



Fondazione Smith Kline

Personalità giuridica riconosciuta (D.P.R. 917 del 9. 9. 1982)

Con il Patrocinio di:



Associazione Italiana Oncologia Medica

WORKSHOP: "PROs in Oncologia"

QUANDO LA QUALITÀ DI VITA DIVENTA FATTORE DI SCELTA TERAPEUTICA

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Oncologia Medica,

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Pavia

TRADITIONAL ENDPOINTS IN ONCOLOGY TRIALS

EFFICACY

Overall Survival

Progression-Free Survival

Response Rate

SAFETY

Adverse Events

Dose modifications



But how well do these endpoints REALLY reflect patient outcomes?

ASSESSMENTS ARE MADE USING STANDARDIZED METHODS

RECIST¹

Measurable lesions defined by unidimensional measurement

Tumour burden based on sum of diameters

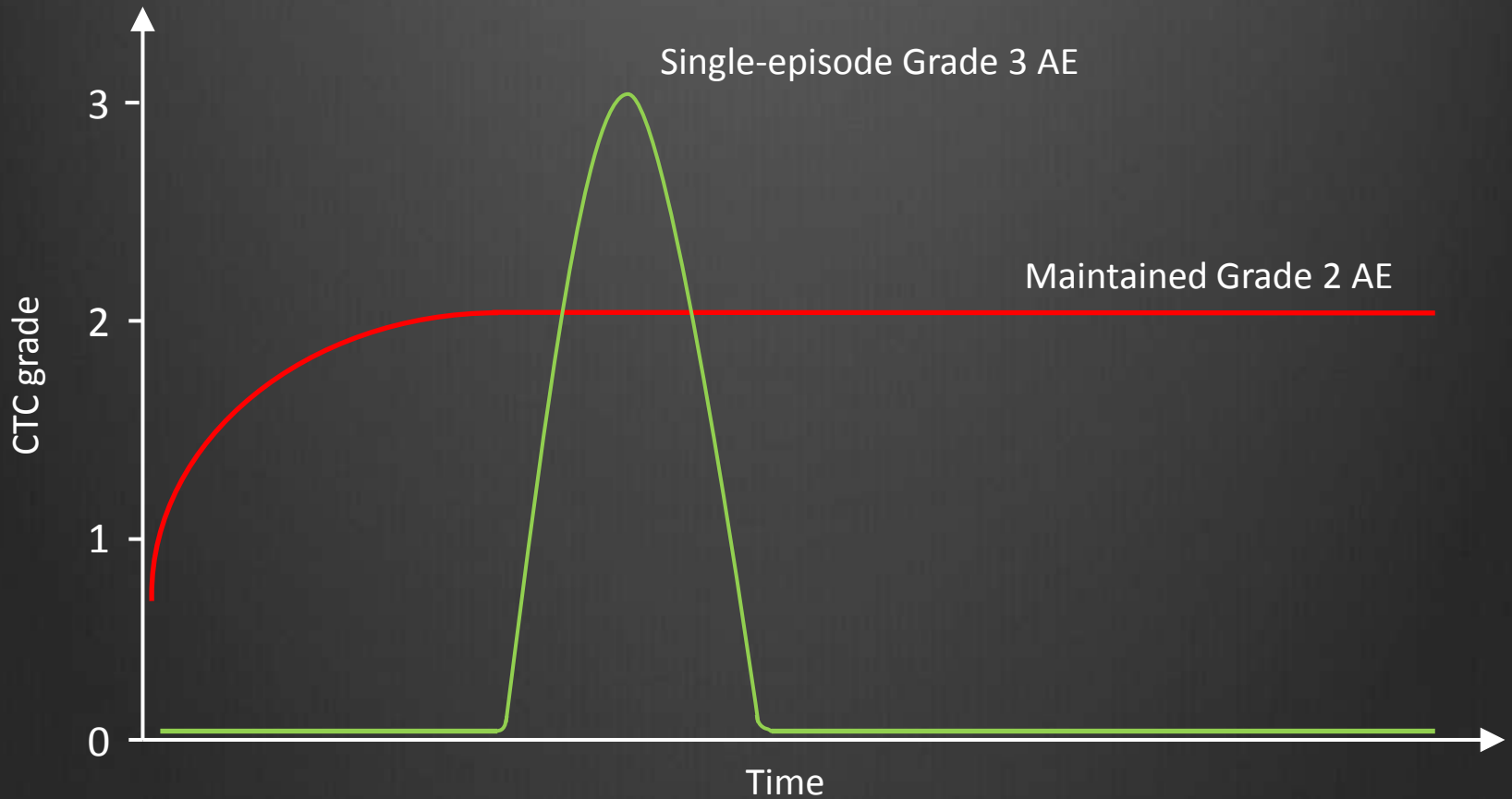
Categories of response: CR; PR (30% ↓), SD; PR (20% ↑)

CTC²

Descriptive terminology used for adverse event (AE) reporting;
if a patient experiences an AE, the highest grade (severity) is
recorded

How effective are these tools for clinical assessment?

DO CTC TRULY REFLECT THE PATIENT EXPERIENCE OF ADVERSE EVENTS?

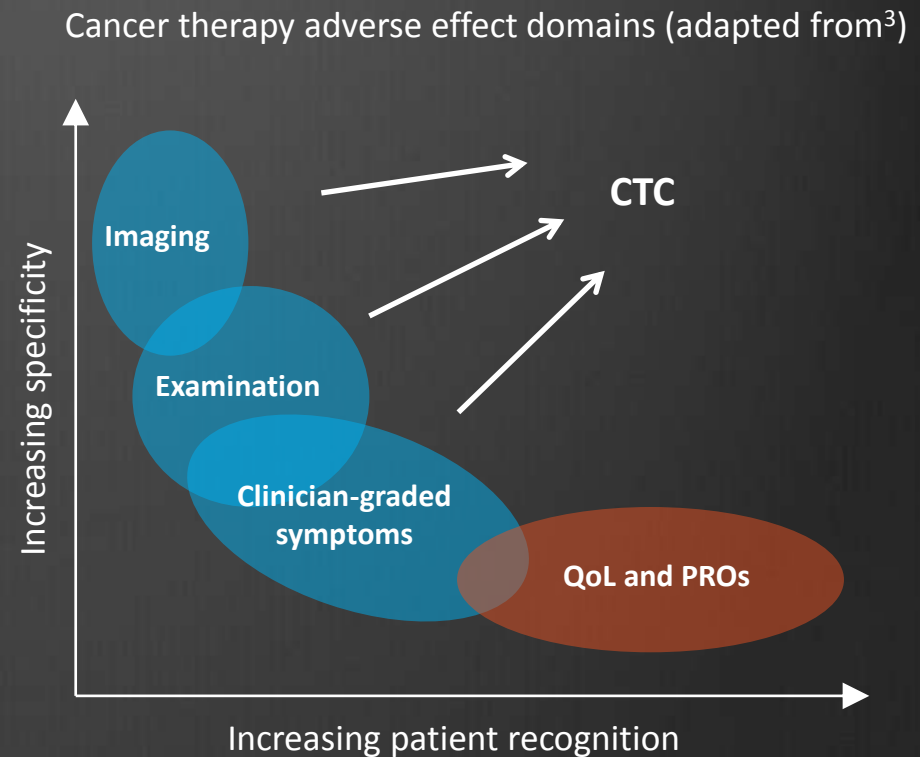


LIMITATIONS OF CTC FOR TARGETED AGENTS

Measure chemotherapy-related toxicity; not toxicity associated with continuous therapy in metastatic disease¹

CTC have not been formally validated²

Do not take into account impact on patient QoL¹



HEALTH

“not merely the absence of disease, but complete physical, mental, and social well being”

(WHO 1948)

HEALTH-RELATED QoL

“Refers to the extent to which one’s usual or expected physical, emotional and social wellbeing are affected by a medical condition and/or its treatment”

(Cella D, 1995)

QoL ACCORDING TO TREATMENT INTENTION

	Clinical purpose	QoL question
Prevention	Reduce incidence	Is toxicity/cost acceptable?
Treatment		
– curative	Eliminate disease	Is toxicity/cost acceptable?
– life-extending	Prolong life	Is added time of value?
– palliative	Improve QoL	Toxicity vs symptom burden

TOXICITY AND QoL: WE KNOW THAT ...

... there is an association between toxicity and QoL^{1,2}

However, several factors influence QoL^{3,4}

efficacy relieving disease symptoms

tolerability of treatment-related AEs

management of treatment-related AEs

low grade toxicities and long treatment duration

QoL: VALIDATED INSTRUMENTS IN RCC (1)

Specificity	Instrument	No. of items	Description
General	EuroQol EQ-5D Index EQ-5D VAS	6	Contains 5 domains: mobility, self-care, social relationships, pain, and mood
	SF-36	36	Contains 8 dimensions across physical and mental health
Cancer-specific	EORTC QLQ-C30	30	Contains 5 functional scales , 3 symptom scales, a global health scale, an HRQOL scale, and single items to assess common cancer symptoms and financial impact
	FACIT FACT-G	27	Physical well-being, social/family well-being, emotional well-being, functional wellbeing
	FACIT-Fatigue	13	A fatigue subscale containing 13 items
	FACT-BRM	40	For patients receiving BRMs; physical and mental subscales containing 14 questions + 27-item FACT-G v.4

BRM: Biological response modifier; DRS: Disease-related symptoms; EORTC: European Organization for Research and Treatment of Cancer; FACIT: Functional Assessment of Chronic Illness Therapy; FACT-G: Functional Assessment of Cancer Therapy-General; FKSI: FACT-Kidney Cancer Symptom Index; HRQOL: Health-related quality of life; QLQ, quality-of-life questionnaire; SF-36: Short Form-36; VAS: Visual analog scale.

QoL: VALIDATED INSTRUMENTS IN RCC (2)

Specificity	Instrument	No. of items	Description
Kidney cancer-specific	FKSI		
	FKSI-DRS	9	Concise list of symptoms caused by RCC
	FKSI-10	10	List of symptoms and concerns of people with RCC
	FKSI-15	15	List of symptoms and concerns of people with RCC
	FKSI-19	19	Revised list of symptoms and concerns of people with RCC (FKSI-15 + 4 additional items)
	RCC Symptom Index	3	List of signs and symptoms of RCC
Treatment-specific	SQLQ	14	Hand/foot soreness and mouth/throat soreness Worst soreness over the past 4 weeks Limitations over the past 4 weeks due to worst soreness Work days missed due to health over the past 4 weeks

BRM: Biological response modifier; DRS: Disease-related symptoms; EORTC: European Organization for Research and Treatment of Cancer; FACIT: Functional Assessment of Chronic Illness Therapy; FACT-G: Functional Assessment of Cancer Therapy-General; FKSI: FACT-Kidney Cancer Symptom Index; HRQOL: Health-related quality of life; QLQ, quality-of-life questionnaire; SF-36: Short Form-36; VAS: Visual analog scale.

QoL: VALIDATED INSTRUMENTS IN RCC (3)

Supplementary Quality of Life Questions

Mouth and Throat Soreness

1. In the past 4 weeks, what was your **WORST** mouth and throat soreness? (circle only one number)

None - I never had any mouth and throat soreness	0
A little bit of mouth and throat soreness	
Quite a lot of mouth and throat soreness	
Severe mouth and throat soreness	

2. In the past 4 weeks, how much did your **WORST** mouth and throat soreness limit you in each of the following activities?

(circle only one number)

	Not Limited	Limited A Little	Limited A Lot	Unable To Do
A) Swallowing	0	1	2	3
B) Drinking	0	1	2	3
C) Eating	0	1	2	3
D) Talking	0	1	2	3
E) Sleeping	0	1	2	3

Hand and Foot Soreness

3. In the past 4 weeks, what was your **WORST** hand soreness?

(Circle only one number)

None - I never had any hand soreness	0
A little bit of hand soreness	1
Quite a lot of hand soreness	2
Severe hand soreness	3

4. In the past 4 weeks, what was your **WORST** foot soreness?

(Circle only one number)

None - I never had any foot soreness	0
A little bit of foot soreness	1
Quite a lot of foot soreness	2
Severe foot soreness	3

How much did your **WORST** foot soreness limit you in each of the following activities?

(circle only one number per row)

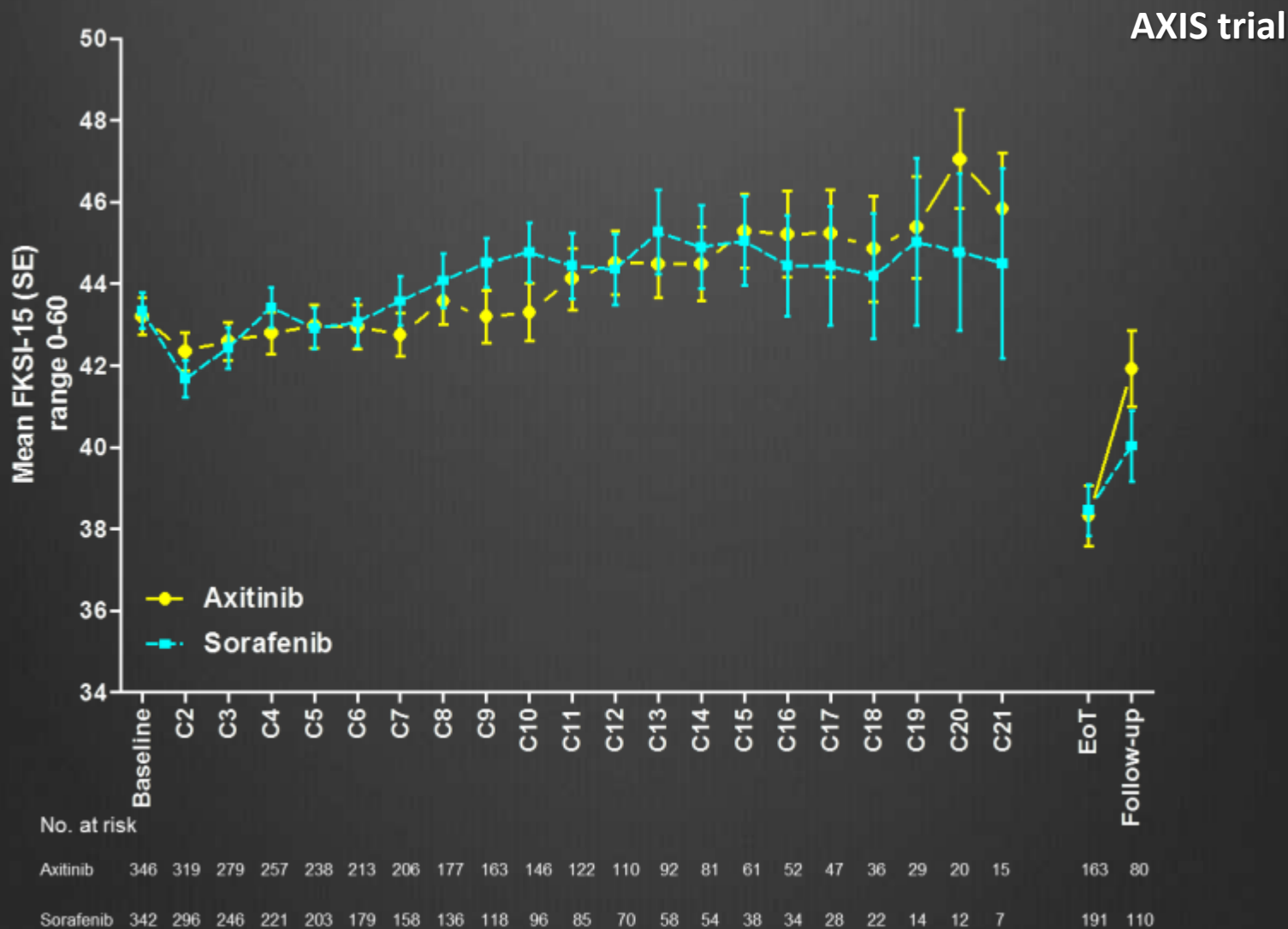
	Limited A Little	Limited A Lot	Unable To Do
A) Walking	1	2	3
B) Running	1	2	3
C) Climbing	1	2	3
D) Staircase	1	2	3
E) Jogging	1	2	3

How many days did you have to take off from work in the past 4 weeks? (circle only one number)
(Do not include days you were off for other reasons)
(Provide a box provided if not applicable)

0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136	137	138	139	140	141	142	143	144	145	146	147	148	149	150	151	152	153	154	155	156	157	158	159	160	161	162	163	164	165	166	167	168	169	170	171	172	173	174	175	176	177	178	179	180	181	182	183	184	185	186	187	188	189	190	191	192	193	194	195	196	197	198	199	200	201	202	203	204	205	206	207	208	209	210	211	212	213	214	215	216	217	218	219	220	221	222	223	224	225	226	227	228	229	230	231	232	233	234	235	236	237	238	239	240	241	242	243	244	245	246	247	248	249	250	251	252	253	254	255	256	257	258	259	260	261	262	263	264	265	266	267	268	269	270	271	272	273	274	275	276	277	278	279	280	281	282	283	284	285	286	287	288	289	290	291	292	293	294	295	296	297	298	299	300	301	302	303	304	305	306	307	308	309	310	311	312	313	314	315	316	317	318	319	320	321	322	323	324	325	326	327	328	329	330	331	332	333	334	335	336	337	338	339	340	341	342	343	344	345	346	347	348	349	350	351	352	353	354	355	356	357	358	359	360	361	362	363	364	365	366	367	368	369	370	371	372	373	374	375	376	377	378	379	380	381	382	383	384	385	386	387	388	389	390	391	392	393	394	395	396	397	398	399	400	401	402	403	404	405	406	407	408	409	410	411	412	413	414	415	416	417	418	419	420	421	422	423	424	425	426	427	428	429	430	431	432	433	434	435	436	437	438	439	440	441	442	443	444	445	446	447	448	449	450	451	452	453	454	455	456	457	458	459	460	461	462	463	464	465	466	467	468	469	470	471	472	473	474	475	476	477	478	479	480	481	482	483	484	485	486	487	488	489	490	491	492	493	494	495	496	497	498	499	500	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525	526	527	528	529	530	531	532	533	534	535	536	537	538	539	540	541	542	543	544	545	546	547	548	549	550	551	552	553	554	555	556	557	558	559	560	561	562	563	564	565	566	567	568	569	570	571	572	573	574	575	576	577	578	579	580	581	582	583	584	585	586	587	588	589	590	591	592	593	594	595	596	597	598	599	600	601	602	603	604	605	606	607	608	609	610	611	612	613	614	615	616	617	618	619	620	621	622	623	624	625	626	627	628	629	630	631	632	633	634	635	636	637	638	639	640	641	642	643	644	645	646	647	648	649	650	651	652	653	654	655	656	657	658	659	660	661	662	663	664	665	666	667	668	669	670	671	672	673	674	675	676	677	678	679	680	681	682	683	684	685	686	687	688	689	690	691	692	693	694	695	696	697	698	699	700	701	702	703	704	705	706	707	708	709	710	711	712	713	714	715	716	717	718	719	720	721	722	723	724	725	726	727	728	729	730	731	732	733	734	735	736	737	738	739	740	741	742	743	744	745	746	747	748	749	750	751	752	753	754	755	756	757	758	759	760	761	762	763	764	765	766	767	768	769	770	771	772	773	774	775	776	777	778	779	780	781	782	783	784	785	786	787	788	789	790	791	792	793	794	795	796	797	798	799	800	801	802	803	804	805	806	807	808	809	810	811	812	813	814	815	816	817	818	819	820	821	822	823	824	825	826	827	828	829	830	831	832	833	834	835	836	837	838	839	840	841	842	843	844	845	846	847	848	849	850	851	852	853	854	855	856	857	858	859	860	861	862	863	864	865	866	867	868	869	870	871	872	873	874	875	876	877	878	879	880	881	882	883	884	885	886	887	888	889	890	891	892	893	894	895	896	897	898	899	900	901	902	903	904	905	906	907	908	909	910	911	912	913	914	915	916	917	918	919	920	921	922	923	924	925	926	927	928	929	930	931	932	933	934	935	936	937	938	939	940	941	942	943	944	945	946	947	948	949	950	951	952	953	954	955	956	957	958	959	960	961	962	963	964	965	966	967	968	969	970	971	972	973	974	975	976	977	978	979	980	981	982	983	984	985	986	987	988	989	990	991	992	993	994	995	996	997	998	999	1000
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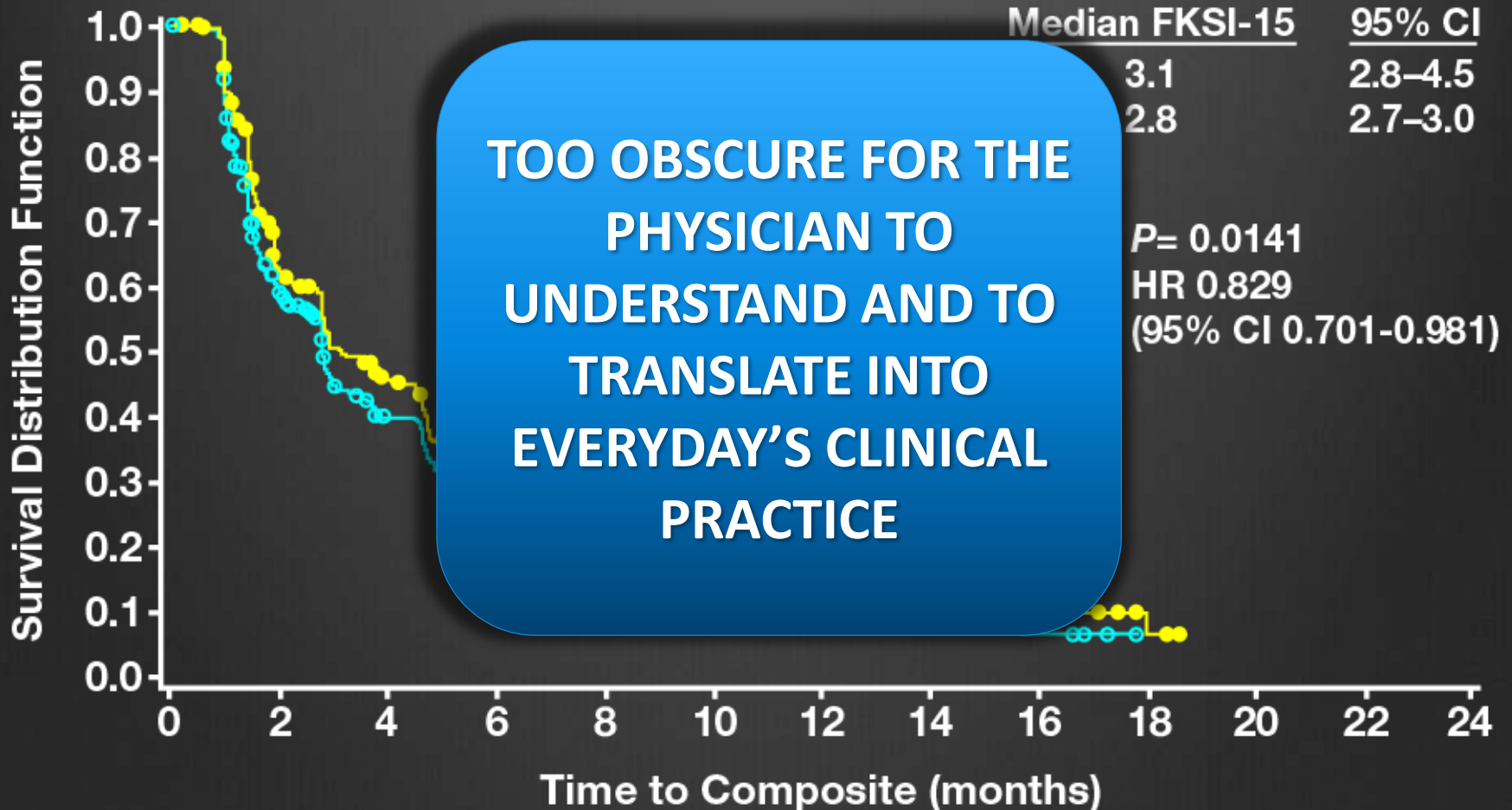
TOO COMPLICATED
FOR THE PATIENTS
TO FILL

QoL FINDINGS IN mRCC TRIALS: FKSI-15



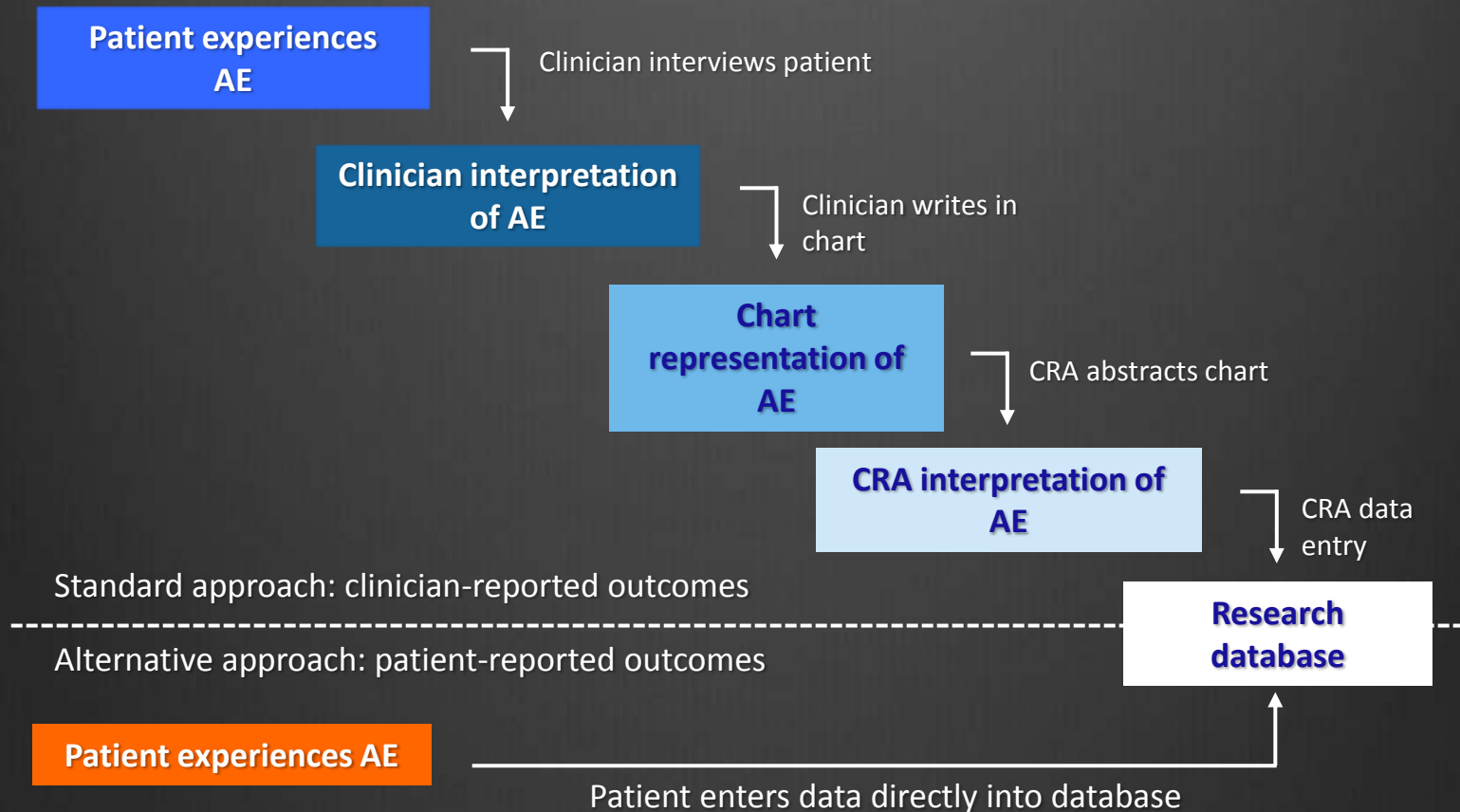
QoL FINDINGS IN mRCC TRIALS: TIME TO DETERIORATION OF FKSI-15

AXIS trial



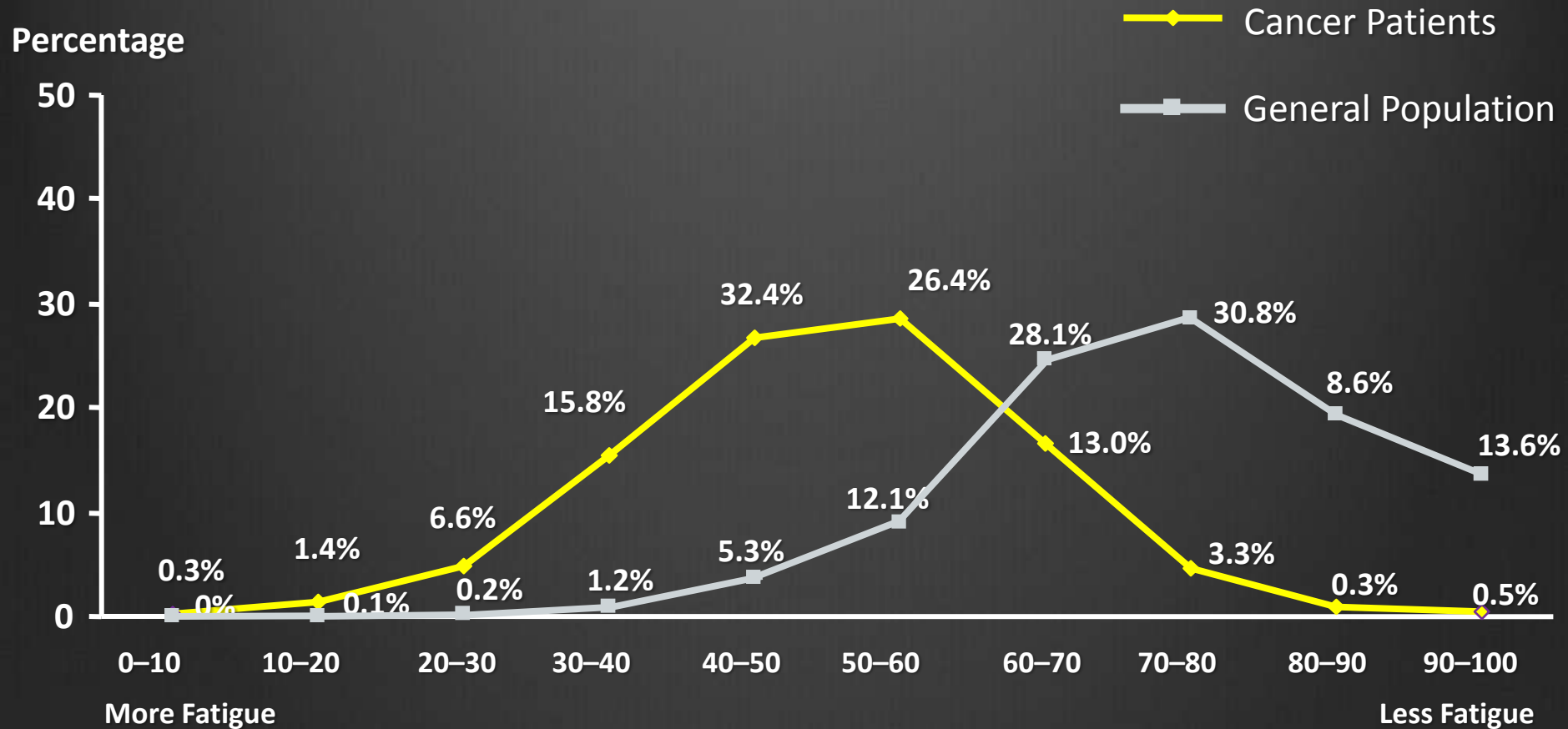
AEs: MEDIATED VS DIRECT TRANSMISSION

Clinician vs. patient-reported outcomes (Adapted from¹)



CRA: Clinical research associate

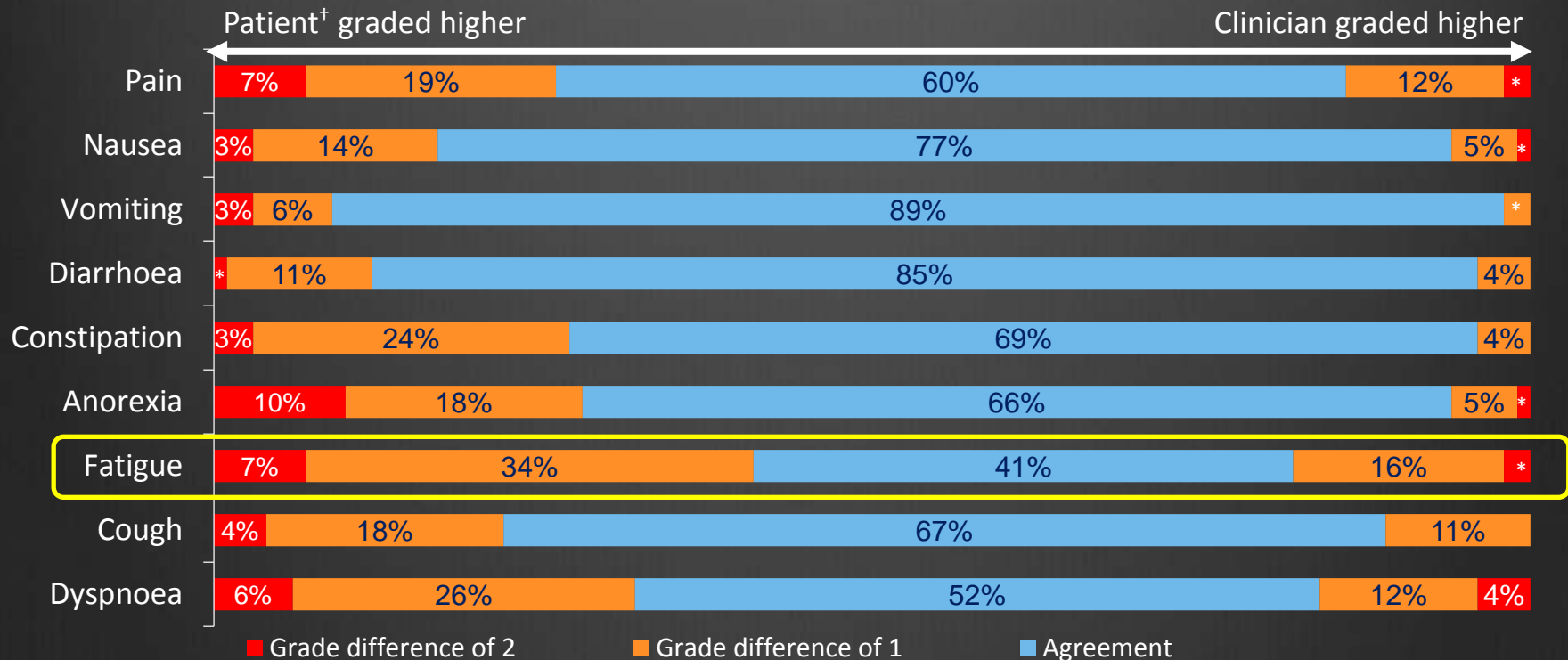
FATIGUE IN CANCER VS GENERAL POPULATION



*There was no general population subject in the first group (0-9.9) and only one in the second group (10-19.9)

Cella D, et al, Cancer, 2001

UNDER REPORTING OF LOW-GRADE TOXICITIES



* ≤2% † Advanced non-small lung cancer patients treated with platinum-based chemotherapy (n=400)

THE EXAMPLE OF FATIGUE IN CANCER PATIENTS

Fatigue in cancer patients is often under-reported, under-diagnosed and under-managed¹

Symptoms that characterise fatigue may not be recorded as fatigue per se²

e.g. feelings of tiredness, exhaustion, depression, feeling unwell, loss of motivation, and reduced capacity for mental work

Patients may report toxicities differently depending on their lifestyle/occupation prior to treatment²

Grade 2 fatigue, defined as difficulties in carrying out daily activities, in retired vs. employed patients

PATIENT PREFERENCE IN ONCOLOGY

Patient-Reported Outcomes (PROs), such as preference, are an increasingly important outcome of cancer therapy, particularly in patients receiving treatment for metastatic disease¹

Increasing emphasis on assessment of QoL, convenience and patient preference, particularly relevant to tolerability of agents²

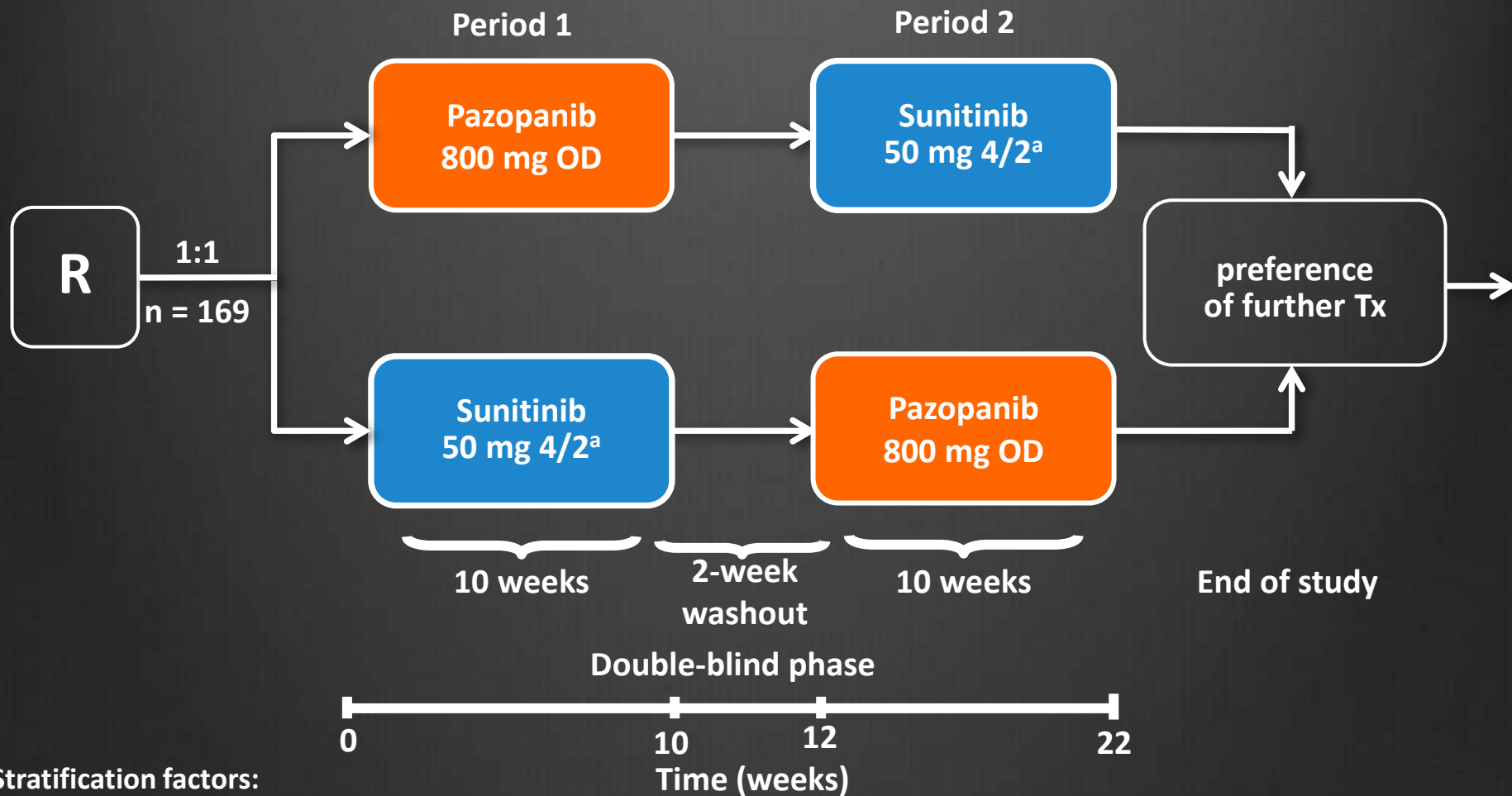
Provides insight into how meaningful differences in key symptomatic toxicities are by assessing the patients preference for one agent over another

Novel endpoint in mRCC (PISCES study)

PATIENT PREFERENCE IN ONCOLOGY: IS IT SOMETHING REALLY NEW?

Year	Trial	Therapy area
2002	Comparison of oral and intravenous treatment regimens ¹	Colorectal cancer
2004	Comparison of patient preference for aromatase inhibitors ²	Breast cancer
2005	Patient preference for once-monthly vs. once-weekly bisphosphonate treatment ³	Prostate cancer
2006	Patient preference for oral vs. intravenous treatment regimens ⁴	Colorectal cancer
2012	Patient preference study of TKIs as first-line therapy ⁵	Renal cell carcinoma

THE PISCES STUDY IN mRCC



Stratification factors:

- ECOG PS (0 vs 1)
- metastatic sites (1 vs ≥ 2)

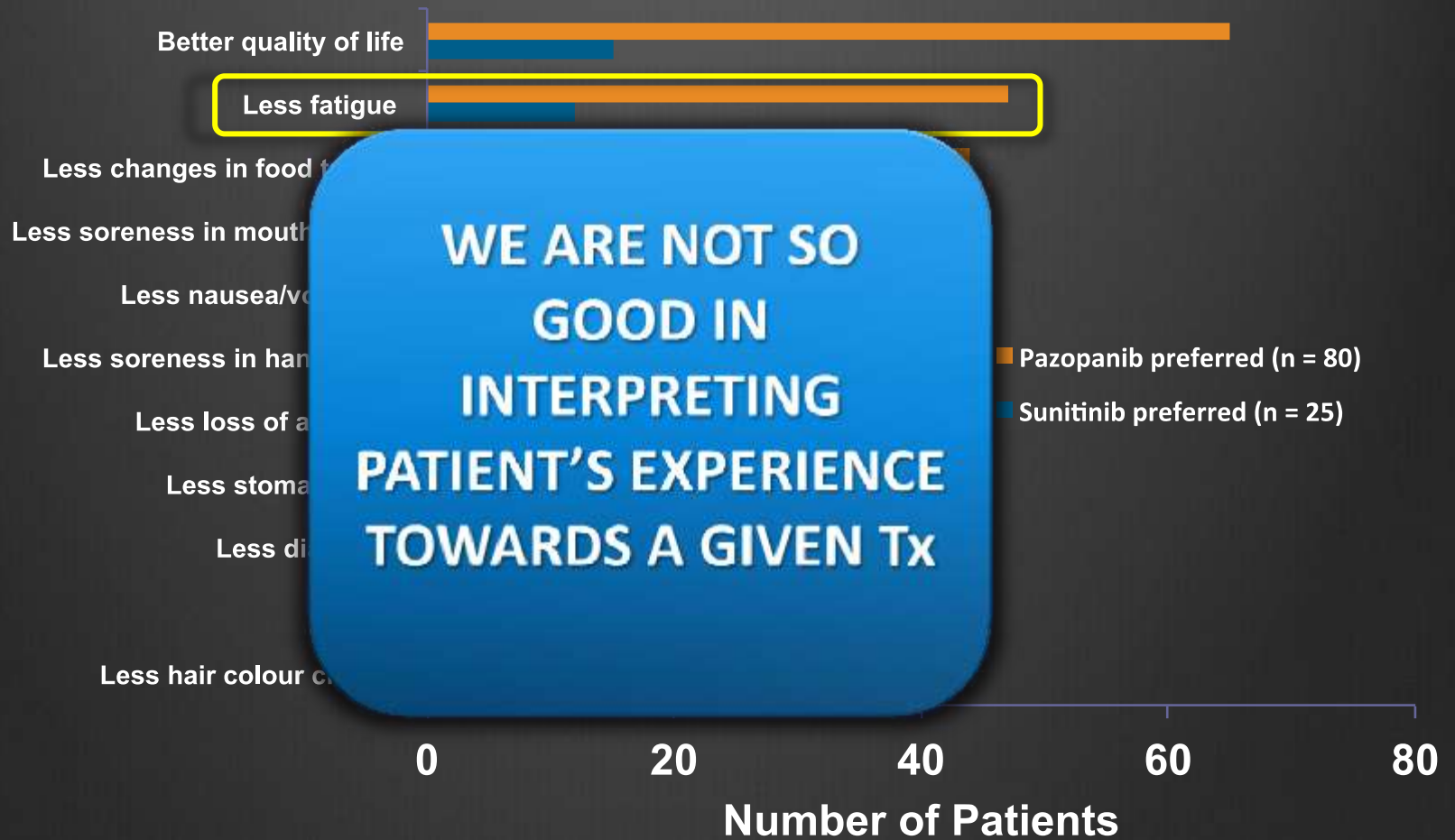
^a4 weeks on treatment → 2 weeks matching placebo → 4 weeks on treatment

FATIGUE IN THE THE PISCES STUDY (1)

Tx-related AEs, as reported by Physicians

Adverse Event	Sunitinib (n = 148)		Pazopanib (n = 153)	
	All Grades	Grade 3/4	All Grades	Grade 3/4
Any AE, %	> 99	47	97	38
Diarrhea	32	< 1	42	< 1
Nausea	30	0	33	< 1
Decreased appetite	19	<1	20	0
Vomiting	16	< 1	14	< 1
Dyspepsia	16	0	10	0
Dysgeusia	27	0	16	0
Mucositis	22	1	16	0
Stomatitis	16	2	5	< 1
Hand-foot syndrome	26	4	16	1
Hair color changes	14	0	17	0
Hypertension	26	9	23	8
Fatigue	30	5	29	4

FATIGUE IN THE THE PISCES STUDY (2)



IF WE DO REALLY PUT PATIENT FIRST ...

... then we do badly need



National Cancer Institute
U.S. National Institutes of Health | www.cancer.gov



National Cancer Institute

Division of Cancer Control and Population Sciences

8015 CENTER FOR DRUG EVALUATION, BETHESDA, MD 20892

Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) Applied Research Program

Background

The NCI Common Terminology Criteria for Adverse Events (CTCAE) (<http://www.commondataelements.org/ctcae/>) is a regulatory standard developed "downstream" of clinical research for use to classify risks to and outcomes in assessing and documenting an array of adverse events. While commonly employed in oncology, the AE is an unrefined tool, including an optional toxicity grading system, or (where required) associated with the use of a medical treatment or intervention that may or may not be considered related to the medical treatment or intervention under investigation. The AE may be either subjective or objective.

An AE is a term that is a unique representation of a specific event used for medical assessment and chronic analysis of treatment efficacy and toxicity. Each AE is typically graded on a scale of 1 (mild to 3 (severe) (WHO) or 1 (mild) to 4 (severe) (CTCAE), but it is not meant for acute AE, such as high risk or life-threatening. The grading requirements for AEs are generally patient-specific and may be unique to that study. That is, the individual patient's AE is to be assessed as a unique observation. The success of the patient's and/or clinical signs, symptoms, and laboratory results obtained as part of medical care of patients. The CTCAE is maintained by the NCI's Cancer Therapy Evaluation Program (CTEP). The CTCAE is updated as it evolves.

There is growing awareness that patient-reported outcomes directly from patients using patient-reported outcomes (PRO) tools can measure the accuracy and efficacy of symptomatic AE data directly. This is based on findings from multiple studies¹⁻³ demonstrating that patients can detect symptomatic function (e.g., fatigue, pain, and severity of common adverse events) more accurately in a study of many with prostate cancer treated with a Prostate Cancer Therapy Evaluation Program (CTEP) than the physician. The physician's assessment was found to be less accurate in assessing common symptomatic adverse events.

In the field of pain management, it has only been recognized that only the patient can accurately

report the onset, severity, and duration of pain and its impact on function. This principle applies to other symptoms, such as fatigue, weight loss, and loss of appetite (or other) which can be found in the CTCAE. The effectiveness of a PRO component to the CTCAE are discussed in an article by Tross et al.⁴

Overview of the PRO-CTCAE

The NCI Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) system parallels a user-based platform to collect patient reports of symptoms that are exacerbating with ongoing treatment, for the purpose of enhancing adverse event (AE) reporting.

<http://www.commondataelements.org/ctcae/>

To date, 31 symptoms of the PRO-CTCAE system have been included on a template for patient reporting. These symptoms have been categorized by organ system (e.g., CTCAE term "muscle weakness" [5007] [muscle]).

For symptoms such as fatigue and pain, the PRO-CTCAE system allows patients to distinguish about symptom frequency, severity, and duration with usual activities. For other symptoms (e.g., hair), questions focus on the presence or absence of the condition. There being no standard template, the PRO-CTCAE system provides an interface to patients, investigators, and clinicians at a secure web-based platform. This tool is a computerized tool to collect data (obtained from National Cancer Center (NCC) data investigators) from patients.

Objectives and Next Steps

The overall goal of the PRO-CTCAE initiative is to employ patient-reported methods to create a system for patient self-reporting of adverse symptoms in cancer that is easy to access and user-generated only, using the PRO-CTCAE system. The system is designed to be compatible with existing adverse event reporting systems, in that it will use systems that assess different attributes (e.g.,

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precision, frequency, severity, interference, or if symptoms that are important to both the CTCAE system and the Common Terminology Criteria for Adverse Events (CTCAE) system. The PRO-CTCAE system allows patients to report symptoms that are exacerbating with ongoing treatment, for the purpose of enhancing adverse event (AE) reporting.

References

1. Burstein HA, Aronson NE. The role of patient self-reports and standardized queries in evaluating the quality of life of patients with chronic disease. *A review.* *J Clin Epidemiol.* 1990;43:743-753.
2. Cohen MH, Lasker JF, Hershman JR, et al. Differences in oncology and patient assessments of health-related quality of life in men with prostate cancer. Results of the Symptom Burden Study. *J Clin Oncol.* 1997;15:1880-1888.
3. Zimmerman SA, Shattuck VL, Stubbins R, et al. Correlation of patient and caregiver ratings of cancer pain. *J Pain Symptom Manage.* 1991;8:33-47.
4. Yipereck NL, Brantner M, Olin DS, et al. Patient, caregiver, and oncologist perceptions of cancer-related fatigue: Results of a multi-institutional survey. *The Fatigue Coalition.* Sanofi-Schering Plough; 2001:34-42.
5. Fennema-Notestane C, Hershman JR, Hershman JR, et al. A brief, low-burden, self-reporting tool for identifying and assessing adverse events. *J Clin Oncol.* 2006;24:1480-1486.
6. Cohen SB, Dorevitz S, Aguirre S, & Cohen AJ. Patient-reported adverse event-related outcomes in oncology: a review. *Health Affairs (Millwood)* 2006;25:1047-1050.
7. Blaskin R, Hershman A, Hershman J, et al. A. Cella A, Hsu M, Zou H, Schrag D. Patient versus clinician symptom reporting using the National Cancer Institute Common Terminology Criteria for Adverse Events: Results of a multicenter-based study. *Lancet Oncology.* 2008;9:823-828.
8. Tross A, Carver AC, Selzer A, & Bause E. Patient-reported outcomes and the evolution of adverse event reporting in oncology. *J Clin Oncol.* 2007;25:1213-1218.
9. Bauer DR. Small patient-reported outcomes as transition for needs-reporting in cancer clinical trials? *J Clin Oncol.* 2007;25:3348-3347.
10. Bause E, Sanchez A, Burt A, Dunn A, Kim MS, Metz D, Page R, Sankaranarayanan J, Proctor R, Fisher H, Williams H, Sankaranarayanan J. Small patient-reported outcomes in patients receiving chemotherapy. *J Clin Oncol.* 2007;25:3374-3376.
11. Bause E, Kim MS, Hwang D, Burt A, Burt A, Proctor R, Sanchez A, Burt A, Kim MS, Sankaranarayanan J. Small patient-reported outcomes in patients receiving chemotherapy. *J Clin Oncol.* 2007;25:3374-3376.

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CONCLUSIONS

Cancer therapies have traditionally been evaluated using efficacy (objective responses and/or survival) and toxicity (AEs according to CTC) criteria

CTC may not be the most appropriate measure for assessing the tolerability of targeted therapies^{1,2}

Evaluation of QoL is often too complicated and its translation into everyday's clinical practice difficult

Traditional endpoints may not truly reflect the patient experience

Patient-reported outcomes are becoming increasingly important in the determination of overall treatment benefit³

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THANK YOU VERY MUCH
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