Exploring the Trajectories of Cognitive Symptoms in Advanced Cancer Patients Receiving IL-2 Immunotherapy: Preliminary findings

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BACKGROUND

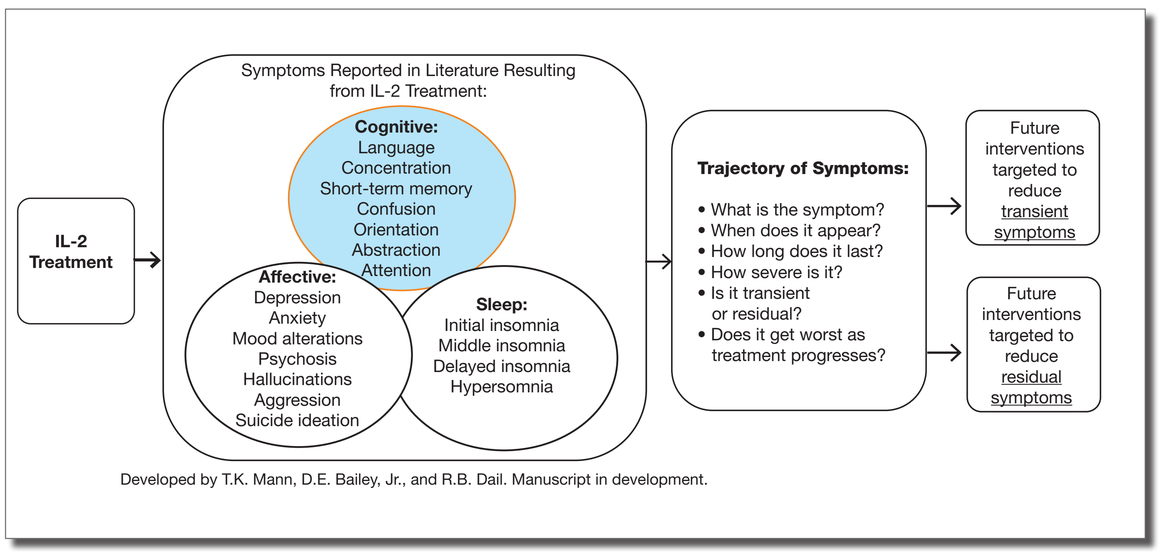
Patients with cancer receiving high-dose Interleukin-2 (IL-2) therapy experience alterations in cognitive functioning[1] including changes in concentration, attention, short-term memory, executive functioning, language, and orientation[2] during treatment. Patients and care partners also report in online forums that cognitive symptoms were inadequately screened for and they were uninformed about potential cognitive alterations during and after treatment.[3] Severe cognitive symptoms may result in early cessation of IL-2 treatment, which results in deficient treatment response. IL-2 is a cytokine produced naturally by the body. High-dose (HD) IL-2 is an immunotherapy produced synthetically and is used as a treatment in patients diagnosed with metastatic renal cell carcinoma (MRCC) to achieve remission or minimize the disease. HD IL-2 is defined as 600,000 IU/kg of IL-2 administered intravenously as a 15-minute bolus every 8-hours for up to 14 treatment doses. These 14 doses comprise one treatment hospitalization; patients can receive up to four treatment hospitalizations.[4] The cognitive symptom trajectory has yet to be described. As such, a description of how symptoms change with each dose within and across hospitalizations is essential to maximize treatment delivery, potentially increasing remission rates in the IL-2 population. ◆

PURPOSE

To describe IL-2—induced cognitive symptoms (language, concentration, confusion, attention, short-term memory, and orientation) longitudinally from the perspective of the patient, care partner, and primary nurse who have first-hand knowledge of symptoms during the treatment course. ◆

STUDY FRAMEWORK

IL-2 symptom trajectory model



METHODS

This exploratory, descriptive study used a mixed-methods case study approach to examine the cognitive symptom trajectory in ten IL-2 cases using qualitative and quantitative data. Each IL-2 case consisted of the IL-2 patient, care partner, and primary nurse.

- Patient Measurement Tools:
  - Montreal Cognitive Assessment (MoCA)[5] and the Attentional Function Index (AFI)[6], evaluating cognitive symptoms at pre- and post-treatment for each hospitalization
  - Semi-structured recorded interview after treatment ended
- Care Partner Measurement Tools:
  - Semi-structured journal entry every 8-hours at the time when a dose of IL-2 was administered
  - Semi-structured recorded interview after treatment ended
- Primary Nurse Measurement Tool:
  - Semi-structured recorded interview after treatment ended providing medical expertise/insight into the treatment trajectory

Measurement Tools:

- The MoCA:
  - Measures global cognitive functioning; max score = 30
  - "Intact global cognitive functioning" = scores ranging from 26 to 30
  - "Impaired global cognitive functioning" = scores less than 26
- The AFI:
  - 13-item scale; scores range from 0-100 for each item measuring perceived changes in attention and working memory
  - Items 1-9: scores of 100 indicate a fully functioning individual
  - Items 10-13: the scale is flipped; scores of 0 indicate a fully functioning individual
  - During analysis items 10-13 were flipped; a total score of 1300 = a fully functioning individual, a score of 0 = a lack of attention/working memory ◆

RESULTS

DEMOGRAPHICS:

Patient(s):

- Two African American women between 45 and 60 years of age
- Eight Caucasian men between 37 and 60 years of age

Care Partner(s):

- Eight spouses
- One daughter
- One significant other

Primary Nurse(s):

- 19 Caucasian nurses
  - 18 females
  - One male
  - Experience ranged from 1.5 to 28 years (mean of 13 years)

SAMPLE SUMMARY STATISTICS:

- Cycles completed by patient (max possible = 4)
  - Six patients completed 2 treatment cycles
  - Four patients completed 4 treatment cycles
- Average doses (max possible = 14) completed per treatment cycle
  - Cycle 1: 8.7 doses
  - Cycle 2: 5.5 doses
  - Cycle 3: 6.75 doses
  - Cycle 4: 5.75 doses
  - Maximum doses received = 11; minimum doses received = 4

MoCA Pre- and Post-Treatment Impaired v. Intact Global Cognitive Functioning per Treatment Cycle

	Cycle 1 (Pre-tx)	Cycle 1 (Post-tx)	Cycle 2 (Pre-tx)	Cycle 2 (Post-tx)	Cycle 3 (Pre-tx)	Cycle 3 (Post-tx)	Cycle 4 (Pre-tx)	Cycle 4 (Post-tx)
# of Pts Completing Cycle:	10	10	10	10	4	4	4	4
Impaired Global Cognitive Functioning:	4 (40%)	4 (40%)	2 (20%)	4 (40%)	1 (25%)	5 (50%)	0 (0%)	0 (0%)
Intact Global Cognitive Functioning:	6 (60%)	6 (60%)	8 (80%)	6 (60%)	3 (75%)	2 (50%)	4 (100%)	4 (100%)

AFI Pre-and Post-Treatment Mean Scores per Treatment Cycle

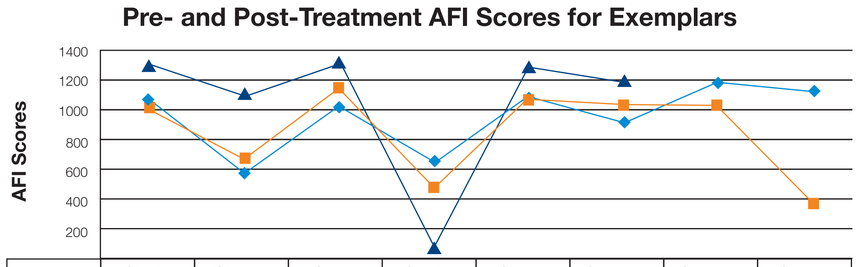
	Cycle 1 (Pre-tx)	Cycle 1 (Post-tx)	Cycle 2 (Pre-tx)	Cycle 2 (Post-tx)	Cycle 3 (Pre-tx)	Cycle 3 (Post-tx)	Cycle 4 (Pre-tx)	Cycle 4 (Post-tx)
# of Pts Completing Cycle:	10	10	10	10	4	4	4	4
Average:	**1113.3**	**789**	**1099**	**871**	**1070**	**992.5**	**1111.66 (n=3)**	**876.66 (n=3)**

*There was a patient-rating error in Cycle 4 on the AFI scale; therefore, the pre-/post-test was omitted.

THREE EXEMPLARS PRESENTED

- Case 4 = "mixed" cognitive symptom trajectory
- Case 7 = "declining" cognitive symptom trajectory
- Case 8 = "stable" cognitive symptom trajectory

Pre- and Post-Treatment AFI Scores for Exemplars



	C1-Pre	C1-Post	C2-Pre	C2-Post	C3-Pre	C3-Post	C4-Pre	C4-Post
Case 4	1085	600	1040	670	1080	930	1185	1120
Case 7	1015	690	1150	490	1070	1040	1030	380
Case 8	1290	1100	1300	100	1290	1200		

Measurement Time Points

*There was a patient-rating error in Cycle 4 on the AFI scale; therefore the pre-/post trearment scores were omitted.
**C = Cycle; Pre = Pre-treatment; Post = Post-treatment

Patient (Case 4):
"Having the ability to focus. My brain could not multi-task. So trying to do things...if there was somebody changing the trash, and the TV on, and you know someone taking my vitals, and a doctor asking me questions, my brain couldn't process all of those things."

Care Partner (Case 7):
"He got really confused um, very argumentative with me…it was probably dose six where I had to start helping him go to the bathroom. Um he was having a hard time telling if he was still peeing. So um, he actually peed on me. Then peed on his shorts and on the floor. And I said, 'Did you go to the bathroom?' He said, 'No, I couldn't go' so just really confused."

Primary Nurse (Case 4):
"Yesterday morning before [the patient] decided to quit [treatment], he said that he was having trouble and that he was just thinking slower. That he had dropped a Gatorade bottle, and it took him a minute to realize that."

CONCLUSION

The use of a case study approach allowed for in-depth exploration of the cognitive symptom trajectory from individuals closest to the symptom experience. Although IL-2 patients only completed measurement scales at two time points (pre- and post-treatment) for each hospitalization, care partners proved to be essential in providing qualitative rich descriptions of symptoms experienced during high-dose IL-2 treatment, and how symptoms changed with each IL-2 dose. Additionally, the care partner played a unique role in identifying and reporting symptoms when the patient may be cognitively impaired. Qualitative reports from the patient, care partner and nurse allowed us to identify symptom changes at the time of each IL-2 dose while also providing context into each symptom trajectory. In the future, specific interventions can be developed for patients receiving IL-2 based on their cognitive symptom trajectory. ◆

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