SACRO CUORE DON CALABRIA
I R C C S

MEMBER OF ECI
Organisation of European Cancer Institutes - EEIG

1° Evento Alumni della Scuola

Patient Reported Outcomes

Dibattito strutturato.
PROs: still a Cinderella outcome?
Giovanni L. PAPPAGALLO
(coordina tutti i relatori)

Quality of life assessment using patient-reported outcome (PRO) measures: still a Cinderella outcome?

L. J. Fallowfield
Sussex Health Outcomes Research & Education in Cancer, Brighton & Sussex Medical School, University of Sussex, Brighton, UK
(E-mail: l.j.fallowfield@sussex.ac.uk)

We have to do better in our evaluation of expensive novel products. The sometimes modest OS or more often PFS gains that excite clinical scientists and pharma share-holders may be of little value to patients experiencing some serious and burden-some side-effects. Conclusions stating that 'patients found side-effects tolerable' should be viewed with some skepticism as trials that are conducted for registration and licensing purposes rarely have lengthy enough follow-up to chart some of the problems that emerge later in the clinic [3].

Parliamone insieme…

… ma facciamo attenzione ai possibili problemi!

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Symptom Endpoints (Patient-Reported Outcomes)

- Blinding is often difficult
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Opel-label design ALSO when masking is feasible…

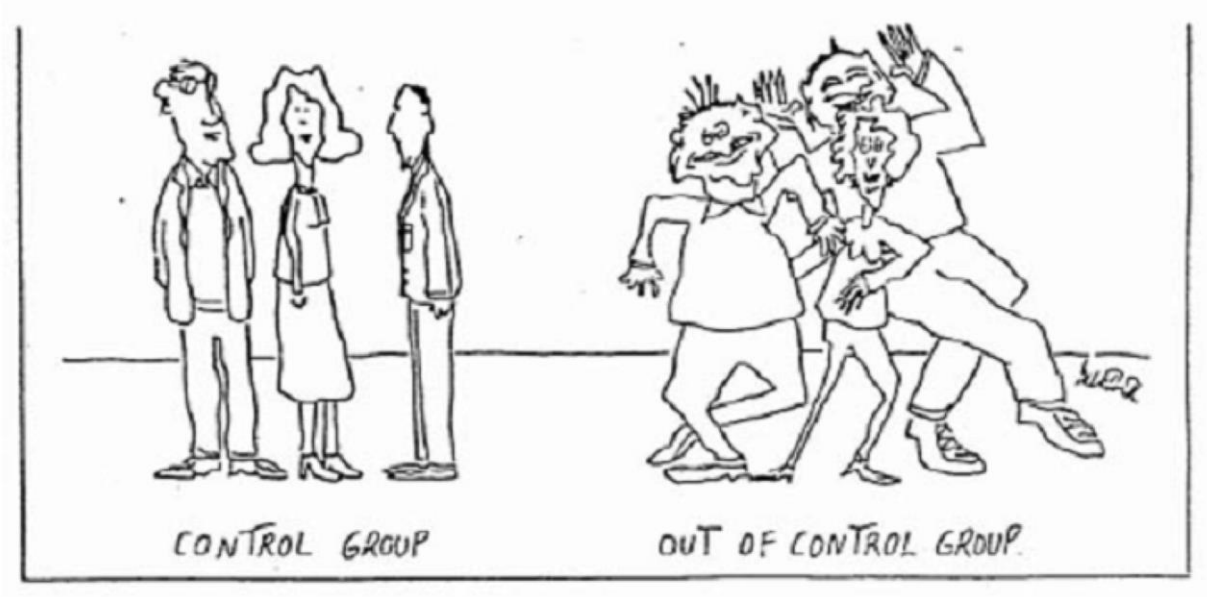
Comparative effectiveness of axitinib versus sorafenib in advanced renal cell carcinoma (AXIS): a randomised phase 3 trial

Brian I Rini, Bernard Escudier, Piotr Tomczak, Andrey Kaprin, Cezary Szczylik, Thomas E Hutson, M Dror Michaelson, Vera A Gorbunova, Martin E Gore, Igor G Rusakov, Sylvie Negrier, Yen-Chuan Ou, Daniel Castellano, Ho Yeong Lim, Hirotsugu Uemura, Jamal Tarazi, David Cella, Connie Chen, Brad Rosbrook, Sinil Kim, Robert J Motzer

Lancet **2011; 378: 1931–39**

Patients and investigators were not masked to study treatment. Progression-free survival and objective response rate were assessed by a masked independent radiology review.

If no patient blinding was performed…



… were they **unbiased** when filling the QoL questionnaire?

Endpoints of benefit and endpoints of harm BOTH contribute to Quality Assessment!

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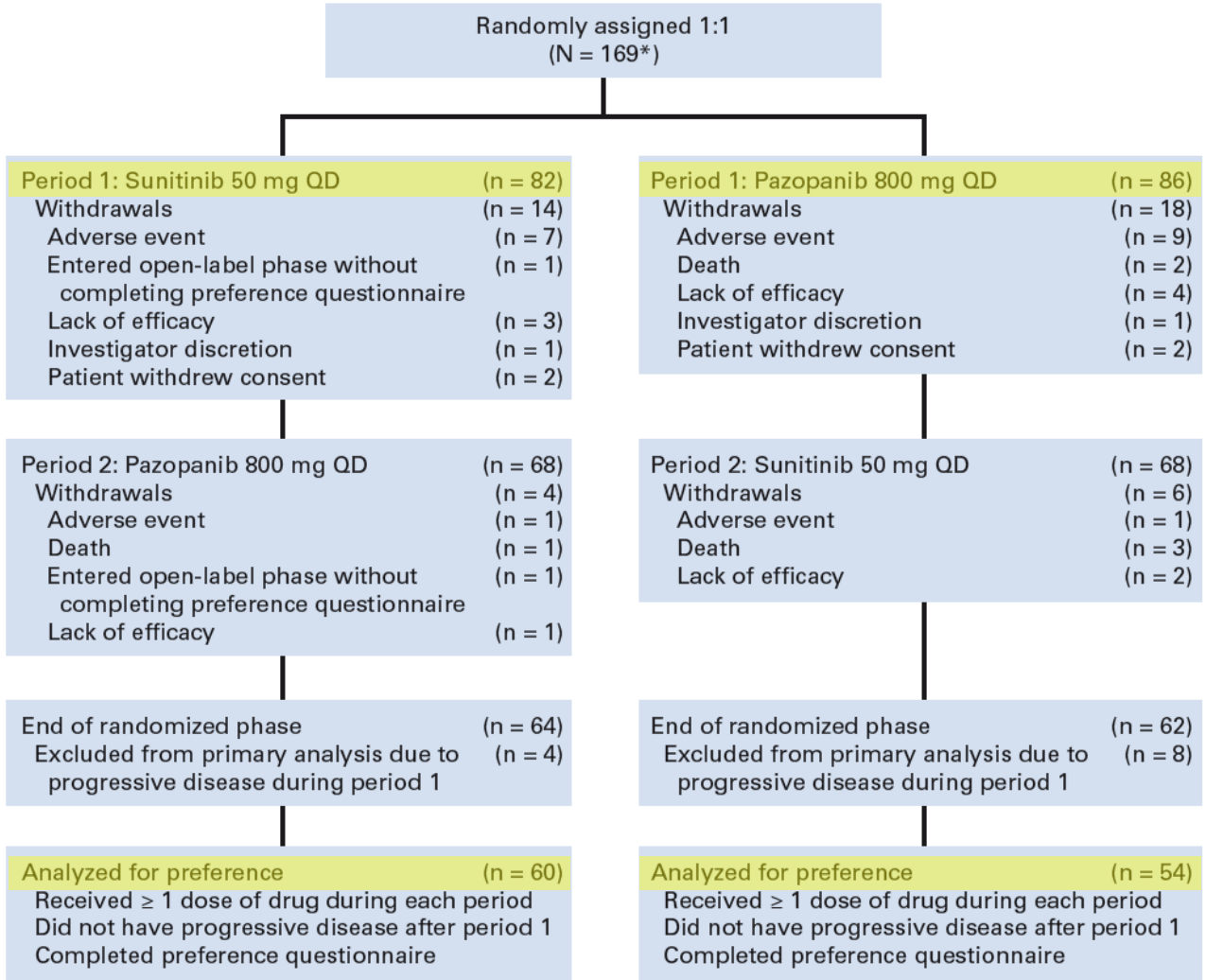
Randomized, Controlled, Double-Blind, Cross-Over Trial Assessing Treatment Preference for Pazopanib Versus Sunitinib in Patients With Metastatic Renal Cell Carcinoma: PISCES Study

Bernard Escudier, Camillo Porta, Petri Bono, Thomas Powles, Tim Eisen, Cora N. Sternberg, Jürgen E. Gschwend, Ugo De Giorgi, Omi Parikh, Robert Hawkins, Emmanuel Sevin, Sylvie Négrier, Sadya Khan, Jose Diaz, Suman Redhu, Faisal Mehmud, and David Cella

J Clin Oncol 32.



Randomized, Controlled, Double-Blind, Cross-Over Trial Assessing Treatment Preference for Pazopanib Versus Sunitinib in Patients With Metastatic Renal Cell Carcinoma: PISCES Study

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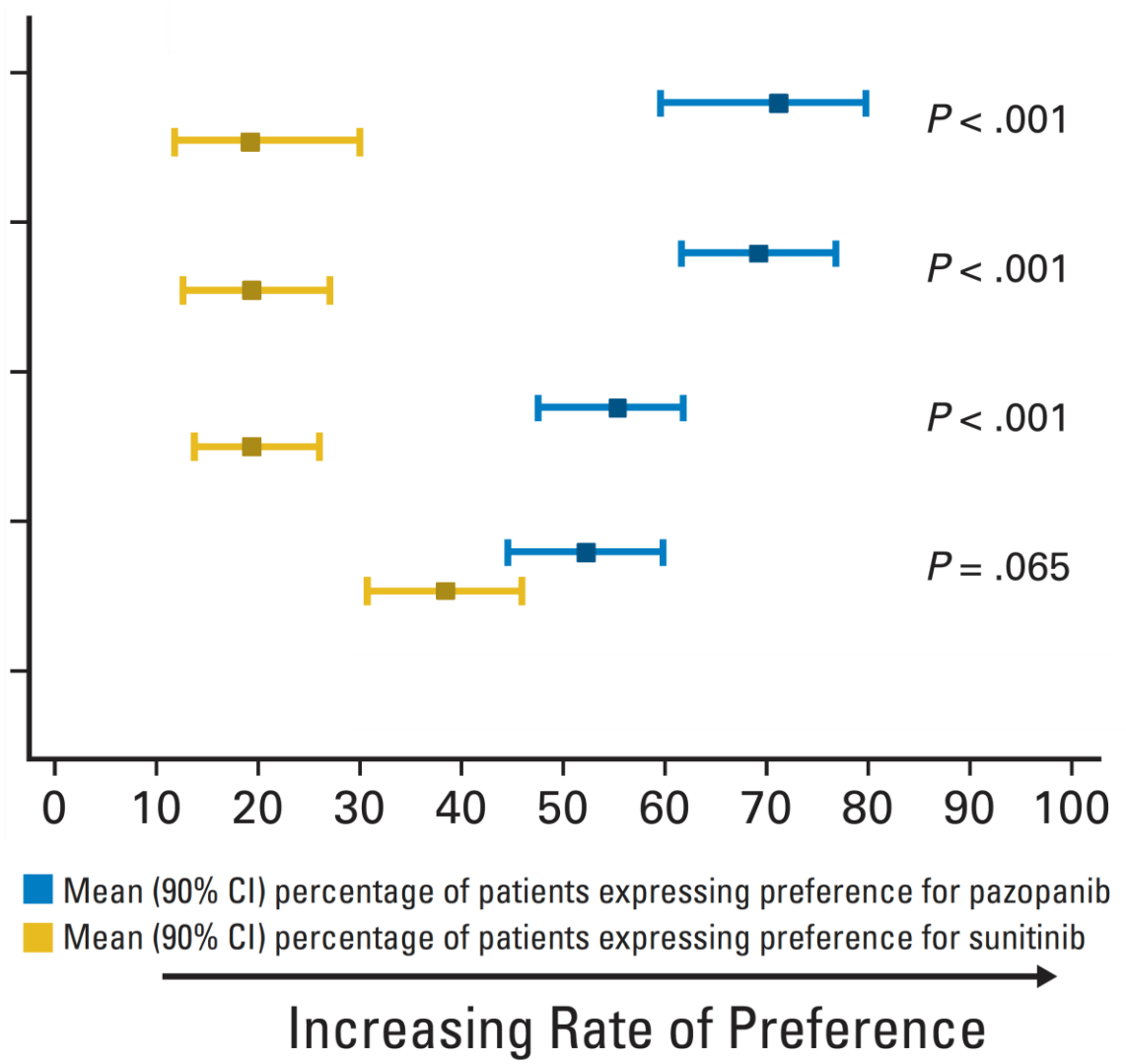
Primary end point (n = 114)

Patients who completed full study treatment (n = 80)

All questionnaires (n = 126)

Worst case: imputation of sunitinib preference for study withdrawals (n = 166)



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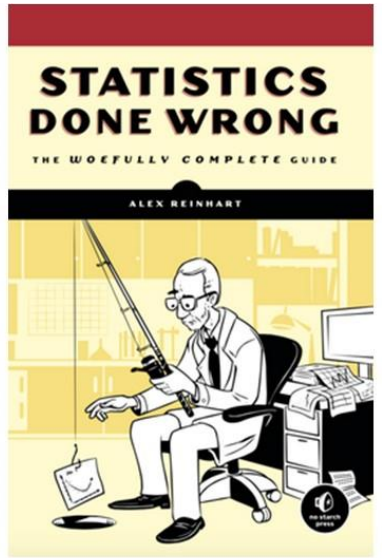
Recent statement by the American Statistical Association about p-values

(Wasserstein & Lazar, Am Stat 2016;70:129-33)



- P-values do not measure the probability that a hypothesis is true.
- Scientific conclusions and policy decisions should not be based only on p <0.05.
- A p-value does not measure the size of an effect or the importance of a result.

UHN Princess Margaret Cancer Centre

ASCO

Pazopanib versus Sunitinib in Metastatic Renal-Cell Carcinoma

Robert J. Motzer, M.D., Thomas E. Hutson, D.O., David Cella, Ph.D., James Reeves, M.D., Robert Hawkins, M.B., B.S., Ph.D., Jun Guo, Ph.D., Paul Nathan, M.B., B.S., Ph.D., Michael Staehler, M.D., Paul de Souza, M.B., B.S., Ph.D., Jaime R. Merchan, M.D., Ekaterini Boleti, M.D., Ph.D., Kate Fife, M.D., Jie Jin, M.D., Robert Jones, Ph.D., Hirotsugu Uemura, M.D., Ph.D., Ugo De Giorgi, M.D., Ulrika Harmenberg, M.D., Ph.D., Jinwan Wang, M.D., Cora N. Sternberg, M.D., Keith Deen, M.S., Lauren McCann, Ph.D., Michelle D. Hackshaw, Ph.D., Rocco Crescenzo, D.O., Lini N. Pandite, M.D., and Toni K. Choueiri, M.D.

N Engl J Med 2013;369:722-31

Table 2. Change in Health-Related Quality of Life during the First 6 Months for 927 Patients Treated in the Study.*

Instrument	Pazopanib	Sunitinib	Difference in Mean Change from Baseline Score with Pazopanib vs. Sunitinib†	P Value§	Drug Favored According to Significant Difference¶	Effect Size‖
	number of patients					
FACIT-F**	377	403	2.32	<0.001	Pazopanib	0.24
FKSI-19**						
Treatment side effects	351	382	0.31	0.03	Pazopanib	0.14
Disease-related physical symptoms	378	407	0.78	0.03	Pazopanib	0.13
Disease-related emotional symptoms	370	402	–0.05	0.41	Neither	–0.04
Functional well-being	378	403	0.31	0.10	Neither	0.09
Total score	377	408	1.41	0.02	Pazopanib	0.14

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FACIT-F**	377	403	2.32	<0.001	Pazopanib	0.24
FKSI-19**						
Treatment side effects	3			0.03	Pazopanib	0.14
Disease-related physical symptoms	3			0.03	Pazopanib	0.13
Disease-related emotional symptoms	3			0.41	Neither	–0.04
Functional well-being	378	403	0.31	0.10	Neither	0.09
Total score	377	408	1.41	0.02	Pazopanib	0.14

Rilevanza dell'effetto da rapportare alla M.I.D. specifica

The Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System: properties, applications, and interpretation

Kimberly Webster, David Cella* and Kathleen Yost

Health and Quality of Life Outcomes 2003, 1:79

Table 1: Minimally important differences for select FACIT scales

Instrument	Scale/Subscale	MID (points)	Reference
FACT-G	PWB	2–3	[28]
	SWB	NA	
	EWB	2*	[28,29]
	FWB	2–3	[28]
	Total FACT-G	3–7	[27,28,30,31]
FACT-Anemia	Fatigue Subscale	3–4	[27,31]
	TOI-Fatigue	5	[27]
	TOI-Anemia	6	
	Total FACT-Anemia	7	
FACT-Breast	Breast cancer subscale	2–3	[30]
	TOI-Breast	5–6	
	Total FACT-Breast	7–8	
FACT-Colorectal	Colorectal cancer subscale	2–3	[32]
	TOI-Colorectal	4–6	
	Total FACT-Colorectal	5–8	
FACT-Head & Neck	Total FACT-Head & Neck	6–12	[33]
FACT-Lung	Lung cancer subscale	2–3	[34]
	TOI-Lung	5–6	

*This MID should be considered tentative as it may be revised based on future research.

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Validity and Reliability of the US National Cancer Institute's Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE)

Amylou C. Dueck, PhD; Tito R. Mendoza, PhD; Sandra A. Mitchell, PhD, CRNP, AOCN; Bryce B. Reeve, PhD; Kathleen M. Castro, RN, MS, AOCN; Lauren J. Rogak, MA; Thomas M. Atkinson, PhD; Antonia V. Bennett, PhD; Andrea M. Denicoff, MS, RN, ANP; Ann M. O'Mara, PhD, RN, FAAN; Yuelin Li, PhD; Steven B. Clauser, PhD, MPA; Donna M. Bryant, MSN, ANP-BC, OCN, CCRC; James D. Bearden III, MD, FACP; Theresa A. Gillis, MD; Jay K. Harness, MD; Robert D. Siegel, MD, FACP; Diane B. Paul, AAS; Charles S. Cleeland, PhD; Deborah Schrag, MD, MPH; Jeff A. Sloan, PhD; Amy P. Abernethy, MD, PhD; Deborah W. Bruner, RN, PhD, FAAN; Lori M. Minasian, MD, FACP; Ethan Basch, MD, MSc; for the National Cancer Institute PRO-CTCAE Study Group

JAMA Oncol. 2015;1(8):1051-1059.

NATIONAL CANCER INSTITUTE

Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) Item Library (version 1)

Certified Translation

This is to certify that the Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) Item Library (version 1) was translated from English to Italian using a universal translation methodology including representation from major Italian speaking regions by qualified translators employed by Italian National Cancer Institute, under the direction of the US National Cancer Institute.

This translation followed the translation methodology recommended by International Society of Pharmacoeconomic and Outcomes Research (ISPOR) a methodology established to ensure that resulting translations of patient-reported outcome measures reflect conceptual equivalence with the source document rendered in language that is culturally acceptable and relevant to the target population. This rigorous methodology requires two forward translations into the target language by native speakers, a reconciled version of the two forward translations done by a third independent translator who is a native speaker of the target language, a back translation of the reconciled version by a native English speaker fluent in the target language, and an independent review by a native speaker trained as a physician or nurse in oncology.

After the translation phase was completed, the PRO-CTCAE Item Library (version 1) was linguistically validated by testing with patients to confirm suitability of the translations for Italian speaking patients. All translation work was performed by members of the Italian translation team to the best of their abilities as native speakers of Italian (or English in the case of the back-translator), and as translators and researchers experienced in the field of health-related quality of life and patient-reported outcomes survey research under the direction of the undersigned.

This translation is, to the best of my knowledge, a valid and accurate translation of the corresponding original English language version of the PRO-CTCAE Item Library (version 1).

Name: Sandra A. Mitchell, PhD, CRNP

Title: Research Scientist and Program Director; Outcomes Research Branch; US National Cancer Institute

Signature:

Date: June 5, 2017

Lise Rene Tamoufe NOTARY PUBLIC Montgomery County State of Maryland My Commission Expires May 1, 2018

6/07/2017

NCI- PRO-CTCAE™ ITEMS-ITALIAN

Item Library Version 1.0

Quando un individuo è in terapia per un tumore, talvolta può sviluppare diversi sintomi ed effetti collaterali. Per ciascuna domanda, fare un segno o una (X) nella casella che meglio corrisponde all'esperienza vissuta negli ultimi sette giorni...

1. PRO-CTCAE™ Symptom Term: Dry mouth				
SENSAZIONE DI BOCCA SECCA				
Negli ultimi 7 giorni, quanto è stata GRAVE la SENSAZIONE DI BOCCA SECCA nel momento PEGGIORE?				
O Per nulla	O Un po'	O Abbastanza	O Molto	O Moltissimo

2. PRO-CTCAE™ Symptom Term: Difficulty swallowing				
DIFFICOLTÀ A DEGLUTIRE				
Negli ultimi 7 giorni, quanto è stata GRAVE la DIFFICOLTÀ A DEGLUTIRE nel momento PEGGIORE?				
O Per nulla	O Un po'	O Abbastanza	O Molto	O Moltissimo

3. PRO-CTCAE™ Symptom Term: Mouth/throat sores				
PIAGHE IN BOCCA O IN GOLA				
Negli ultimi 7 giorni, quanto sono state GRAVI le PIAGHE IN BOCCA O IN GOLA nel momento PEGGIORE?				
O Per nulla	O Un po'	O Abbastanza	O Molto	O Moltissimo
Negli ultimi 7 giorni, in che misura le PIAGHE IN BOCCA O IN GOLA HANNO INTERFERITO con le Sue attività abituali o quotidiane?				
O Per nulla	O Un po'	O Abbastanza	O Molto	O Moltissimo

4. PRO-CTCAE™ Symptom Term: Cracking at the corners of the mouth (cheilosis/cheilitis)				
SCREPOLATURE AGLI ANGOLI DELLA BOCCA				
Negli ultimi 7 giorni, quanto sono state GRAVI le SCREPOLATURE AGLI ANGOLI DELLA BOCCA, nel momento PEGGIORE?				
O Per nulla	O Un po'	O Abbastanza	O Molto	O Moltissimo

The PRO-CTCAE™ items and information herein were developed by the Division of Cancer Control and Population Sciences in the NATIONAL CANCER INSTITUTE at the NATIONAL INSTITUTES OF HEALTH, in Bethesda, Maryland, U.S.A. Use of the PRO- CTCAE™ is subject to NCI's Terms of Use.

Version date: 6/3/2017

https://healthcaredelivery.cancer.gov/pro-ctcae/pro-ctcae_italian.pdf