



ImmunoScience Academy

Partnering for Education & Optimizing Treatment in ImmunoScience

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Workshop A2

The challenge of survivorship care in the field of immunotherapy

Convention room 3, Floor 1

Anne Rogiers, MD

*Head of Clinic, Neurocognitive Remediation Unit,
Psychiatric Department, CHU Brugmann – Site Horta*

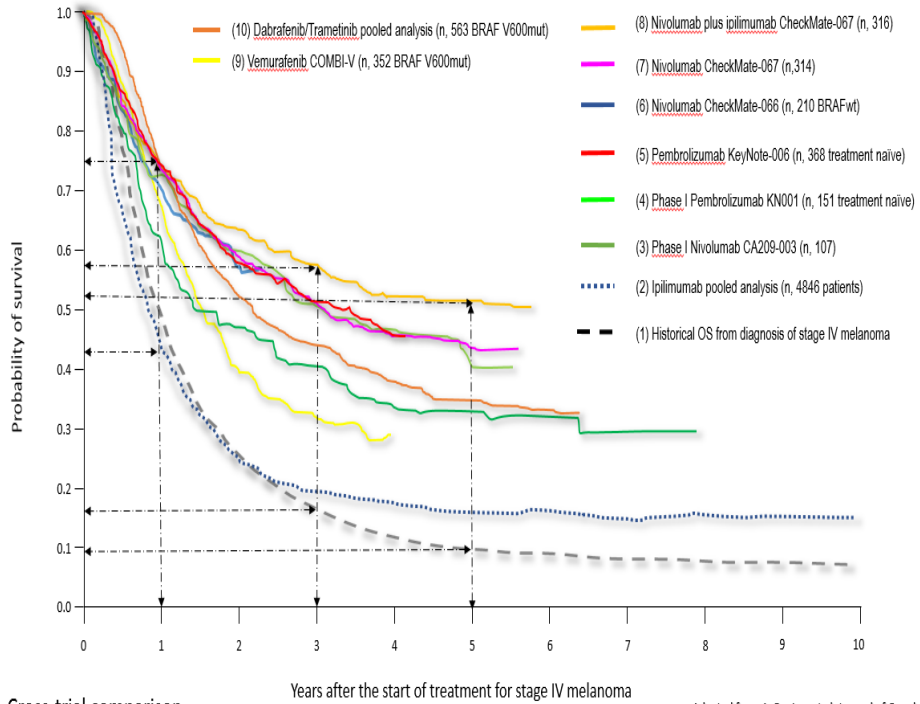
Moderated by:

Bart Neyns, MD

Head of Department, Medical Oncology, UZ Brussel

SURVIVAL RATE

Overall Survival of Advanced Melanoma Patients on First Line Therapy



IMMUNERELATED ADVERSE EVENTS

- Rash
- Diarrhoea
- Colitis
- Hepatitis
- Neurological
- Fatigue
- Other irAE

PSYCHOSOCIAL OUTCOME



No studies on long-term psychosocial outcome of patients treated with immunotherapy

- ▶ Case report
- ▶ Three clinical studies investigating psychosocial outcome and health related quality of life (HRQoL) of advanced melanoma survivors treated with immune checkpoint inhibitors
- ▶ Melanoma survivors are at risk for emotional distress impacting HRQoL and in need for tailored care.



Patient



When?
Psychological?
Physical stressors?
Neuro-cognitive consequences?
Social consequences?

Survivor



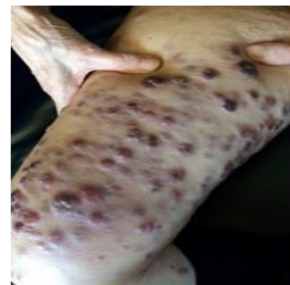
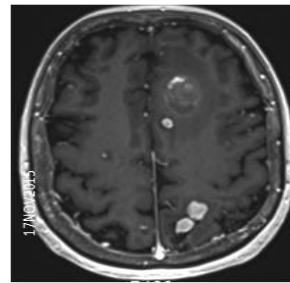
Disease related distress

Survivorship related issues

Immune therapy related

- Confrontation with a potentially mortal disease
- Traumatic experience of melanoma progression
- Brain metastasis
- Frequent relapses of disease

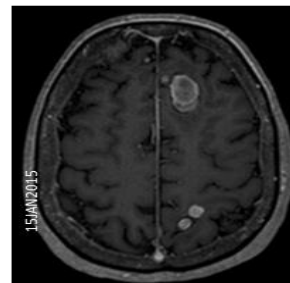
72y F, stage IV-M1c; BRAF V600E, failed Vemurafenib, complete remission on PEMBRO



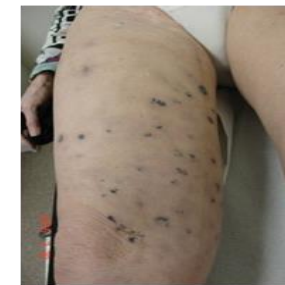
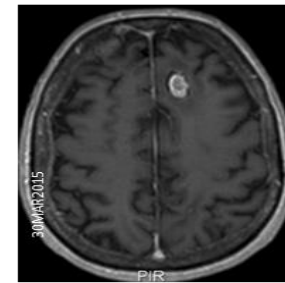
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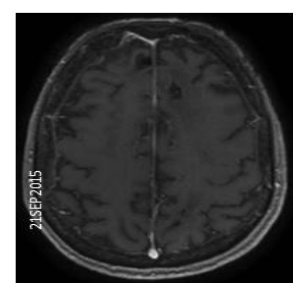
administrations of pembrolizumab



9DEC2014



30MAR 2015



SEPT 2015



**Disease
related
distress**

**Survivorship
related
issues**

**Immune
therapy**

- Depression, anxiety
- Fatigue
- Neurocognitive dysfunction
- Impact on social relationships and return to work
- Physical sequels adjuvant therapy



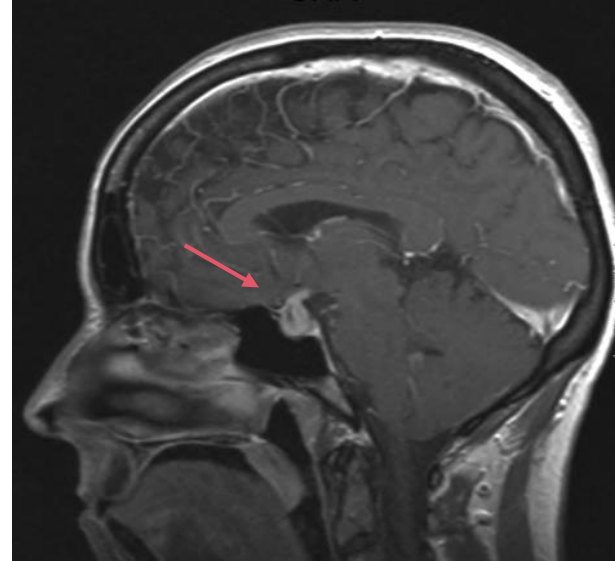
Emotional burden in advanced melanoma survivors

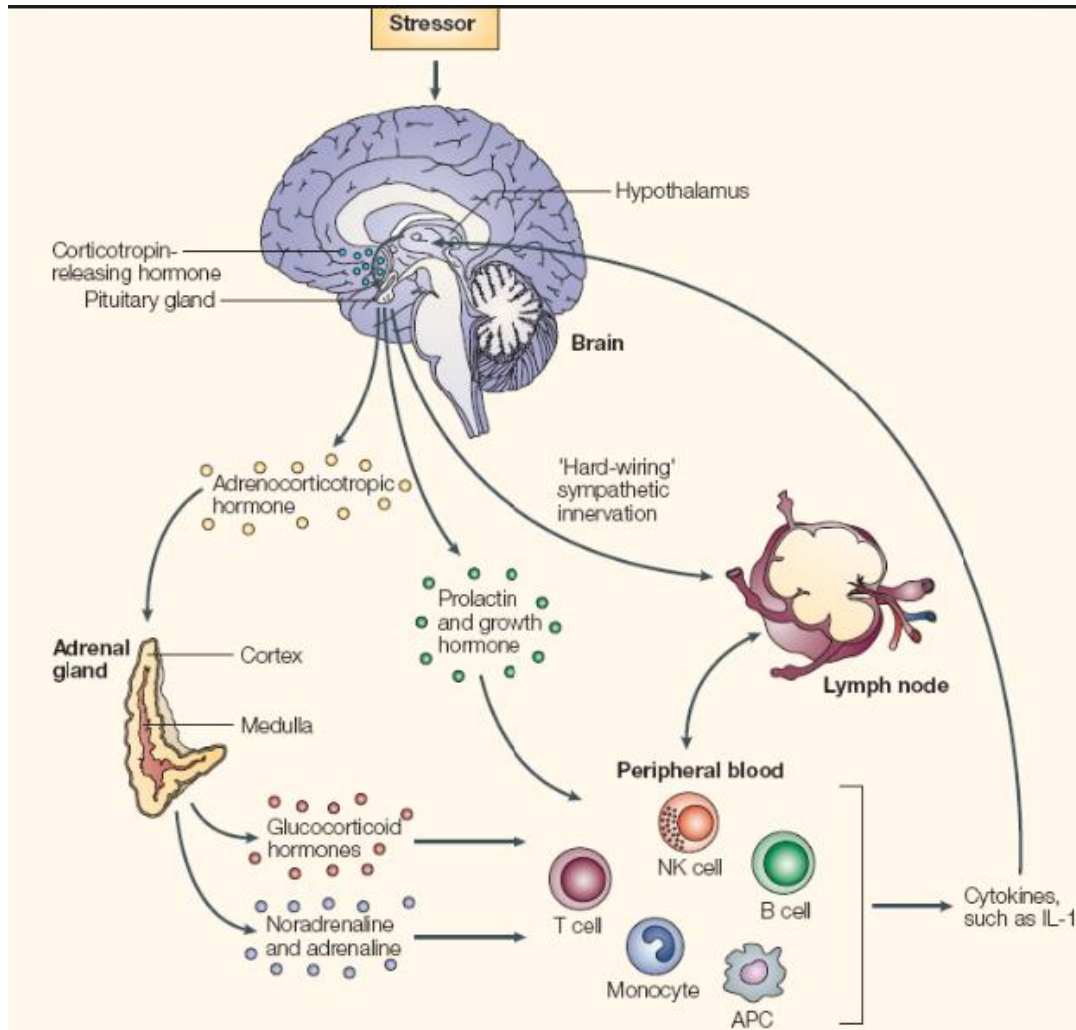
**Disease
related
distress**

**Survivorship
related
issues**

**Immune
therapy
related**

- ▶ Uncertainty of caregivers in terms of long-term OS
- ▶ Potential interaction between IRAE and neuro-endocrine system
- ▶ Complex interaction between inflammation, the neuro-endocrine system, sleep-wake cycle and the central nervous system with possible behavioral changes





ROBERT M. SAPOLSKY

Author of *A Primate's Memoir*

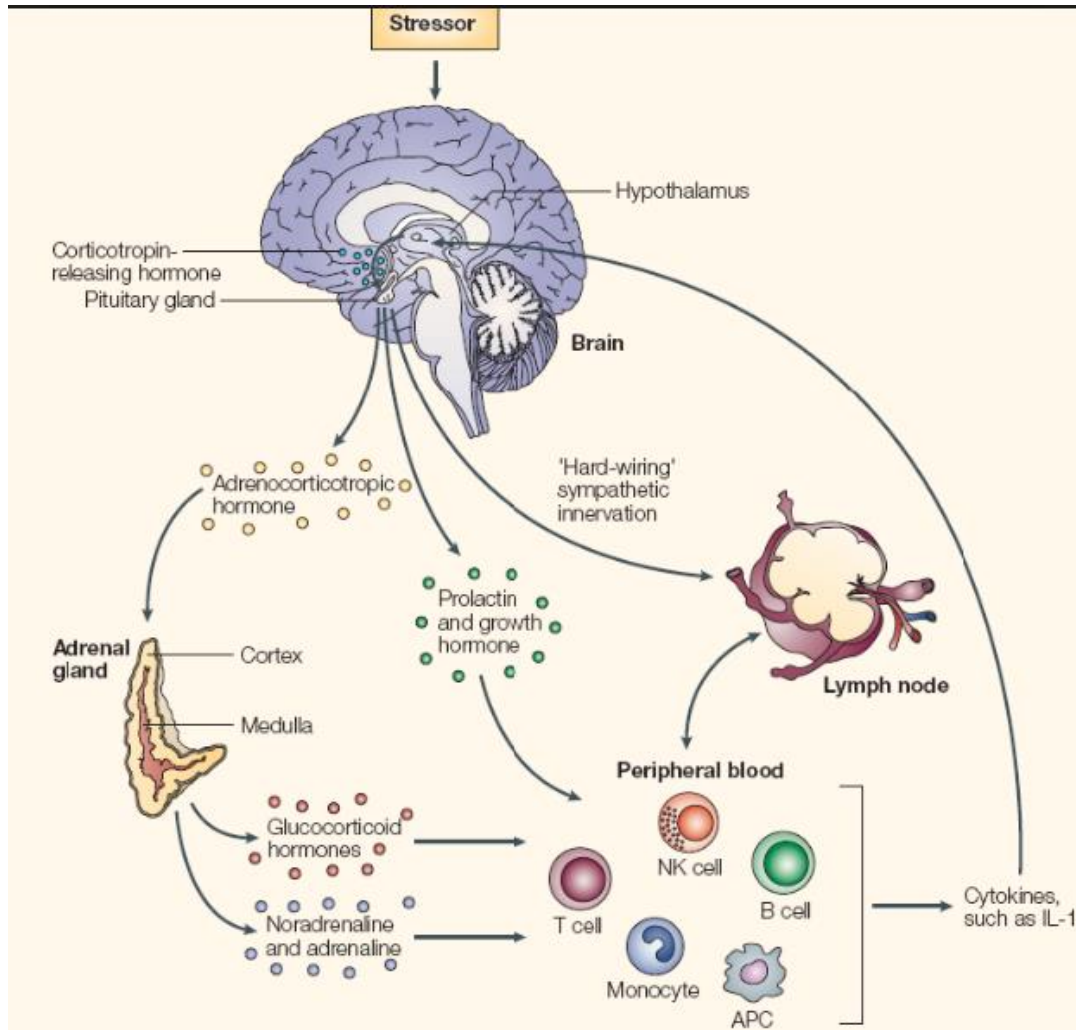
WHY ZEBRAS DON'T GET ULCERS

The Acclaimed Guide to Stress, Stress-Related Diseases, and Coping—Now Revised and Updated

"One of the best science writers of our time,"

—Oliver Sacks





Stress
Social support
Cancer
Cancer treatment



Inflammation
Fatigue
Depression/Anxiety
Cognition




Clinical experience first patients on immunotherapy and BRAF/MEK-inhibitors

- ▶ **During treatment:** cognitive problems, fatigue, anxiety and depressive symptoms
- ▶ **After remission of disease:** persisting cognitive problems, fatigue, difficulties with socio-professional reintegration, and acute suicidal ideation in 3 patients





Health-related quality of life, emotional burden, and neurocognitive function in the first generation of metastatic melanoma survivors treated with pembrolizumab: a longitudinal pilot study

A. Rogiers^{1,2}  · C. Leys³ · J. De Cremer⁴ · G. Awada⁵ · A. Schembri⁶ · P. Theuns⁴ · M. De Ridder² · B. Neyns⁵

Received: 28 June 2019 / Accepted: 31 October 2019

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**Baseline assessment
T0 (N=25)**

Patients were recruited from the parental study and invited to participate at the moment of their planned visit as defined in the parental study .

**Follow up visit
T1 (N=18)
3 - 4 months**

**Follow up visit
T2 (N=24)
5 - 7 months**

**Follow up visit
T3 (N=6)
8 - 9 months**

**Follow up visit
T4 (N=24)
10 - 12 months**

1. Semistructured psychiatric interview (SCID-IV-CV)
2. Assessment of HRQOL, anxiety, depression, fatigue (EORTC QLQ C30, HADS, FSS)
3. Computerised neurocognitive testing

1. Assessment of HRQOL, anxiety, depression, fatigue (EORTC QLQ C30, HADS, FSS)
2. Computerised neurocognitive testing



Anxiety and Depression

HADS

14 questions:

7 Anxiety

7 Depression

Screening tool

EORTC QLQ-C30

EORTC-QLQ-C30

30 questions:

Global health status

Functional scales

Symptom scales

Fatigue

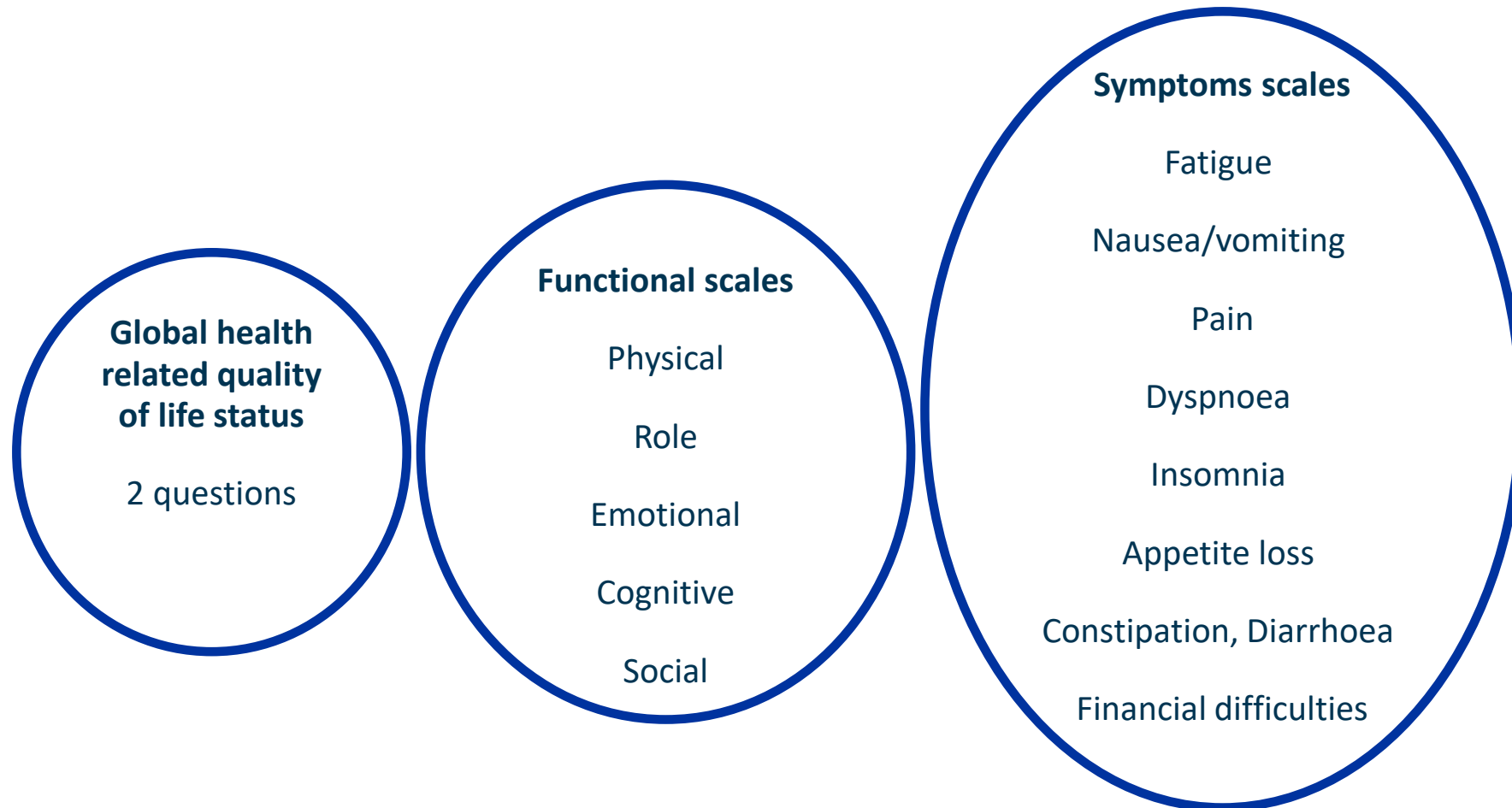
Fatigue severity scale

7 questions:

Cut-off score of 4



Health Related Quality of Life: EORTC-QLQ C30

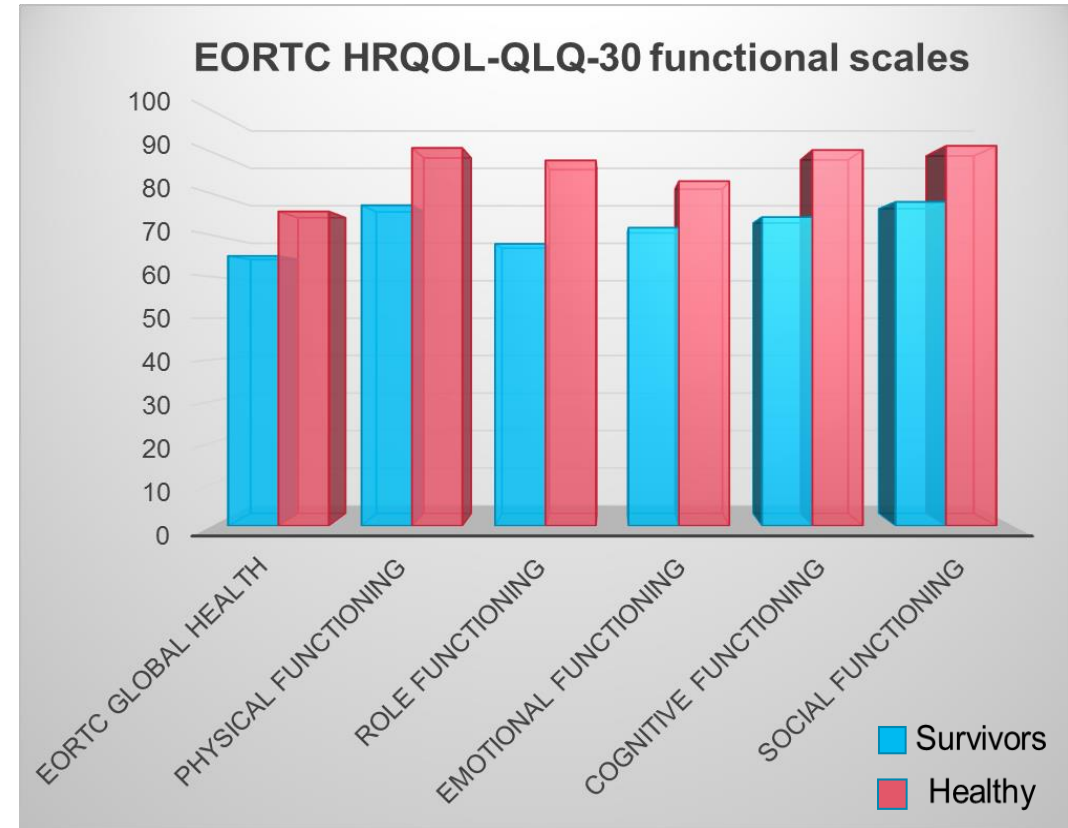


Results



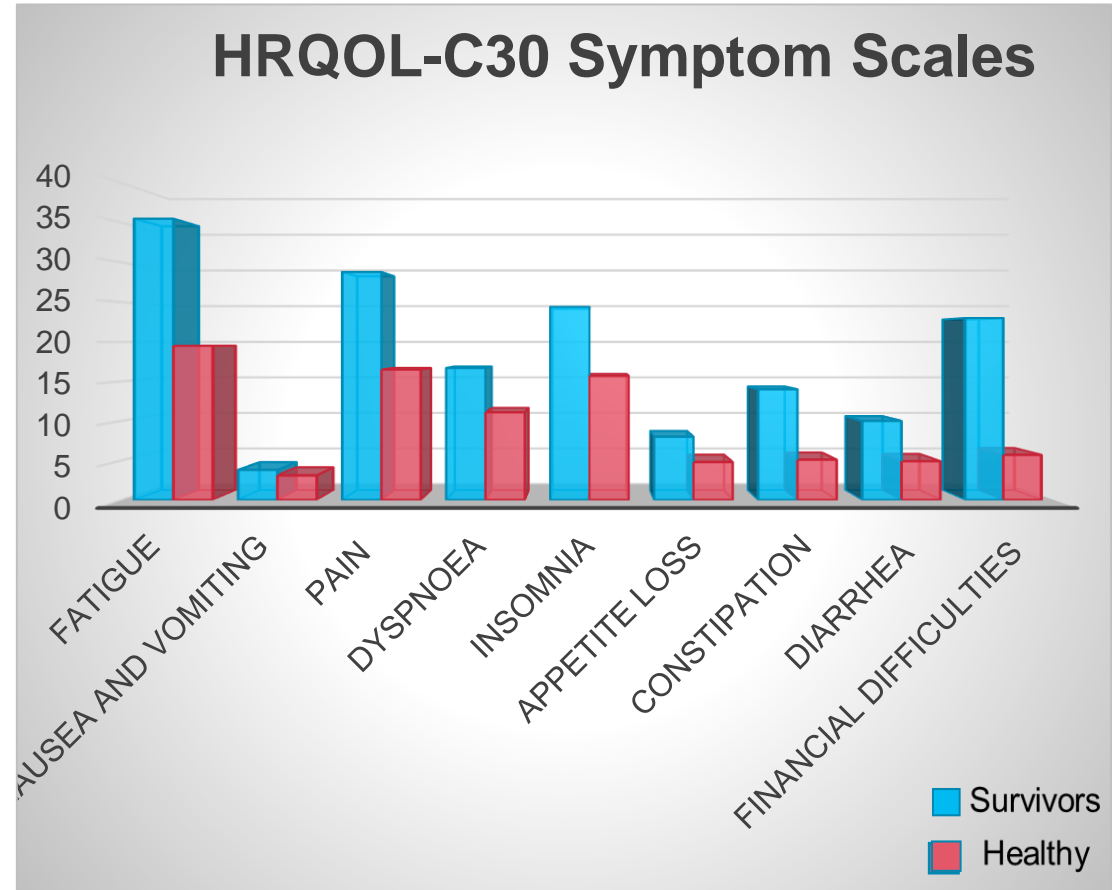
Health Related Quality of Life: Functional

- Global HRQOL ($p=0,009$)
 - Physical ($p=0,0005$)
 - Role function ($p=0,001$)
 - Emotional ($p=0,05$)
 - Cognitive ($p=0,0005$)
 - Social functioning ($p=0,001$)
- ▶ Compared to the healthy population ¹



Health Related Quality of Life: Symptoms

- Fatigue (p=0,0005)
 - Pain (p=0,02)
 - Insomnia (p=0,01)
 - Constipation (p=0,025)
 - Financial difficulties (p=0,01)
- *Compared to the healthy population*¹



Anxiety and depression (HADS)

Score ≥ 11

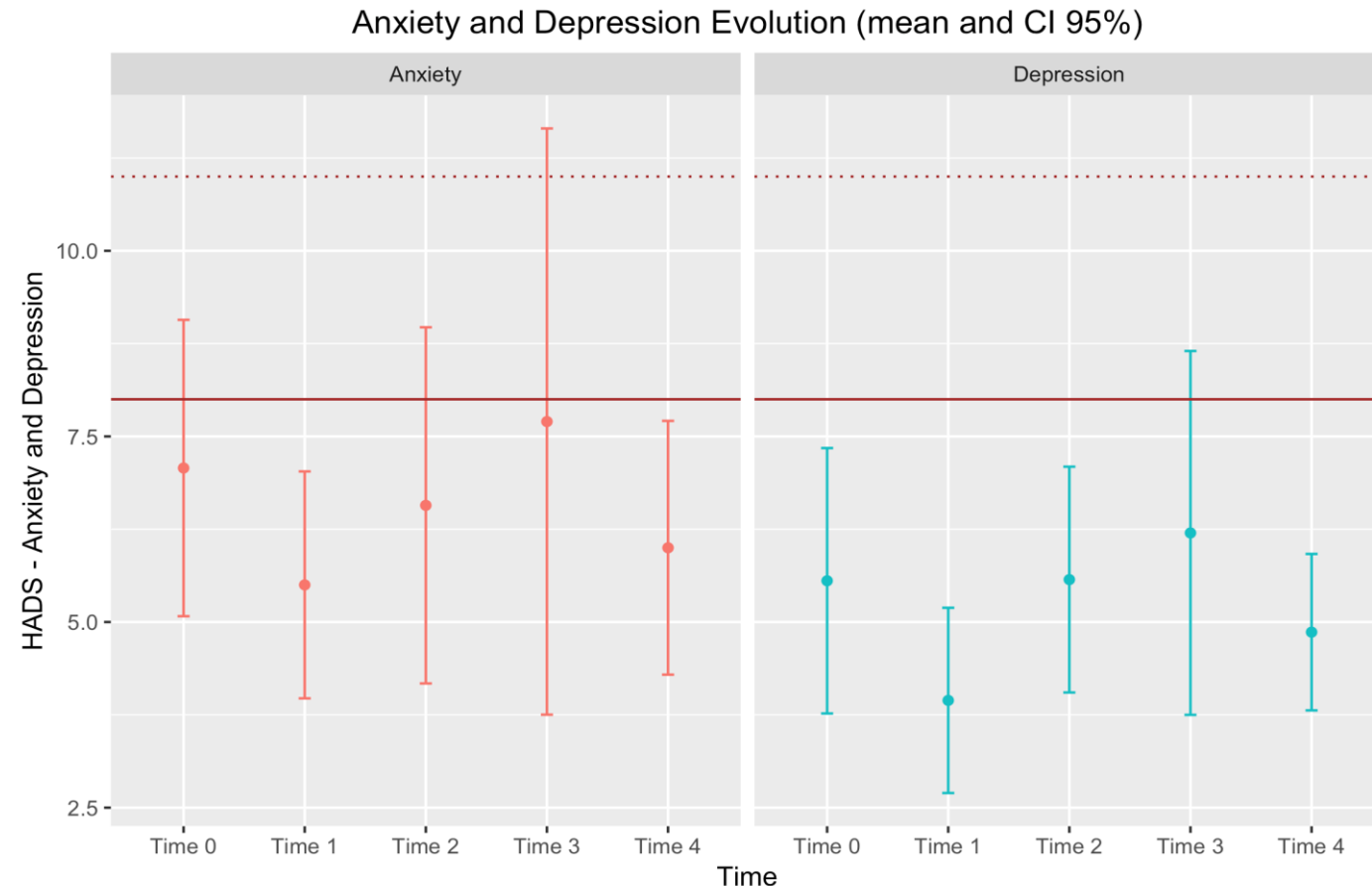
8 pts severe depression/anxiety

Score ≥ 8 :

Anxiety: 9 pts (35%)

Depression: 7 pts (27%)

15 pts (64%) anxiety/depression
> 1 Timepoint



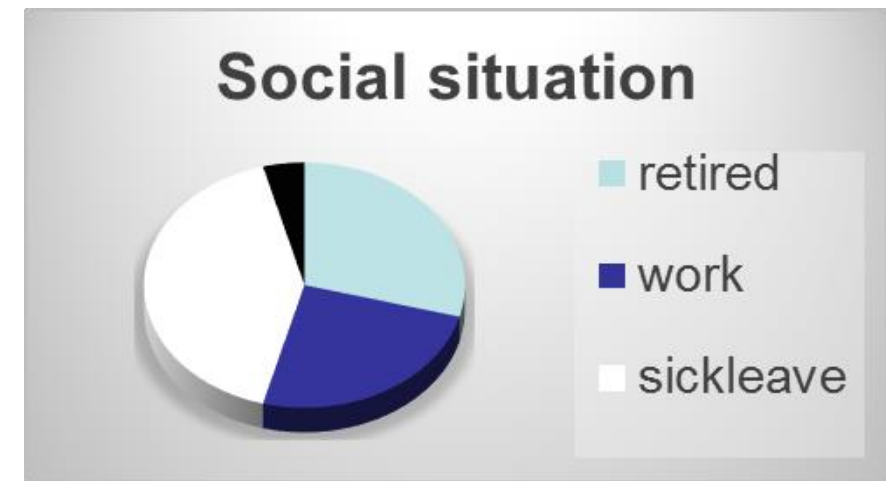
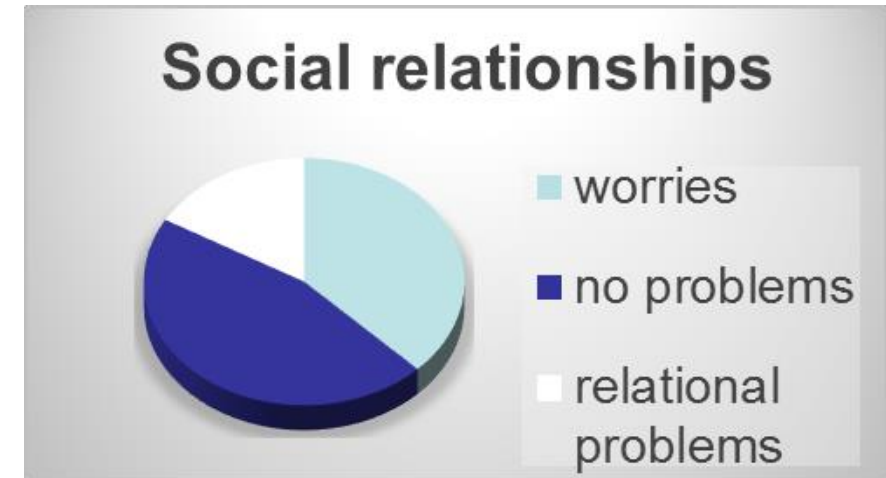
Psycho-Social outcome

> 50% concerns: impact of disease on their families

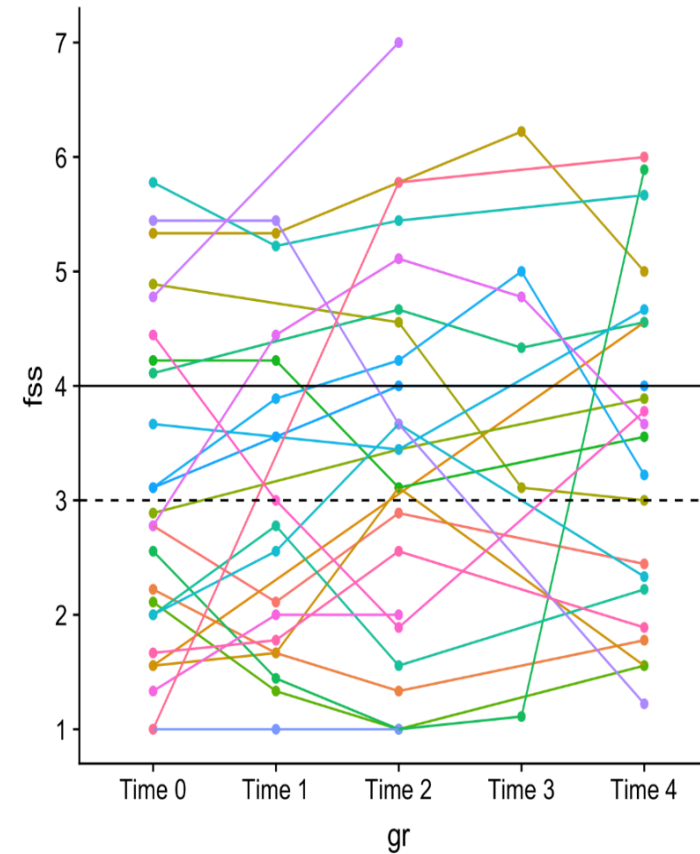
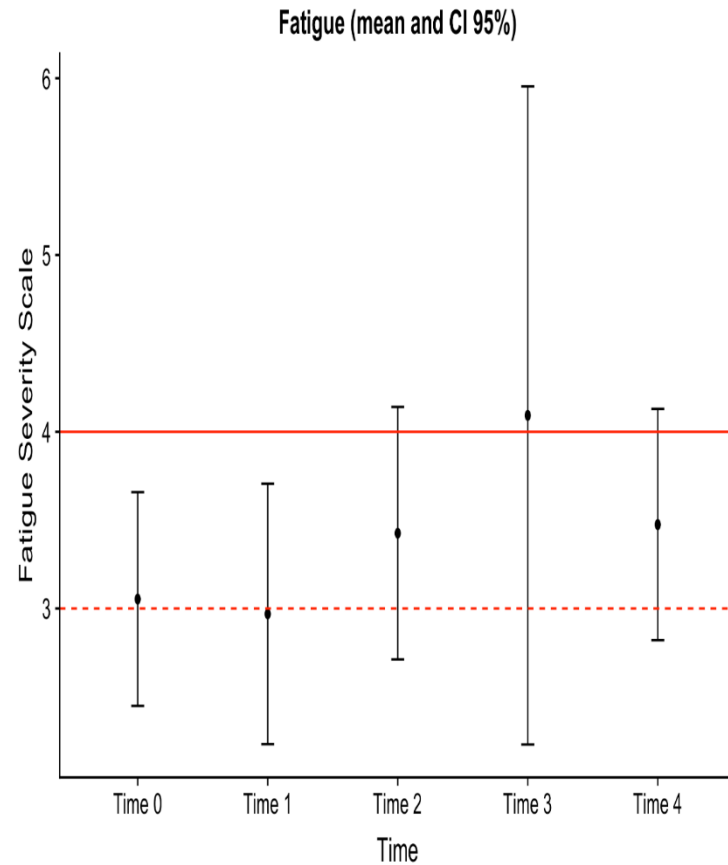
> 30% financial problems

6 of the pts continued working

- 4/6 still under immunotherapy



Fatigue (FSS)



Baseline: 11 pts: fatigue (FSS > 4)

During survey: 15 pts (60 %) FSS > 4 during at least one timepoint



Semi-structured interview

7 patients developed transient suicidal ideation

- 1 pt suicide attempt: 8 months after CR
- 2 pts just after stopping PEMBRO

Not detectable during the oncological consult

In the context of a Post Traumatic Stress Disorder

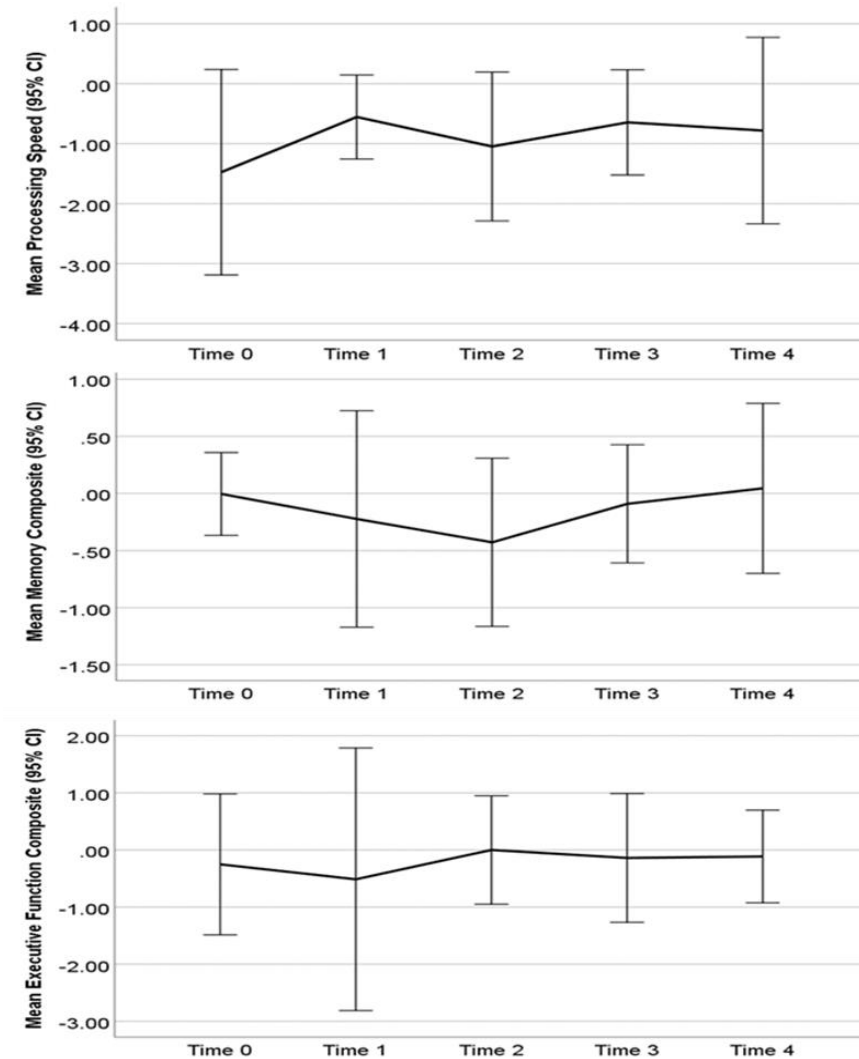
12 pts (48%) suffered from Post Traumatic Stress Disorder

Suicidality was reversible after tailored multidisciplinary care and trauma oriented intervention



Computerized Cognitive Testing

- 10 ptn (40%): ≥ 2 or more tests.
- 5 ptn (20%): global cognitive impairment, only 1 with brain meta
- Subjective cognitive dysfunction: correlated with fatigue, anxiety, depression, Global HRQOL
- Objective cognitive dysfunction: NO statistical significant correlation with fatigue, anxiety and Global HRQOL



Key Findings

Diminished HRQoL

- Diminished, social, emotional & cognitive functioning
- High symptom burden of fatigue, pain, constipation, insomnia and financial difficulties

High levels of fatigue and emotional distress

High levels of objective cognitive dysfunction

HRQoL, fatigue, anxiety, depression and subjective cognitive functioning highly correlated

Distress in context of PTSD and not in the context of depression

Supportive Care in Cancer

<https://doi.org/10.1007/s00520-019-05168-3>

ORIGINAL ARTICLE



Health-related quality of life, emotional burden, and neurocognitive function in the first generation of metastatic melanoma survivors treated with pembrolizumab: a longitudinal pilot study

A. Rogiers^{1,2} • C. Leys³ • J. De Cremer⁴ • G. Awada⁵ • A. Schembri⁶ • P. Theuns⁴ • M. De Ridder² • B. Neyns⁵

Received: 28 June 2019 / Accepted: 31 October 2019

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Key Findings

Psychosocial outcome:

- High levels of emotional distress
- PTSD present in 6/17 (35%)
- Persistent fatigue in 7/17 (41%)
- Anxiety/depression in 9/17 (53%)
- Objective cognitive impairment: 7/17 (41%)

Immune related adverse events:

- 3 patients had hypophysitis:
 - Persisting fatigue
 - Depression (2/3)
- 1 patient Guillain Barré:
 - Persisting depression
 - Severe depression

All cases of skin toxicity (N=8), hepatitis (N=2), colitis (N=2), and sarcoidosis (N=2) resolved without impact on HRQoL

Neurocognitive function, psychosocial outcome and health-related quality of life of long-term melanoma survivors treated with ipilimumab

Anne Rogiers^{1,2}, Christophe Leys³, Justine Lauwyck⁴, Adrian Schembri⁵, Gil Awada⁴, Julia Katharina Schwarze⁴, Jennifer De Cremer⁶, Peter Theuns⁶, Paul Maruff⁵, Mark De Ridder², Bart Neyns⁴

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⁵ Clinical Science Department, Cogstate Ltd, Melbourne, Australia

⁶ Faculty of Psychology, Vrije Universiteit Brussel, Brussels,

Submitted to Cancers: in review
Presented at ASCO SITC



Key Findings

- In this multicenter matched cohort study that included 89 survivors and 265 matched controls:
 - Lower physical, role, cognitive and social functioning than matched controls
 - Higher symptom burden of fatigue, dyspnea and financial impact than matched controls.
- These differences were indicated as clinically relevant.
- Survivorship care models interventions should be focused on physical, role, cognitive and social morbidity



Recent published studies

- ▶ O'Reilly et al found that 73 patients had:
 - Lower physical, social functioning and general health levels, compared with a healthy population
 - HRQoL results were established in 30% of patients on various ICI treatments
 - Non-cancer-specific measurement (SF-36)
 - Heterogeneous patient population
 - Cross-sectional

- ▶ Lai Kwon et al found that 69 long-term responders to ICI experienced:
 - Chronic treatment toxicities and psychological morbidity
 - 75% of the patients were receiving various active treatment
 - General HRQoL was not assessed
 - Heterogeneous patient population
 - Cross-sectional



Conclusions

- ▶ Advanced melanoma survivors are at high risk for suffering from severe emotional disturbances
 - Special attention is indicated for pts with a history of trauma, frequent relapses of disease, younger patients, patients with CNS related irAE and hypophysitis
- ▶ Neurocognitive dysfunction was present in about 40 % of the cases and impacts social functioning and wellbeing
 - Further research is necessary to understand the complex interactions between the immune system and neurocognition/emotions
- ▶ Timely detection of neurocognitive and/or emotional coping problems is important in order to offer tailored care and make the most of survivorship



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