La méthode du temps jusqu'à détérioration d'un score de qualité de vie dans les essais cliniques de phase III en cancérologie: une revue systématique de la littérature

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Séminaire Qualité de Vie 2018

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Analyse longitudinale de la Qualité de Vie (QdV)

Le temps jusqu'à détérioration (TJD) d'un score de QdV

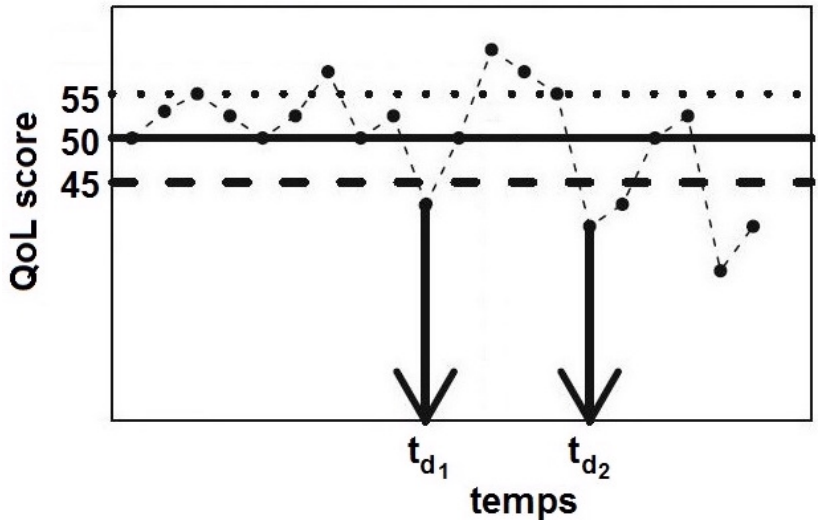
- **Situation adjuvante : TJD**
  - ▷ 1ère détérioration significative du score de QdV p/r au score à l'inclusion

  (Hamidou Z, *The Oncologist*, 2011)
- **Situation avancée/métastatique : Temps jusqu'à détérioration définitive (TJDD)**
  - ▷ sans amélioration suivante p/r au score à l'inclusion
  - ▷ incluant décès ou non comme évènement (**Survie sans détérioration de la QdV**)

  (Bonnetain F, *Eur J Cancer*, 2010)
- DMCI incluse dans la définition de l'évènement

(Anota A, *QoL Research*, 2013)

- Score élevé = haut niveau de QdV
- t_{d_1} : première détérioration
- t_{d_2} : détérioration définitive

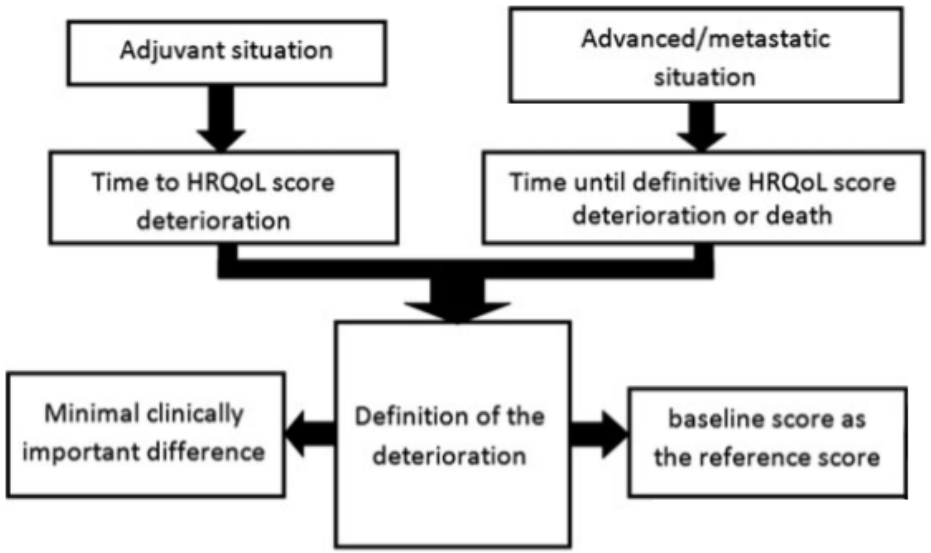


Analyse longitudinale de la Qualité de Vie (QdV)

QUANTITATIVE METHODS SPECIAL SECTION

Time to health-related quality of life score deterioration as a modality of longitudinal analysis for health-related quality of life studies in oncology: do we need RECIST for quality of life to achieve standardization?

Amélie Anota · Zeinab Hamidou · Sophie Paget-Bailly · Benoist Chibaudel · Caroline Bascoul-Mollevi · Pascal Auquier · Virginie Westeel · Frederic Fiteni · Christophe Borg · Franck Bonnetain



recommandations proposées

(Anota A, *QoL Research*, 2013)

Objectif de cette revue

Evaluer comment la méthode du TJD a été définie et rapportée dans les essais cliniques randomisés (ECR) depuis 2014

Stratégie de recherche

- PubMed/Medline
- Central (Librairie Cochrane)
- Recherches manuelles

→ Etudes publiées entre janvier 2014 et juin 2018

Critère de sélection

- Article en anglais
- ECR de phase III en cancérologie
- QdV ou tout autre patient-reported outcomes (PROs)
- Méthode TJD appliquée

Extraction des données

- Dédoublonnage des articles
- Identification des articles à inclure ou exclure par 2 examinateurs
- Inclusion/exclusion selon le "titre/abstract" puis le "manuscrit"
- Désaccords résolus après discussion entre les 2 examinateurs

Articles retenus

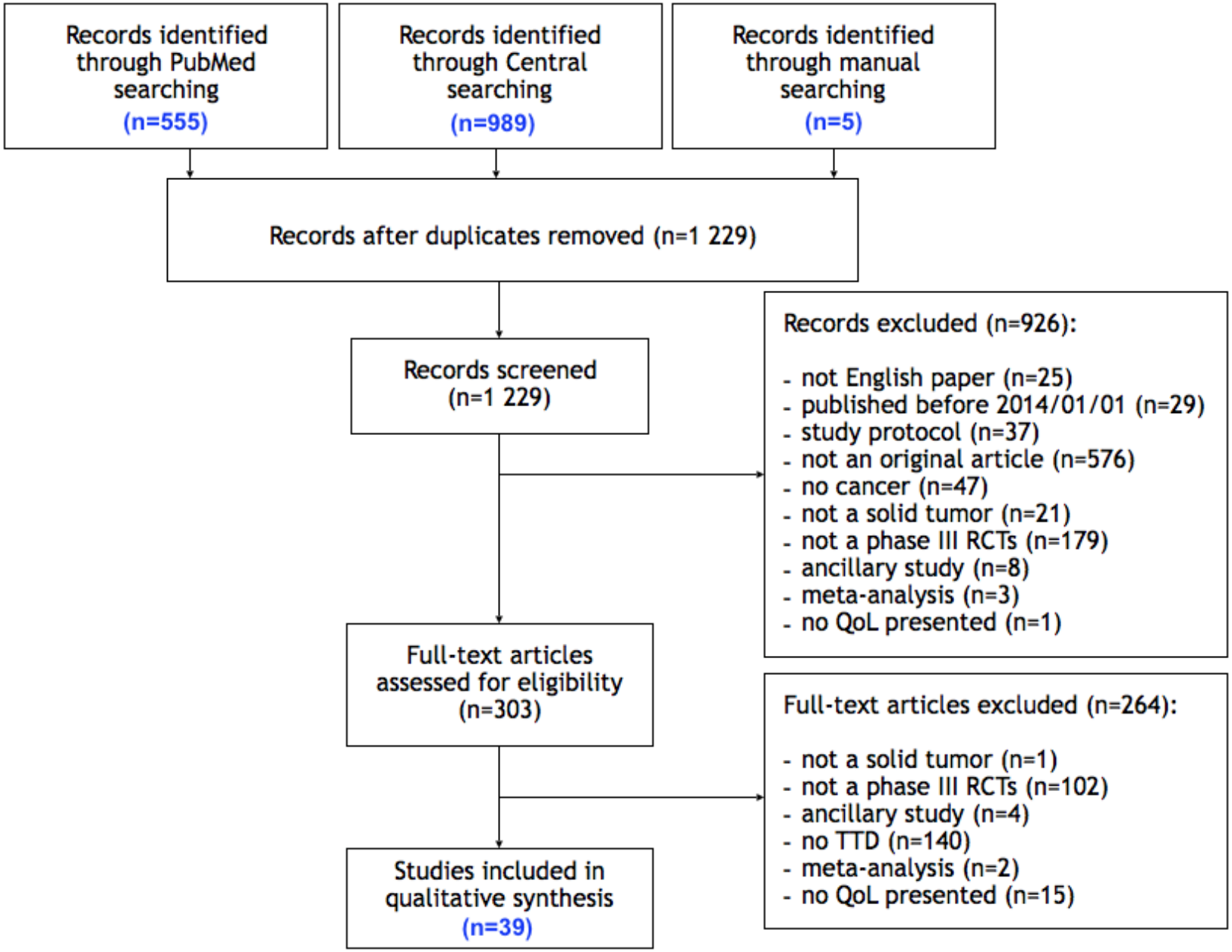
- Collecte de données par 2 examinateurs
- Désaccords résolus après discussion entre les 2 examinateurs

Collecte de données

- Information générale de l'étude
- Evaluation des PROs
- L'approche du TJD
- Présentation des résultats

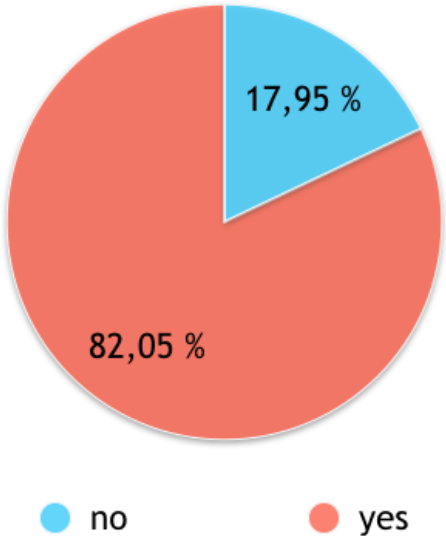
↪ **Analyses descriptives (fréquences et pourcentages)**

Flow diagram : 1 549 articles identifiés

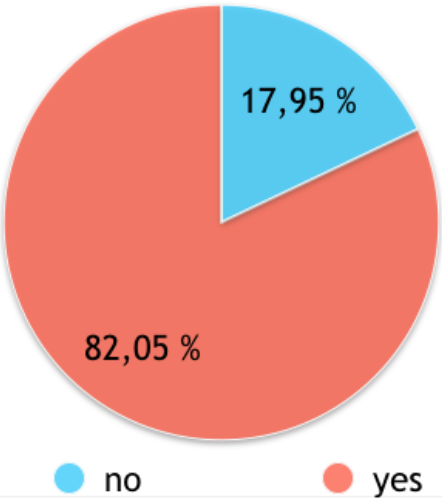


Informations générales : 39 articles inclus

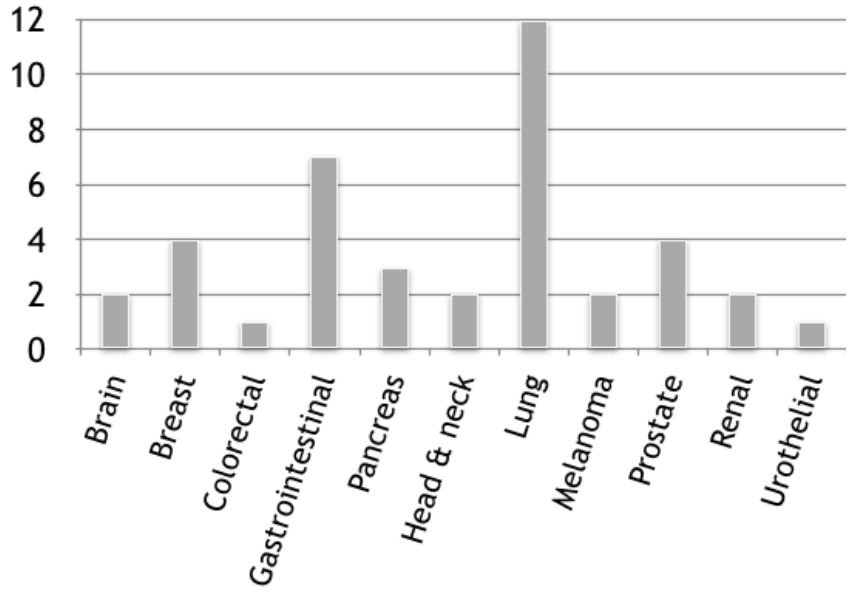
International study



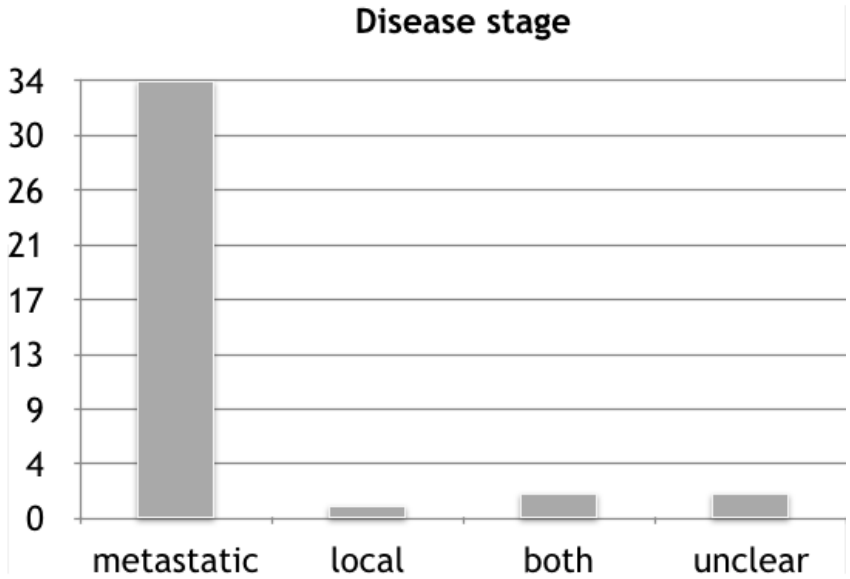
Second paper focused on PROs analyses



Disease site

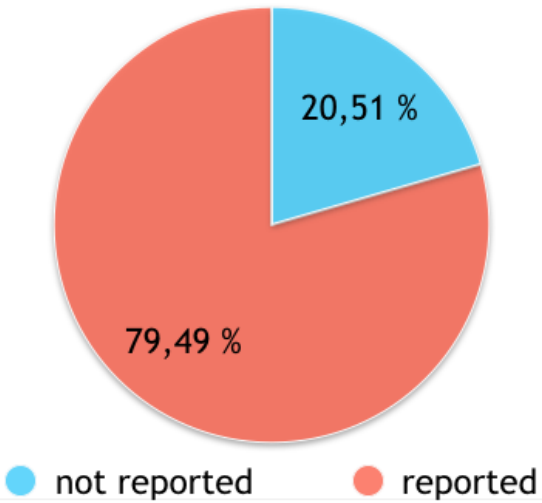


Disease stage

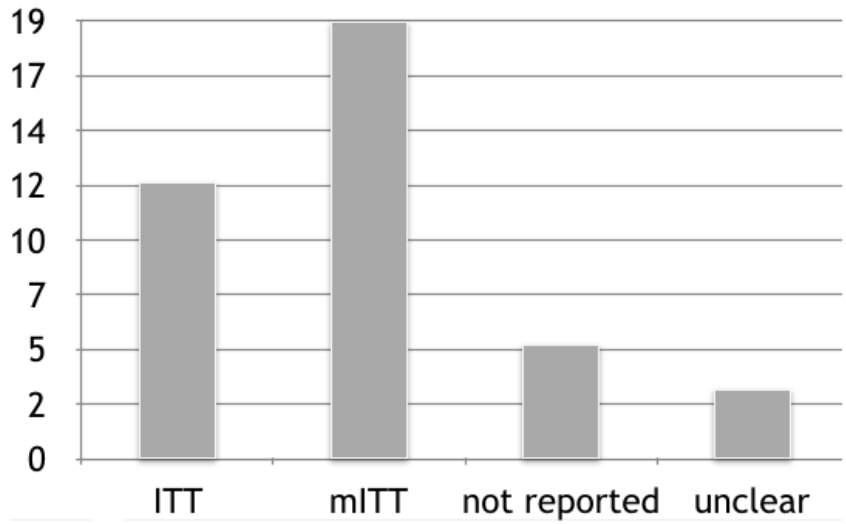


Informations générales : 39 articles inclus

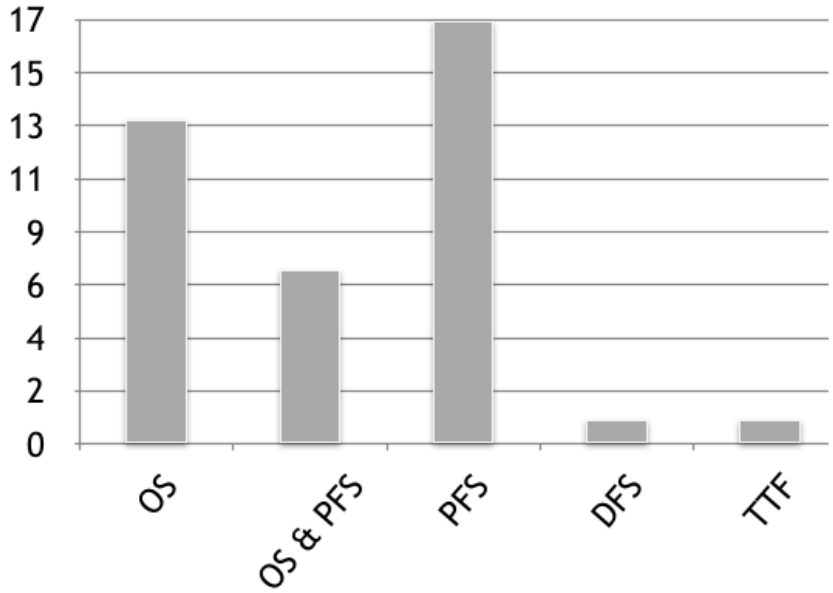
Baseline PRO sample size



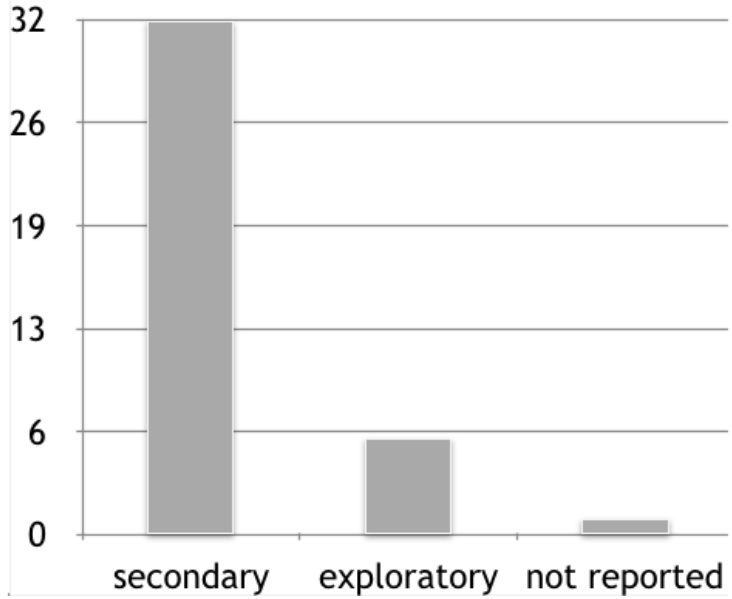
PRO population



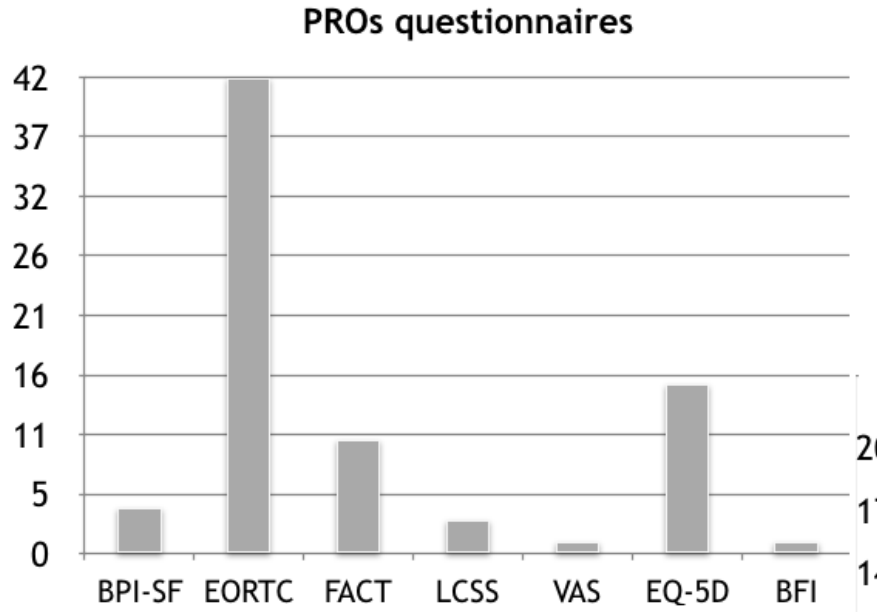
Primary endpoint(s)

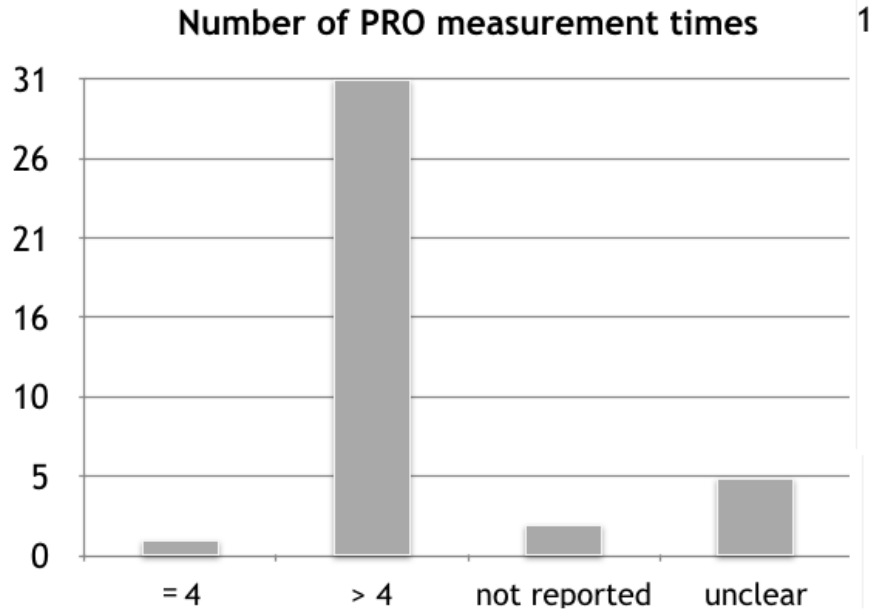


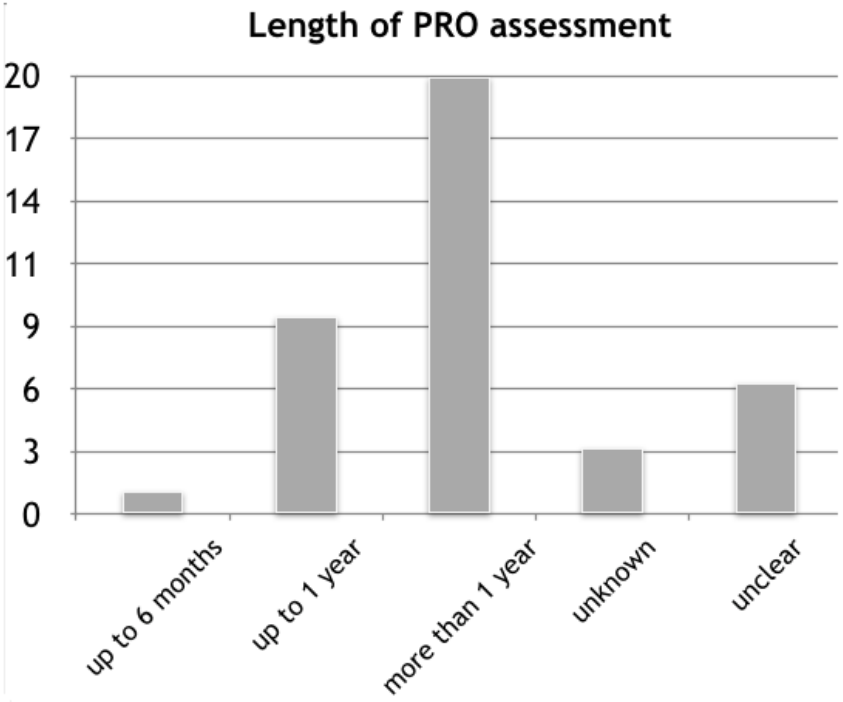
PRO endpoint



Evaluation des PROs : 39 articles inclus







Méthode du temps jusqu'à détérioration : 39 articles inclus

	n	%
Deterioration was considered as		
first deterioration (reversible)	14	35.90
a priori first deterioration but not specify	7	17.95
definitive deterioration (maintained over time)	10	25.64
confirmed deterioration (two consecutive)	6	15.38
first and confirmed deterioration	1	2.56
unclear	1	2.56
Reference score to qualify the deterioration		
baseline	31	79.49
not defined	5	12.82
unclear	3	7.69
Composite definitions		
yes	**16**	**41.03**
deterioration in several HRQoL scales	1	6.25
death	9	56.25
death and disease progression	5	31.25
increased of analgesic use	1	6.25
no	**23**	**58.97**
MCID to qualify the deterioration		
same value for each score	29	65.91
different according to the score	8	18.18
different according to the patient (relative deterioration)	2	4.55
not defined	4	9.09
unclear	1	2.27

Targ Oncol (2016) 11:815–824
DOI 10.1007/s11523-016-0462-5

ORIGINAL RESEARCH ARTICLE

Patient-Reported Outcomes and Quality of Life with Sunitinib Versus Placebo for Pancreatic Neuroendocrine Tumors: Results From an International Phase III Trial

Aaron Vinik[1] · Andrew Bottomley[2] · Beata Korytowsky[3] · Yung-Jue Bang[4] · Jean-Luc Raoul[5] · Juan W. Valle[6] · Peter Metrakos[7] · Dieter Hörsch[8] · Rajiv Mundayat[3] · Arlene Reisman[3] · Zhixiao Wang[3] · Richard C. Chao[9] · Eric Raymond[10]

TTD was retrospectively assessed. This was a composite endpoint defined as time from randomization to death, tumor progression, or clinically meaningful (≥10 points) change from baseline in functioning, symptoms, or global HRQoL in two consecutive cycles.

Lancet Oncol 2017; 18: 1600-09

Health-related quality-of-life results for pembrolizumab versus chemotherapy in advanced, PD-L1-positive NSCLC (KEYNOTE-024): a multicentre, international, randomised, open-label phase 3 trial

Julie R Brahmer, Delvys Rodríguez-Abreu, Andrew G Robinson, Rina Hui, Tibor Csőszi, Andrea Fülöp, Maya Gottfried, Nir Peled, Ali Tafreshi, Sinead Cuffe, Mary O'Brien, Suman Rao, Katsuyuki Hotta, Jin Zhang, Gregory M Lubiniecki, Anne C Deitz, Reshma Rangwala, Martin Reck

time to deterioration of the composite of cough, chest pain, and dyspnoea in the QLQ-LC13 (defined as time to first onset of a 10-point or greater decrease from baseline in cough, chest pain, or dyspnoea, confirmed by a second adjacent 10-point or greater decrease from baseline in any of these three symptoms)

Méthode du temps jusqu'à détérioration : 39 articles inclus

- En situation métastatique (n=34 articles)

	n	%
Deterioration was considered as		
first deterioration (reversible)	13	38.24
a priori first deterioration but not specify	6	17.65
definitive deterioration (maintained over time)	7	20.59
confirmed deterioration (two consecutive)	6	17.65
first and confirmed deterioration	1	2.94
unclear	1	2.94

	n	%
Death considered in the deterioration definition		
first deterioration (reversible)	4/13	30.77
a priori first deterioration but not specify	2/6	33.33
definitive deterioration (maintained over time)	5/7	71.43
confirmed deterioration (two consecutive)	1/6	16.67
first and confirmed deterioration	1/1	100.00

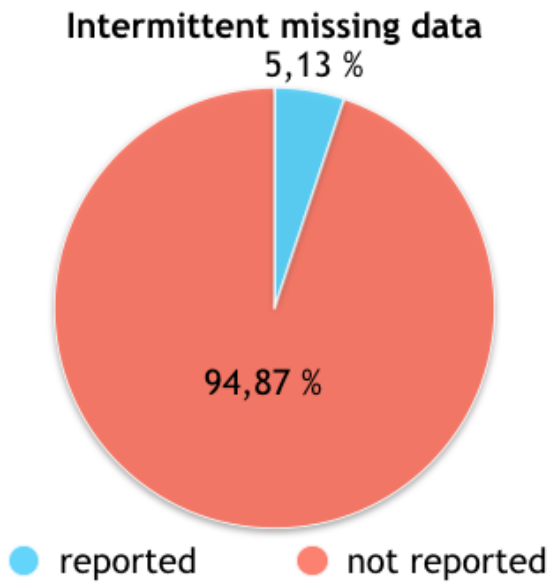
Effect of enzalutamide on time to first skeletal-related event, pain, and quality of life in men with castration-resistant prostate cancer: results from the randomised, phase 3 AFFIRM trial

Karim Fizazi, Howard I Scher, Kurt Miller, Ethan Basch, Cora N Sternberg, David Cella, David Forer, Mohammad Hirmand, Johann S de Bono

	Definition of secondary endpoint
Time to pain progression	Time from randomisation to the date of pain progression (ie, an increase above baseline in the score of "I have pain" on FACT-P with confirmation at a consecutive visit at least 3 weeks later)
Time to HRQoL deterioration	Time from date of randomisation to the date of first HRQoL deterioration (defined as a ≥10-point decrease in the global FACT-P score at a post-baseline assessment compared with baseline) or death from any cause, whichever occurs first

Méthode du temps jusqu'à détérioration : 39 articles inclus

	n	%
Baseline missing scores was considered as		
Articles identified (n=39)		
a censor	2	5.13
not reported	9	23.08
unclear	13	33.33
n/a (if mITT population or no baseline missing scores)	15	38.46
Articles where PROs were analyzed in intent-to-treat population (n=12)		
a censor	2	16.67
not reported	4	8.33
unclear	5	33.33
n/a (if mITT population or no baseline missing scores)	1	41.67



The Oncologist — Gastrointestinal Cancer

Quality of Life in the Trastuzumab for Gastric Cancer Trial

Taroh Satoh,[a] Yung-Jue Bang,[b] Evgeny A. Gotovkin,[c] Yasuo Hamamoto,[d] Yoon-Koo Kang,[e] Vladimir M. Moiseyenko,[f] Atsushi Ohtsu,[g] Eric Van Cutsem,[h] Nedal Al-Sakaff,[i] Alexa Urspruch,[i] Julie Hill,[j] Harald A. Weber,[i] Hyun-Cheol Chung[k] for the ToGA Trial Investigators

made following PD, when compliance is typically poor. If a definitive deterioration was observed after a missing value, it was assumed that the deterioration occurred at the time of the missing value. Moreover, it was mandatory for data manage-

Lancet Oncol 2014; 15: 1147-56

Effect of enzalutamide on time to first skeletal-related event, pain, and quality of life in men with castration-resistant prostate cancer: results from the randomised, phase 3 AFFIRM trial

Karim Fizazi, Howard I Scher, Kurt Miller, Ethan Basch, Cora N Sternberg, David Cella, David Forer, Mohammad Hirmand, Johann S de Bono

To take into account that missing values were likely to be related to the poor health state of the patient, it was assumed that the deterioration had occurred at the time of the missing value.

Présentation des données : 39 articles inclus

How were deterioration results reported	n
Deterioration curve by treatment arm	27
Forest plots	10
HR with confidence interval	34
HR without confidence interval	1
Median with confidence interval	20
Median without confidence interval	12
Plot of differences in median time to symptom worsening	1
Event reported for dimensions specified in the method section	
yes	14
yes, for some dimensions	1
no	24
Event reported for each component in case of composite definitions	
yes	3
unclear	1
no	12

- Primary endpoint(s) in favor of the experimental arm : n=29
  - ↪ PRO endpoint favors the experimental arm : n=23
- No statistical significant $\neq$ between treatment arms in primary endpoint(s) : n=10
  - ↪ PRO endpoint favors the experimental arm : n=5
  - ↪ PRO endpoint favors the control arm : n=1

Présentation des données : 39 articles inclus

- Recommandations proposées non suivies
- Besoin d'un travail d'harmonisation
  - ↪ Quelle définition doit-on considérer ?
  - ↪ Dans le cas d'évènements composites, quels évènements doit-on considérer ?
- Variabilité des définitions du TJD
  - ↪ Essais semblables non comparables

Merci de votre attention

www.umqvc.org & www.qualitedeviecancer.fr