Developing a supportive and palliative care intervention for patients with allogeneic stem cell transplantation: protocol of a multicentre mixed-methods study (allo-PaS)

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ABSTRACT

Introduction: Although allogeneic stem cell transplantation (allo-SCT) is a curative treatment for many haematological malignancies, it is often associated with a high morbidity and mortality. Yet, little is known about the needs for supportive and palliative care among allo-SCT recipients. Moreover, targeted interventions that reduce symptom burden and suffering are still lacking. The present study aims to inform a supportive-palliative care intervention for patients with allo-SCT and their informal carers by exploring their experiences and assessing their needs, especially their existential concerns, regarding four research topics: symptom burden and quality of life; coexistence of a chance for cure and a relevant risk of dying; change in goals of care; dying phase.

Methods and analysis: This is a descriptive mixed-methods study in progress with a convergent parallel design. Data on the four research topics will be collected and analysed separately in three steps: (1) qualitative semi-structured interviews among 20 patients, 20 informal carers and 12 healthcare providers (HCPs) and focus groups among 12–24 HCPs; (2) a quantitative cross-sectional survey with validated questionnaires, but also includes self-developed questions and self-developed questions among 100 patients, 100 informal carers and 50 HCPs; (3) a retrospective case analysis of all deceased patients who underwent an allo-SCT between 2010 and 2019, with collection of quantitative and qualitative data. The qualitative and quantitative data sets will be finally merged for comparison and interpretation. Results will serve to develop a supportive-palliative care intervention.

Ethics and dissemination: The Ethics Commission of the Faculty of Medicine of the University of Cologne approved this study (20–1370_2). The study results will be published in peer-review journals, be presented at congresses and will be translated into clinical practice through the development of the palliative-supportive care intervention.

Trial registration number: DRKS00027290 (German Clinical Trials Register).

INTRODUCTION

Allogeneic stem cell transplantation (allo-SCT) is a curative treatment modality for several primary or relapsed haematological malignancies, in which healthy blood stem cells are transferred from a donor to the patient. However, it is associated with a substantial rate of complications. In particular, acute and chronic graft-versus-host disease (GvHD) and infections cause significant morbidity and mortality. The 5-year survival of transplanted patients, all diagnoses included, is about 50%. Patients are thus often in need of supportive and palliative care to best manage their severe symptomatology and suffering, until the very end of life.

Physical symptoms, psychological distress and reduced quality of life are very common in allo-SCT recipients and survivors, but also among their informal carers. The most frequent physical symptom within patients...
in both the early months and the years after allo-SCT is fatigue.\(^3\) In addition, gastrointestinal disorders such as loss of appetite, nausea, diarrhoea or constipation, as well as sleep disturbances often occur mainly in the first 3 months after allo-SCT.\(^6\) \(^7\) \(^8\) Further long-term symptoms persisting for at least 1 year after transplantation are mainly pain and sexual dysfunction.\(^3\) \(^6\) \(^9\) \(^10\) Fatigue might persist even 5 years after transplantation.\(^20\) Acute and chronic GvHD, especially in their more severe forms, are associated with a higher burden of psychological distress, mainly pain and sexual dysfunction.\(^3\) \(^6\) \(^9\) \(^10\) \(^21\) Psychological distress is also highly prevalent.\(^2\) \(^3\) \(^4\) \(^5\) \(^6\) \(^7\) \(^8\) \(^9\) \(^10\) \(^11\) \(^12\) In a prospective, multicentre study, the prevalence of anxiety was significantly increased before allo-SCT, while depression was diagnosed more frequently after transplantation, compared with the general population and this up to 10 years after the procedure.\(^22\) Post-traumatic stress disorder is also a major concern after allo-SCT.\(^4\) \(^23\) \(^24\) \(^25\) \(^26\) Further, studies indicate that mental health is impaired by acute and chronic GvHD.\(^10\) \(^21\) \(^27\) Quality of life is also reduced compared with pre-transplantation scores, mainly until 1 year post-allo-SCT.\(^4\) \(^10\) \(^27\) In allo-SCT survivors, chronic GvHD has a major impact on quality of life.\(^3\) \(^21\) In view of the many burdensome symptoms and needs of allo-SCT recipients, survivors and those relapsing, the (early) integration of specialist palliative care into the transplantation trajectory has gained increasing attention during recent years.\(^5\) \(^7\) \(^15\) \(^23\) \(^28\) \(^29\) \(^30\) Integrating palliative care early into oncological procedures is a well-established concept for solid tumours and is part of international evidence-based recommendations.\(^31\) \(^32\) \(^33\) \(^34\) However, such clinical concepts are still largely lacking for haematological malignancies, although recent pioneer research shows the effectiveness of palliative care integration.\(^5\) \(^7\) \(^15\) \(^35\) \(^36\) \(^37\) With regard to allo-SCT, El-Jawhari et al conducted a first randomised clinical trial investigating a palliative consultation service integrated into standard SCT procedures. The intervention was shown to be effective in reducing the symptom burden, controlling anxiety, depression and post-traumatic stress symptoms and optimising quality of life.\(^25\) \(^26\) Depression symptoms were also reduced among the informal carers. Other palliative care aspects in the context of allo-SCT, like discussions on goals of care, referral to hospice and maintaining hope after talking to palliative care specialists, were subject of some further prospective studies, which also showed a positive effect of integrating early specialist palliative care services.\(^7\) \(^38\) \(^39\) Although these results are promising, overall there is a paucity of data on the benefits of specialist palliative care interventions for patients with allo-SCT and their informal carers. Moreover, the broad applicability of these results in the real-world setting and in various healthcare systems is still very limited. Further research is warranted.\(^15\)

Treatment with allo-SCT simultaneously entails the chance for a long-term remission, but also the risk of a burdensome course with many complications and, ultimately, death. Little is known about the experience of patients, their informal carers and the healthcare providers (HCPs) facing such a situation of simultaneous chance of cure and risk of dying. In advanced cancer, it is now well-known that the confrontation with fundamental changes and losses triggered by the diagnosis of an incurable malignancy can cause existential distress.\(^40\) Existential concerns have hardly been investigated in haematological malignancies, in which a risk of dying coexists with a real chance of cure. Few studies in the allo-SCT context have investigated existential concerns. They operationalised these concerns as uncertainty, fear of cancer progression and fear of death, and found some clinically relevant distress that deems further investigation.\(^41\) \(^42\) \(^43\) \(^44\) \(^45\) Regarding patients’ resources, positive psychological attitudes like optimism and hope have been investigated: they might have a positive impact on health-related outcomes in patients with SCT.\(^46\) In summary, more research is needed to explore the exact dimensions of existential distress, patients’ and informal carers’ resources and coping strategies and the support that HCPs might best offer.

Compared with patients with solid tumours, patients with haematological malignancies receive specialist palliative care less frequently and they more often undergo invasive treatments until the end of life. How dying is disclosed also differs, as patients with haematological cancer are less frequently informed about the nearing death.\(^47\) \(^48\) \(^49\) Potential reasons for this have been described in the literature, for instance the prognostic uncertainty of haematological malignancies, unrealistic expectations on the part of patients or HCPs and the fear that involving the palliative care team might deprive patients of hope.\(^5\) \(^49\) \(^50\) \(^51\) There is a research void on how patients after allo-SCT and their informal carers experience the change from a curative to a palliative goal of care, what is burdensome and how HCPs should ideally complete such a process.

The little literature available to date on the last phase of life and dying phase in patients after allo-SCT reveals a high burden of physical symptoms.\(^52\) \(^53\) There is a lack of data on further patients’ and informal carers’ burdens, on their coping strategies and on the best possible end-of-life care.

**Objectives**

To fill in these research gaps, our study aims to broadly assess and to in-depth explore needs, burdens and coping strategies among allo-SCT recipients, survivors and those relapsing after allo-SCT, their informal carers and HCPs, including haematologists and oncologists, palliative care specialists, nurses and psycho-oncologists, using a mixed-methods design. It will answer the following research questions:

1. **Symptoms, burden, quality of life.** What are the symptoms, burdens, problems of patients and their informal carers, how is the quality of life and what is the transplant’s impact on their everyday life? How do they cope with their situation? How can quality of life be optimised?

2. **Coexistence of a chance of cure and a relevant risk of dying.** How do patients, their informal carers and HCPs cope with this situation? What causes distress, especially fear?
of death, what intensifies or reduces it? How can patients and their informal carers best be supported?

3. Change of goals of care. How is a change from a curative to a palliative goal of care perceived by patients, informal carers, HCPs? What is challenging and burdensome, what is helpful? What is the best way to carry out the process of changing goals of care?

4. Dying phase. How is the last phase of life experienced by patients and their informal carers or, if the situation has not yet arisen, what is their view on it? How is the experience of HCPs? What are the special challenges? How can patients and informal carers best be supported?

The results from this mixed-methods study will subsequently inform the development of a palliative-supportive care intervention, aiming to optimise the quality of life of patients with allo-SCT and their informal carers, to best manage their symptoms and distress, to adequately communicate a change in goals of care and to accompany them at the end of life (table 1).

**METHODS AND ANALYSIS**

**Study design**

This is a descriptive mixed-methods study in progress that started in February 2022 and will be completed at the end of 2023. It employs a convergent parallel design, that is, qualitative and quantitative data will be collected and analysed in parallel, before both data sets will be converged by comparison, to finally derive interpretations. The main reason for mixing methods in our study is to reach a greater validity through finding triangulation. Data collection will be conducted in three methodologically different steps: part I, qualitative interviews and focus groups, part II, cross-sectional survey and part III, retrospective chart review. This will permit to broadly explore and to gain a comprehensive understanding of patients’, informal carers’ and HCPs’ experience with allo-SCT (table 2).

The study data, together with two literature reviews, will constitute a reliable basis to later conceptualise, pilot and finalise a supportive-palliative care intervention (table 1). In this article, we focus on the description of the mixed-methods study as a preliminary key element for the development of the intervention.

**Setting and recruitment**

Participants are being recruited through a multicentre network of oncology centres across Germany. The Stem Cell Transplantation Section and the Centre of Palliative Medicine of the University Hospital of Cologne are coordinating the study. The Stem Cell Transplantation Section in Cologne consists of an inpatient ward and an outpatient clinic, where 80–100 patients undergo an allo-SCT every year. It is part of the Centre for Integrated Oncology, a joint tumour centre of the University Hospitals of Aachen, Bonn, Cologne and Düsseldorf (CIO-ABCD). Further German oncology centres will help recruiting participants. All participants are receiving detailed verbal and written information about the study. Informed consent for participation is being obtained.

**Part I** For the qualitative interviews, the patients and their informal carers have been enrolled consecutively at the Stem Cell Transplantation Section of Cologne since February 2022. The inclusion criteria (table 2) are being checked by the research assistants. Included are adult patients at one of these three time points along the allo-SCT trajectory: (T1) from establishing the indication for allo-SCT to allo-SCT; (T2) on the inpatient SCT unit after allo-SCT; (T3) in the outpatient clinic after discharge from the transplantation ward and until 1 year after allo-SCT. To recruit patients, HCPs are identifying potential participants and are forwarding them to the study team. For enrolling informal carers, the participating patients are being suggested to name a close relative involved in their care. HCPs are being recruited at the CIO-ABCD.

**Part II** Patients and informal carers will be invited to participate in the survey via displayed flyers or via the HCPs of the participating centres of the oncology networks. During the initial screening by telephone, the inclusion criteria will be checked by the research assistants (table 2). The inclusion criteria are the same as for part I (see table 2). HCPs in the participating oncology centres will be recruited via different digital channels (e.g., mailing lists, networks).

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Table 1 Key elements of the supportive-palliative intervention
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| **(I) Qualitative** | Patients | In-depth qualitative interviews | ► Deemed eligible for allo-SCT or having undergone allo-SCT.  
► ≥18 years.  
► Informed consent. | ► Non-sufficient German language skills.  
► Severe physical impairment.  
► Severe cognitive impairment. | 20 | T1, T2 or T3 | Exploration, assessment and description of:  
► Symptoms, burden, individual quality of life.  
► Experience and coping with the coexistence of chance of cure and risk of dying.  
► Experience and wishes on the process of a change in goals of care.  
► Fears, hope and wishes on the last phase of life. |
| | Informal carers | In-depth qualitative interviews | ► Informal carers of a patient with allo-SCT.  
► ≥18 years.  
► Informed consent. | | | |
| | HCPs | In-depth qualitative individual interviews | ► Belonging to a relevant professional group (physicians, nurses, psycho-oncologists, chaplains, physiotherapists, music/art therapists, social workers).  
► ≥18 years.  
► Informed consent. | ► Non-sufficient experience in caring for patients with allo-SCT.  
► Non-sufficient German language skills. | 12 | n.a. | |
| | Focus groups | | | | | |
| **(II) Survey** | Patients | Cross-sectional survey | As for part I | As for part I | 100 | T1, T2 or T3 | |
| | Informal carers | | | | 100 | |
| | HCPs | | | | 50 | n.a. | |
► ≥18 years. | n.a. | Total population 2010–2019 | n.a. | Assessment and description of clinical trajectory, symptoms, complications, survival time, etc. |

*T1: time from establishing the indication for allo-SCT to allo-SCT; T2: time on the inpatient stem cell transplantation unit after allo-SCT; T3: time in the outpatient clinic after discharge from stem cell transplantation ward and until 1 year after allo-SCT.

table: The table describes the mixed-methods study design, including the study parts, participants, methods, inclusion and exclusion criteria, sample size, time points of data collection, and main objectives.
Part III: The records of all deceased patients with an allo-SCT performed at the Stem Cell Transplantation Section of the University Hospital of Cologne between 2010 and 2019 will be identified.

Sample size
For the qualitative interviews (part I), the sample size of patients, informal carers and HCPs as presented in table 2 is expected to result in a saturation of content, based on literature and own previous experience. The sample size is an estimate and will be finalised after content saturation.

For the survey (part II), the sample sizes of 100 patients and 100 informal carers, and of 50 HCPs (see table 2) are about sufficient to estimate proportions with a precision (SE) of maximum ±0.05 and 0.07, respectively (Stata/SE V.15.1, StataCorp, College Station, Texas, USA; cii proportions, exact).

Part III is a total population analysis of the deceased patients with an allo-SCT carried out in a period of 10 years. The expected sample is about 300 deceased persons.

Data collection
Part I: For the qualitative parts of the study, all interviews are being conducted by two experienced and trained research assistants. As the study intends to explore a broad range of experiences, in-depth face-to-face (or online) interviews and focus groups are carried out with semi-structured interview guides addressing the issues raised in the research questions and have been developed for the three relevant project stakeholders (patients, informal carers and HCPs). The interviews and the focus groups are scheduled for 30–90 min. If some topics addressed have not (yet) been experienced by the patients or the informal carers at the time of the interview (eg, a change in goals of care or the last phase of life), the questions are formulated hypothetically (‘Imagine…’). The interviews are audio-recorded and transcribed verbatim. Socio-demographic and clinical data, particularly on allo-SCT and its complications, are also collected.

Part II: For the quantitative survey among patients and informal carers, we will send by post a self-administered paper–pencil questionnaire with the possibility of telephone support by the research team. We will have a first personalised contact with the participants by telephone before they start answering the questionnaire, given the sensitive topic of the survey, which deals with dying and death. This will allow for feedback, when needed. The survey among HCPs will be performed via an online survey tool and be digitally sent to participants. Each test battery for each participants’ groups (patients, informal carers and HCPs) consists of standardised and validated questionnaires as well as of self-developed questions addressing the four main research topics. Some open-ended questions will allow for free-text responses. We will also ask patients, informal carers and HCPs for socio-demographic information as well as for patients’ clinical data. All three test batteries will be piloted for comprehensibility, readability, plausibility and possible strain, among a group of researchers, clinicians with experience in allo-SCT and the target population (patients, informal carers and HCPs). In the following, we present the standardised questionnaires that will be implemented for the survey.

Patients’ questionnaires
We will assess the distress that arises from cancer and its treatments using the German version of the self-report Cancer- and Treatment Distress Scale. It consists of 23 items scored on a 4-point Likert scale (0 ‘no distress’ to 3 ‘severe distress’). The items cover six subscales: uncertainty, family strain, identity, health burden, medical demands and finances. It has been validated in English for SCT recipients. The first four subscales include items on various existential concerns, among others fear of progression.

Death anxiety will be measured with the validated German version of the Death and Dying Distress Scale. The 15 items assess the distress arising from the confrontation with one’s own finitude as well as with the dying process. We will adapt them to our population, using the wording ‘your possible death’ instead of ‘your death’, as the main participants are in a curable state of their disease despite the relevant mortality rate. The items are rated on a 6-point Likert scale (0 ‘no distress’ to 5 ‘extreme distress’).

Demoralisation, a common form of existential distress, has been defined as a maladaptive coping form in patients facing a stressor event like an advanced illness, and is characterised by a loss of meaning, hope and purpose. The Demoralisation Scale-II is a 16-item revised questionnaire with two subscales (meaning and purpose; distress and coping ability) and was validated in German in a cancer population. Items are rated on a 5-point Likert scale (0 ‘never’ to 2 ‘often’).

Adaptation to a life-threatening medical situation will be measured by means of the Loss Orientation and Life Engagement in Advanced Cancer Scale, a tool with 21 items scored on a 5-point Likert scale (0 ‘not at all’ to 4 ‘nearly all the time’). The scale builds on the concept of dual orientation when facing severe loss, especially at the end of life: patients might focus on past or anticipated loss, like preoccupation with death and dying (‘loss orientation’), or on engaging in meaningful activities (‘life engagement’). Coping strategies including end-of-life preparation, distraction and hope are measured.

The validated Spiritual Well-being Scale of the Functional Assessment of Chronic Illness Therapy questionnaire is a widely used self-report instrument to measure the spiritual well-being as a resource in patients with cancer and is available in German (www.facit.org). It consists of 12 items assessing the religious and the existential well-being with constructs like peace, meaning and faith. A 5-point Likert scale is used for answering the items from 0 ‘not at all’ to 4 ‘very much’.

We will investigate death acceptance, as this life attitude might be adaptive in terms of existential distress. We will use the corresponding subscale of the Life Attitude Profile-Revised, which has been validated in German. The subscale death acceptance includes eight items scored on a 7-point Likert scale (1, ‘strongly disagree’ to 7, ‘strongly agree’).

Psychological distress operationalised as anxiety and depression symptoms will be measured with the validated German versions of the Patient Health Questionnaire and of the Generalised Anxiety Disorder Questionnaire. The items are answered on a 4-point Likert scale from 0 (not at all) to 3 (nearly every day).

We will use the validated Functional Assessment of Cancer Therapy–Bone Marrow Transplant to assess the quality of life of patients with allo-SCT. A German version is available. It includes 47 items divided into five subscales: physical, social, emotional, functional well-being and SCT-specific concerns. Responses are given on a 5-point Likert scale that ranges from 0 ‘not at all’ to 4 ‘very much’.

The self-developed questions around the four research topics ask for: the estimated prognosis (chance for cure and risk of death); the time points in the transplantation trajectory when perceived life threat and fear of death is highest; when is the best time and what is the best manner to address this topic and with which HCPs; support needs for existential concerns; and, how to be best prepared for the end of life in the event of a fatal course of the disease.

Informal carers’ questionnaires

The quality of life of relatives of patients with allo-SCT will be measured with the Family Reported Outcome Measure. The 16-item questionnaire assesses how the fact of having a sick family member affects the relatives’ quality of life. It has been validated in German in a population of relatives of patients with chronic diseases. The answer scale ranges from 0 (‘not at all’) to 2 (‘a lot’).

We assess the informal carers’ burden with the 7-item Short Form of the Zarit Burden Interview (ZBI-7), a self-report questionnaire, which originated as a 29-item tool. ZBI-7 has been validated in German for the palliative care setting. Response options on a 5-point scale range from 0 ‘never’ to 4 ‘nearly always’.

The self-developed questions for informal carers cover the same topics as those described above for patients.

HCPs’ questionnaire

The Death Attitude Profile-Revised measures attitudes towards death by means of 32 items covering five dimensions: fear of death (negative thoughts and feelings about death and dying), death avoidance (avoiding thoughts about death to reduce death anxiety), neutral acceptance (view of death as something that is neither feared nor welcomed), approach acceptance (view of death as a gateway to a positive afterlife) and escape acceptance (view of death as an escape from a painful existence). The items are quoted on a 7-point Likert scale (1, strongly disagree, to 7, strongly agree). The scale was translated and validated in German in a healthy population.

The self-developed questions address the HCPs’ view on the patients’ experience as well as their own attitudes: which existential concerns are most prominent; time points in the transplantation trajectory when perceived life threat and fear of death are highest; when is the best time to address this topic and with which HCPs; HCPs’ attitudes when confronted with the issue of dying and death; challenges and helps in establishing and addressing a change in goals of care; time points to best address a change in goals of care with the patients and their informal carers; needs and best support at the end of life, especially in the dying phase, that is, in the very last days of life.

Part III: In the retrospective case analysis, the medical records of all patients with an allo-SCT carried out between 2010 and 2019 and who died until 2020 will be analysed. The following data will be collected: socio-demographic and clinical data; integration of specialist palliative care, of pain service, of psycho-oncology or chaplaincy; post-transplantation survival and place of death. In addition, the records of the deceased patients who underwent an allo-SCT in 2019 will be analysed in more detail for data like antitumour therapies, comorbidities and complications, symptoms, pharmacological symptom control. Notes from the patients’ records on existential concerns resulting from the coexistence of a chance of cure and the risk of dying, or from the change of goals of care, as well as issues on the end of life will be collected for qualitative text analysis.

Data analysis

According to the convergent parallel design of mixed-methods studies, we will first analyse the results of the three study parts separately and then merge them for interpretation.

Part I: To ensure a quality report, the researchers will be guided by the ‘Consolidated criteria for reporting qualitative research (COREQ)’. All tape-recorded and verbatim transcribed interviews will be analysed using Qualitative Content Analysis (QCA) according to Kuckartz. In the European context, QCA is often used as a synonym for thematic analysis. This is a systematic and content-oriented approach to manage and structure data by detecting themes and categories. It draws on the information of the data material, defines categories and creates a content structure. Moreover, it searches for connections between categories and helps to clearly present resulting themes. The analysis of the interview content will be conducted independently by two to three researchers to minimise the subjectivity of data interpretation. At every analysis stage, findings will be discussed among the research team and the results of these discussions will be incorporated to refine data analysis. The software MAXQDA will be used to support data management and analysis.

Open access
Part II: To complete and report the survey, we will follow the ‘STROBE Statement—Checklist of items that should be included in reports of cross-sectional studies’. The statistical analyses will be mainly descriptive. Empirical distributions are characterised by the usual measures of location and dispersion, that is, absolute and relative (\%) frequency for qualitative characteristics; mean, SD and percentiles (0, 25, 50, 75, 100) for quantitative characteristics. In addition, we will describe relationships/association for any two variables (bivariate) by the correlation coefficient or, if required, for three or more variables (multivariate) via multivariable regression models. Subgroup analyses will be performed by gender and age, as well as other covariates. To facilitate clinical interpretation, unadjusted 95% CIs will also be provided where relevant. Free-text responses will be analysed qualitatively with content analysis.

Part III: The same measures as for study part II (quantitative data) will be calculated. Again, subgroup analyses will be performed by gender, age and other covariates. Further, the relevant text passages from the medical records of patients with an allo-SCT carried out in 2019 will be analysed qualitatively with content analysis.

Comparison and interpretation: To merge the qualitative and quantitative data sets, we will first compare them, looking for convergent findings as well as for divergent ones. We will so elaborate a robust framework for a comprehensive understanding of the experiences of patients and informal carers undergoing allo-SCT. The results will serve as a basis for the subsequent development of the supportive-palliative intervention.

Patient and public involvement
Patients and informal carers are directly involved in the design of study part II by piloting the survey (see Methods section). Subsequently, they will also be directly implicated in designing the supportive-palliative intervention. Overall, the intervention will build on the patients and informal carers’ views that will be comprehensively explored and collected in the study presented here.

ETHICS AND DISSEMINATION
This study was approved by the Ethics Commission of the Faculty of Medicine of the University of Cologne on 23 March 2022 (20-1370_2). It follows the ethical principles of the Declaration of Helsinki and its amendments. Informed consent is obtained from all participants after informing them individually about all goals and procedures of the study. They are especially informed that participation is voluntary and that they can withdraw their participation at any time. All collected data are pseudonymised before analysis. The participants are informed about their right not to answer certain interview or survey questions. If some patients or their informal carers might feel burdened by dealing with existential issues or by their illness situation during an interview, it is planned to interrupt the interview and to give the participants sufficient time and space to address the burden. Only if they agree, the interview will be continued. Regarding the survey, we will have a preliminary individual phone call with all participants, where they will be encouraged to contact their HCPs or the research team in case of feeling burdened.

The results of the study will be published in peer-review journals. They will also be presented at congresses and specialist events for HCPs and patients. Furthermore, the findings will be used to develop a clinical intervention intending to respond to palliative and supportive care needs of patients with allo-SCT and their informal carers.

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Contributors
STS, MHerling and UH designed the study and coordinated the research project. AP wrote the first draft of this article. MHellmich, MHallek and CScheid revised the study protocol. All authors revised the manuscript, approved it and agreed with its submission.

Competing interests
None declared.

Patient and public involvement
Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication
Not applicable.

Provenance and peer review
Not commissioned; externally peer reviewed.

Data availability statement
Availability of data: Yes. Type of data provided: Anonymised participant data underlying the published results. Date of data availability: 12 months after publication of the results. Target group: The data are available to researchers who provide a methodologically sound proposal. Objective of data use: Aims outlined in the approved proposal. Method of data acquisition: Proposals should be addressed to the corresponding author.

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REFERENCES


75 Eilsner SA, Salek SS, Finlay AY, et al. Validation of the German version of the family reported outcome measure (FROM-16) to assess the impact of disease on the partner or family member. Health Qual Life Outcomes 2021;19:106.


