calreticulin in myeloproliferative neoplasms. N Engl J Med. 2013;369 (25):2379-2390.
6. Nangalia J, Massie CE, Baxter EJ, et al. Somatic CALR mutations in myeloproliferative neoplasms with nonmutated JAK2. N Engl J Med. 2013;369(25):2391-2405.
7. Rotunno G, Mannarelli C, Guglielmelli P, et al. Impact of calreticulin mutations on clinical and hematological phenotype and outcome in essential thrombocythemia. Blood. 2014;123(10):1552-1555.
8. Tefferi A, Guglielmelli P, Lasho TL, et al. CALR and ASXL1 mutations-based molecular prognostication in primary myelofibrosis: an international study of 570 patients. Leukemia. 2014;28(7):1494-500.
9. Ortmann CA, Kent DG, Nangalia J, et al. Effect of mutation order on myeloproliferative neoplasms. N Engl J Med. 2015;372(7):601-612.
10. Verstovsek S, Kantarjian H, Mesa RA, et al. Safety and efficacy of INCB018424, a JAK1 and JAK2 inhibitor, in myelofibrosis. N Engl J Med. 2010;363(12):1117-1127.
11. Verstovsek S, Mesa RA, Gotlib J, et al. A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis. N Engl J Med. 2012;366(9):799-807.
12. Harrison C, Kiladjian JJ, Al-Ali HK, et al. JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis. N Engl J Med. 2012;366(9):787-798.
13. Verstovsek S, Mesa RA, Gotlib J, et al. Efficacy, safety, and survival with ruxolitinib in patients with myelofibrosis: results of a median 3-year follow-up of COMFORT-I. Haematologica. 2015;(4):479-488.
14. Cervantes F, Vannucchi AM, Kiladjian JJ, et al. Three-year efficacy, safety, and survival findings from COMFORT-II, a phase 3 study comparing ruxolitinib with best available therapy for myelofibrosis. Blood. 2013;122(25):4047-4053.
15. Guglielmelli P, Biamonte F, Rotunno G, et al. Impact of mutational status on outcomes in myelofibrosis patients treated with ruxolitinib in the COMFORT-II study. Blood. 2014;123(14):2157-2160.
16. Hagop K, Kiladjian J-J, Gotlib J, et al. A pooled overall survival analysis of the COMFORT studies: 2 randomized phase 3 trials of ruxolitinib for the treatment of myelofibrosis. Blood. 2013;122(21):abstract 2820.
17. Wilkins BS, Radia D, Woodley C, Farhi SE, Keohane C, Harrison CN. Resolution of bone marrow fibrosis in a patient receiving JAK1/JAK2 inhibitor treatment with ruxolitinib. Haematologica. 2013;98(12):1872-1876.
18. Al-Ali HK, Hubert K, Lange T, et al. Complete clinical, histopathologic and molecular remission of primary myelofibrosis with long-term treatment with the JAK1/2 inhibitor ruxolitinib. 56th ASH Annual Meeting. San Fransisco, CA, USA. 6-9, 2014. Abstract 1836.
19. Galli S, McLornan D, Harrison C. Safety evaluation of ruxolitinib for treating myelofibrosis. Expert Opin Drug Saf. 2014;13(7):967-976.
20. Hasselbalch HC. Chronic inflammation as a promotor of mutagenesis in essential thrombocythemia, polycythemia vera and myelofibrosis. A human inflammation model for cancer development? Leukemia Res. 2013;37(2):214-220.
21. Massa M, Rosti V, Campanelli R, Fois G, Barosi G. Rapid and long-lasting decrease of T-regulatory cells in patients with myelofibrosis treated with ruxolitinib. Leukemia. 2014;28(2):449-451.
22. Rudolph J, Cornez I, Brossart P, Wolf D. The JAK1/JAK2 inhibitor ruxolitinib substantially affects NK cell biology. Blood. 2013;122(21):16.
23. Wolschke C, Alchalby H, Ayuk F, et al. The Pan- JAK inhibitor ruxolitinib impairs T-cell activation, cytokine production and proliferation in vivo and in vitro. Blood. 2013;122(21):2001.
24. Campanelli R, Fois G, Poletto V, et al. Decrease of T regulatory cells in patients with myelofibrosis receiving ruxolitinib. Blood. 2013;122(21):4057.
25. Kordasti SY, Seidl T, Abellan PP, et al. JAK inhibition reduces CD25 high CD27+ FOXp3+ T regulatory cells and causes a silencing of T effector cells in patients with myeloproliferative neoplasms whilst promoting a TH17 phenotype. Blood. 2013;122(21):4092.
26. Kwatra SG, Dabade TS, Gustafson CJ, Feldman SR. JAK inhibitors in psoriasis: a promising new treatment modality. J Drugs Dermatol. 2012;11(8):913-918.
27. Ghoreschi K, Gadina M. Jakpot! New small molecules in autoimmune and inflammatory diseases. Exp Dermatol. 2014;23(1):7-11.
28. Xing L, Dai Z, Jabbari A, et al. Alopecia areata is driven by cytotoxic T lymphocytes and is reversed by JAK inhibition. Nature Med. 2014;20(9):1043-1049.
29. Spoerl S, Mathew NR, Bscheider M, et al. Activity of therapeutic JAK 1/2 blockade in graft-versus-host disease. Blood. 2014;123(24):3832-3842.
30. Vannucchi AM, Kiladjian JJ, Griesshammer M, et al. Ruxolitinib versus standard therapy for the treatment of polycythemia vera. N Engl J Med. 2015;372(5):426-435.

Ofatumumab and its role as immunotherapy in chronic lymphocytic leukemia

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The therapy of chronic lymphocytic leukemia (CLL) is in an era of momentous change from chemotherapy towards targeted therapy. The first phase was the introduction of monoclonal antibodies, especially the anti-CD20 antibodies rituximab, ofatumumab, and obinutuzumab in combination immunochemotherapy. More recently, small molecular inhibitors have emerged which target the B-cell receptor signaling pathways (ibrutinib and idelalisib), BCL-2 (ABT-199), and immunomodulation [immunomodulatory drugs (IMiDs), lenalidomide]. In this rapidly changing landscape, what is the role of the anti-CD20 monoclonal antibody ofatumumab in CLL?

Ofatumumab in relapsed/refractory chronic lymphocytic leukemia

Ofatumumab recognizes a different epitope to rituximab that includes both the large and small extracellular domains of CD20, and has a slower dissociation rate compared to rituximab. These characteristics have suggested potentially superior activity.[1,2] Single agent ofatumumab was first utilized in relapsed/refractory (R/R) CLL and demonstrated overall response rates of approximately 50%, though these mainly consisted of partial responses. As such, the United States Food and Drug Administration (FDA) granted accelerated approval for the use of ofatumumab in previously treated CLL in October 2009. In April 2010, the European Medicines Agency (EMA) recommended a conditional marketing authorization for the use of ofatumumab in fludarabine- and alemtuzumab-refractory CLL.

These approvals were largely based on two trials: Coiffier *et al.* (2008)[3] and Wierda *et al.* (2010).[4] The first trial was a phase I-II dose escalating multicenter study of ofatumumab in 33 patients with R/R CLL who had received a median of 3 prior treatment regimens. They reported an overall response rate (ORR) of 48% (13 of 27 patients) with no complete responses (CR). The median progression-free survival (PFS) was 106 days. Grade 3 or more adverse events included infection, thrombocytopenia and neutropenia. The second trial was a phase II international trial using ofatumumab in fludarabine- and alemtuzumab-refractory (FA-ref) CLL and in

Table 1. Clinical studies of single agent ofatumumab in relapsed/refractory CLL.

STUDY	Phase	Number	Patients' characteristics				Treatment	ORR (%)	CR (%)	Median PFS	Median OS	Grade 3-4 adverse events
			17pdel (%)	β2M (%)	Unmutated IGHV (%)	Median prior treatments						
Coiffier 2008[3]	I/II	27 (Cohort C)	ND	ND	ND	3	Ofa	48	0	106 days	ND	Infection Neutropenia Thrombocytopenia
Wierda 2010[4]	II	138 59 & 79	22	ND	ND	5 & 4	Ofa in FA-ref & BF-ref	58 & 47	0&1	5.7 & 5.9 mos	13.7 & 15.4 mos	Neutropenia Infection
Moreno 2015[5]	IV	103	21 (11/52)	ND	84 (42/50)	4	Observational study	22	3	5	11	Neutropenia Thrombocytopenia Infection
Byrd 2014[6]	III	391	32 *vs.* 33	78 *vs.* 74	ND	3 *vs.* 2	Ibrutinib *vs.* Ofa	43 *vs.* 4	0 *vs.* 0	Ibrutinib NR (88% at 6 mos) *vs.* 8.1 mos Ofa	Both groups NR. At 12 mos: 90 *vs.* 81%.	Similar both arms: Neutropenia Pneumonia Thrombocytopenia Anemia

ORR: overall response rates; CR: complete response; PFS: progression-free survival; OS: overall survival; Ofa: ofatumumab; FA-ref: fludarabine- and alemtuzumab-refractory; BF-ref: fludarabine-refractory with bulky (>5cm) lymphadenopathy; β2M: Beta-2 microglobulin >3.5mg/L in percentage; ND: No data provided; NR: Not reached; mos: months.

fludarabine-refractory CLL with bulky (>5cm) lymphadenopathy (BF-ref). At the interim analysis, there were 59 and 79 patients with a median of 5 and 4 prior treatments in the FA-ref and BF-ref groups, respectively. The ORR was 58% and 47% in the FA-ref and BF-ref groups, respectively. All responders achieved a partial response (PR) except for one in the BF-ref who attained a CR. Median PFS and overall survival (OS) were 5.7 and 13.7 months in the FA-ref group, respectively, and 5.9 and 15.4 months in the BF-ref group, respectively. The grade 3 or more adverse event profile included infection and neutropenia. One patient did develop progressive multifocal leukoencephalopathy (PML).

In this issue, Moreno and colleagues[5] conducted a study on behalf of the European Research Initiative on CLL (ERIC group) in response to the conditional authorization of the drug in Europe. They report the results of a phase IV, non-interventional, observational study on single agent ofatumumab in poor-prognosis CLL. Notably, they were not able to reproduce similar ORR to that demonstrated by Coiffier *et al.*[3] and Wierda *et al.*[4] which raises questions over the use of ofatumumab as monotherapy in R/R CLL. One hundred and three patients with R/R CLL who had received a median of 4 prior treatment regimens were reported to have an ORR based on an intention-to-treat (ITT) of 22% (3CR, 1CR incomplete, 19PR). This is less than half that observed in the two pivotal trials upon which both FDA and EMA approval was obtained, despite consisting of patients with similar disease-risk profile. Median PFS and OS times were 5 and 11 months, respectively. These were shorter than those reported by Wierda *et al.* (6 and 14 months, respectively).[4] The adverse event profile is comparable to that seen in the two previous trials and included infusion-related reactions, cytopenias, and infections. Two patients developed PML.

With the introduction of novel therapies, the Bruton tyrosine kinase (Btk) inhibitor, ibrutinib, was compared directly with ofatumumab in a randomized clinical trial in this setting of R/R CLL. Ibrutinib demonstrated markedly improved duration of PFS, OS and response rates when compared to ofatumumab monotherapy. Byrd *et al.*[6] published a report last year showing their results at a median follow up of 9.4 months; the median duration of PFS was not reached in the ibrutinib group (88% at 6 months) as compared to a median PFS of 8.1 months in the ofatumumab group. OS at 12 months was 90% and 81% in the ibrutinib and ofatumumab groups, respectively. ORRs were significantly higher in the ibrutinib group (43% *vs.* 4%) consisting of only partial responses. Grade 3 or more adverse events included neutropenia (16% ibrutinib *vs.* 14% ofatumumab), anemia (5% ibrutinib *vs.* 8% ofatumumab), and pneumonia (7% ibrutinib *vs.* 5% ofatumumab). In the light of the efficacy and safety data of ibrutinib, it now has FDA and EMA approval for use in previously treated CLL. Given the efficacy seen with ibrutinib, the role of single agent ofatumumab in R/R setting now appears questionable (Table 1).

Other roles of ofatumumab in R/R CLL are being explored, particularly combination studies (bendamustine and ofatumumab;[7] dexamethasone and ofatumumab;[8] lenalidomide and ofatumumab[9]) and in maintenance studies[10] which do look promising (Table 2), and these are likely to map out future treatment options in this setting.

Ofatumumab in first-line treatment for chronic lymphocytic leukemia

The use of ofatumumab in combination with chemotherapy (fludarabine (F) and cyclophosphamide (C)) in fit, treatment-naïve CLL patients has been discouraging, represented by a lower ORR than its counterpart monoclonal anti-CD20 antibody, rituximab, in combination with the same chemotherapy (FCR: ORR 90%, CR 44%).[11,12] The ORR and CR for the 500 mg and the 1000 mg ofatumumab cohorts were 77% *versus* 73% and 32% *versus* 50%, respectively. Wierda *et al.*[12] postulate that the reduced ORR may reflect the proportion of higher-risk profiles of the patient population [13% 17p deletion and 64% Beta(β)-2-microglobulin (β2M) >3.5mg/L]. However, even though there was a lower proportion of patients with del(17p) in the FCR group (8%)

Table 2. Clinical studies of ofatumumab used in combinations or as maintenance in relapsed/refractory CLL.

Study	Phase	Number	Patients' characteristics	Treatment	ORR (%)	CR (%)	Median PFS	Median OS	Grade 3-4 adverse events
Cortelezzi 2014[7]	II	47	61% had 1 previous line of therapy, remainder had 2, 66% IgHV mutation, 17% Del(17p)/TP53 mutations	Ofa and Bendamustine	72 Del(17p) 37.5 (3 out of 8 patients)	17 Del(17p) 0	23.6 mos	OS 83.6% at 24.2 mos	Neutropenia Infection
Doubek 2015[8]	II	33	3 median prior therapies, 94% IgHV mutation, 24% Del(17p)/TP53 mutations	Ofa and Dexamethasone	67 Del(17p) 63	15 Del(17p) 25	10 months	34 months	Infection Neutropenia
Costa 2014[9]	II	21	2 median prior therapies	Sequential treatment with ofa and lenalidomide	47.6			21.5 months	Neutropenia Thrombocytopenia
vanOers 2014[10]	III	474	CLL responded to treatment at relapse	Ofa *vs.* observation	Time to next therapy 38 *vs.* 27.4 months	-	28.6 *vs.* 15.2 months	No differences in OS at the interim analysis	Infection Neutropenia

ORR: overall response rates; CR: complete response; PFS: progression-free survival; OS: overall survival; Ofa: ofatumumab.

Table 3. Clinical studies of anti-CD20 monoclonal antibodies, with emphasis on ofatumumab, in treatment-naïve chronic lymphocytic leukemia.

STUDY	Phase	Number	Patients' characteristics 17pdel (%)	B2M (%)	Unmutated IGHV (%)	Treatment	ORR (%)	CR (%)	Median PFS	Median OS events	Grade 3-4 adverse
Hallek 2010[11]	III	817	7 *vs.* 10 (avg 8)	33 *vs.* 32 (avg 32)	63 *vs.*63 (avg 63)	FCR *vs.*FC	90 *vs.*80	44 *vs.*22	52 *vs.* 33mo 3yrs	87% *vs.* 83% 3yrs	Neutropenia Leukopenia Thrombocytopenia Infection
Wierda 2011[12]	II	61	6 *vs.*20 (avg13)	61 *vs.*67 (avg64)	52 *vs.*30 (avg41)	Ofa (500 mg *vs.* 1000 mg) with FC	77 *vs.* 73	32 *vs.* 50	Could not be estimated follow up 8 months	Could not be estimated follow up 8 months	Neutropenia Thrombocytopenia Anemia Infection
Hillmen 2013[13]	III	447	5 *vs.* 8 (avg 6)	71 *vs.* 78 (avg 75)	57 *vs.* 56 (avg 56)	Ofa-Clb *vs.* Clb alone	82 *vs.* 69	12 *vs.* 1	22.4 *vs.*13.1 months	Not reached at 29 months	Neutropenia Infection
Goede 2014[14] & Goede 2015[15]		781	8	Not reported	61	G-Clb *vs.* Clb R-Clb *vs.* Clb Clb alone	33 (G-Clb) *vs.* 28 (R-Clb)		29.2 (G-Clb) *vs.* 15.4 (R-Clb) months, 29.9 (G-Clb) *vs.* 11.1 (Clb) months	No statistically significant OS of G-Clb over R-Clb (HR0.70, 95%CI, 0.47- 1.02)	Neutropenia Infection

ORR: overall response rates; CR: complete response; avg: average; Ofa: ofatumumab; G: obinutuzumab; Clb: chlorambucil; R: rituximab.

compared to the O-FC group (13%), the ORR and the CR for this subgroup are not markedly different (68% and 5% for FCR *vs.* 63% and 13% for O-FC) with a higher proportion achieving CR in the O-FC cohort. The proportion of patients with β2M>3.5mg/L in the O-FC cohort was 2-fold that of FCR. Response to FCR treatment in the prognostic subgroup β2M was not provided,[11] but with O-FC, the ORR and CR in patients with β2M>4mg/L were 68% and 29%, respectively. Interestingly, the O-FC group also had a higher rate of neutropenia when compared to that seen in FCR treated patients.

Hillmen *et al.*[13] examined the use of ofatumumab plus chlorambucil (Clb) *versus* chlorambucil monotherapy in treatment-naive patients in whom fludarabine-based therapy was deemed inappropriate (due to advanced age or comorbidities). They reported promising ORR and CR of 82% and 12%, respectively, with the combination of O-Clb compared to 69% and 1% with Clb alone. The median PFS was significantly longer with the addition of ofatumumab (22.4 *vs.* 13.1 months). Median overall survival (OS) was not reached at a median follow up of 29 months for either group. In April 2014, FDA approved the use of ofatumumab for patients in this setting. Late in 2014, Goede *et al.*[14,15] published data on the anti-CD20 antibodies, rituximab (R) and obinutuzumab (G) in combination with chlorambucil in a similar patient cohort that had significant morbidity or a creatinine clearance between 30 and 69 mL/min. G-Clb compared to Clb alone had a significantly longer median PFS (29.9 *vs.* 11.1 months). Similarly, R-Clb compared to Clb alone had a significantly longer median PFS (16.3 *vs.* 11.1 months). The combination of G-Clb had a longer median PFS when compared to the combination of R-Clb (29.2 *vs.* 15.4 months). These trials suggest that the obinutuzumab combination is superior to the ofatumumab combination, based on median PFS. A direct comparison of G-Clb and O-Clb would be required to confirm this in this

group of frail patients, but this is unlikely to occur in the present environment where currently planned trials with obinutuzumab with either ibrutinib or Abt-199 are starting in this setting.

In summary, in the R/R CLL setting, the role of ofatumumab as monotherapy has been superseded by novel agents, and, more specifically, with ibrutinib showing substantially superior activity in a direct comparison.[6] However, there may be an emerging role for ofatumumab in combination therapies and in maintenance. In the fit, treatment naïve CLL patient, FCR remains standard of care given the lower efficacy rates seen with O-FC. In the unfit, treatment-naïve CLL patient, despite having received FDA approval, the current use of ofatumumab in combination with Clb is not clear, given the demonstrated improved efficacy with the combination of obinutuzumab and Clb.

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References

1. Teeling JL, French RR, Cragg MS, et al. Characterisation of new human CD20 monoclonal antibodies with potent cytolytic activity against non-Hodgkin lymphomas. Blood. 2004;104:1973-1800.
2. Teeling JL, Marcus WJ, Wiegman LJ, et al. The biological activity of human CD20 monoclonal antibodies is linked to unique epitopes on CD20. J Immunol. 2006;177:362-371.
3. Coiffier B, Lepretre S, Pedersen LM, et al. Safety and efficacy of ofatumumab, a fully human monoclonal anti CD20 antibody, in patients with relapsed or refractory B- cell chronic lymphocytic leukemia: a phase 1-2 study. Blood. 2008;111:1094-1100.
4. Wierda WG, Kipps TJ, Mayer J, et al. Ofatumumab as a single-agent CD20 immunotherapy in fludarabine-refractory chronic lymphocytic leukemia. J Clin Oncol. 2010;28:1749-1755.
5. Moreno C, Montillo M, Panayiotidis P, et al. Ofatumumab in poor-prognosis chronic lymphocytic leukemia: A phase 4, non-interventional, observational study from the European Research Initiative on CLL (ERIC). Haematologica. 2015(4):511-516.
6. Byrd JC, Brown JR, O'Brien S, et al. Ibrutinib versus ofatumumab in previously treated chronic lymphoid leukemia. N Engl J Med. 2014; 371:213-223.
7. Cortelezzi A, Sciumè M, Liberati AM, et al. Bendamustine in combination with ofatumumab in relapsed or refractory chronic lymphocytic leukemia: a GIMEMA Multicenter Phase II Trial. Leukemia. 2014;28: 642-648.
8. Doubek M, Brychtova Y, Panovska A, et al. Ofatumumab Added to Dexamethasone in Patients with Relapsed or Refractory Chronic Lymphocytic Leukemia. Results from a Phase II Study. Am J Haematol. 2015 Feb 2. doi: 10.1002/ajh.23964. [Epub ahead of print]
9. Costa LJ, Fanning SR, Stephenson J Jr, et al. Sequential Ofatumumab and Lenalidomide for the Treatment of Relapsed and Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma. Leuk Lymphoma. 2014 Aug 17:1-15. [Epub ahead of print]
10. van Oers MHJ, Kuliczkowski K, Smolej L, et al. Ofatumumab (OFA) Maintenance Prolongs PFS in Relapsed CLL: Prolong Study Interim Analysis Results. Am Soc Hematology Oral Presentation. Abstract 21. December 6, 2014.
11. Hallek M, Fischer K, Fingerle-Rowson G, et al. International Group of Investigators, German Chronic Lymphocytic Leukaemia Study Group-CLL8 Study: Addition of rituximab to fludarabine and cyclophosphamide in patients with chronic lymphocytic leukaemia: a randomised, open-label, phase 3 trial. Lancet. 2010;376:1164-1174.
12. Wierda WG, Kipps TJ, Dürig J, et al. 407 Study Investigators. Chemoimmunotherapy with O-FC in previously untreated patients with chronic lymphocytic leukemia. Blood. 2011; 117: 6450-8.
13. Hillmen P, Robak T, Janssens A, et al. Ofatumumab + chlorambucil versus chlorambucil alone in patients with untreated chronic lymphocytic leukemia (CLL): results of the phase III study complement 1 - Am Soc Haematology Oral presentation. 2013;122:1266–1270.
14. Goede V, Fischer K, Busch R, et al. Obinutuzumab plus chlorambucil in patients with CLL and coexisting conditions. N Engl J Med. 2014; 370: 1101-10.
15. Goede V, Fischer K, Engelke A, et al. Obinutuzumab as frontline treatment of chronic lymphocytic leukemia: Updated results of the CLL11 study. Leukemia. 2015. [Epub ahead of print]

Hematopoietic cell transplantation for acute leukemia: selecting donors

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In this issue of *Haematologica*, Gorin and colleagues compare the outcomes after T-cell-replete haploidentical transplantation and autologous transplantation for adults with acute myeloid or lymphoblastic leukemia.[1]

Following induction of complete remission, most adults with acute myeloid or lymphoblastic leukemia are referred for hematopoietic cell transplantation. However, donor choice varies. There is general agreement that an HLA-matched sibling is the most suitable donor. As only about a third of patients who may benefit from hematopoietic cell transplantation have an HLA-matched sibling donor, alternative donor choices include mismatched relatives, unrelated donors (volunteer adults or umbilical cord blood) or self (autologous). In the report by Gorin and colleagues,[1] overall and leukemia-free survival rates after T-cell-replete haploidentical and autologous transplantation were comparable when the haploidentical transplants were performed at experienced transplant centers defined as performing five or more haploidentical transplants over a 6-year period. When haploidentical transplants were performed at centers that performed fewer such transplants, overall and leukemia-free survival rates were better after autologous transplantation.

Selecting a suitable donor for hematopoietic cell transplantation requires careful review of the available literature. A recent report from the National Marrow Donor Program suggests most Caucasians will have an HLA-matched adult unrelated donor or one who is HLA-mismatched at a single locus.[2] However, use of T-cell-replete grafts from haploidentical donors is appealing and increasingly offered to patients. But transplant conditioning regimens and graft-*versus*-host disease prophylaxis vary by graft source and center practice. Consequently, in the absence of appropriately designed clinical trials, comparison and interpretation of outcomes between donor sources are challenging. Gorin and colleagues recommend autolo-