can promote this right to a *chance of cure*. This statement was approved in principle by the following representatives of these study groups in San Diego in December 2003:

- Associazione Italiana di Ematologia ed Oncologia Pediatrica (AIEOP): M Arico, G Basso, A Biondi, V Conter, G Masera, G Tognoni, MG Valsecchi
- Berlin-Frankfurt-Münster Group (BFM): G Cario, H Gadner, O Haas, J Harbott, R Panzer, H Riehm, M Schrappe, A Stackelberg, M Stanulla, M Zimmermann
- Children's Oncology Group (COG): B Camitta, W Carroll, P Gaynon, S Hunger, J Nachman, K Schultz, N Winick
- Cooperative Study Group for Childhood Acute Lymphoblastic Leukemia (COALL): M Horstmann, G Janka-Schaub
- Czech Pediatric Hematology (CPH): J Stary, J Trka
- Dana-Farber Cancer Institute (DFCI) ALL Consortium: S Sallan, L Silverman
- Dutch Childhood Oncology Group (DCOG): R Pieters, A Veerman
- European Organization for Research and Treatment of Cancer-Childhood Leukemia Group (EORTC-CLG): Y Bertrand, S Suciu
- French Acute Lymphoblastic Leukemia Study Group (FRALLE): G Leverger
- Japan Association of Childhood Leukemia Study (JACLS): K Horibe
- NCRI/Medical Research Council Childhood Working Party, United Kingdom Acute Lymphoblastic Leukemia (MRC-UKALL): OB Eden, C Harrison, B Gibson
- Nordic Society of Pediatric Haematology and Oncology (NOPHO): E Forestier, K Schmiegelow, K Vettenranta
- St. Jude Children's Research Hospital (SJCRH): D Campana, E Couston-Smith, WE Evans, R Handgretinger, C-H Pui, MV Relling
- Taiwan Pediatric Oncology Group (TPOG): D-C Lang
- Tokyo Children's Cancer Study Group (TCCSG): A Manabe, M Tsuchida
- D Pinkel.

Chronic myeloid leukemia-specific T-cell responses

In chronic myeloid leukemia (CML), the chimeric p210 fusion protein resulting from the bcr-abl fusion gene produced by the t(9;22)(q34; q11) translocation, in virtue of the unique sequence of amino acids contained in the junctional regions, which is CML-specific, furnished the rationale for a peptide vaccine strategy in this disease.[1] Although treatment of CML has bee revolutionized by imatinib mesylate (see previous articles in this journal)[2-12] a portion of patients are or become resistant to this drug,[13] so that alternative treatments have been proposed.[14-17] Theoretically, CML-specific T cells might be useful for therapeutic purposes. As discussed by Posthuma and co-workers in this issue,[18] a prerequisite for a CML-specific T-cell response is proteasomal degradation of intracellular BCR/ABL protein resulting in presentation of BCR/ABL-specific oligopeptides by HLA class I or HLA class II molecules on the membrane of leukemic cells and the presence of T-cells with a T-cell receptor (TCR) that can recognize these peptide-HLA complexes. Until now there is no definite proof of the existence of such CML-specific responses *in vivo*. In their work, Posthuma and co-workers[18] show that proteosomal degradation of BCR/ABL protein can generate a CML-specific HLA-A*0301 restricted peptide, but high-avidity T-cells recognizing this BCR/ABL-specific antigen could not be demonstrated.

References

1. Bocchia M. Is there any role left for p210-derived peptide vaccines in chronic myeloid leukemia? Haematologica 2002;87:675-7.
2. Besalduch J, Guti Rrez A, Parody R, Bernu ST. Chromosomal abnormalities in Philadelphia (Ph)-negative cells of patients with chronic myeloide leukemia treated with Imatinib (ST1571). Haematologica 2003;88:ELT03.
3. Cervantes F, Hernandez-Boluda JC, Steegmann JL, Conde E, Alvarez-Larran A, Lopez-Jimenez J, et al. Imatinib mesylate therapy of chronic phase chronic myeloid leukemia resistant or intolerant to interferon: results and prognostic factors for response and progression-free survival in 150 patients. Haematologica 2003;88:1117-22.
4. Kiani A, Habermann I, Schake K, Neubauer A, Rogge L, Ehninger G. Normal intrinsic Th1/Th2 balance in patients with chronic phase chronic myeloid leukemia not treated with interferon-alpha or imatinib. Haematologica 2003;88:754-61.
5. Lange T, Bumm T, Otto S, Al-Ali HK, Kovacs I, Krug D, et al. Quantitative reverse transcription polymerase chain reaction should not replace conventional cytogenetics for monitoring patients with chronic myeloid leukemia during early phase of imatinib therapy. Haematologica 2004;89:49-57.
6. Marin D, Marktel S, Bua M, Armstrong L, Goldman JM, Apperley JF, et al. The use of imatinib (STI571) in chronic myelod leukemia: some practical considerations. Haematologica 2002;87:979-88.
7. Marktel S, Marin D, Foot N, Szydlo R, Bua M, Karadimitris A, et al. Chronic myeloid leukemia in chronic phase responding to imatinib: the occurrence of additional cytogenetic abnormalities predicts disease progression. Haematologica 2003;88:260-7.
8. O'Dwyer M. Current use of imatinib in the treatment of chronic myeloid leukemia. Haematologica 2003;88:241-4.
9. Rosti G, Trabacchi E, Bassi S, Bonifazi F, de Vivo A, Martinelli G, et al. Risk and early cytogenetic response to imatinib and interferon in chronic myeloid leukemia. Haematologica 2003;88:256-9.
10. Steegmann JL, Moreno G, Alaez C, Osorio S, Granda A, de la Camara R, et al. Chronic myeloid leukemia patients resistant to or intolerant of interferon alpha and subsequently treated with imatinib show reduced immunoglobulin levels and hypogammaglobulinemia. Haematologica 2003;88:762-8.
11. Sureda A, Carrasco M, de Miguel M, Martinez JA, Conde E, Sanz MA, et al. Imatinib mesylate as treatment for blastic transformation of Philadelphia chromosome positive chronic myelogenous leukemia. Haematologica 2003;88:1213-20.

12. Luzzatto L, Frassoni F, Melo JV. Imatinib: can one outwit chronic myeloid leukemia? Haematologica 2002;87:898-901.
13. Agirre X, Fontalba A, Andreu EJ, Odero MD, Larrayoz MJ, Montiel C, et al. Lack of Bcr-Abl point mutations in imatinib chronic myeloid leukemia patients in chronic phase before initiation of treatment is not predictive of response. Haematologica 2003;88:1425-6.
14. Olavarria E. Autotransplantation for chronic myeloid leukemia: is it useful? Haematologica 2002;87:3-6.
15. Cervantes F, Camos M, Boque C, Besses C, Alcala A, Sureda A. Polyethylene glycol interferon-a2b alone or in combination with low-dose Ara-C in patients newly diagnosed with chronic myeloid leukemia. Haematologica 2004;89:870-1.
16. Hernandez-Boluda JC, Carreras E, Cervantes F, Marin P, Arellano-Rodrigo E, Rovira M, et al. Collection of Philadelphia-negative stem cells using recombinant human granulocyte colony-stimulating factor in chronic myeloid leukemia patients treated with alpha-interferon. Haematologica 2002;87:17-22.
17. Sayer HG, Kasper C, Mugge LO, Schilling K, Scholl S, Hoffken K. Allogeneic blood stem cell transplantation in advanced chronic myeloid leukemia--high response rate associated with increased chronic graft-versus-host disease. Haematologica 2003;88:831-3.
18. Posthuma EFM, van Bergen CAM, Kester MGD, de Paus RA, van Veelen PA, de Ru AH, et al. Proteosomal degradation of BCR/ABL protein can generate a CML-specific HLA-A*0301 restricted peptide, but high-avidity T-cells recognizing this BCR/ABL-specific antigen could not be demonstrated. Haematologica 2004;89: 1062-71.

Molecular basis of von Willebrand disease and its clinical implications

Von Willebrand's disease (VWD) is an autosomally inherited bleeding disorder caused by a deficiency or abnormality of von Willebrand factor (VWF). Castaman and co-workers[1] have recently reviewed the molecular basis of VWD in this journal. VWD has a prevalence of about 1% in the general population, but the figure for clinically relevant cases is lower (about 100/million inhabitants). Most cases appear to have a partial quantitative deficiency of VWF (type 1 VWD) with variable bleeding tendency, whereas qualitative variants (type 2 VWD), due to a dysfunctional VWF, are clinically more homogeneous. Type 3 VWD is rare and the patients have a moderate to severe bleeding diathesis because of the virtual absence of VWF, and a recessive pattern of inheritance.

In this issue, Hilbert and co-worker[2] report studies on a new mutation in the VWF gene that causes type 2A VWD. These patients may be poorly responsive to desmopressin and should receive FVIII/VWF concentrates in cases of prolonged mucosal bleeding and major surgery. This study provides an example of the relevance of molecular studies for clinical practice.

Other studies on VWF or VWD recently published in this journal are listed below.[3-8]

References

1. Castaman G, Federici AB, Rodeghiero F, Mannucci PM. Von Willebrand's disease in the year 2003: towards the complete identification of gene defects for correct diagnosis and treatment. Haematologica 2003;88:94-108.
2. Hilbert L, Federici AB, Baronciani L, Dellagiovanna S, Mazurier C. A new candidate mutation, G1629R, in a patient with type 2A von Willebrand disease: basic mechanisms and clinical implications. Haematologica 2004;89:1128-33.
3. Coppola R, Mari D, Lattuada A, Franceschi C. Von Willebrand factor in Italian centenarians. Haematologica 2003;88:39-43.
4. Franchini M, Gandini G, Manzato F, Lippi G. Evaluation of the PFA-100 system for monitoring desmopressin therapy in patients with type 1 von Willebrand's disease. Haematologica 2002;87:670.
5. Sanchez-Luceros A, Meschengieser SS, Woods AI, Blanco AN, Kempfer AC, Casais P, et al. Acquired von Willebrand factor abnormalities in myeloproliferative disorders and other hematologic diseases: a retrospective analysis by a single institution. Haematologica 2002;87:264-70.
6. Perutelli P. Immunostaining of von Willebrand factor multimers on agarose gels and nitrocellulose filters. Haematologica 2002; 87:223-4.
7. Federici AB. The factor VIII/von Willebrand factor complex: basic and clinical issues. Haematologica 2003 Jun;88:EREP02.
8. Federici AB, Canciani MT, Forza I, Mannucci PM, Marchese P, Ware J, et al. A sensitive ristocetin co-factor activity assay with recombinant glycoprotein Ibα for the diagnosis of patients with low von Willebrand factor levels. Haematologica 2004;89:77-85.