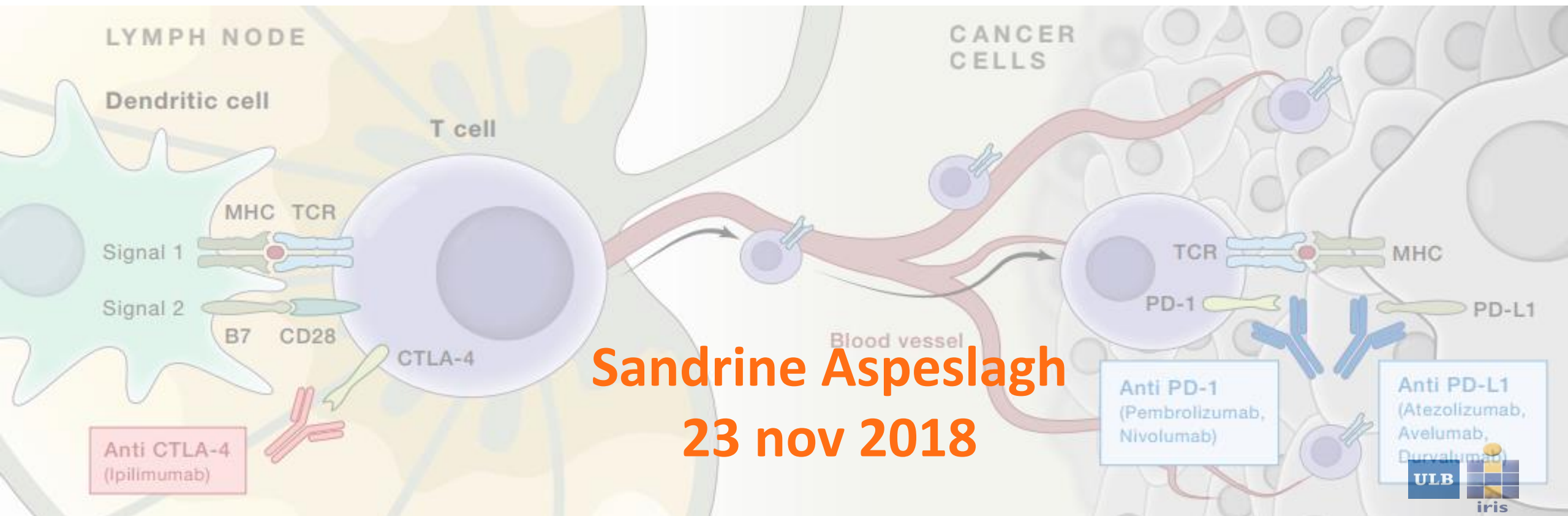




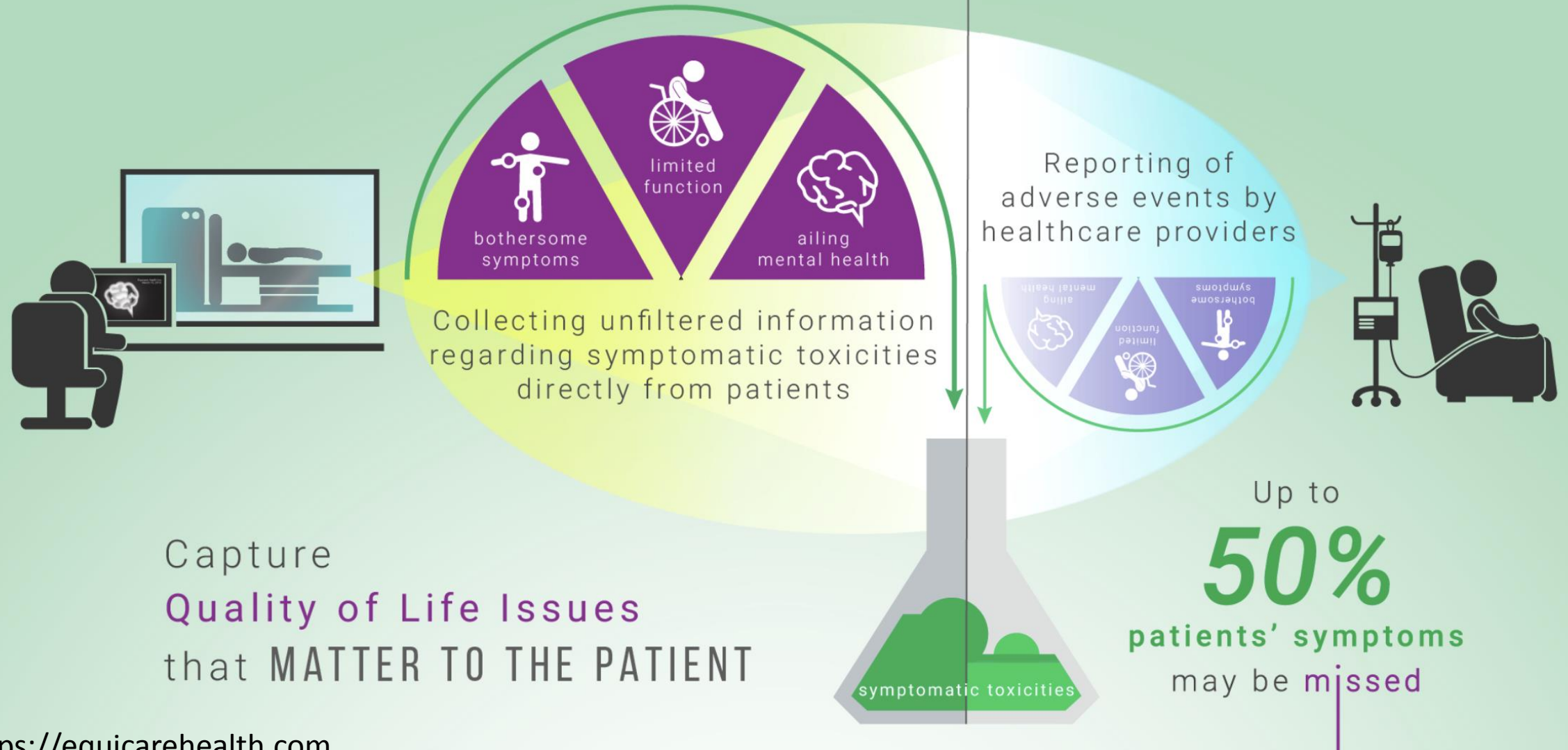
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**JULES BORDET**  
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# Patients-reported outcomes and Immune Checkpoint Blockade: Where are we now ??



**Sandrine Aspeslagh**  
**23 nov 2018**

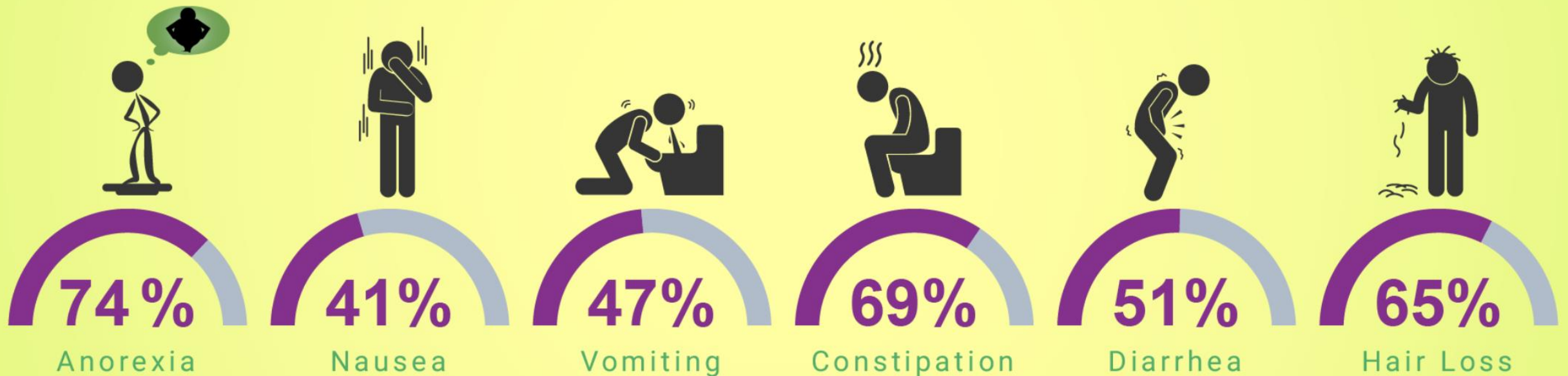
# CANCER CARE WITH & WITHOUT PATIENT REPORTED OUTCOMES



# Why PRO?

## TREATMENT-RELATED SUBJECTIVE PATIENT EXPERIENCES OFTEN UNDERREPORTED BY PHYSICIANS

Nature Reviews | Clinical Oncology Vol 13 May 2016 pp319-325



Proportion of patients with self-reported treatment-associated toxicities in any of the treatment cycles that were not reported at all by their physicians. Data from 3 randomized controlled trials.

# Goal PRO

- ◆ Adjust clinical care to the **exact needs** of the patient
- ◆ Basis for global **health economic** assesment of therapies
- ◆ **Global** picture of patients well being (will complete what the physician and paramedics misses)
- ◆ Basis for **FDA/EMA approval** (eg bisphosphonates for prevention of morbidity form bone lesions in onco-hematology)

# PRO instruments

- ◆ EORTC-QLQ-C30
  - ◆ 81 languages
  - ◆ 12 disease specific modules can be added: eg lung cancer LC13
  - ◆ CAT version (computerized)
- ◆ EuroQoL-ED-5D products
- ◆ PROMIS
- ◆ MDASI
- ◆ ...



# QOL Questionnaire development @ EORTC QOL group

**Phase I: generation of QL issues**



**Phase II: construction of item list**



**Phase III: Pre-testing**



**Phase IV: Field-testing**



# Symptom and QOL measures are different!

- ◆ **Symptom**: symptom questionnaire, adapt to research question (depression vs cough)
- ◆ **QOL**:
  - ◆ HRQoL:
    - ◆ General health: EORTC-QLQ-C30 (or CAT version), EQ-5D-3L
    - ◆ Disease specific: EORTC-LC13, LSCC
  - time to deterioration
- ◆ Patients with symptoms can have good QOL (eg wheelchair), some symptoms have impact on QOL: diarrhea, pain, ...

# EORTC-QLQ-C30: 30 questions

- ◆ Functional testing
  - ◆ Physical function
  - ◆ Role performance
  - ◆ Emotional function
  - ◆ Cognitive function
  - ◆ Social function
- ◆ Global health status
- ◆ Symptom scales/items: fatigue, nausea/vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhea, financial difficulties

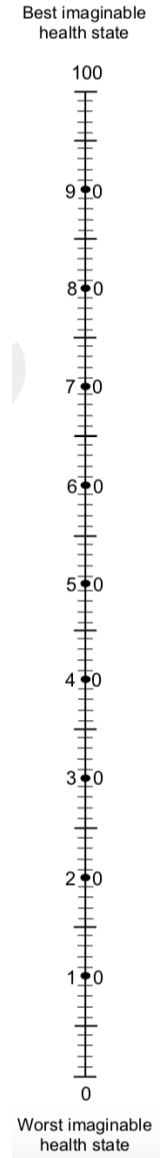


# EQ-5D-3L

- ◆ Descriptive part:
  - ◆ scale: no probl, some probl, extreme probl
    1. mobility
    2. self-care
    3. usual activities
    4. pain/discomfort
    5. anxiety/depression

- VAS for health status

**Your own health  
state today**



# Head & Neck CA



# Merkel CA



# Hodgkin



# Melanoma



# Lung CA



# RCC



# Bladder CA



Reimbursement Immunecheckpoint blockade Belgium nov 2018

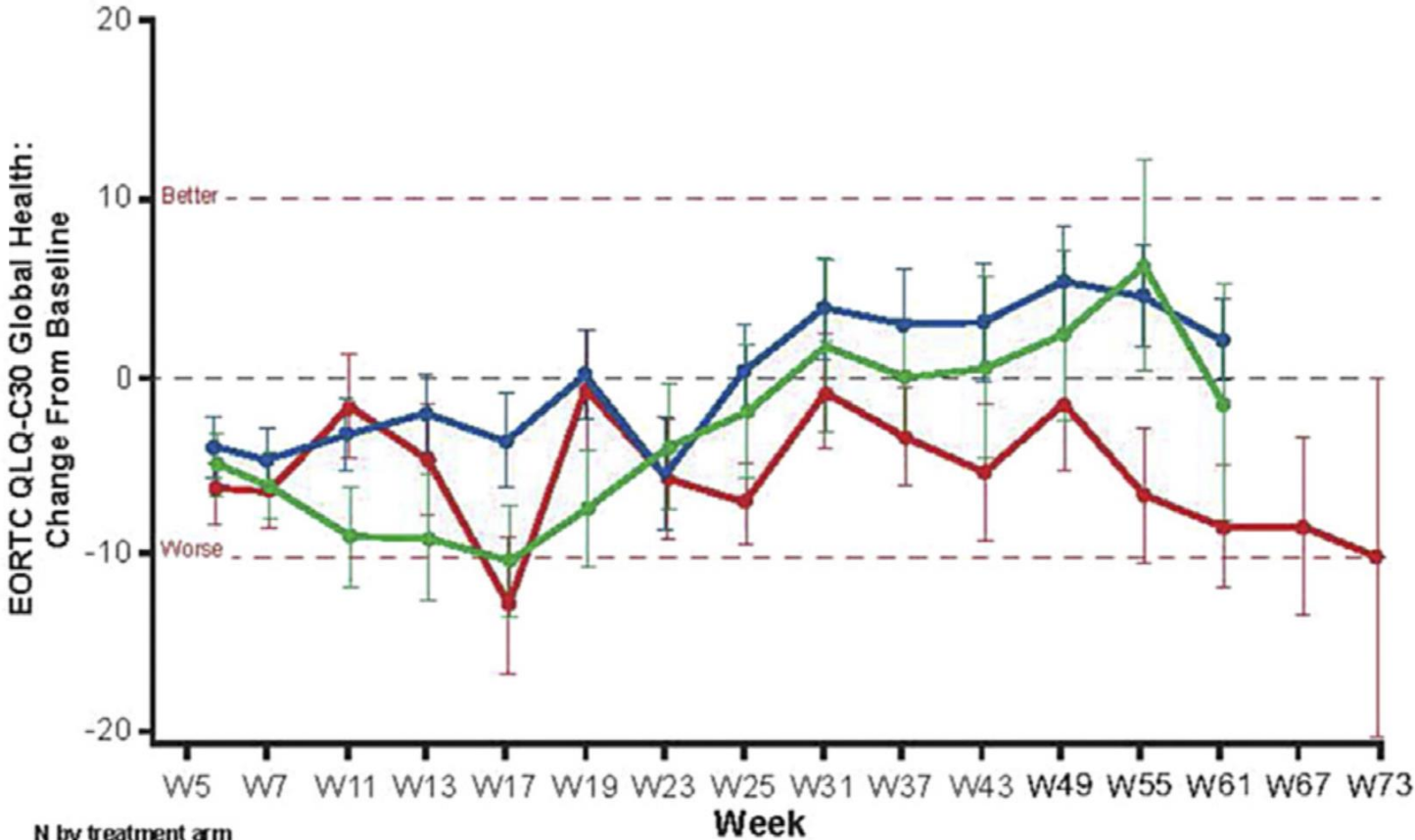
# Melanoma metastatic setting

- ◆ **Keynote-002:** pembro vs CT (ipilimumab R): QLQ-C30 : HRQoL better maintained for pembrolizumab vs CT (-2,6 vs -9,  $p=0,01$ ) (Schadendorf D et al, 2016, EJC)
- ◆ **Keynote-006:** pembrolizumab vs ipilimumab (1<sup>st</sup> or 2<sup>nd</sup> line) : QLQ-C30, EQ-5D-3L: HRQoL acc to both scales better maintained for pembrolizumab vs ipilimumab (-2,5 vs -10,  $p<0,001$ ) (Petrella T et al, 2017, EJC)
- ◆ **Checkmate 067:** nivolumab + ipilimumab vs nivolumab vs ipilimumab 1<sup>st</sup> line: QLQ-C30, EQ-5D-3L: no difference between 3 groups and grade  $\frac{3}{4}$  AE: no clinical meaningful differences in HRQoL (Schadendorf D et al, 2017, EJC)
- ◆ **Checkmate 066:** nivolumab vs dacarbazine 1<sup>st</sup> line QLQ-C30, EQ-5D-3L HRQoL for nivolumab maintained, after week 13: high attrition rate for CT (Long G et al, 2016, Ann of Onc)

# Checkmate 067: nivo + ipi vs nivo vs ipi 1<sup>st</sup> line

## subanalysis of pts with grade 3/4 toxicities

Nivolumab  
Nivolumab + Ipilimumab  
Ipilimumab



N by treatment arm

Nivolumab	94	96	73	73	58	62	45	51	41	34	30	28	22	12	4	0
Nivolumab + ipilimumab	127	128	63	60	40	53	46	57	53	53	39	34	28	19	10	5
Ipilimumab	117	108	64	51	35	42	30	30	19	18	16	14	8	6	4	0

QLQ-C30

# Psychosocial outcome & quality of life in advanced melanoma survivors



Anne Rogiers<sup>123</sup>, J. De Cremer<sup>3</sup>, L. Ben Salama<sup>23</sup>, M. De Ridder<sup>123</sup>, J. L. Bernheim<sup>3</sup>, P. Theuns<sup>3</sup>, B. Neyns<sup>23</sup>

1. Centre Hospitalier Universitaire Brugmann; 2. Universitair Ziekenhuis Brussel; 3. Vrije Universiteit Brussel

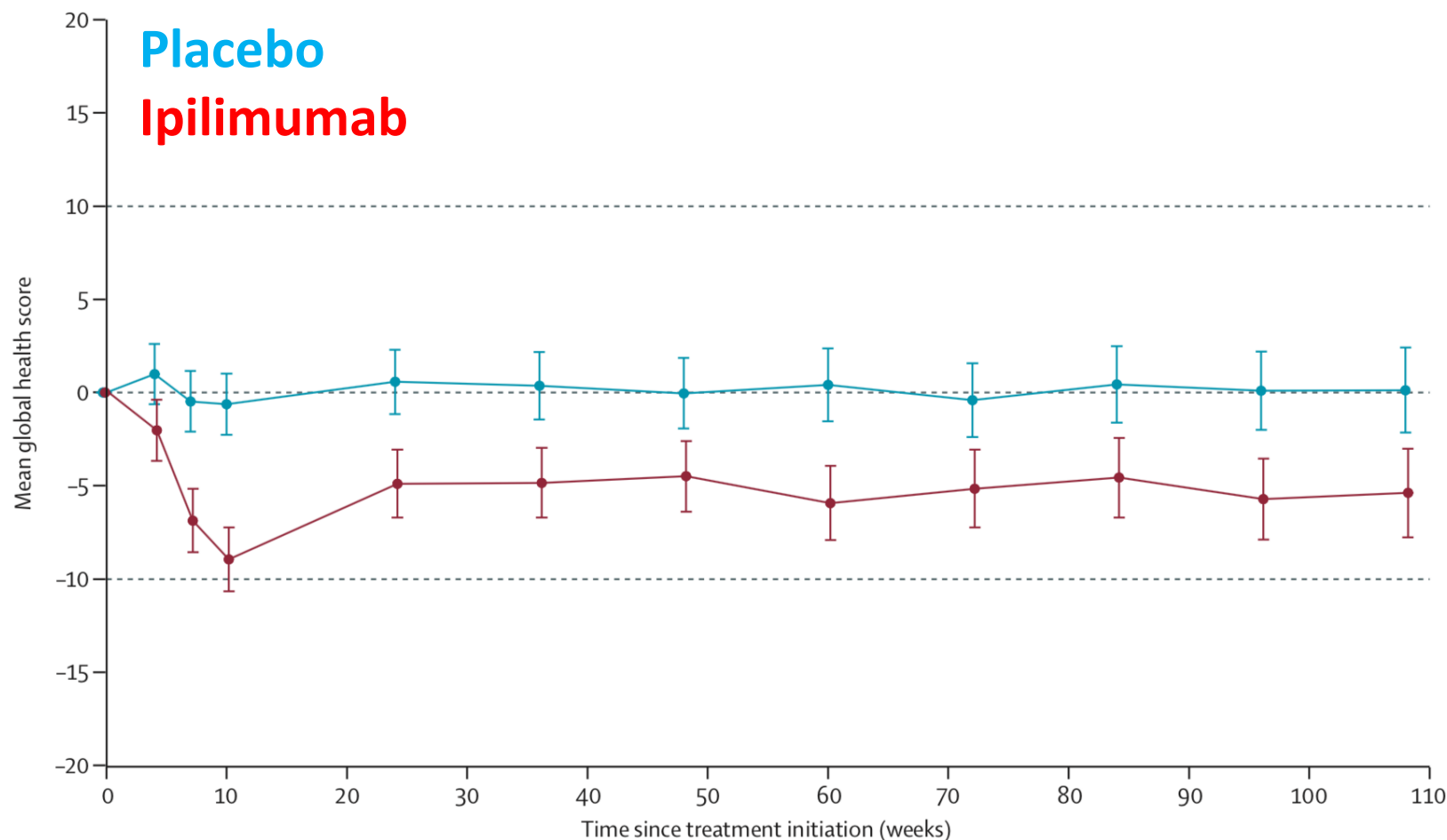


## Advanced melanoma, in complete remission at least 1y after treatment initiation with ICPI

Single centered ongoing study using semi-structured interview, computer assisted cognitive testing and PRO's: HADS, FSS, ESS, Brugmann fatigue scale, CFQ, and EORTC-QLQ-30). FU 2y

- ◆ Semi-Structured Psychiatric Examination revealed that survivors of advanced melanoma suffer from **severe emotional disturbances and cognitive problems** affecting their subjective wellbeing.
- ◆ Mean EORTC Global Health Score revealed that **HRQOL was significant lower** than the European Mean ( $t(23)=2.713$ ,  $p=0.006$ )
- ◆ Some differences in results on fatigue scales
- ◆ CFQ seems not to detect subjective cognitive complaints
- ◆ **Timely detection is important to offer adapted psycho-social care in advanced melanoma survivors treated with immune-therapy**

# Melanoma adjuvant setting: ipilimumab vs placebo



After 4 cycles of ipilimumab: no differences in HRQoL

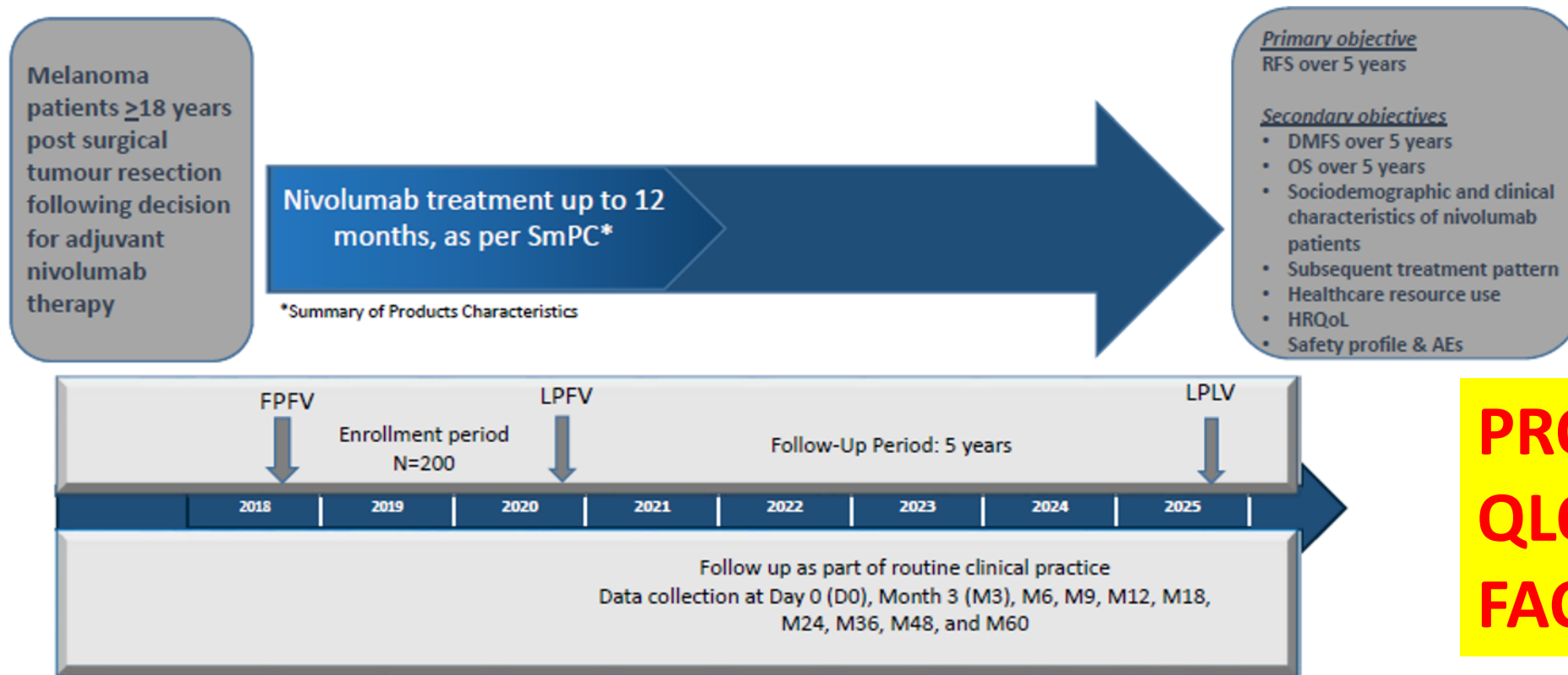
## Number of observations

Placebo (N=476)	442	421	412	404	347	307	276	255	248	227	214	175
Ipilimumab (N=475)	446	400	360	356	300	290	275	242	217	205	199	159



# CA209-8RX: Adjuvant Nivolumab Real World Evidence Study

Title: A Belgian National, Prospective, Therapeutic Non-Interventional Clinical Trial in Patients Receiving Adjuvant Nivolumab for Resected Melanoma



**PRO:  
QLQ-C30  
FACT-M**

# Head & Neck CA



# Merkel CA



# Hodgkin



# Melanoma



# Lung CA



# RCC



# Bladder CA



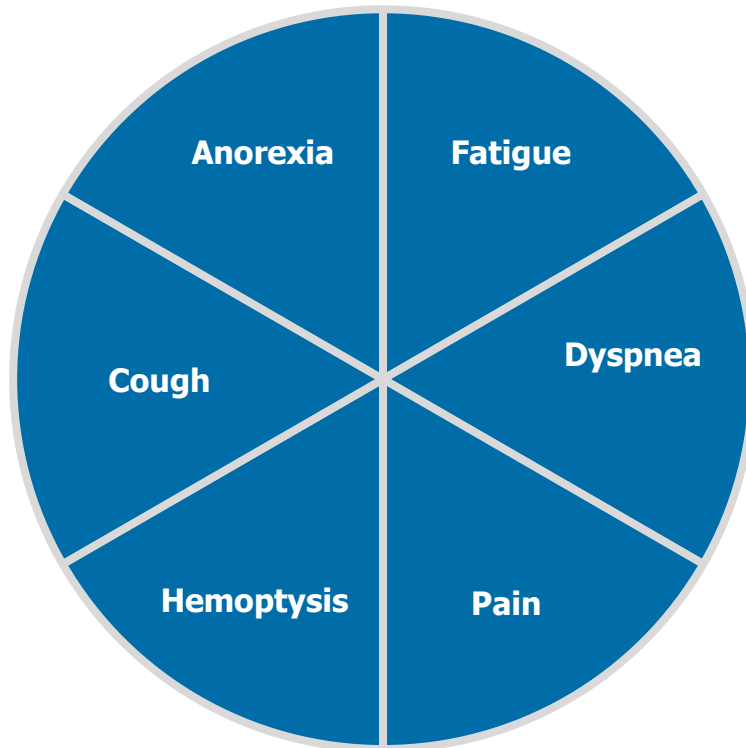
Reimbursement Immunecheckpoint blockade Belgium nov 2018

# Lung Cancer specific questionnaires: LSCC, EORTC-LC13

## Average Symptom Burden Index (ASBI)

(0–100)

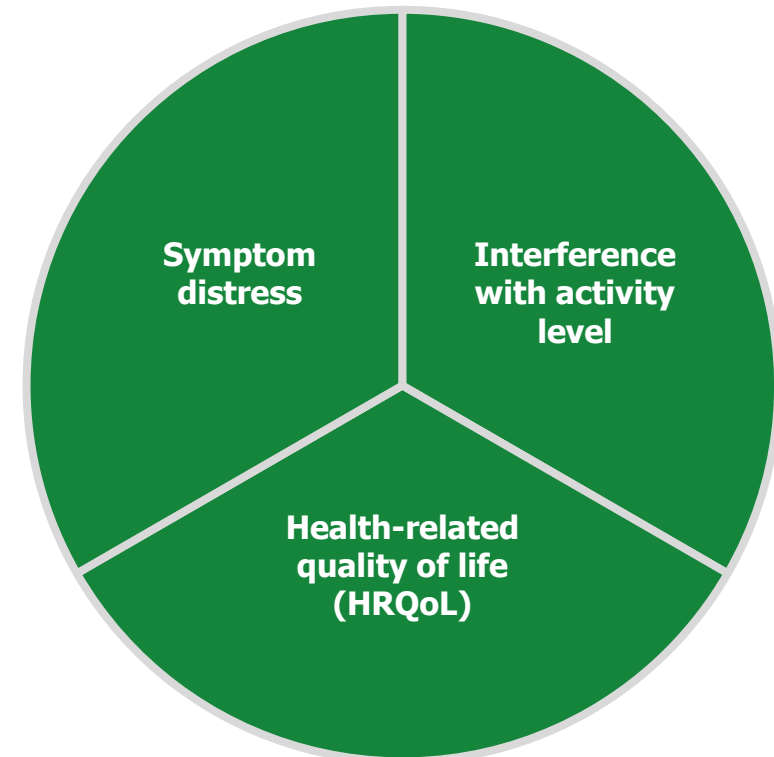
(MID  $\geq 10$ ; higher is worse)



## 3-Item Global Index (3-IGI)

(0–300)

(MID  $\geq 30$ ; higher is better)

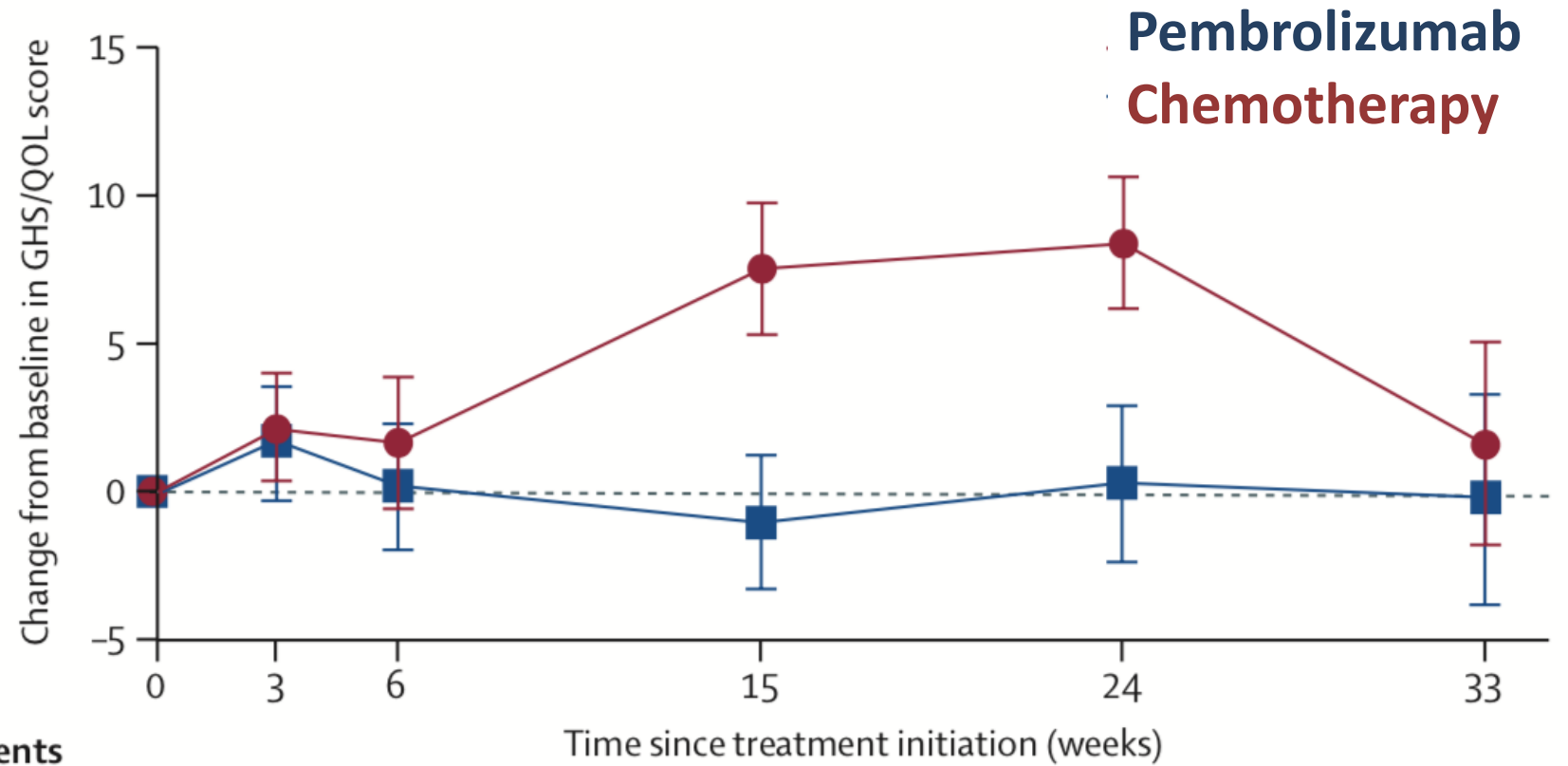


# Lung cancer metastatic setting

- ◆ **Keynote-024:** phase III: 1<sup>st</sup> line pembrolizumab vs platinum-based CT in PDL1+ (50%) pts: QLQ-C30, EQ-5D-3L, EORTC-LC13 less deterioration with pembro compared to CT (Brahmer J et al 2017, Lancet Onco)
- ◆ **Checkmate 057:** phase III nivolumab vs docetaxel in non sq NSCLC (after platinum): EQ-5D-3L, LSCC: improvement with nivo and not with docetaxel (Reck M et al, 2018, EJC)
- ◆ **Checkmate 017:** phase III nivolumab vs docetaxel in sq NSCLC (after platinum): EQ-5D-3L, LSCC: improvement with nivo and decrease with docetaxel (Reck M et al, 2018, JTO)
- ◆ **OAK:** A Phase III Study of atezolizumab Versus docetaxel (after platinum): QLQ-C30, EORTC-LC13 atezo tends to prolong time to worsening of disease-related symptoms (Bordoni R et al 2018, Clinical Lung Cancer)

# Keynote-024: 1<sup>st</sup> line pembrolizumab vs platinum-based CT in PDL1+ (50%) pts: global health score improves with pembro

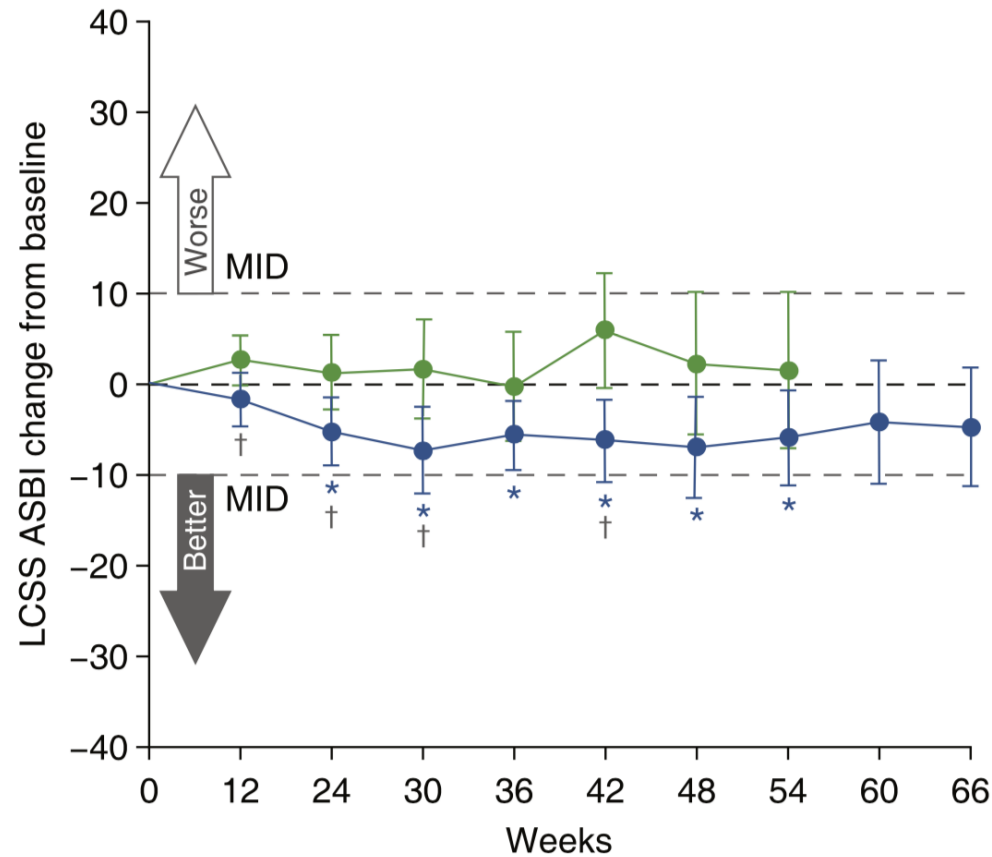
QLQ-C30



Number of patients (number missing)						
Pembrolizumab	145 (5)	126 (24)	117 (33)	105 (45)	93 (57)	63 (87)
Chemotherapy	138 (9)	114 (33)	102 (45)	85 (62)	71 (76)	44 (103)

# Checkmate 057: nivolumab vs docetaxel 1<sup>st</sup> line: less disease specific symptom burden; improves with nivo

Nivolumab  
Docetaxel



EQ-5D-3L, LSCC

No. of patients:

Nivolumab	206	112	69	59	49	43	38	39	29	27
Docetaxel	202	98	40	29	22	12	11	7	3	1

Reck M et al, 2018, EJC

High attrition  
rate with CT



# Future perspectives

- ◆ Integration social media (FB, twitter, ...) and technology
- ◆ Reimbursement/price setting according to QOL improvement or stabilisation
- ◆ Medical team is informed in real-time on patient QOL: treatment can be adapted accordingly

# Technology and Convergence of PROs & PerfOs: “Wearables”

- PRO Measures

- Physical Health
- Mental Health
- Social Health

**Jawbone**  
*Health Watch*

- 100MM nights
- 50B activity
- 1MM personal

years  
per week  
per week



**Cave digital literacy**



# Conclusion

- ◆ PRO and immunotherapy: at the very beginning (all mentioned studies exploratory analysis)
- ◆ HR QOL results for IT: very encouraging
- ◆ Difference between study patients and real life patients?
- ◆ Huge group of scientists are working on the questionnaires: final result depends on **close collaboration between physician and patient...**

# Thanks

- ◆ Anne Rogiers
- ◆ Bart Neyns
- ◆ Patrick Miqueu
- ◆ Bordet CTCU team
- ◆ Bordet B1 team

