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Berdel2,† and Dario Neri1,†1Department of Chemistry and Applied Biosciences, ETH Zürich, Wolfgang-Pauli-Strasse 10, CH-8093 Zurich, Switzerland.2Department of Medicine A, Hematology and Oncology, University Hospital Muenster, D-48129 Muenster, Germany.3Phloggen SpA, I-53018 Sovicelle (SI), Italy.4Department of Medical Oncology, University Hospital and University of Berne, CH-3010 Berne, Switzerland.5Department of Pathology, Hematopathology Section and Lymph Node Registry, University of Kiel, D-24105 Kiel, Germany. *†Corresponding author. E-mail: berdel[at]uni-muenster.de (W.E.B.); neri[at]pharma.ethz.ch (D.N.)Page 3Katrin L. Gutbrodt1,* , Christoph Schliemann2,* , Leonardo Giovannoni3, Katharina Frey1, Thomas Pabst4, Wolfram Klapper5, Wolfgang E. Berdel2,† and Dario Neri1,†1Department of Chemistry and Applied Biosciences, ETH Zürich, Wolfgang-Pauli-Strasse 10, CH-8093 Zurich, Switzerland.2Department of Medicine A, Hematology and Oncology, University Hospital Muenster, D-48129 Muenster, Germany.3Phloggen SpA, I-53018 Sovicelle (SI), Italy.4Department of Medical Oncology, University Hospital and University of Berne, CH-3010 Berne, Switzerland.5Department of Pathology, Hematopathology Section and Lymph Node Registry, University of Kiel, D-24105 Kiel, Germany. *†Corresponding author. E-mail: berdel[at]uni-muenster.de (W.E.B.); neri[at]pharma.ethz.ch (D.N.)Page 4 04 September 2013 Vol 5, Issue 201 By Katrin L. Gutbrodt, Christoph Schliemann, Leonardo Giovannoni, Katharina Frey, Thomas Pabst, Wolfram Klapper, Wolfgang E. Berdel, Dario Neri By Minbiao Ji, Daniel A. Orringer, Christian W. Freudiger, Shakti Ramkissoon, Xiaohui Liu, Darryl Lau, Alexandra J. Golby, Isaiah Norton, Marika Hayashi, Nathalie Y. R. Agar, Geoffrey S. Young, Cathie Spino, Sandro Santagata, Sandra Camelo-Piragua, Keith L. Ligon, Oren Sagher, X. Sunney Xie By Ishita Das, Joo-Min Park, Jung H. Shin, Soo Kyeong Jeon, Hernan Lorenzi, David J. Linden, Paul F. Worley, Roger H. Reeves As allogeneic stem cell transplantation (alloSCT) can be a very taxing treatment, psychosocial variables should be considered in order to optimize the treatment benefit for patients.In a prospective longitudinal study, we assessed the influence of anxiety, depression and resilience on patients' QoL during and after alloSCT. Resilience means the ability of individuals to deal successfully with stressful situations. A high degree of resilience can help patients to adapt to their challenging situation.1, 2The study was conducted at the center for stem cell transplantation of the University Hospital Muenster, Germany, was approved by the local Ethics Committee (2011-255-f-5) and registered at the German Clinical Trials Register (DRKS00007945).The study focused on patients undergoing therapy without relapse since the event of a relapse will change the treatment strategy. Applied instruments were EORTC Quality of Life Questionnaire (EORTC QLQ-C30),3 Resilience Scale (RS-25),4, 5 and Hospital Anxiety and Depression Scale (HADS).6, 7Semi-structured interviews of 30 min focused on patients' understanding of the concepts QoL and resilience (see Supplementary Information). Qualitative content analysis8, 9 was used to evaluate the interviews.Over a period of 12 months, all patients meeting the inclusion criteria and willing to participate, were included consecutively in the study. Inclusion criteria were as follows: age ≥18 years, ability to complete questionnaires without external help. Patients with various diseases were included. Treatment regimens of the miscellaneous disease entities are different in nature, but all patients received their conditioning therapy followed by alloSCT in the specialized care unit with laminar air flow and/or HEPA filtered ventilation. Exclusion criteria were psychiatric disorders and lack of knowledge of the German language.Patient recruitment was from March 2014 to February 2015, the data were collected till October 2015. During the time of recruitment, 133 patients were treated at the stem cell transplant unit. Of 85 patients meeting the inclusion criteria, 65 were willing to participate in the study (full analysis collective).QoL, resilience, anxiety and depression were assessed at three time points: at beginning (T1) and end (T2) of inpatient treatment as well as 6 months after discharge (T3).From 65 patients at T1, 49 were able to complete questionnaires at T2. Eight patients died during inpatient treatment, one patient relapsed. Four patients decided to participate no longer in the study and three patients were physically not able to fill out the questionnaires at T2. From those 49 patients, 30 completed questionnaires at T3. Six patients died, four patients relapsed and a further six patients were physically not able to complete the questionnaires. Two patients decided not to participate any more, one patient had become clinically depressed. The complete case collective consists of the 30 patients who filled out the questionnaires at all time points (Supplementary Figure S1).The interviews were scheduled for 1 year after alloSCT, when patients had adapted to their life situation. Twenty patients agreed to be interviewed.Standard descriptive analyses were performed. QoL was analyzed using multivariate linear mixed models for the longitudinal data.10, 11 Missing values were treated as missing at random. Model selections were performed, where, among others, resilience was removed as an influencing variable based on the likelihood-ratio (LR) test. The final model included the main effects of sex, HADS-anxiety at T1, HADS-depression at T1, and time point and the interaction effect sex x time point as influencing variables. Repeated measurements of QoL were modeled using a random intercept for patient and a heterogeneous residual variance for each time point. Results are reported as regression coefficients and corresponding 95% confidence intervals (95% CI), or global P-values of the F-test. Resilience, QoL and their changes are presented via boxplots.As sensitivity analysis, all analyses were repeated in the complete case collective.Transcriptions of the interviews were categorized and a content analysis was done by counting the frequencies of statements in each category.Statistical analyses were performed using SAS software V9.4. All P-values and confidence intervals have to be interpreted in an exploratory sense. Consequently, no significance levels were defined and no adjustment for multiplicity was performed. P-values were considered as statistically noticeable in cases where P≤0.05.The study collective consisted of 43 men (66%) and 22 women (34%) between 27 and 73 years (see Supplementary Table S1). Median age was 58 years, with no statistically noticeable difference between males (57 years) and females (59 years). Of these patients, 29 had AML or ALL, 10 patients myelodysplastic syndrome, 13 lymphoma, 3 CML or CLL, and 10 patients had other disorders (aplastic anemia, paroxysmal nocturnal hemoglobinuria, myelofibrosis).Supplementary Table S2 shows the assessment of QoL, resilience and HADS at each time point.The longitudinal data of QoL are shown in Figure 1a. In the univariate analysis, no statistically noticeable effects on resilience were found for age or gender. No relevant changes in resilience over time could be observed (Figure 1b).Figure 1 Boxplots of Global Quality of Life EORTC QLQ-C30, Resilience Scale. (a) Boxplots of Global Quality of Life EORTC QLQ-C30 (QoL) and absolute changes since T1 separated by gender. (b) Boxplots of Resilience Scale and absolute changes since T1 separated by gender.In the multivariable linear mixed model for QoL, the HADS-depression score at T1 has a statistically noticeable effect (P=0.0053, Table 1). Per one point increase on the HADS-depression scale the mean QoL decreases by -2.4 units. HADS-anxiety score at T1 showed no noticeable effect, whereas the interaction between sex and time point influences QoL noticeably (P=0.0123). This means females and males have a different development of QoL over time. Male patients showed a noticeable decrease of -15.3 units between T1 and T2. But, this decrease was compensated between T2 and T3 by an increase of 15.3. Females started at T1 with a lower QoL compared to males and showed a slight increase to T2 (9.7) and stayed on this level until T3. At T3, no difference in QoL between male and female patients could be detected. The detailed linear regression model equation can be found in Supplementary Table S3. Resilience at T1 was removed as independent variable in the model selection step because the influence on QoL was not noticeable and only small (LR-test, P=0.506). In the sensitivity analysis of QoL, the complete case collective has a similar course over time and the QoL differences between females and males were similar to the differences in the full analysis collective.Table 1 Linear mixed model estimates of the global quality of lifeCorrelations between QoL, HADS, emotional functioning and resilience at each time point are shown in Supplementary Table S5.The interviews reveal that patients are not necessarily familiar with the concept of resilience. Ten of the 20 patients interviewed stated they had never heard the term nor did they know the meaning of it. The other 10 patients were at least able to circumscribe the meaning ('being able to deal successfully with stressful situations'). The concept QoL is much better understood. Ten patients stated autonomy as the central point of their individual QoL ('being self-determined'), seven patients stated an intact family life as most important. Being asked how the alloSCT influenced their life, 17 patients declared they had to learn to live with a number of physical and psychological restrictions and 11 patients complained about the loss of light-heartedness. Asked what helped them most while undergoing treatment, 18 patients named the social support they received from family, friends and medical personnel.The different primary disease entities showed no association with QoL, the HADS-depression score at T1 has a statistically noticeable effect (P=0.0053, Table 1). Per one point increase on the HADS-depression scale the mean QoL decreases by -2.4 units. HADS-anxiety score at T1 showed no noticeable effect, whereas the interaction between sex and time point influences QoL noticeably (P=0.0123). This means females and males have a different development of QoL. This could be due to gender-specific behavior and coping strategies.12The mean resilience score at T1 in our sample (140.3) was slightly higher than the standard value (133.78) for the German population.5 Contrary to our expectations, resilience seems to have only a small influence on patients' QoL during treatment. This might be due to the fact that patients need time to adapt to the situation of alloSCT-treatment. Furthermore, during treatment, the powerful influence of somatic aspects might override psychological factors.HADS-depression and anxiety scores are not in the pathologically abnormal range.13 The impact of the HADS-depression score (T1) on QoL is not surprising. Depression is discussed as possible risk factor for survival after alloSCT.14, 15The content analysis of the interviews shows that patients rely on the emotional support, which they get not only from their family but as well from the medical staff.Our study bears some limitations. All inference statistics have only an exploratory interpretation. The multivariable models were fitted data-driven and were not determined before data collection. Therefore, the applied statistical models are not valid to make assumptions about population inference. Due to the sample size, fitting of larger multivariable models with further clinically relevant covariables was not possible. Consequently, prospective studies are needed to confirm a relationship between resilience and QoL and to identify factors that influence QoL after alloSCT. Further, there could be a bias in the development of QoL due to drop-outs and the missing at random assumption could be violated. Comparisons between drop-outs and completers are presented in Supplementary Table S4. However, the results of QoL in the complete case collective were similar to those in the full analysis collective at T1 and T2.In order to provide adequate psychological care for patients undergoing alloSCT, it is necessary to pay attention to pre-transplant depression because this factor has a strong impact on patients' QoL. When monitoring QoL during treatment, one has to be aware of the fact that men and women might have a different development in their QoL over time. Managing depression and QoL deterioration during treatment will help to ease the burden of alloSCT for patients.15Schumacher A, Sauerland C, Silling G, Berdel WE, Stelljes M. Resilience in patients after allogeneic stem cell transplantation. Support Care Cancer 2014; 22: 487-493.Article PubMed Google Scholar 2Hou WK, Law CC, Yin J, Fu YJ. Resource loss, resource gain, and psychological resilience and dysfunction following cancer diagnosis: a growth mixture modeling approach. 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All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee and with the declaration of Helsinki (1964) and its later amendments or comparable ethical standards. The authors declare no conflict of interest. Supportive Care in Cancer (2021)

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