Biscayne Boulevard, Suite 3600
Miami, FL 33131

This email was sent to you by Dr Neil Love and Research To Practice. To unsubscribe from future emails in this series, [click here](#). To unsubscribe from all email communications, including CME/CNE activities sent by Research To Practice, [click here](#). To update your information on our current distribution lists, [click here](#).

Obinutuzumab (GA101) in Relapsed/Refractory Non-Hodgkin Lymphoma

Presentations discussed in this issue

Salles GA et al. **Efficacy and safety of obinutuzumab (GA101) monotherapy in relapsed/refractory indolent non-Hodgkin's lymphoma: Results from a Phase I/II study (BO20999).** *Proc ASH 2011*; [Abstract 268](#).

Sehn LH et al. **Randomized Phase II trial comparing GA101 (obinutuzumab) with rituximab in patients with relapsed CD20+ indolent B-cell non-Hodgkin lymphoma: Preliminary analysis of the GAUSS study.** *Proc ASH 2011*; [Abstract 269](#).

Radford J et al. **Obinutuzumab (GA101) in combination with FC or CHOP in patients with relapsed or refractory follicular lymphoma: Final results of the Phase I GAUDI study (BO21000).** *Proc ASH 2011*; [Abstract 270](#).

Slides from presentations at ASH 2011 and transcribed comments from recent interviews with Jonathan W Friedberg, MD, MMSc (1/11/12) and Brad S Kahl, MD (1/26/12)

Efficacy and Safety of Obinutuzumab (GA101) Monotherapy in Relapsed/Refractory Indolent Non-Hodgkin's Lymphoma: Results from a Phase I/II Study (GAUGUIN, BO20999)¹

Randomized Phase II Trial Comparing GA101 (Obinutuzumab) with Rituximab in Patients with Relapsed CD20+ Indolent B-Cell Non-Hodgkin Lymphoma: Preliminary Analysis of the GAUSS Study²

Obinutuzumab (GA101) in Combination with FC or CHOP in Patients with Relapsed or Refractory Follicular Lymphoma: Final Results of the Phase I GAUDI Study (BO21000)³

¹ **Salles GA et al.**
Proc ASH 2011; Abstract 268.

² **Sehn LH et al.**
Proc ASH 2011; Abstract 269.

³ **Radford J et al.**
Proc ASH 2011; Abstract 270.

Research
To Practice®

Efficacy and Safety of Obinutuzumab (GA101) Monotherapy in Relapsed/Refractory Indolent Non-Hodgkin's Lymphoma: Results from a Phase I/II Study (GAUGUIN, BO20999)

Salles GA et al.

Proc ASH 2011;Abstract 268.

Research
To Practice®

Background

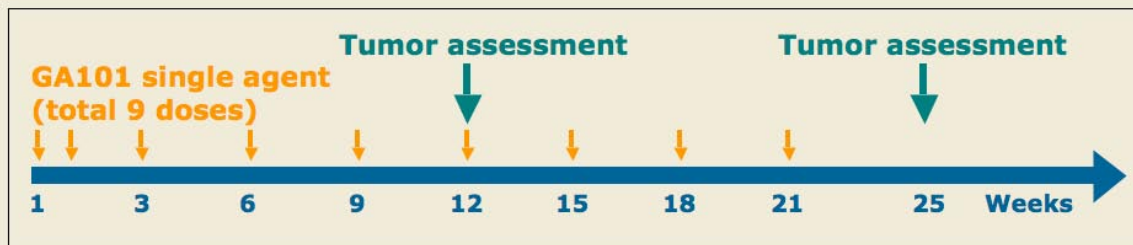
- GA101 is a Type II glycoengineered, humanized anti-CD20 monoclonal antibody with superior preclinical activity to Type I antibodies in vitro and in vivo.
- Anti-CD20 antibodies with different functional activity from rituximab may have better efficacy.
- GAUGUIN is a Phase I/II study of GA101 in patients with relapsed/refractory non-Hodgkin lymphoma (NHL).
- **Objectives:**
 - Evaluate the safety, pharmacokinetics (PK) and clinical activity of escalating doses of GA101 in a Phase I study.
 - Compare end-of-treatment response, safety, PK, best overall response and progression-free survival (PFS) of 2 dose regimens of GA101 in a Phase II study.

Salles GA et al. *Proc ASH 2011;Abstract 268.*

Research
To Practice®

GAUGUIN Phase I Study Design

- Eligibility: Patients with relapsed/refractory/indolent CD20+ NHL for whom “no treatment of higher priority was available” (FL: n = 13, small lymphocytic lymphoma: n = 1, lymphoplasmacytic lymphoma: n = 1, Waldenstrom’s lymphoma, n = 1)
- Nonrandomized, adaptive dose-escalation design



Salles GA et al. *Proc ASH* 2011;Abstract 268.

Research
To Practice®

Phase I Dose Escalation Design

Cohort (n = 3/group)	GA101 dose (mg) Dose 1/doses 2-9
1	50/100
2	100/200
3	200/400
4	400/800
5	800/1,200
6	1,200/2,000
7	1,600/1,600/800*

* Dose 1/dose 2/dose 3-9

Re-treatment with GA101 on relapse was allowed.

Salles GA et al. *Proc ASH* 2011;Abstract 268.

Research
To Practice®

Responses in Phase I Study

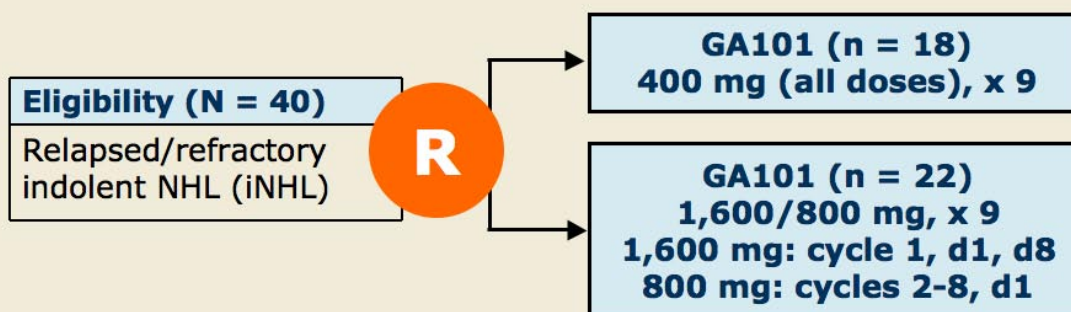
	Best overall response	End of treatment
Overall response rate (ORR)	56%	44%
Complete response (CR)	31%	25%
Partial response (PR)	25%	19%

- Responses were observed across all dose levels
 - No clear dose-response relationship
- Median duration of response: 32 mo

Salles GA et al. *Proc ASH* 2011;Abstract 268.

Research
To Practice®

GAUGUIN Phase II Study Design



GA101 schedule: d1 and d8 cycle 1, d1 of cycles 2-8, 3 weekly cycles

Primary endpoint: End-of-treatment response, assessed 4 weeks after last infusion

Secondary endpoint: Safety, PK, best overall response, progression-free survival (PFS)

Salles GA et al. *Proc ASH* 2011;Abstract 268.

Research
To Practice®

Phase II End-of-Treatment Response

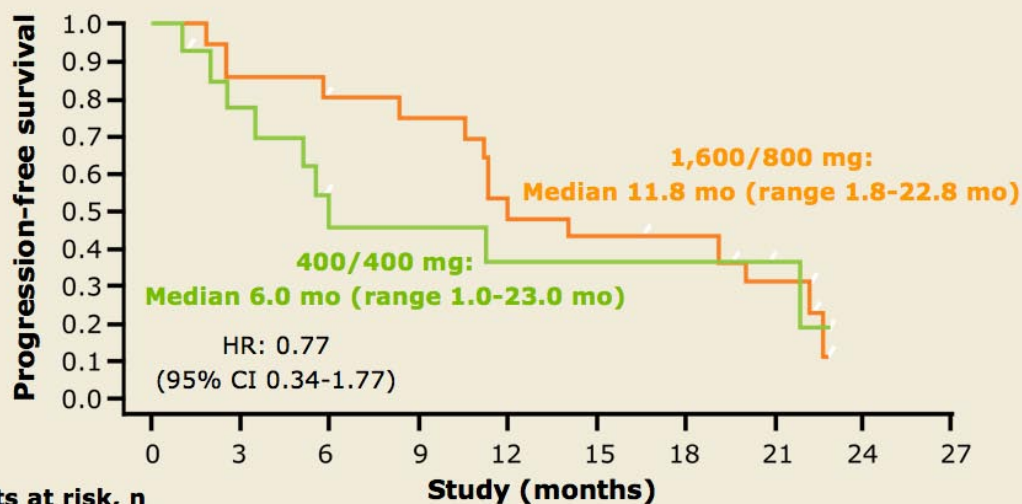
Overall population	400/400 mg (n = 18)	1,600/800 mg (n = 22)
ORR	17%	55%
CR/CRu	—	9%
PR	17%	45%
Stable disease	33%	27%
Progressive disease	50%	18%
Rituximab-refractory population	(n = 12)	(n = 10)
ORR	8%	50%
CR/CRu	—	10%
PR	8%	40%
Stable disease	33%	30%
Progressive disease	58%	20%

CRu = unconfirmed CR
 Median duration of response: 17 mo

Salles GA et al. *Proc ASH* 2011;Abstract 268.

Research
To Practice®

PFS in Patients with FL



Patients at risk, n	0	3	6	9	12	15	18	21	24	27
400/400 mg	14	10	5	5	4	4	4	2	0	0
1,600/800 mg	20	17	15	14	9	8	7	5	0	0

Median observation time: 23.1 mo

With permission from Salles GA et al. *Proc ASH* 2011;Abstract 268.

Research
To Practice®

Phase II: Select Grade 3-4 Treatment-Related Adverse Events (AEs)

AE	400/400 mg (n = 18)	1,600/800 mg (n = 22)
Thrombocytopenia	0%	5%
Lymphopenia	6%	9%
Neutropenia/febrile neutropenia	0%	19%
Infections and infestations	0%	5%
Infusion-related reactions	0%	9%
Asthenia	0%	5%
Cytolytic hepatitis	0%	5%

Total AEs = 1 in 400/400-mg arm and 12 in 1,600/800-mg arm

Salles GA et al. *Proc ASH* 2011;Abstract 268.

Research
To Practice®

Author Conclusions

- GA101 as a single agent has encouraging efficacy in this group of patients with heavily pretreated relapsed/refractory iNHL.
 - A higher response was observed with the 1,600/800-mg dose of GA101 vs the 400/400-mg dose.
 - A response rate of 50% was observed in patients with rituximab-refractory disease in this cohort.
- Promising PFS and response duration for GA101 as a single agent were observed.
- GA101 demonstrated an acceptable safety profile in both dose regimens.
- Based on these data and pharmacokinetic results a 1,000-mg dose will be taken forward for future studies.

Salles GA et al. *Proc ASH* 2011;Abstract 268.

Research
To Practice®

Investigator Commentary: GA101 Monotherapy in Relapsed or Refractory Indolent NHL

GA101 has several features that differentiate it from rituximab. It is a Type 2 monoclonal antibody, which means that when it binds to the CD20 epitope, the intracellular cascade that occurs is different. It is believed that a Type 2 antibody may have more direct cytotoxicity and cell death and slightly less complement-dependent cytotoxicity.

The results from this study hint that GA101 might be better than rituximab. This was not a comparative study, but one can say that because responses occurred in patients with rituximab-refractory disease. However, you have to keep in mind that if you were refractory to rituximab long ago and you receive it again, there might be a response.

In terms of tolerability, despite the fact that it is a humanized antibody, studies suggest that the initial infusion-related reactions in particular are worse than those with rituximab. Many trials now include a low dose on the first day of administration. Most oncologists are comfortable managing even severe infusion reactions. Otherwise the tolerability is similar to rituximab, with not much immunosuppression or other toxicity.

Interview with Jonathan W Friedberg, MD, MMSc, January 11, 2012

Randomized Phase II Trial Comparing GA101 (Obinutuzumab) with Rituximab in Patients with Relapsed CD20+ Indolent B-Cell Non-Hodgkin Lymphoma: Preliminary Analysis of the GAUSS Study

Sehn LH et al.

Proc ASH 2011;Abstract 269.

Research
To Practice®

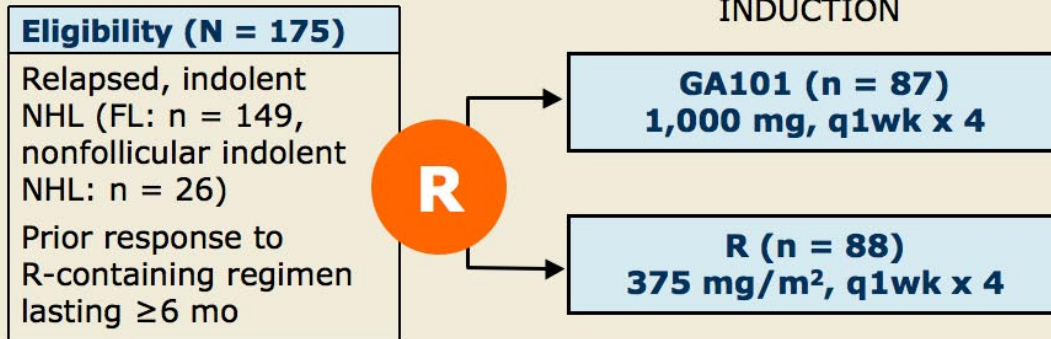
Background

- In preclinical models GA101 has demonstrated enhanced direct cell death and increased ADCC compared to other anti-CD20 antibodies.
- GA101 single-arm clinical studies have demonstrated responses in patients with relapsed/refractory NHL and CLL.
- However, no direct comparisons to rituximab (R) have been reported to date.
- **Objective:** Compare the efficacy and safety of monotherapy with GA101 to those of R in patients with relapsed indolent NHL.

Sehn LH et al. *Proc ASH 2011*;Abstract 269.

Research
To Practice®

GAUSS Study Design



Patients with no disease progression after induction received maintenance GA101 or R every 2 months for 2 years at the same dose.

Primary endpoint: Overall response rate (ORR) in the FL population

Secondary endpoints: PFS, overall survival (OS), safety

Sehn LH et al. *Proc ASH 2011*;Abstract 269.

Research
To Practice®

Response to GA101 versus Rituximab (Abstract)

Response	FL population			
	GA101 (n = 74)		R (n = 75)	
	INV	IRF	INV	IRF
ORR	43.2%	43.2%	38.7%	28%
CR/CRu	10.8%	NR	6.7%	NR
Disease progression	20.3%		17.3%	
FL+ nonfollicular indolent NHL				
Response	GA 101 (n = 88)		R (n = 87)	
	INV	IRF	INV	IRF
ORR	43.2%	42.0%	35.6%	24.1%

INV = investigator assessment; IRF = independent central blinded radiology review;
NR = not reported

End-of-treatment response assessed 28-42 d after last induction dose

Sehn LH et al. *Proc ASH* 2011;Abstract 269.

Research
To Practice®

Select Adverse Events (AEs) (Abstract)

AE	GA101 (n = 88)	Rituximab (R) (n = 87)
Infusion-related reaction (IRR)		
Any grade	72%	49%
Grade 3/4	11%	5%
Fatigue (any grade, ≥5%)	23%	17%
Back pain (any grade, ≥5%)	7%	2%
Decreased appetite (any grade, ≥5%)	7%	2%
Insomnia (any grade, ≥5%)	5%	0%

- Serious AEs: GA101 arm (n = 5) due to IRR (n = 2), febrile neutropenia (n = 1), pleural effusion (n = 1), nephrolithiasis (n = 1); R arm (n = 9)
- Deaths: GA101 (n = 1) due to pulmonary aspergillosis, R (n = 1) due to cardiopulmonary arrest
- Discontinuations: GA101 (n = 4, 3 due to IRR, 1 due to orthostatic hypotension), R (n = 7)

Sehn LH et al. *Proc ASH* 2011;Abstract 269.

Research
To Practice®

Author Conclusions

- Treatment with GA101 in patients with relapsed NHL resulted in higher response rates compared to R as assessed by both investigators and the IRF at an early time point.
- GA101 was well tolerated. Although a higher rate of IRRs were noted, the majority were Grade 1/2 in severity and did not result in significant differences in treatment discontinuation.
- This first head-to-head trial of GA101 against R demonstrated higher response rates without appreciable differences in safety.
- GA101 is under study in Phase III trials in combination with chemotherapy (NCT01287741, NCT01332968, NCT01059630).

Sehn LH et al. *Proc ASH 2011*;Abstract 269.

Research
To Practice®

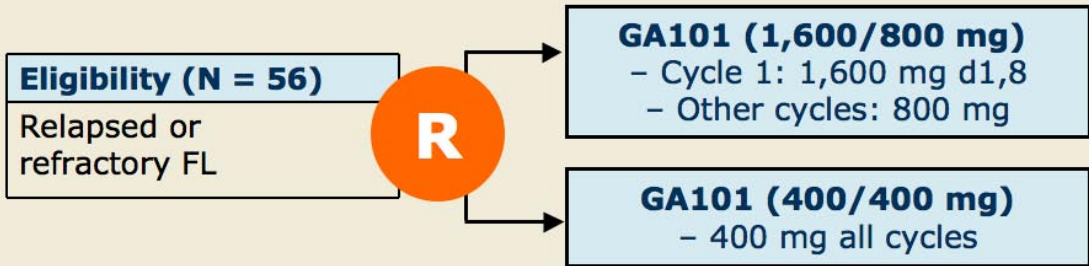
Obinutuzumab (GA101) in Combination with FC or CHOP in Patients with Relapsed or Refractory Follicular Lymphoma: Final Results of the Phase I GAUDI Study (BO21000)

Radford J et al.

Proc ASH 2011;Abstract 270.

Research
To Practice®

GAUDI Study Design



- Patients were stratified by prior chemotherapy regimens before randomization:
 - **CHOP** (n = 28): 6-8, 21-d cycles
 - **Fludarabine/cyclophosphamide (FC)** (n = 28): 4-6, 28-d cycles
- Patients responding to GA101 were offered maintenance treatment for 2 years or until progression.

Primary endpoint: Safety
Secondary endpoint: Response rate

Radford J et al. *Proc ASH* 2011;Abstract 270.

Research
To Practice®

Adverse Events (Abstract)

Adverse event	G-CHOP (n = 28)	G-FC (n = 28)
Infusion-related reactions (IRR)*		
Any grade	64%	79%
Grade 3/4	7%	7%
Neutropenia (Grade 3/4)	39%	50%
Cycles delayed due to hematologic toxicity or infections	6%	10%
Dose of chemotherapy reduced due to toxicity	29%	36%

* IRRs were mostly during the first infusion.

G = GA101

- No evidence of increased toxicity with the 1,600/800-mg dose vs 400/400 mg
- 28/28 pts in G-CHOP, 22/28 pts in G-FC completed treatment

Radford J et al. *Proc ASH* 2011;Abstract 270.

Research
To Practice®

Response to Therapy (Abstract)

Response*	G-CHOP (n = 28)	G-FC (n = 28)
ORR	96.4%	92.9%
CR	39.3%	50.0%
PR	57.1%	42.9%
Stable disease	3.6%	0%
Progressive disease	0%	3.6%

* Assessed by IWG criteria modified to classify unconfirmed CR as PR

- 3.6% of patients in G-FC arm were not assessed.
- Response rates in the G-CHOP arm compared favorably to those in the rituximab in combination with CHOP cohort from the EORTC 20981 study in a matched-pair analysis.

Radford J et al. *Proc ASH* 2011;Abstract 270.

Research
To Practice®

Author Conclusions

- GA101 can be safely combined with chemotherapy regimens used in the treatment of FL and demonstrated a high level of activity compared to historical controls.
- G-CHOP could be delivered at the protocol-specified 3-weekly interval in most patients.
- G-FC in a more heavily pretreated population showed worse tolerability than G-CHOP.
- Following these promising results, GA101 will be studied in combination with CHOP and other chemotherapies in a randomized Phase III study against the standard of care, R-CHOP (NCT01287741).

Radford J et al. *Proc ASH* 2011;Abstract 270.

Research
To Practice®

Investigator Commentary: Comparison of GA101 to Rituximab in Relapsed CD20+ Indolent NHL

The GAUSS study, which I was a part of, showed 2 important results. The first is that both CR rates and overall response rates were slightly higher in the GA101 group compared to the rituximab group. However, it was disappointing that the PFS data presented at the meeting showed overlapping curves for the GA101 and rituximab groups. So the higher response rate did not translate into an improvement in PFS. This Phase II study was powered to investigate response, not to study differences in PFS. Even though these data are preliminary, they are still disappointing. Despite these results, a Phase III study to determine the durability of GA101 has been planned.

Interview with Jonathan W Friedberg, MD, MMSc, January 11, 2012

GA101 in Combination with FC or CHOP in Relapsed or Refractory FL

The GAUDI study was a pilot study that showed that GA101 can be safely combined with CHOP chemotherapy. It gives the investigators confidence that they can go ahead with the big Phase III study comparing R-CHOP to G-CHOP (NCT01287741).

Interview with Brad S Kahl, MD, January 26, 2012