Differences in attitudes and beliefs toward end-of-life care between hematologic and solid tumor oncology specialists

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Background: Patients with hematologic malignancies often receive aggressive care at the end-of-life. To better understand the end-of-life decision-making process among oncology specialists, we compared the cancer treatment recommendations, and attitudes and beliefs toward palliative care between hematologic and solid tumor specialists.

Patients and methods: We randomly surveyed 120 hematologic and 120 solid tumor oncology specialists at our institution. Respondents completed a survey examining various aspects of end-of-life care, including palliative systemic therapy using standardized case vignettes and palliative care proficiency.

Results: Of 240 clinicians, 182 (76%) clinicians responded. Compared with solid tumor specialists, hematologic specialists were more likely to favor prescribing systemic therapy with moderate toxicity and no survival benefit for patients with Eastern Cooperative Oncology Group (ECOG) performance status 4 and an expected survival of 1 month (median preference 4 versus 1, in which 1 = strong against treatment and 7 = strongly recommend treatment, P < 0.0001). This decision was highly polarized. Hematologic specialists felt less comfortable discussing death and dying (72% versus 88%, P = 0.007) and hospice referrals (81% versus 93%, P = 0.02), and were more likely to feel a sense of failure with disease progression (46% versus 31%, P = 0.04). On multivariate analysis, hematologic specialty [odds ratio (OR) 2.77, P = 0.002] and comfort level with prescribing treatment to ECOG 4 patients (OR 3.79, P = 0.02) were associated with the decision to treat in the last month of life.

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Introduction

Despite advances in cancer therapeutics, patients with advanced hematologic malignancies such as refractory leukemias and lymphomas have a poor prognosis and often die as a result of their disease. These patients have significant symptom burden and psychosocial needs along the disease trajectory [1–3]. In the last days of life, patients with hematologic malignancies often receive aggressive interventions such as chemotherapy, prolonged hospitalizations, and intensive care unit (ICU) admissions [4–6]. Furthermore, few have early access to palliative care and hospice care compared with patients with advanced solid tumors [7–10]. It is unclear if these differential end-of-life care practices are because of differences in patient characteristics, disease trajectory, perceived prognosis, treatment risks and benefits, or oncology professionals’ attitudes toward end-of-life care.

A handful of qualitative studies have explored end-of-life decision-making in the hematologic setting from the patients’, caregivers’ and nurses’ perspective [11–13]. We identified only two small qualitative studies that examined the end-of-life care practices from the medical perspective [14, 15]. A better understanding of the oncology specialists’ decision-making process for palliative systemic therapies at the end-of-life, and their attitudes and beliefs towards palliative care could help us to develop targeted interventions to improve the quality of end-of-life care for patients with hematologic malignancies. In this survey, we compared the cancer treatment recommendations between hematologic and solid tumor oncology specialists for patients with advanced cancer using standardized case vignettes. We also examined factors associated with cancer treatment recommendations, and compared the attitudes and beliefs toward palliative care between hematologic and solid tumor specialists.

Methods

Participants

The Institutional Review Board at The University of Texas MD Anderson Cancer Center (MDACC) approved this study and waived the requirement for review and informed consent. Study participants were medical oncologists or mid-level providers (MLPs, i.e. advanced nurse practitioners or physician assistants) practicing either hematologic oncology or solid tumor oncology at MDACC. Clinicians who regularly provide care to both patients with solid tumor and those with hematologic malignancies (e.g. phase I program and general oncology) were excluded. Because of the wide variations in cancer treatment resources and palliative care access across cancer centers in the USA [16], we specifically designed this as a single-institution study to minimize inferences related to regional practices and resource availability on our primary outcome.

Survey Development

We designed the survey based on the literature and input from our expert panel, consisting of a solid tumor oncologist, a hematologic oncologist, two specialists dually trained in palliative care and medical oncology, and a palliative care specialist. This survey examined three aspects of end-of-life care: (i) palliative systemic therapy, (ii) palliative care delivery, and (iii) palliative care referral (reported separately). The full survey can be found in supplementary material, available at Annals of Oncology online.

We provided respondents with three case vignettes to determine their decision-making preferences for palliative systemic therapy. These vignettes were adapted from a previous study that examined cancer treatment decisions [17]. In keeping with the original format, we did not provide the specific cancer diagnosis to customize this variable for each respondent (e.g. a leukemia specialist only sees leukemia patients in her clinic). Instead, we provided many parameters previously known to be associated with treatment decision-making [17]. Each vignette described a patient with advanced incurable cancer and a strong outpatient treatment wish; for whom, the next systemic therapy option had moderate toxicity, 15% chance of tumor response, and no expected survival gain. The three cases were identical except for the patient’s Eastern Cooperative Oncology Group (ECOG) performance status (PS) being 2, 3, or 4, with corresponding expected median survival of 6 months, 3 months, and 1 month, respectively. Respondents were asked to provide their treatment recommendation for each patient using a 7-point Likert Scale from 1 (strongly against palliative systemic therapy) to 7 (strongly recommend palliative systemic therapy).

We assessed the clinicians’ perceived proficiency in palliative care delivery, such as symptom control, end-of-life discussions, and hospice referral. These questions were generated based on the core palliative care skillsets outlined by the Institute of Medicine, National Consensus Project, and the literature [18, 19]. We also included questions based on a qualitative study that examined oncologists’ attitudes toward end-of-life care [20]. A detailed description for the full survey is available in supplementary material, available at Annals of Oncology online. For each question, respondents were asked to rate their level of agreement (‘strongly agree’, ‘agree’, ‘neither agree nor disagree’, ‘disagree’, and ‘strongly disagree’).

Respondents also provided their demographics, such as years of clinical experience, palliative care training, and percentage of advanced cancer patients referred to palliative care.

Survey Process

We randomly sampled 60 individuals from each of the four strata among 67 hematologic oncologists, 97 solid tumor oncologists, 103 hematologic oncology MLPs, and 99 solid tumor MLPs. All potential participants received an initial invitation with an e-mail that included a link to the survey in a secured website. At the same time, they also received a hard copy of the invitation letter and survey accompanied by a $10 gift certificate. They were asked to complete the survey anonymously and to return it by mail or electronically. Reminders were sent to non-respondents at 2, 4, 6, and 12 weeks. Data collection was carried out between May and August 2014.

Statistical Analysis

Our primary outcome was the proportion of oncologists and MLPs who recommended palliative systemic therapy for patients with ECOG PS of 4 and estimated survival of 1 month. This was chosen because of the

Conclusions: We found significant differences in attitudes and beliefs toward end-of-life care between hematologic and solid tumor specialists, and identified opportunities to standardize end-of-life care.

Key words: chemotherapy, decision making, end-of-life care, hematologic neoplasms, palliative care, quality of health care
A consensus that starting a new line of chemotherapy in the last 30 days of life is an indicator of aggressive end-of-life care [21]. We decided a priori to combine the responses from oncologists and MLPs for our primary analysis. With an anticipated response rate of 60% (therefore, 72 evaluable specialists per group), we had 93% power to detect an effect size as small as 0.588 (i.e. 1-point difference in the 7-point scale with standard deviation of 1.7) using a two-sided two-sample t-test with a 5% significance level.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Hematologic oncology</th>
<th>Solid tumor oncology</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Faculty N (%)</td>
<td>MLP N (%)</td>
<td>Both N (%)</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–29</td>
<td>0 6 (14) 6 (7)</td>
<td>0 5 (9) 5 (5)</td>
<td>0.35</td>
</tr>
<tr>
<td>30–39</td>
<td>14 (33) 13 (31) 27 (32)</td>
<td>6 (14) 18 (34) 24 (25)</td>
<td></td>
</tr>
<tr>
<td>40–49</td>
<td>13 (30) 9 (21) 22 (26)</td>
<td>23 (52) 11 (21) 34 (35)</td>
<td></td>
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<td>50–59</td>
<td>11 (26) 10 (24) 21 (25)</td>
<td>10 (23) 16 (30) 26 (27)</td>
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</tr>
<tr>
<td>60–69</td>
<td>3 (7) 3 (7) 6 (7)</td>
<td>5 (11) 3 (6) 8 (8)</td>
<td></td>
</tr>
<tr>
<td>70 or greater</td>
<td>2 (5) 1 (2) 3 (4)</td>
<td>0 0 0</td>
<td></td>
</tr>
<tr>
<td>Female sex</td>
<td>15 (35) 38 (90) 53 (62)</td>
<td>18 (41) 52 (98) 70 (72)</td>
<td>0.16</td>
</tr>
<tr>
<td>Department</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>0 0 0</td>
<td>7 (16) 8 (15) 15 (15)</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>0 0 0</td>
<td>6 (14) 10 (19) 16 (16)</td>
<td></td>
</tr>
<tr>
<td>Genitourinary</td>
<td>0 0 0</td>
<td>8 (18) 12 (23) 20 (21)</td>
<td></td>
</tr>
<tr>
<td>Leukemia</td>
<td>18 (42) 17 (40) 35 (41)</td>
<td>0 0 0</td>
<td></td>
</tr>
<tr>
<td>Lymphoma/myeloma</td>
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<td>0 0 0</td>
<td></td>
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<tr>
<td>Melanoma</td>
<td>0 0 0</td>
<td>4 (9) 8 (15) 12 (12)</td>
<td></td>
</tr>
<tr>
<td>Neuro</td>
<td>0 0 0</td>
<td>7 (16) 6 (11) 13 (13)</td>
<td></td>
</tr>
<tr>
<td>Sarcoma</td>
<td>0 0 0</td>
<td>1 (2) 6 (11) 7 (7)</td>
<td></td>
</tr>
<tr>
<td>Stem cell Transplantation</td>
<td>13 (30) 15 (36) 28 (33)</td>
<td>0 0 0</td>
<td></td>
</tr>
<tr>
<td>Thoracic/head and neck</td>
<td>0 0 0</td>
<td>11 (25) 3 (6) 14 (14)</td>
<td></td>
</tr>
<tr>
<td>Years of post-graduate clinical experience, median (IQR)</td>
<td>12 (9, 20) 7.5 (3.8, 14.5) 10 (6, 17)</td>
<td>15 (9, 20) 9 (3, 15) 10 (6, 16)</td>
<td>0.91</td>
</tr>
<tr>
<td>Training in palliative care</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Formal palliative care fellowship (1 year or more)</td>
<td>0 1 (2) 1 (1)</td>
<td>1 (2) 0 1 (1)</td>
<td>0.93</td>
</tr>
<tr>
<td>Formal palliative care rotation (1 month or more)</td>
<td>12 (28) 4 (10) 16 (19)</td>
<td>15 (34) 5 (9) 20 (21)</td>
<td>0.76</td>
</tr>
<tr>
<td>Palliative care courses, continuing medical education lectures, or conferences</td>
<td>17 (40) 18 (43) 35 (41)</td>
<td>21 (48) 28 (53) 49 (51)</td>
<td>0.21</td>
</tr>
<tr>
<td>No training</td>
<td>22 (51) 22 (52) 44 (52)</td>
<td>15 (34) 23 (43) 38 (39)</td>
<td>0.09</td>
</tr>
<tr>
<td>Approximate % of advanced cancer patients referred to palliative care, median (IQR)</td>
<td>10 (5, 25) 20 (10, 45) 10 (9, 30)</td>
<td>30 (20, 25.2) 50 (20, 75) 43 (20, 70)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*Unless otherwise specified.
*Comparisons were made between all hematologic oncology specialists and all solid tumor oncology specialists using the Wilcoxon rank sum test for continuous variables and χ² or Fisher’s exact test for categorical variables.
IQR, interquartile range; MLP, mid-level providers including physician assistants and advance nurse practitioners.

**Table 2. Cancer treatment preferences**

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Hematologic oncology</th>
<th>Solid tumor oncology</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Faculty median (IQR)</td>
<td>MLP median (IQR)</td>
<td>Both median (IQR)</td>
</tr>
<tr>
<td>Performance status 4, expected survival: 1 month</td>
<td>4 (2, 6) 4 (2, 6) 4 (2, 6)</td>
<td>1 (1, 3.5) 2 (1, 3) 1 (1, 3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Performance status 3, expected survival: 3 months</td>
<td>4 (3, 6) 4.5 (3, 6) 4 (3, 6)</td>
<td>3 (2.5) 3 (2.5) 3 (2.5)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Performance status 2, expected survival: 6 months</td>
<td>5 (4, 6) 5 (4, 6) 5 (4, 6)</td>
<td>5 (4, 6) 5 (5, 6) 5 (4, 6)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

*Respondents were asked to provide their treatment recommendation for each patient using a 7-point Likert Scale from 1 (strongly against palliative systemic therapy) to 7 (strongly recommend palliative systemic therapy).
*Comparisons were made between all hematologic oncology specialists and all solid tumor oncology specialists using the Wilcoxon rank sum test.
IQR, interquartile range; MLP, mid-level providers including physician assistants and advance nurse practitioners.
Annals of Oncology


Figure 1. Cancer treatment recommendation in the last month of life. Respondents were asked to provide their treatment recommendation using a 7-point Likert Scale from 1 (strongly against palliative systemic therapy) to 7 (strongly recommend palliative systemic therapy) for a hypothetical patient with incurable advanced cancer and a strong outspoken treatment wish. The treatment had a 15% chance of tumor response, moderate toxicity, and no expected survival gain. (A) For a patient with ECOG performance status of 4 and median survival of 1 month, hematologic specialists were significantly more likely than solid tumor specialists to favor prescribing systemic cancer therapy (median preference 4 versus 1, \( P < 0.0001 \)). A bimodal distribution was observed for both hematologic and solid tumor specialists. (B) For a patient with ECOG performance status of 3 and median survival of 3 months, hematologic specialists were also significantly more likely to favor prescribing cancer therapy (median preference 4 versus 3, \( P = 0.0002 \)). (C) For a patient with ECOG performance status of 2 and median survival of 6 months, no difference was found (median preference 5 versus 5, \( P = 0.18 \)).

We summarized the data using standard descriptive statistics. We combined the answers 'strongly agree' and 'agree' for reporting purposes. We compared the responses between the solid tumor oncology teams and hematologic malignancy teams using the \( \chi^2 \) test or Fisher’s exact test for categorical variables and the Wilcoxon rank sum test for nonparametric continuous variables. We conducted similar testing with the dependent variable being comfort level to administer treatment to patients with ECOG PS = 4 (agree/strongly agree versus others). We then examined the association between the treatment recommendation for patients with ECOG PS = 4 and 1 month of life expectancy and various clinician characteristics with univariate logistic regression analysis. For this outcome, values between 5 and 7 were coded as recommending treatment, and values between 1 and 4 were coded as not recommending treatment. Variables with a \( P \)-value of <0.10 were considered in a multivariate logistic regression model.

The Statistical Analysis Software 9.3 (SAS Institute, Inc., Cary, NC, USA) software was used for statistical analysis. Statistically significance was declared when the \( P \)-value is <0.05.

results

response rate

The overall response rate was 182/240 (76%). Specifically, 43/60 (72%) hematologic oncologists, 44/60 (73%) solid tumor oncologists, 42/60 (70%) hematologic oncology MLPs, and 53/60 (88%) solid tumor MLPs completed the survey.

clinician demographics

The characteristics of clinicians who completed the survey are summarized in Table 1. Briefly, both hematologic and solid tumor specialists reported a median of 10 years of experience in practice. Few received formal palliative care training.

recommendations for palliative systemic therapy

Table 2 and Figure 1 show the treatment recommendations for the three hypothetical patients in the standardized case vignettes between the two groups of oncology specialists. Hematologic specialists were more likely than solid tumor specialists to favor prescribing systemic cancer therapy to patients with ECOG PS = 4 and an expected survival of 1 month (median preference 4 versus 1, \( P < 0.0001 \)). Figure 1A illustrates a bimodal distribution, emphasizing that this decision is highly polarized.

palliative care skills and attitudes

A vast majority (>80%) of hematologic and solid tumor specialists reported that they were comfortable with managing symptoms, counseling patients, discussing prognosis and advance care planning, and that they had a close relationship with patients and their families (Table 3). Compared with solid tumor specialists, hematologic specialists were less comfortable discussing death and dying with their patients (72% versus 88%, \( P = 0.007 \)) and referring patients to hospice (81% versus 93%, \( P = 0.02 \)). Hematologic specialists were also more likely to report feeling a sense of failure when they were not able to alter the course of disease (46% versus 31%, \( P = 0.04 \)).

Slightly more than half of the respondents perceived that they derived satisfaction providing end-of-life care to dying patients, and that they received adequate collegial support for caring for dying patients. Only a minority (<30%) of hematologic and solid tumor specialists felt comfortable prescribing systemic therapy to patients with ECOG PS of 3 and 4 (Table 3).
On univariate logistic regression analysis, hematologic specialty (odds ratio [OR] 2.79, 95% confidence interval [CI] 1.49–5.32, \( P = 0.002 \)), self-reported comfort level with counseling (OR 3.54, 95% CI 1.14–15.56, \( P = 0.027 \)), and self-reported comfort level with prescribing systemic therapies to patients with ECOG 4 (OR 4.03, 95% CI 1.45–12.25, \( P = 0.007 \)) were associated with recommendation of systemic therapy for patients with expected life expectancy of 1 month. Multivariate regression revealed that hematologic malignancy (OR 2.77, 95% CI 1.45–529, \( P = 0.002 \)) and comfort level in prescribing systemic therapy to patients with ECOG PS of 4 (OR 3.79, 95% CI 1.29–11.15, \( P = 0.02 \)) were associated with the decision to treat (Table 4).

In turn, comfort level in prescribing treatment to patients with ECOG PS of 4 was associated with older clinicians (\( P = 0.02 \)), comfortable with giving chemotherapy to patients with ECOG 3 (89% versus 14%, \( P \leq 0.001 \)), deriving satisfaction in providing end-of-life care (89% versus 60%, \( P = 0.02 \)), and comfortable with discussing death and dying (100% versus 79%, \( P = 0.03 \)).

discussion

We found significant variations in the attitudes and beliefs toward end-of-life care among oncology specialists. Hematologic specialists were more willing to recommend systemic therapy in the last month of life than solid tumor specialists, more likely to report a sense of failure when they were not able to alter the course of disease, and less comfortable with certain aspects of end-of-life care, such as discussing death and dying and referring patients to hospice care. Our findings support the need to develop evidence-based guidelines, decision aids, and care pathways to standardize oncology specialists’ end-of-life care practices.

Palliative chemotherapy, used to describe non-curative intent treatment, is often given by oncologists to provide symptom control, sustain hope, and improve survival; however, this term is sometimes considered an oxymoron because of the possibility of significant adverse effects, particularly when given to debilitated patients.
patients at the end-of-life. It is thus important for oncologists to carefully weigh the risks and benefits, and to help patients and their families clearly understand the implications of such therapies. Administration of systemic cancer therapy in the last 30 days of life is considered a poor quality of care indicator by the American Society of Clinical Oncology and the National Quality Forum for both patients with solid tumor and hematologic malignancies [21, 22]. Our group and others have previously reported that patients with hematologic malignancies were much more likely to receive chemotherapy and targeted agents in the last days of life compared with those with advanced solid tumors [4, 6, 23, 24]; however, it had been unclear if this finding was because of differences in patient characteristics, curability, prognosis, treatment risks, and benefits, and whether clinician attitudes contribute to this process. By controlling for many of these variables in our vignettes, we found that hematologic specialists remained significantly more likely to offer treatments to patients at the end-of-life. This finding implies that the attitudes of oncology professionals toward treatment at the end-of-life have a critical role in the decision-making process.

In contrast to the decisions for patients earlier in the disease trajectory, the treatment decision for patients in the last month of life was highly polarized—oncology specialists were either strongly favoring treatment or strongly against it (Figure 1A). In multivariate regression, hematologic specialty and feeling comfortable with prescribing treatment to patients with ECOG PS of 4 were associated with the decision to treat. Curiously, only 13% of hematologic specialists and 7% of solid tumor specialists reported that they felt comfortable prescribing treatment to patients with ECOG PS of 4 despite a larger proportion strongly recommending treatment to similar patients in the case vignette, suggesting that other factors such as patient preference may influence clinicians’ recommendation. Further research is needed to better understand why some oncology specialists feel comfortable offering treatments to very debilitated patients.

Clinician demographics, hematologic subspecialty (i.e. leukemia, lymphoma/myeloma and stem cell transplant), perceived palliative care proficiency, and attitudes toward hospice referral were not significantly associated with treatment recommendations. Our analysis was limited by a lack of variance in some dependent variables. For example, a vast majority of respondents perceived themselves as comfortable with palliative care skills and a small minority reported having formal palliative care training. Moreover, there may be other unexplored clinician factors such as the level of hope and optimism, personality (risk adverse versus risk taking), and oncology training that may affect the treatment decisions. Additional research should consider examining these factors.

This study has several limitations. First, we used case vignettes to assess decision-making for cancer treatments. This may not fully reflect the complex decision-making process in the real world, which is often longitudinal in nature and involves emotionally charged conversations. Second, we did not conduct formal testing of clinicians’ palliative care skills, but relied on self-reporting. Third, all participants were from a single tertiary care cancer center, which may limit its generalizability. Because higher rates of chemotherapy use in the last month of life among patients with hematologic malignancies are not unique to our institution but have been widely reported [6, 25], our findings represent the first step to better understand this phenomenon. Finally, we excluded oncologists who provide care to both patients with solid tumor and those with hematologic malignancies, such as general oncologists. Further studies are needed to examine their end-of-life care practices.

In summary, controlling for many known variables in decision-making, hematologic specialists and those who felt comfortable prescribing cancer treatments to patients with ECOG PS of 4 were more likely to recommend treatments for patients entering the last month of life, although wide variations exist. Hematologic specialists were also less comfortable with death and dying and reported more self-blame. These factors may contribute to the lower quality of end-of-life care among hematologic patients, such as high rates of ICU admission and prolonged hospitalizations in the last 30 days of life [4]. Specific interventions targeting hematologic specialists are needed to improve the end-of-life care process and outcomes for patients with hematologic malignancies.

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**Disclosure**

The authors have declared no conflicts of interest.

**References**

Association of proinflammatory cytokines and chemotherapy-associated cognitive impairment in breast cancer patients: a multi-centered, prospective, cohort study‡

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Background: Existing evidence suggests that proinflammatory cytokines play an intermediary role in postchemotherapy cognitive impairment. This is one of the largest multicentered, cohort studies conducted in Singapore to evaluate the prevalence and proinflammatory biomarkers associated with cognitive impairment in breast cancer patients.

Patients and methods: Chemotherapy-receiving breast cancer patients (stages I–III) were recruited. Proinflammatory plasma cytokines concentrations [interleukin (IL)-1β, IL-2, IL-4, IL-6, IL-8, IL-10, granulocyte–macrophage colony-stimulating factor, interferon-γ and tumor necrosis factor-α] were evaluated at 3 time points (before chemotherapy, 6 and 12 weeks after chemotherapy initiation). The FACT-Cog (version 3) was utilized to evaluate patients’ self-perceived cognitive disturbances and a computerized neuropsychological assessment (Headminder™) was administered to evaluate

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