Year in Review

Proceedings from a Multitumor CME Symposium Focused on the Application of Emerging Research Information to the Care of Patients with Common Cancers

Diffuse Large B-cell and T-Cell Lymphomas — Michelle A Fanale, MD

Select Publications

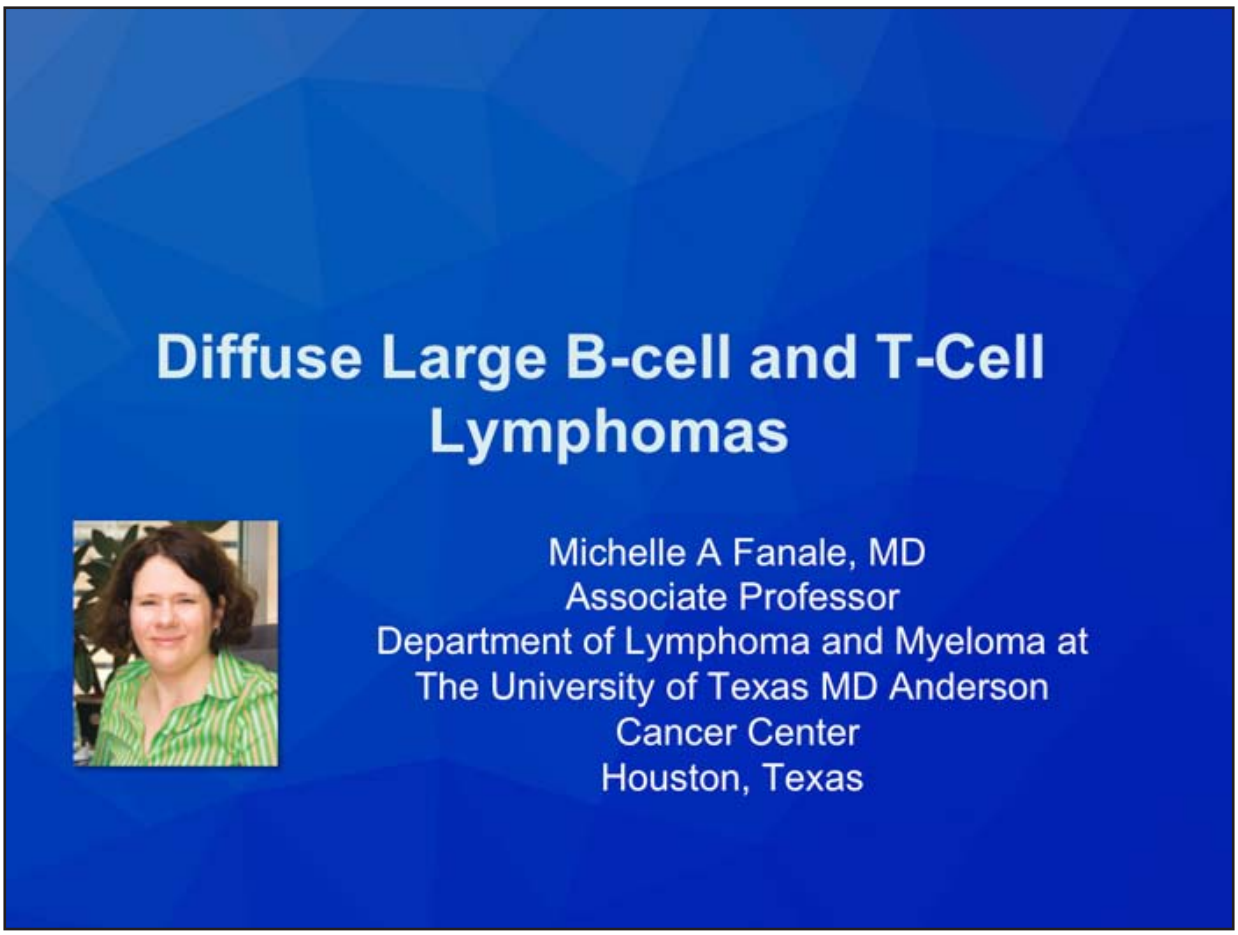
Dupuis J et al. **Final analysis of the RO-CHOP Phase Ib/II study: Romidepsin in association with CHOP in patients with peripheral T-cell lymphoma (PTCL).** *Proc ASH* 2014;**Abstract 504**.

Jacobsen ED et al. **Brentuximab vedotin demonstrates objective responses in a phase 2 study of relapsed/refractory DLBCL with variable CD30 expression.** *Blood* 2015;125(9):1394-402.

Kochenderfer JN et al. **Chemotherapy-refractory diffuse large B-cell lymphoma and indolent B-cell malignancies can be effectively treated with autologous T cells expressing an anti-CD19 chimeric antigen receptor.** *J Clin Oncol* 2015;33(6):540-9.

Nowakowski GS et al. **Lenalidomide combined with R-CHOP overcomes negative prognostic impact of non-germinal center B-cell phenotype in newly diagnosed diffuse large B-cell lymphoma: A phase II study.** *J Clin Oncol* 2015;33(3):251-7.

Nowakowski GS et al. **Randomized, phase III trial of the efficacy and safety of lenalidomide plus R-CHOP vs R-CHOP in patients with untreated ABC-type diffuse large B-cell lymphoma.** *Proc ASCO* 2015;**Abstract TPS8600**.

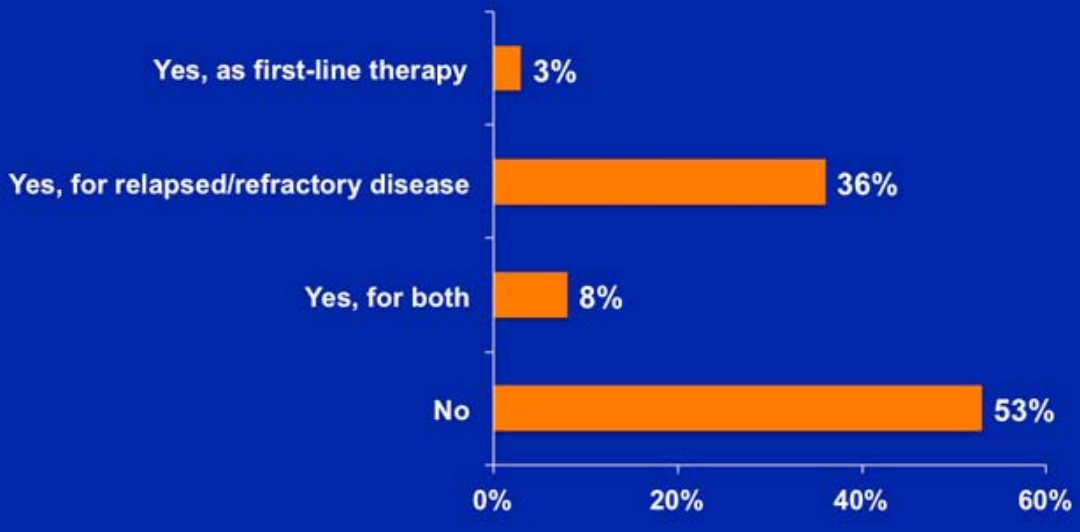


Disclosures

Consulting Agreements	Merck, Spectrum Pharmaceuticals Inc; Contracted Research: Bristol-Myers Squibb Company, Celgene Corporation, Genentech BioOncology, Gilead Sciences Inc, MedImmune Inc, Merck, Novartis Pharmaceuticals Corporation, Onyx Pharmaceuticals, an Amgen subsidiary, Seattle Genetics, Takeda Oncology
Data and Safety Monitoring Board	Amgen Inc; Honoraria: Merck, Seattle Genetics, Spectrum Pharmaceuticals Inc, Takeda Oncology

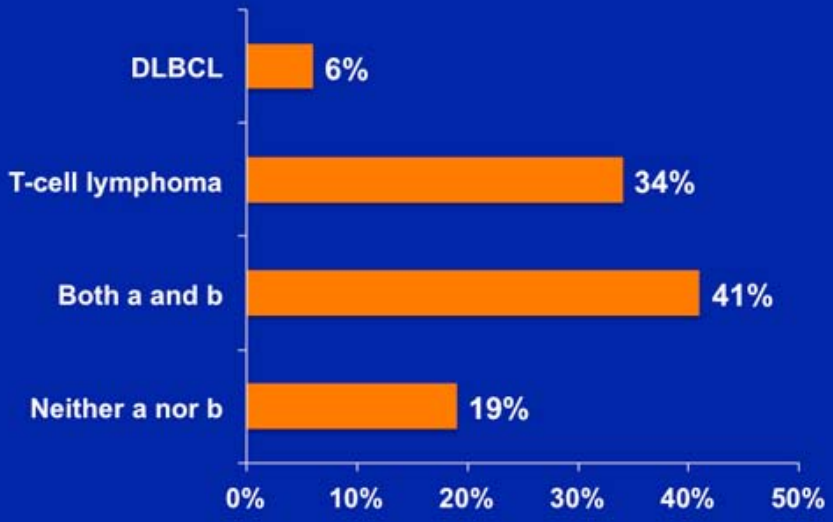
AUDIENCE POLL

Do you generally use lenalidomide outside of a protocol setting for patients with diffuse large B-cell lymphoma (DLBCL)?



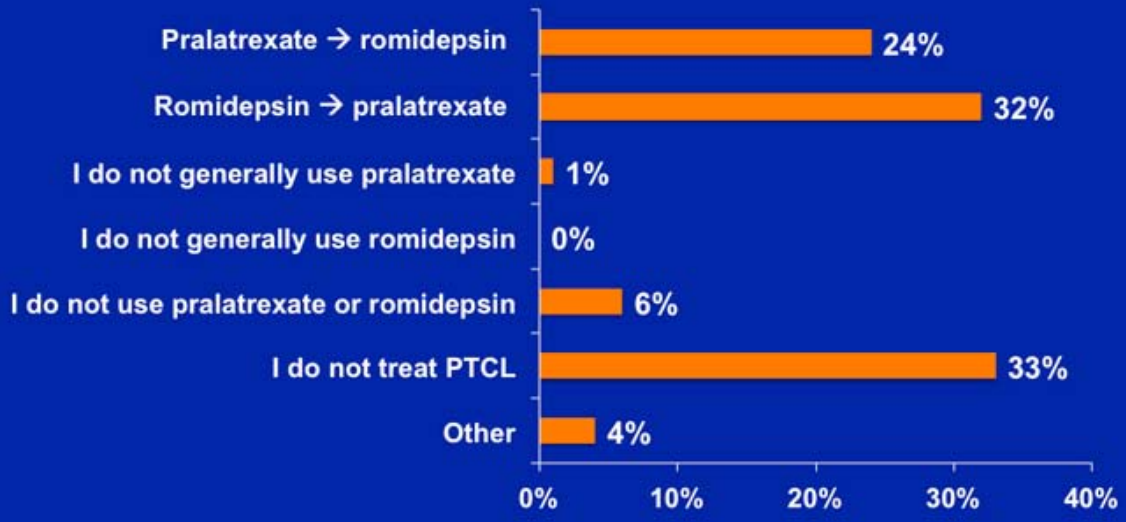
AUDIENCE POLL

Do you generally recommend CD30 testing for your patients with…



AUDIENCE POLL

How do you generally sequence pralatrexate and romidepsin for an otherwise healthy patient with slowly progressing relapsed peripheral T-cell lymphoma (PTCL) who is asymptomatic?



VOLUME 33 · NUMBER 3 · JANUARY 20 2015

JOURNAL OF CLINICAL ONCOLOGY

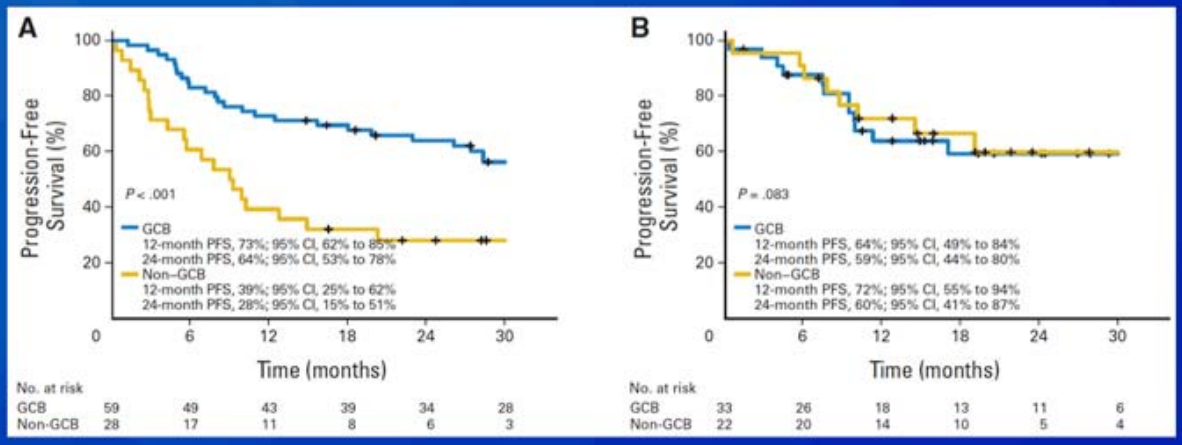
ORIGINAL REPORT

Lenalidomide Combined With R-CHOP Overcomes Negative Prognostic Impact of Non–Germinal Center B-Cell Phenotype in Newly Diagnosed Diffuse Large B-Cell Lymphoma: A Phase II Study

Grzegorz S. Nowakowski, Betsy LaPlant, William R. Macon, Craig B. Reeder, James M. Foran, Garth D. Nelson, Carrie A. Thompson, Candido E. Rivera, David J. Inwards, Ivana N. Micallef, Patrick B. Johnston, Luis F. Porrata, Stephen M. Ansell, Randy D. Gascoyne, Thomas M. Habermann, and Thomas E. Witzig

Progression-Free Survival by Germinal Center B-Cell Phenotype

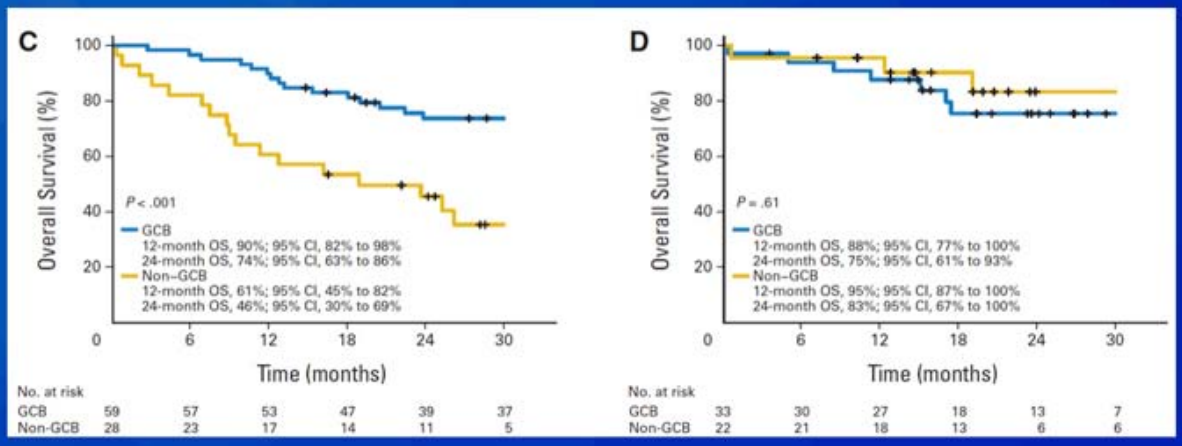
Historical Controls: R-CHOP **R²-CHOP**



Nowakowski GS et al. *J Clin Oncol* 2015;33(3):251-7.

Overall Survival by Germinal Center B-Cell Phenotype

Historical Controls: R-CHOP **R²-CHOP**



Nowakowski GS et al. *J Clin Oncol* 2015;33(3):251-7.

Conclusions

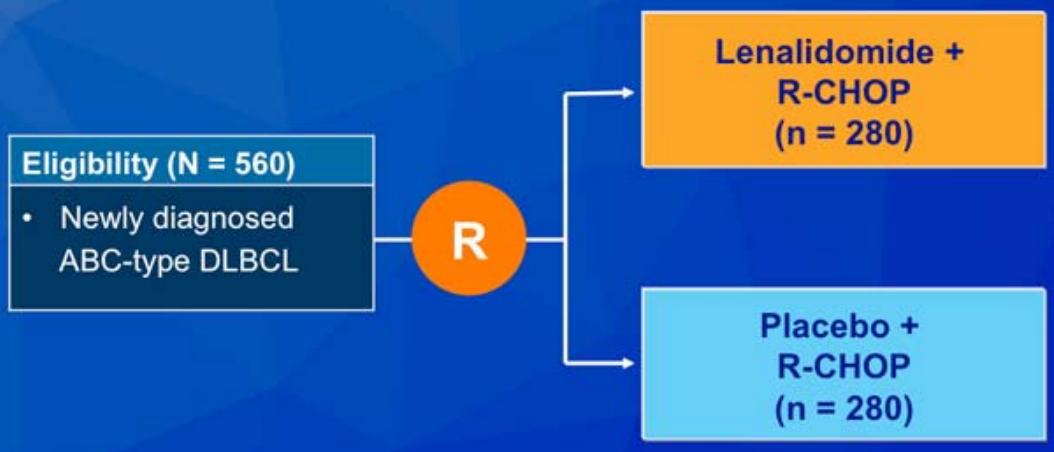
Critical finding(s): The addition of lenalidomide to R-CHOP seems to be able to neutralize the negative impact typically seen particularly on both CRR and PFS for patients with non-germinal center B-cell diffuse large B-cell lymphoma (DLBCL).

Clinical implication(s): While these data are promising, a confirmatory Phase III trial is ongoing, so at least at this point I would recommend to first await the data from that trial.

Conclusions

Research relevance: Additional trials evaluating the role of lenalidomide are ongoing or planned to open soon, including the "Smart Start" trial of my colleague Dr Jason Westin, which is a Phase Ib/II study of rituximab, lenalidomide, ibrutinib and EPOCH in patients with newly diagnosed DLBCL, as well as a Phase III confirmatory trial of lenalidomide plus R-CHOP vs R-CHOP for patients with untreated ABC-type DLBCL.

ROBUST: Phase 3 Study of Lenalidomide plus R-CHOP vs R-CHOP in DLBCL



Primary Endpoint: Progression-free survival

Nowakowski GS et al. *Proc ASCO* 2015;Abstract TPS8600. (NCT02285062)

Regular Article

CLINICAL TRIALS AND OBSERVATIONS

Brentuximab vedotin demonstrates objective responses in a phase 2 study of relapsed/refractory DLBCL with variable CD30 expression

Eric D. Jacobsen,[1] Jeff P. Sharman,[2] Yasuhiro Oki,[3] Ranjana H. Advani,[4] Jane N. Winter,[5] Celeste M. Bello,[6] Gary Spitzer,[7] Maria Corinna Palanca-Wessels,[8] Dana A. Kennedy,[8] Pamela Levine,[8] Jing Yang,[8] and Nancy L. Bartlett[9]

[1]Dana-Farber Cancer Institute, Boston, MA; [2]Willamette Valley Cancer Institute and Research Center/US Oncology Research, Eugene, OR; [3]University of Texas MD Anderson Cancer Center, Houston, TX; [4]Stanford University Medical Center, Stanford, CA; [5]Northwestern University, Chicago, IL; [6]H. Lee Moffitt Cancer Center, Tampa, FL; [7]St. Francis Hospital, Upstate Oncology Associates, Greenville, SC; [8]Seattle Genetics, Inc., Bothell, WA; and [9]Washington University School of Medicine, St. Louis, MO

Blood. 2015;125(9):1394-1402

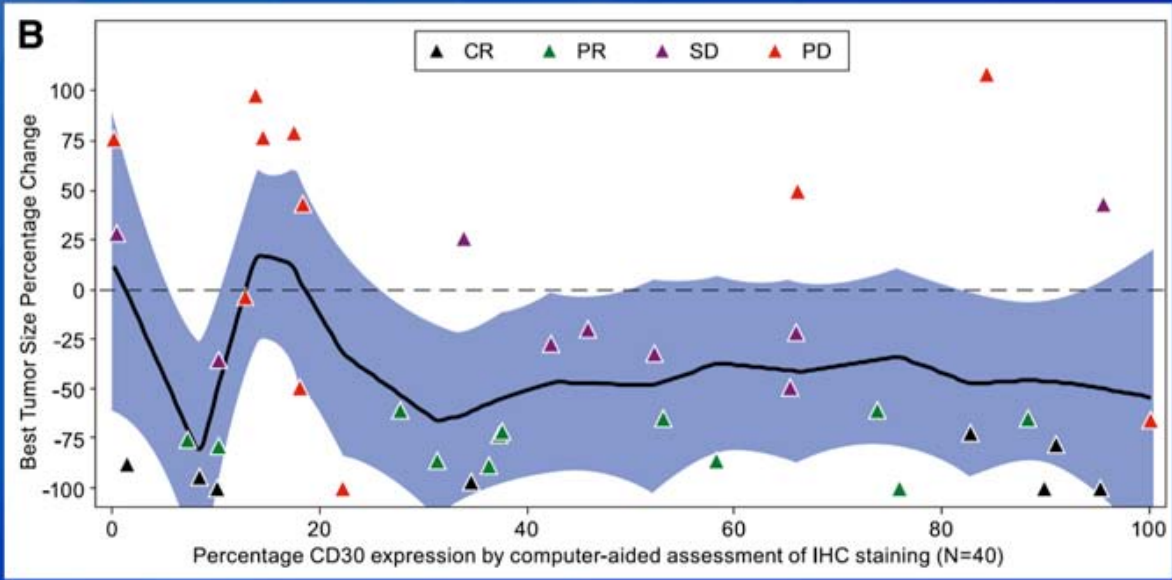
Best Response to Single-Agent Brentuximab Vedotin

	Refractory DLBCL (n = 39)		Relapsed DLBCL (n = 8)		Total DLBCL (n = 48)		Other B-cell (n = 19)	
	No.	%	No.	%	No.	%	No.	%
Objective response rate	17	44%	3	38%	21	**44%**	5	26%
Best clinical response								
CR	6	15%	2	25%	8	17%	3	16%
PR	11	28%	1	13%	13	27%	2	11%
SD	8	21%	3	38%	11	23%	7	37%
PD	14	36%	2	25%	16	33%	6	32%
Disease control rate	25	64%	6	75%	32	67%	12	63%

- No statistical correlation between response and level of CD30 expression
- However, all responding patients had quantifiable CD30 by computer-assisted assessment of IHC

Jacobsen ED et al. *Blood* 2015;125(9):1394-1402.

Maximum Tumor Size Reduction by Quantitative CD30 Expression in Patients with DLBCL



Jacobsen ED et al. *Blood* 2015;125(9):1394-1402.

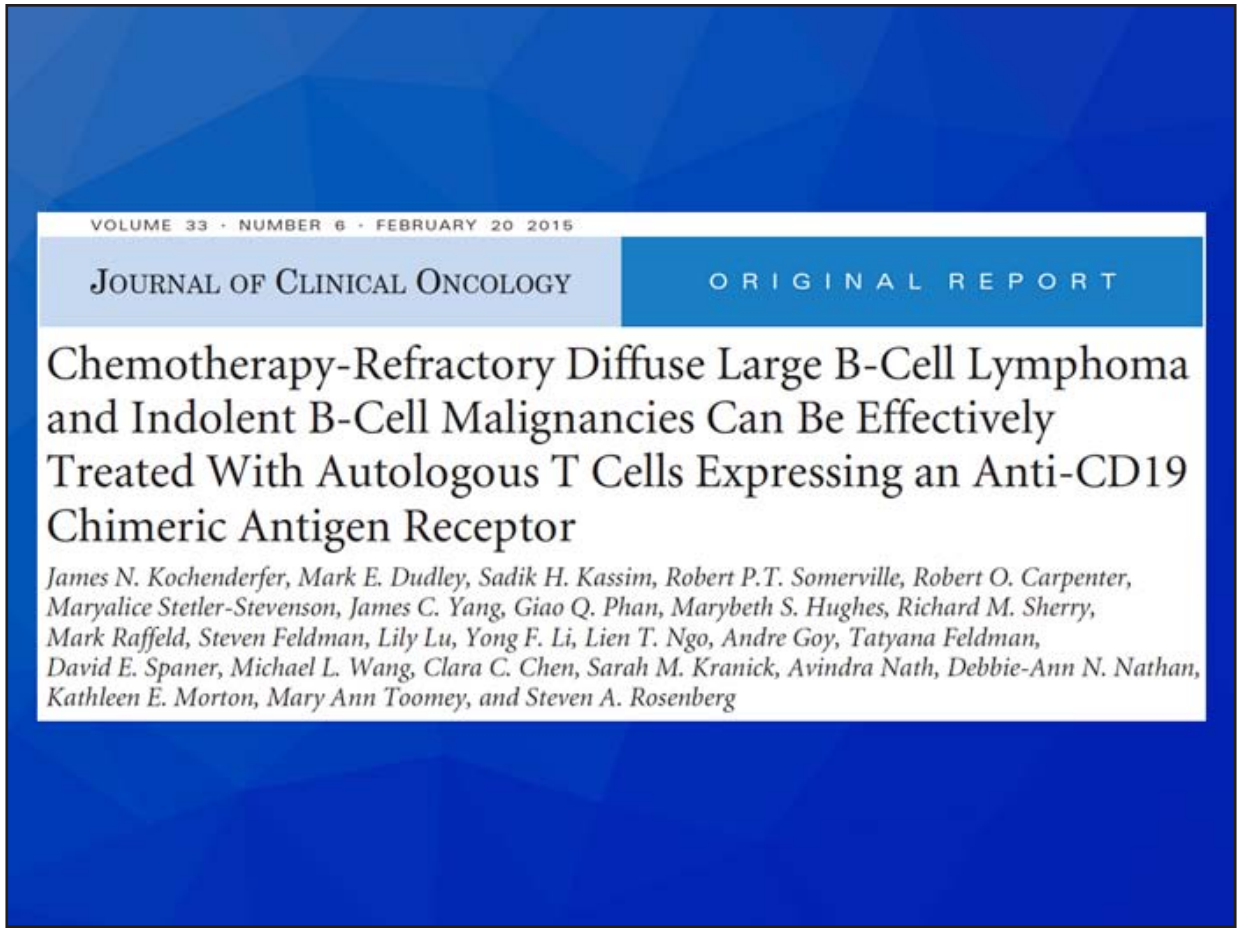
Conclusions

Critical finding(s): CRR of nearly 20% with a duration of response of approximately 17 months was respectable for single-agent therapy, and interestingly there was not a clear statistical correlation similar to what has been seen in the trial for relapsed non-ALCL PTCL for level of response and CD30 expression levels. However, all patients did show some level of positivity for CD30.

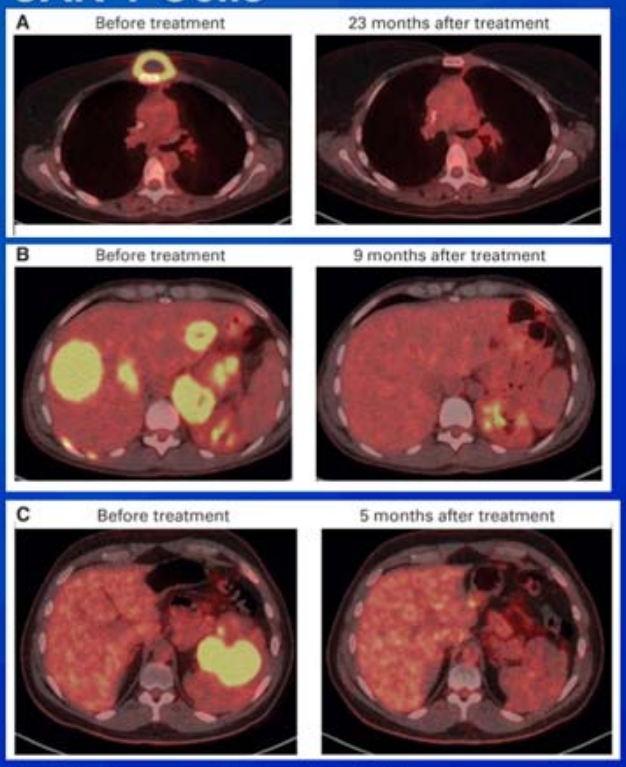
Clinical implication(s): Positive benefit has now been seen for targeting CD30 expression in non-HL and non-ALCL lymphomas, albeit at lower levels of response than is seen for these diagnoses.

Conclusions

Research relevance: Data from a Phase II trial combining brentuximab vedotin plus R-CHOP for front-line therapy for DLBCL have also been reported at ASCO 2015 by N Bartlett and colleagues with an ORR of 80%, a CRR of 67% and a 12-month PFS of 65%. However, a randomized trial would be needed to confirm this relative benefit.



Complete Remissions in Patients Receiving Anti-CD19 CAR-T Cells



Kochenderfer JN et al. J Clin Oncol 2015;33:540-49.

Conclusions

Critical finding(s): First publication of successful treatment of DLBCL with anti-CD19 CAR T cells. High response rates with a CRR of 53% and a CRR for the 7 patients with chemotherapy-refractory DLBCL of 57%, with durations now out to 22 months.

Clinical implication(s): Although there are clearly potential toxicities, including fever, hypotension, delirium and other neurologic toxicities, the benefit seen is pronounced for patients who otherwise would often have dismal outcomes.

Conclusions

Research relevance: CAR T-cell therapies are expected to continue to improve via refinements in gene therapy vectors, CAR design and T-cell culture methods, and they have broad-based potential clinical applicability toward management of B-cell lymphomas, with a multitude of ongoing clinical trials.

Final Analysis of the RO-CHOP Phase Ib/II Study: Romidepsin in Association with CHOP in Patients with Peripheral T-Cell Lymphoma (PTCL)

Dupuis J et al.

Proc ASH 2014;Abstract 504.

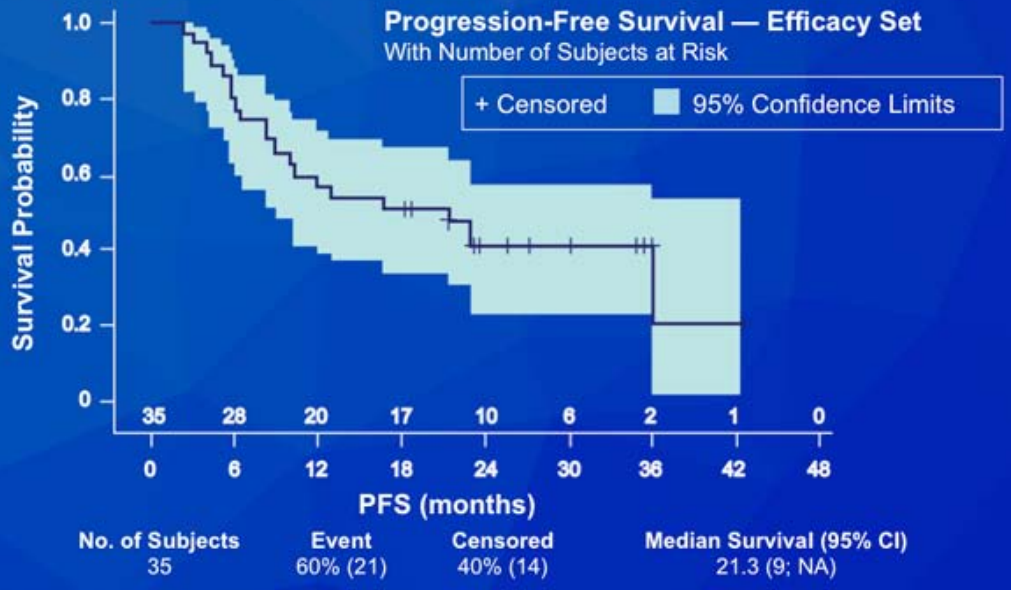
Responses After 8 Cycles (Evaluable Patients)

Response	N = 35
Complete response	51%
Partial response	17%
Progressive disease (PD)	26%

- Two patients experienced early cardiac events (myocardial infarction) and were excluded from the efficacy analysis.

Dupuis J et al. *Proc ASH* 2014;Abstract 504.

Progression-Free Survival (PFS)



- 1-year estimated PFS = 57%
- Median follow-up = 30 months

Dupuis J et al. *Proc ASH* 2014;Abstract 504.

Conclusions

Critical finding(s): The ORR was 68% with a CRR of 51% and an estimated PFS of 57% at 18 mo.

Romidepsin can be combined with CHOP but with the known risks of hematologic toxicities and also potential cardiovascular events that might or might not be related to the treatment.

Clinical implication(s): This trial adds to the overall data for combining targeted agents with chemotherapy for front-line management of PTCL, including data for COEP plus pralatrexate, CHOP plus belinostat and CHP plus brentuximab vedotin.

Conclusions

Research relevance: A confirmatory Phase III randomized trial is ongoing for Ro-CHOP vs CHOP. Also for other combinations, such as the ECHELON-2 Phase III trial for CHP plus brentuximab vedotin versus CHOP for CD30+ PTCL including ALCL. Whether targeted therapy doublets and triplets being developed in the relapsed setting might eventually replace CHOP-based chemotherapy in the front-line setting remains to be seen.