Les PS supérieurs à 1

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Liens d’intérêt

- Aucun lien d’intérêt à déclarer en relation avec cette présentation

Plan du cours

1. Que signifie indice de performance (« performance status »)?
2. Echelles et reproductibilité de la mesure
3. L'indice de performance: rôle pronostique
4. Prise en charge des patients avec un indice de performance altéré dans les CBNPC
    1. Traitements à visée curative
    2. Chimiothérapie
    3. Traitements ciblés
    4. Immunothérapie

Que signifie indice de performance?

- Mesure de l'état général du patient et des besoins en soins médicaux
- Permet de décrire les capacités fonctionnelles et physiques
- Pas restreint à une description des co-morbidités (ex. échelle de Charlson)

Echelles disponibles

Karnofsky

- Echelle de 0-100

Cancer 1948,1,634-656

TABLE 1

PERFORMANCE STATUS

Definition	*%*	*Criteria*
Able to carry on normal activity and to work. No special care is needed.	100	Normal; no complaints; no evidence of disease.
	90	Able to carry on normal activity; minor signs or symptoms of disease.
	80	Normal activity with effort; some signs or symptoms of disease.
Unable to work. Able to live at home, care for most personal needs. A varying amount of assistance is needed.	70	Cares for self. Unable to carry on normal activity or to do active work.
	60	Requires occasional assistance, but is able to care for most of his needs.
	50	Requires considerable assistance and frequent medical care.
Unable to care for self. Requires equivalent of institutional or hospital care. Disease may be progressing rapidly.	40	Disabled; requires special care and assistance.
	30	Severely disabled; hospitalization is indicated although death not imminent.
	20	Very sick; hospitalization necessary; active supportive treatment necessary.
	10	Moribund; fatal processes progressing rapidly.
	0	Dead.

ECOG/Zubrod/OMS

- Echelle de 0-5

Am J Clin Oncol 1982, 5, 649-52

TABLE 2

Performance Status

Grade	ECOG	Karnofsky	Analgesic Code
0	Fully active, able to carry on all pre-disease performance without restriction	100—Normal, no complaints; no evidence of disease 90—Able to carry on normal activity; minor signs or symptoms of disease	1—None 2—Mild, e.g., aspirin 3—Occasional oral narcotics 4—Regular oral narcotics
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work	80—Normal actiity with effort, some signs or symptoms of disease 70—Cares for self but unable to carry on normal activity or to do active work	5—Parenteral narcotics 6—Uncontrollable
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours	60—Requires occasional assistance but is able to care for most of personal needs 50—Requires considerable assistance and frequent medical care	
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours	40—Disabled; requires special care and assistance 30—Severely disabled; hospitalization is indicated although death not imminent	
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair	20—Very ill; hospitalization and active supportive care necessary 10—Moribund	
5	Dead	0—Dead	

Lansky

- Echelle de 0-100
- Pédiatrie

Cancer 1987, 60, 1651-6

Echelle ECOG

	description
0	Asymptomatique (activité normale : aucune restriction à poursuivre les activités précédant l'affection).
1	Symptomatique (gêné pour les activités physiques soutenues mais capable de se déplacer seul et d'assurer un travail léger ou sédentaire, par exemple un travail de bureau ou le ménage).
2	Symptomatique, alité moins de 50 % de la journée (capable de se déplacer seul et de s'occuper de soi-même mais incapable de produire un travail léger).
3	Symptomatique, alité plus de 50 % de la journée, sans y être confiné (capable de prendre soin de soi-même de manière limitée, alité ou confiné au fauteuil plus de 50 % de la journée).
4	Confiné au lit (totalement dépendant, incapable de prendre soin de soi-même, confiné au lit ou au fauteuil).
5	Mort.

Adapté de J Chron Dis 1960,11,7-33

Echelle de Karnofsky

		Définition
Capable d'exercer une activité normale Aucun soin particulier n'est nécessaire	100	Normal; Aucune plainte, aucune preuve de maladie
	90	Capable d'exercer une activité normale; signes ou symptômes mineurs de la maladie
	80	Activité normale avec effort; certains signes ou symptômes de la maladie
Incapable de travailler, capable de vivre à la maison, s'occuper de la plupart des besoins personnels; une quantité variable d'assistance est nécessaire	70	Prendre soin de soi, incapable d'exercer une activité normale ou faire un travail actif
	60	Nécessite une assistance occasionnelle, mais peut prendre soin de la plupart de ses besoins
	50	Nécessite une aide considérable et des soins médicaux fréquents
Incapable de s'occuper de soi-même; nécessite des soins institutionnels ou hospitaliers équivalents; la maladie peut progresser rapidement	40	handicapé; nécessite soins spécialisés et une assistance
	30	Sévèrement handicapé; l'hospitalisation est indiquée, bien que la mort ne soit pas imminente
	20	Très malade; hospitalisation nécessaire, un traitement de soutien actif est nécessaire
	10	Moribond; processus fatal progressant rapidement
	0	Décès

Adapté de Cancer 1948,1,634-656

Peut-on comparer les échelles?

Eur J Cancer, Vol. 28A, No. 8/9, pp. 1328–1330, 1992.
Printed in Great Britain

0964–1947/92 $5.00 + 0.00

Can Karnofsky Performance Status be Transformed to the Eastern Cooperative Oncology Group Scoring Scale and Vice Versa?

Eugenia Verger, Manel Salamero and Carlos Conill

Table 2. Equivalences between ECOG and KPS

KPS	Expected ECOG: Point estimation	66% confidence interval	95% confidence interval
100	0	0–1	0–1
90	1	0–1	0–2
80	1	1–2	0–2
70	2	1–2	1–3
60	2	2–3	1–3
50	3	2–3	2–4
40	3	3–4	2–4
30	4	3–4	3–4
20	4	4	3–4

KPS = Karnofsky performance status, ECOG = Eastern Cooperative Oncology Group.

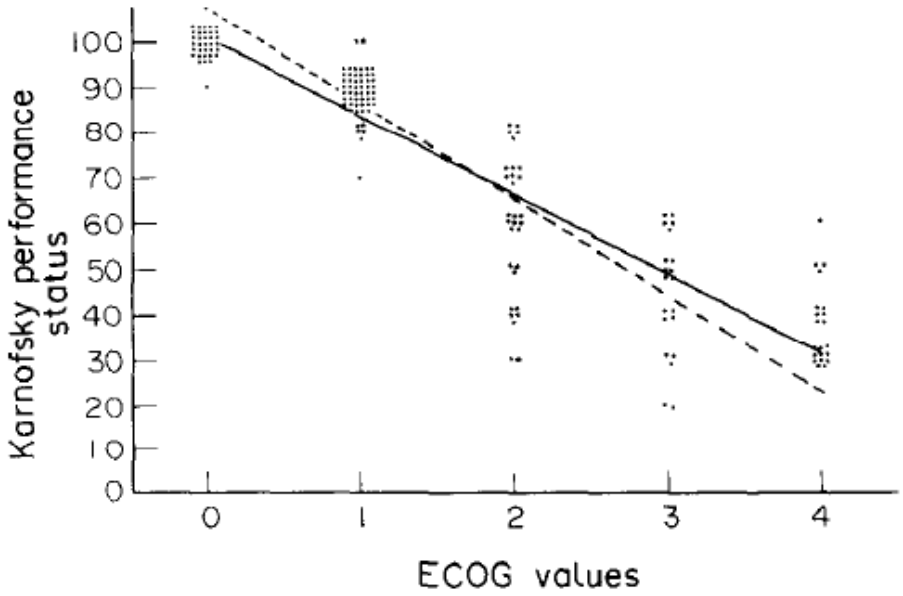


Fig. 1. Plot of Karnofsky performance status (KPS) and Eastern Cooperative Oncology Group (ECOG) values for each patient (n = 150) and regression lines for expected KPS and ECOG scores. _ Expected KPS; ---- expected ECOG.

Karnofsky and ECOG Performance Status Scoring in Lung Cancer: A Prospective, Longitudinal Study of 536 Patients From a Single Institution

Eur J Cancer 1996: 1135-41

G. Buccheri, D. Ferrigno and M. Tamburini

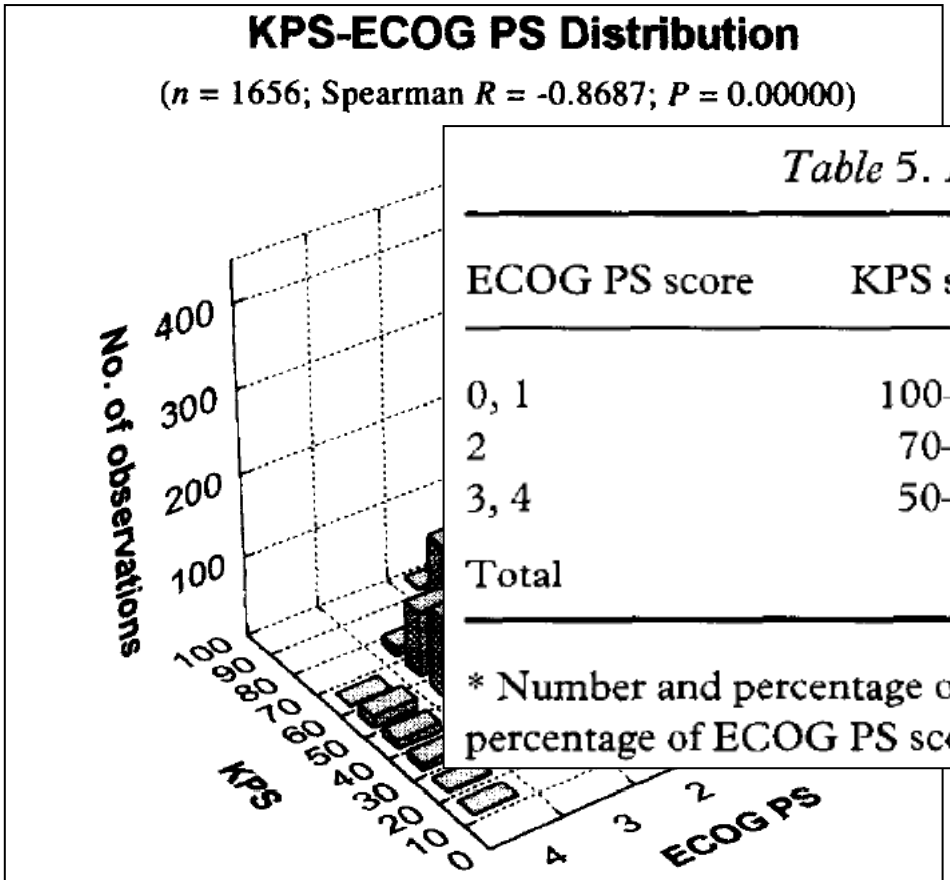


Figure 1. Distribution of Karnofsky's index and Eastern Cooperative Oncology Group performance status scoring (in all, 1656 paired assignments).

Table 5. Proposed ECOG PS–KPS conversion table

ECOG PS score	KPS score	Hits (%, 95% CI)*	Hits (%, 95% CI)†
0, 1	100–80	658/732 (90, 84–96%)	658/739 (89, 82–96%)
2	70–60	589/686 (86, 78–93%)	589/755 (78, 69–87%)
3, 4	50–10	146/238 (61, 51–72%)	146/162 (90, 84–96%)
Total		1393/1656 (84, 76–92%)	

* Number and percentage of KPS scores correctly predicted by ECOG PS. † Number and percentage of ECOG PS scores correctly predicted by KPS.

Reproductibilité de l'évaluation de l'indice de performance

Echelles et reproductibilité de la mesure

Table 1 Challenges in Evaluating Performance Status

Variety of scales	Karnofsky, Eastern Cooperative Oncology Group, World Health Organization
Influenced by cancer-related factors	Anorexia, fatigue, weight loss, pain
Influenced by other factors	Comorbidities, medications, age, psychosocial issues
Influenced by assessor	Physician, healthcare provider, patient, family member

Semin Oncol 31(suppl 11):3-7 © 2004

Evaluation of Patients with Advanced Cancer Using the Karnofsky Performance Status

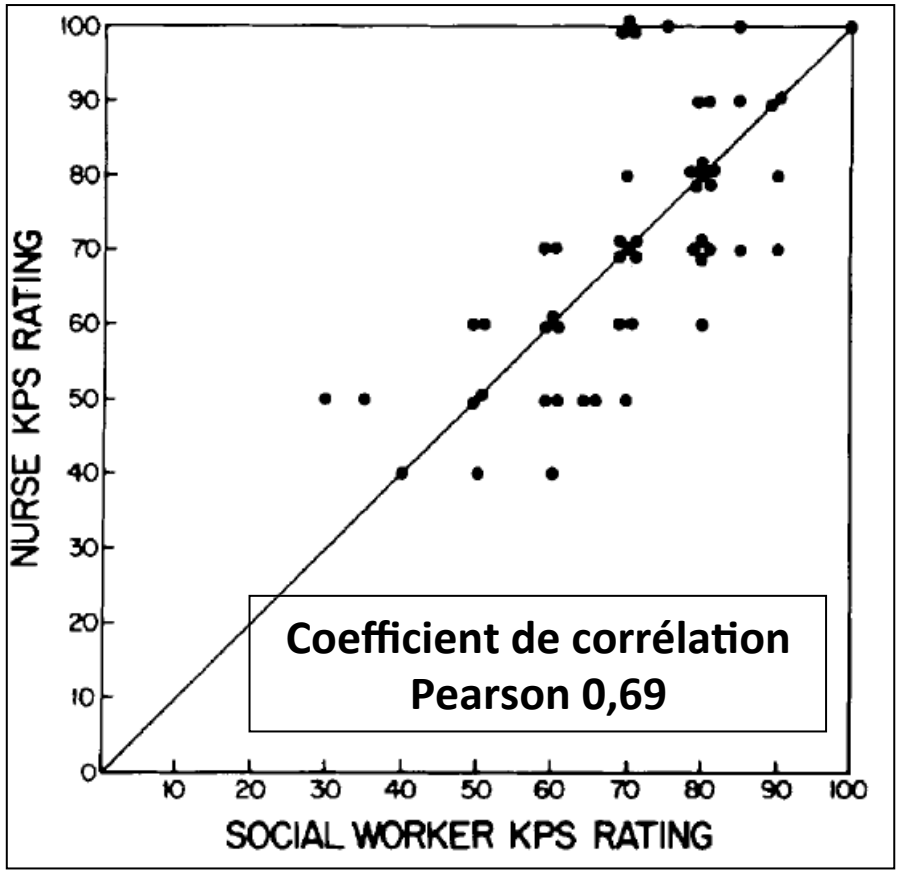


TABLE 4. Correlations (Pearson) between KPS and Other Variables ($45 \leq N \leq 49$)

Variable	Correlation with KPS*
1. Desire for food	.40 ($P < .002$)
2. Sleep	.24 ($P < .050$)
3. Difficulty with balance	.61 ($P < .001$)
4. Difficulty with stairs	.63 ($P < .001$)
5. Pain level	−.37 ($P < .006$)
6. Happiness	.12 (not significant)
7. Positive affect	.54 ($P < .001$)
8. Negative affect	−.09 (not significant)
9. Satisfaction with life	.36 ($P < .007$)
10. Overall condition	.39 ($P < .004$)

* All variables except pain level and negative affect are coded such that a higher score represents a higher level of functioning.

Meilleure corrélation pour l'évaluation paramètres physiques que psychologiques

Cancer 45:2220–2224, 1980.

Performance status assessment in cancer patients. An inter-observer variability study

Table IV Kappa statistics for assessment of ECOG performance status among 100 cancer patients by three observers

ECOG score	*Kappa*	*95% confidence limits*
0	0.55	(0.44–0.67)
1	0.48	(0.37–0.60)
2	0.31	(0.19–0.42)
3	0.43	(0.32–0.55)
4	0.33	(0.22–0.45)

Overall Kappa 0.44 (95% confidence limits 0.38–0.51).

3 médecins oncologues

Table V Simplified performance status assessment among 100 cancer patients by three observers

ECOG score	*Agreement (proportion of cases with agreement among all three observers)*
0–2	0.92
3–4	0.82

Br. J. Cancer (1993), **67**, 773–775

Intra and interobserver variability in cancer patients' performance status assessed according to Karnofsky and ECOG scales

Table 2. Interobserver agreement of Karnofsky performance status.

Observer A \ Observer B	20	30	40	50	60	70	80	90	100	Total
20										0
30	1	3	3							7
40		1	3	1						5
50		1	1	11						13
60				5	3	6				14
70				1	1	25	17	1		45
80						3	42	3		48
90							12	12	5	29
100							6	12	30	48
Total	1	5	7	18	4	34	77	28	35	209

Table 3. Interobserver agreement of ECOG performance status.

Observer A \ Observer B	0	1	2	3	4	Total
0	49	25				74
1	2	69	3			74
2		9	17	2		28
3			3	16	2	21
4				1	11	12
Total	51	103	23	19	13	209

The interobserver correlation was very high and similar for KPS (K = 0.921) (Table 2) and EPS (K = 0.914)

Table 5. Intraobserver (A, B) agreement on Karnofsky and ECOG performance status evaluated by direct interview or by examining patient self-evaluation scales.

Observer*	Mean values (± S.D.)	Weighted K
Karnofsky		
A	77.99 (± 18.15)	
A1	75.26 (± 21.44)	0.851
A2	75.17 (± 21.60)	0.852
B	77.27 (± 17.51)	
B1	77.27 (± 20.04)	0.897
B2	76.75 (± 19.97)	0.871
ECOG		
A	1.15 (± 1.18)	
A1	0.94 (± 1.22)	0.870
A2	0.96 (± 1.22)	0.876
B	1.23 (± 1.11)	
B1	1.17 (± 1.24)	0.905
B2	1.20 (± 1.24)	0.896

Annals of Oncology 2: 437–439, 1991.

Prognostic value of performance status assessed by patients themselves, nurses, and oncologists in advanced non-small cell lung cancer

206 CBNPC
12 oncologues
45 infirmières

Table 3 Agreement in assessment of ECOG PS between patients and oncologists (n = 206)

Oncologist's score	Patient's score				
	0	1	2	3	4
0	17	22	0	0	0
1					
2					
3					
4					

Kappa 0.53 (95% CI 0.45–0.61)

Table 5 Prognostic value of ECOG PS graded by patients, nurses, and oncologists: results of analyses separately included in the Cox model

Variables	Multivariate-adjusted hazard ratios[a] (95% CI)		
	Patient-assessed PS	Nurse-assessed PS	Oncologist-assessed PS
PS Score			
0	reference	reference	reference
1	1.63 (0.97–2.83)	1.79 (1.07–3.12)	1.63 (1.04–2.64)
2	1.60 (0.89–2.93)	2.08 (1.06–4.13)	1.95 (1.00–3.79)
3	2.77 (1.46–5.33)	2.25 (1.15–4.49)	4.28 (2.23–8.10)
4	3.90 (1.81–8.25)	2.99 (1.18–7.16)	3.43 (1.61–7.07)
P-trend	< 0.001	0.018	< 0.001

Table
nurses

Nurse score	
0	
1	
2	
3	
4	

British Journal of Cancer (2001) **85**(11), 1634–1639

Performance status score: do patients and their oncologists agree?

Table 4 Performance status (PS) scores (NSCLC and SCLC) as assessed by patient (vertical axis) and oncologist (horizontal axis)

		ONCOLOGIST				
	Score	**0**	**1**	**2**	**3**	**4**
PATIENT	**0**	*10*	10	2	0	0
	1	10	*22*	8	2	0
	2	0	11	*11*	1	0
	3	0	2	3	*8*	0
	4	0	0	0	1	*0*

weighted κ score = 0.45 (0.33, 0.59

British Journal of Cancer (2003) 89, 1022–1027

Table 2 Survival by performance status (NSCLC and SCLC) assessed by (a) patient[a] and (b) oncologist[b]

Score	Median survival (months)	Cumulative survival (95% CI) at 1 year
(a) *Patient*		
0	12.9	52% (31, 73)
1	11.3	40% (25, 55)
2	6.5	17% (2, 33)
3–4	2.2	14% (0, 32)
(b) *Doctor*		
0	18.9	67% (44, 88)
1	8.2	41% (26, 57)
2	6.5	17% (2, 35)
3–4	2.1	17% (0, 38)

Should Patient-Rated Performance Status Affect Treatment Decisions in Advanced Lung Cancer?

TABLE 2. Patients' and Physicians' Agreement in Rating of PS

		MD-PS				
	Score	**0**	**1**	**2**	**3**	**4**	**Total**
Pt-PS							
	0	7	12				19
	1	5	30	5	1		41
	2	3	6	6			15
	3	3	11	11	7		32
	4		1		1		2
Total		18	60	22	9		109

kappa coefficient = 0.42

J Thorac Oncol. 2008;3: 1133–1136

L’indice de performance: rôle pronostique

The Impact of Additional Prognostic Factors on Survival and their Relationship with the Anatomical Extent of Disease Expressed by the 6th Edition of the TNM Classification of Malignant Tumors and the Proposals for the 7th Edition

TABLE 2. Multivariate Analysis of Prognostic Factors for Survival in NSCLC, Using General Characteristic Variables (Clinical TNM Stage as Proposed by IASLC Staging Project, Age, Gender, PS, Histological Cell Type)

Variable	*n*/*N* (%)	HR (95% CI)	*P*
Stage II	1531/12426 (12%)	1.80 (1.65, 1.97)	<0.001
Stage IIIA	2048/12426 (16%)	2.71 (2.49, 2.95)	<0.001
Stage IIIB/IV	7280/12426 (59%)	5.34 (4.95, 5.76)	<0.001
Age (continuous)	*N* = 12426	1.01 (1.00, 1.01)	<0.001
Squamous cell type	5304/12426 (43%)	0.93 (0.89, 0.97)	<0.001
Male gender	9764/12426 (79%)	1.17 (1.11, 1.23)	<0.001
PS 1 (vs.0)	6294/12426 (51%)	1.38 (1.32, 1.44)	<0.001
PS 2 (vs. 0)	1423/12426 (11%)	2.09 (1.95, 2.23)	<0.001
PS 3–4 (vs. 0)	579/12426 (5%)	3.48 (3.17, 3.83)	<0.001

Sculier et al, J Thorac Oncol 2008

COMORBIDITY AND KPS ARE INDEPENDENT PROGNOSTIC FACTORS IN STAGE I NON–SMALL-CELL LUNG CANCER

Table 2. Summary of univariate analysis of various prognostic factors on the surgical and RT groups and all patients

	Surgical group	RT group	Whole group
Histologic type (non-SCC vs. SCC)	0.007	NS	<0.001
Grade (well/mod vs. Poorly dif)	NS	NS	NS
cT stage (cT1 vs. cT2)	NS	NS	0.065
T size (CT) (<4 vs. ≥4 cm)	NS	NS	0.062
Age (<70 vs. ≥70 y)	NS	0.025	NS
Tobacco use (≤40 vs. >40 py)	0.047	0.039	<0.001
KPS (≥70 vs. <70)	0.002	0.021	<0.001
CIRS-G(4) [(−) vs. (+)]	0.001	0.018	<0.001
SI (≤2 vs. >2)	0.005	0.040	<0.001
Charlson score (≤2 vs. >2)	NS	0.018	0.004

Int. J. Radiation Oncology Biol. Phys., Vol. 52, No. 4, pp. 1047–1057, 2002

COMORBIDITY AND KARNOFKSY PERFORMANCE SCORE ARE INDEPENDENT PROGNOSTIC FACTORS IN STAGE III NON–SMALL-CELL LUNG CANCER: AN INSTITUTIONAL ANALYSIS OF PATIENTS TREATED ON FOUR RTOG STUDIES

"A multivariate analysis with clinical stage, KPS, and comorbidity (SI) showed that a KPS 70 (p = 0.028, relative risk 1.6, and 95% confidence interval 1.1–2.6) and SI of 2 (p < 0.0001, relative risk 2.6, 95% confidence interval 1.8–4) were independently associated with an inferior OS. »

Int. J. Radiation Oncology Biol. Phys., Vol. 54, No. 2, pp. 357–364, 2002

Pronostique aussi pour les stades loco-régionaux

Early mortality in lung cancer: French prospective multicentre observational study

Michel Grivaux[1*], Didier Debieuvre[2], Dominique Herman[3], Christine Lemonnier[4], Jean-Michel Marcos[5], Jacky Crequit[6], Sylvie Vuillermoz-Blas[7], Patricia Barre[8], Marie Saillour[9] and Francis Martin[10]

		Vital status at					
		1 month			3 months		
		Alive	Dead		Alive	Dead	
	N	*N* = 6,303	*N* = 678	*p-value*	*N* = 5,360	*N* = 1,621	*p-value*
Performance status at diagnosis		***n* = 6,235**	***n* = 672**	***<0.001***	***n* = 5,299**	***n* = 1,608**	***<0.001***
0- Fully active, n (%)	1,885	1,855 (29.8)	30 (4.5)		1,765 (33.3)	120 (7.5)	
1- Restricted in heavy physical work, n (%)	2,872	2,749 (44.1)	123 (18.3)		2,462 (46.5)	410 (25.5)	
2- Up and about more than half the day, n (%)	1,273	1,103 (17.7)	170 (25.3)		812 (15.3)	461 (28.7)	
3- In bed or sitting in a chair more than half the day, n (%)	685	460 (7.4)	225 (33.5)		231 (4.4)	454 (28.2)	
4- In bed or in a chair all the time, n (%)	192	68 (1.1)	124 (18.5)		29 (0.6)	163 (10.1)	

Facteur pronostique pour la mortalité à court terme

BMC Pulmonary Medicine (2016) 16:45

Determinants of Improved Outcome in Small-Cell Lung Cancer: An Analysis of the 2,580-Patient Southwest Oncology Group Data Base

Favorable Variables Entire Data Base (n = 1,316)	Significance, Overall Survival* P	Hazards Ratio
Performance status 0-1	< .00005	1.4
Recent studies since 1978	< .00005	1.4
Age < 70 years	< .00005	1.5
Female sex	.0001	1.3
Study 8269	.0009	1.5
White race	.0095	1.3

Albain et al J Clin Oncol 1990

The Impact of Additional Prognostic Factors on Survival and their Relationship with the Anatomical Extent of Disease Expressed by the 6th Edition of the TNM Classification of Malignant Tumors and the Proposals for the 7th Edition

TABLE 7. Multivariate Analysis of Prognostic Factors for Survival in SCLC, Using General Characteristic Variables (Limited vs. Extensive Stage, Age, Gender, PS)

Variable	*n*/*N* (%)	HR (95% CI)	*P*
Age	*N* = 6609	1.01 (1.01, 1.02)	<0.001
Extensive stage (vs Lim.)	3739/6609 (57%)	2.13 (2.02, 2.25)	<0.001
Male (vs. female)	4368/6609 (66%)	1.25 (1.19, 1.32)	<0.001
PS 1	3161/6609 (48%)	1.36 (1.28, 1.44)	<0.001
PS 2	1060/6609 (16%)	1.93 (1.78, 2.09)	<0.001
PS 3–4	349/6609 (5%)	3.45 (3.05, 3.89)	<0.001

Sculier et al, J Thorac Oncol 2008

Karnofsky Performance Score, Radiation Dose and Nodal Status Predict Survival of Elderly Patients Irradiated for Limited-disease Small-cell Lung Cancer

Characteristic	Survival at 1 Year (%)	2 Year (%)	3 Year (%)	*p*-Value[a] Univariate analysis	Multivariate analysis
Gender					
Female (n=10)	70	20	0		
Male (n=26)	58	23	15	0.87	
Karnofsky performance score					
≤70 (n=12)	17	0	0		
>70 (n=24)	75	38	17	**<0.001**	**<0.001**

Prise en charge des patients avec un indice de performance altéré dans les CBNPC

Traitements à visée curative

- Manque de données spécifiques
- Chirurgie:
  - Si altération de l'indice de performance lié à co-morbidités fonctionnelles contre-indiquant une chirurgie

  ⇒Radiothérapie

  ⇒Radiothérapie stéréotaxique

Table 1 Primary Tumor Control Results After Stereotactic Ablative Body Radiation of Stage I Non–Small Cell Lung Cancer

Reference	Sample Size	Total Dose	Fractions	Primary Tumor Control
McGarry et al[26]	47	24.0–72.0 Gy in escalating doses; increments of 2 Gy per fraction	3	74% (crude)
Zimmermann et al[28]	30	24.0–37.5 Gy	3	87% (3 y)
Nyman et al[29]	45	45.0 Gy	3	80% (crude)
Fritz et al[31]	33	30.0 Gy	1	94% (crude)
Baumann et al[33]	57	15.0 Gy	3	92% (3 y)
Nagata et al[30]	45	12.0 Gy	4	94% (3 y)
Xia et al[34]	43	5.0 Gy	10	95% (3 y)
Lagerwaard et al[32]	206	20.0 Gy; 12.0 Gy; 7.5 Gy	3; 5; 8	93% (crude)
Timmerman et al[27]	59	18.0 Gy	3	98% (3 y)

JNCCN 2014: 1015

REVIEW ARTICLE

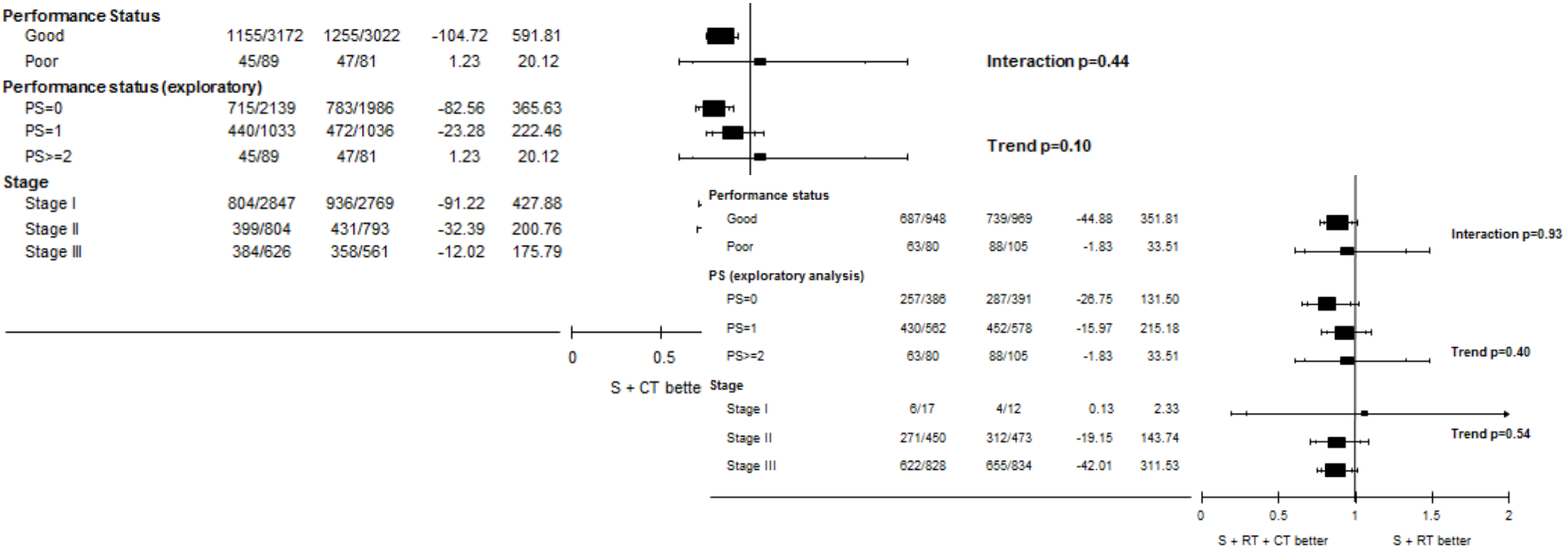
A systematic review of outcomes following stereotactic ablative radiotherapy in the treatment of early-stage primary lung cancer

[1]PATRICK MURRAY, MD, FRCR, [1]KEVIN FRANKS, FRCR and [2]GERARD G HANNA, PhD, FRCR

Br J Radiol 2017; **90**: 20160732.

Chimiothérapie adjuvante

Performance status†				
Good	3172 (74%)	3022 (73%)	948 (72%)	969 (72%)
Poor	96 (2%)	83 (2%)	81 (6%)	105 (8%)
Unknown	76 (2%)	58 (1%)	22 (2%)	16 (1%)
Not supplied	961 (22%)	979 (24%)	264 (20%)	255 (19%)



Cochrane Database of Systematic Reviews 2015, Issue 3. Art. No.: CD011430.

La chimiothérapie conventionnelle
Analyses rétrospectives

Outcome of Patients with a Performance Status of 2 in Eastern Cooperative Oncology Group Study E1594

A Phase III Trial in Patients with Metastatic Nonsmall Cell Lung Carcinoma

Arm	Regimen	Schedule
PC	Paclitaxel 135 mg/m^2 over 24 hours on day 1 and cisplatin 75 mg/m^2 on Day 2	Every 21 days
GC	Gemcitabine 1 g/m^2 on Days 1, 8, and 15 and cisplatin 100 mg/m^2 on Day 1	Every 28 days
DC	Docetaxel 75 mg/m^2 on Day 1 and cisplatin 75 mg/m^2 on Day 1	Every 21 days
PCb	Paclitaxel 225 mg/m^2 over 3 hours on Day 1 and carboplatin AUC 6 on Day 1	Every 21 days

	Treatment arm[a]				
Measure	PC	GC	DC	PCb	Overall
Response rate (no.)	18	13	18	15	64
CR (%)	0	0	0	0	0
PR (%)	17	23	6	13	14
Time to progression (months) (no.)	1.4 (21)	4.6 (13)	1.4 (19)	1.5 (15)	1.7 (68)
Median survival (months)	7.0	7.9	2.3	4.6	4.1
Overall 1-yr survival (%)	19	38.5	10.5	13.3	19.1

Fatal Events

GC arm
- Renal failure related to therapy
- Progressive mental obtundation and seizures

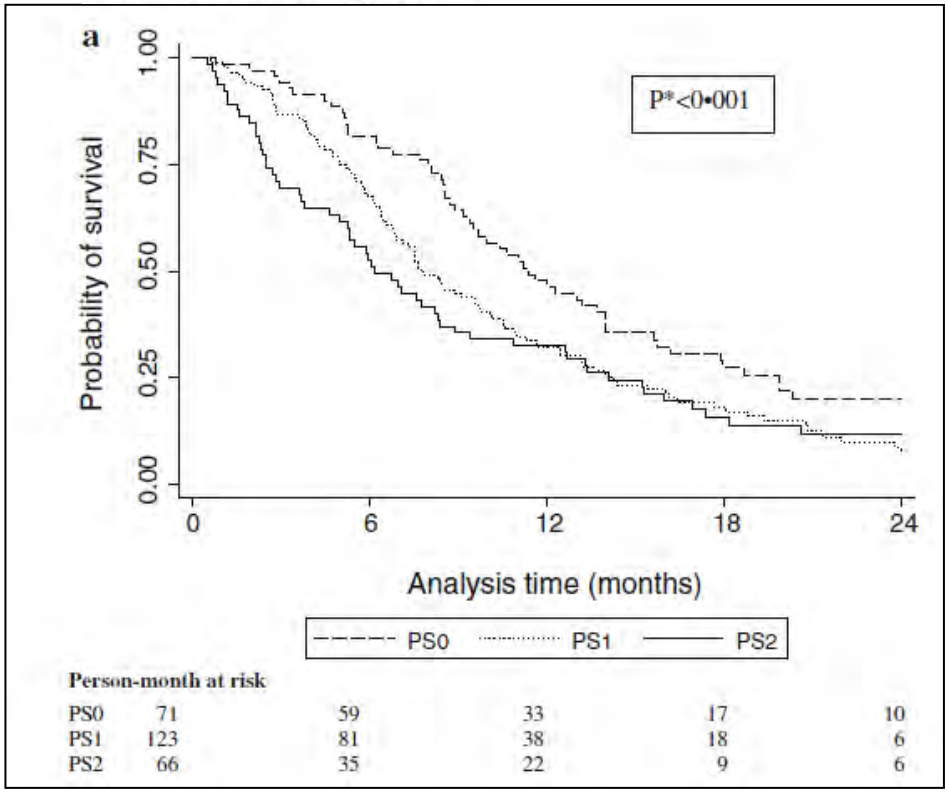
DC arm
- Hemoptysis without thrombocytopenia
- Infection with Grade 4 neutropenia
- DVT with progressive respiratory insufficiency

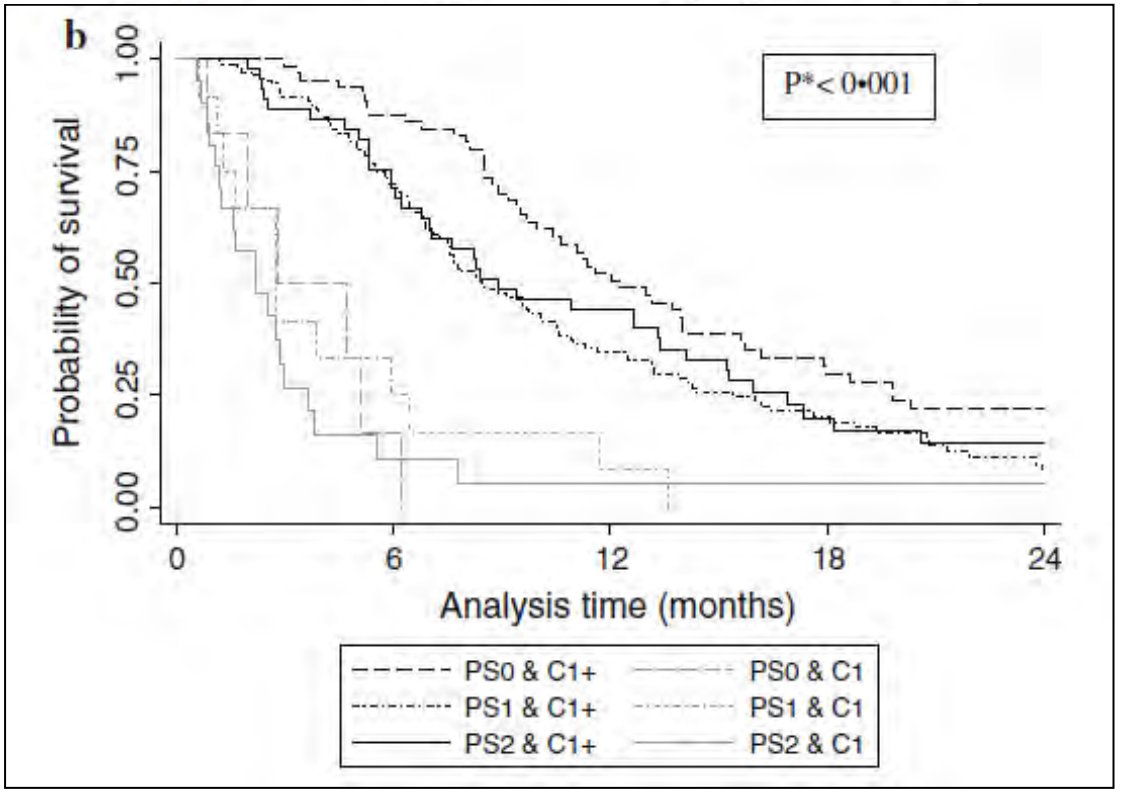
Sous-groupe de patients PS 2 ont une toxicité plus importante et un avantage clinique (RR, survie) moindre que les PS 0-1

Cancer 2001: 2639-47

Results of platinum-based chemotherapy in unselected performance status (PS) 2 patients with advanced non-small cell lung cancer: a cohort study

Symptoms improved	92 (35.4)	66 (33.70)	26 (39.4)	0.40
Clinical toxicity				
Febrile neutropenia	56 (21.5)	43 (21.9)	13 (19.7)	0.88
Other toxicities (grade 3/4)	12 (4.6)	7 (3.6)	5 (7.6)	0.22

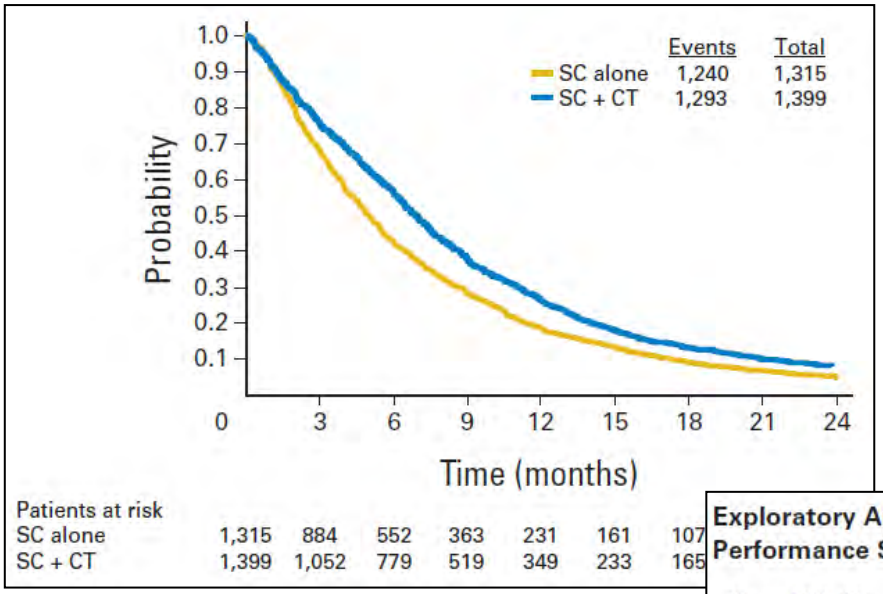


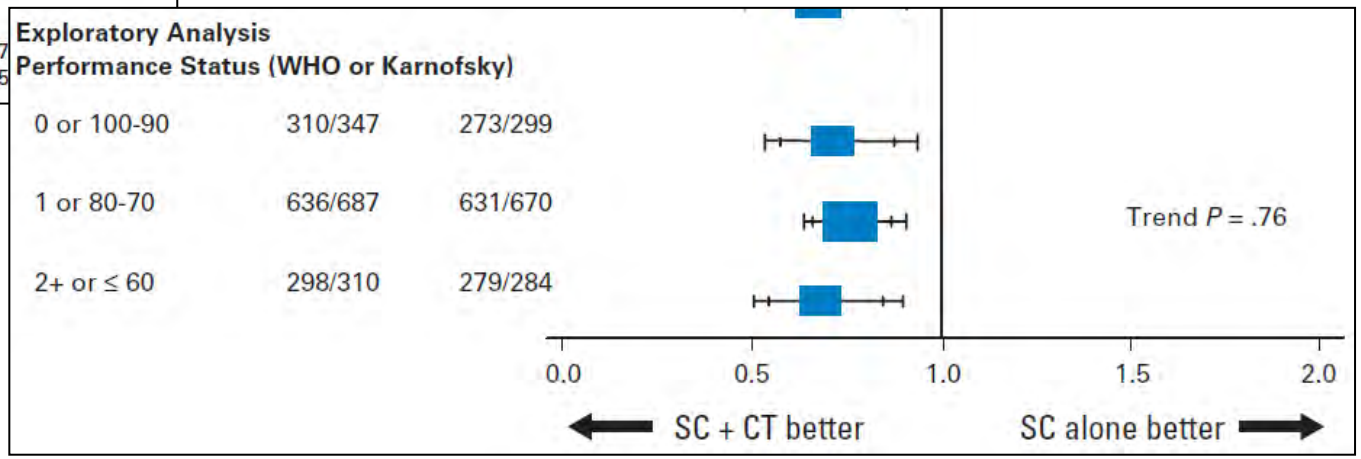


Jouveshomme et al Med Oncol 2013: 544

Chemotherapy in Addition to Supportive Care Improves Survival in Advanced Non–Small-Cell Lung Cancer: A Systematic Review and Meta-Analysis of Individual Patient Data From 16 Randomized Controlled Trials

NSCLC Meta-Analyses Collaborative Group





J Clin Oncol 26:4617-4625. © 2008

Chemotherapy improves low performance status lung cancer patients

TABLE 2 Response distribution to the first three courses of induction gemcitabine+ifosfamide+cisplatin chemotherapy according to initial performance status (PS)

	PS 80–100	PS 60–70	p-value
Patients	387	98	
Objective response	147 (38)	27 (28)	0.06
No change	99 (26)	16 (16)	
Progression	98 (25)	25 (26)	
Tumoural necrosis	2	1	
Early death malignant	7	10	
Toxic death	8	9	
High toxicity and stop treatment	14	5	
Not evaluable	12	5	

Analyse rétrospective d'une étude randomisée de 485 patients

20% mauvais PS.

Amélioration clinique (obtention d'un bon PS sous CT) dans 25% des mauvais PS

- 38% parmi répondeurs
- 20% parmi maladies stables
- 14% parmi progresseurs

Survie des patients avec mauvais PS était significativement moindre, mais la survie des répondeurs était similaire, indépendamment du PS de base.

On notait plus de morts toxiques parmi les patients avec mauvais PS (9,2 versus 2,1%).

Sculier Eur Respir J 2007: 1186-92

Table IV. Health related Quality of Life Responses according to Performance Status

	PS 0/1				PS 2				
	%				%				
	n	Improved	Stable	Worse	n	Improved	Stable	Worse	p
Function									
Global QOL	276	32	24	44	93	48	13	39	<0,01
Physical function	278	20	26	54	94	27	20	53	0,26
Role function	278	26	15	59	94	38	20	42	0,01
Emotional function	277	35	40	25	94	37	32	31	0,29
Social function	277	31	19	50	94	34	17	49	0,80
Cognitive function	277	26	33	41	94	39	18	43	<0,01
Symptoms									
Fatigue	278	32	11	57	94	48	8	44	0,03
Pain C30	278	36	29	35	94	48	20	32	0,09
Chest pain LC13	275	20	45	35	94	32	42	26	0,06
Arm/shoulder pain LC13	277	21	50	29	94	30	39	31	0,12
Pain elsewhere LC13	274	26	39	35	91	32	34	34	0,50
Dyspnea C30	278	29	35	36	93	54	20	26	<0,01
Dyspnea LC13	276	32	17	51	94	44	13	43	0,10
Swallowing problems	277	10	68	22	94	17	54	29	0,04
Cough	277	45	37	18	94	45	30	25	0,26
Hemoptysis	278	8	81	11	94	10	80	10	0,76
Nausea/vomiting	278	19	38	43	94	29	30	41	0,13
Insomnia	278	34	37	29	94	43	39	19	0,11
Sore mouth	277	9	57	34	93	9	60	31	0,87
Neuropathy	275	13	57	30	94	9	52	39	0,20
Hair loss	276	6	59	35	94	6	57	37	0,93
Appetite loss	278	26	36	38	94	40	26	34	0,02
Constipation	273	15	29	56	94	22	29	49	0,23
Diarrhea	278	25	53	22	94	20	56	24	0,66

Acta Oncologica 2009: 1019-25

Survival among Non-Small Cell Lung Cancer Patients with Poor Performance Status after First Line Chemotherapy

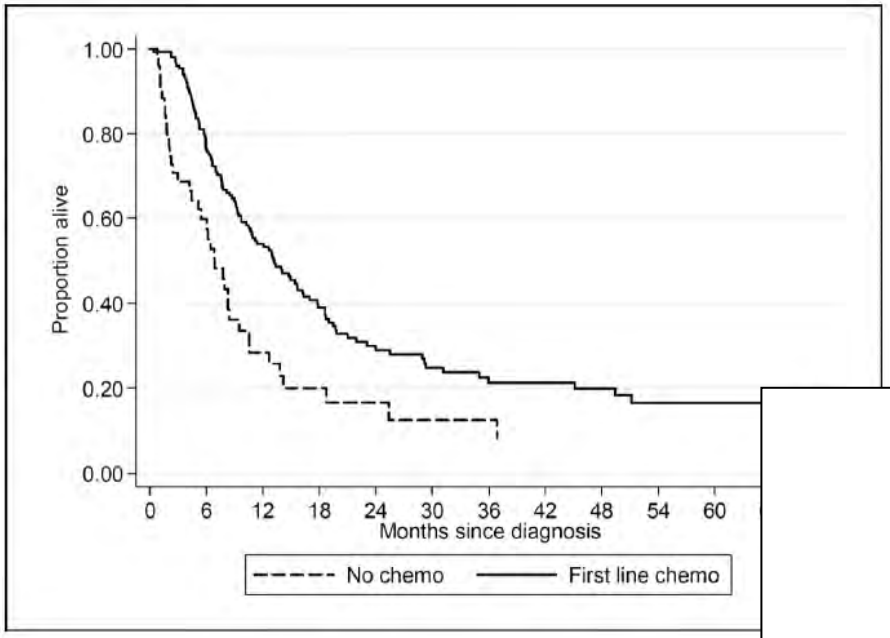


Figure 1.
Survival of advanced non-small cell lung cancer patients, ECOG perform
with first line chemotherapy (solid line) vs. no chemotherapy (dashed lin

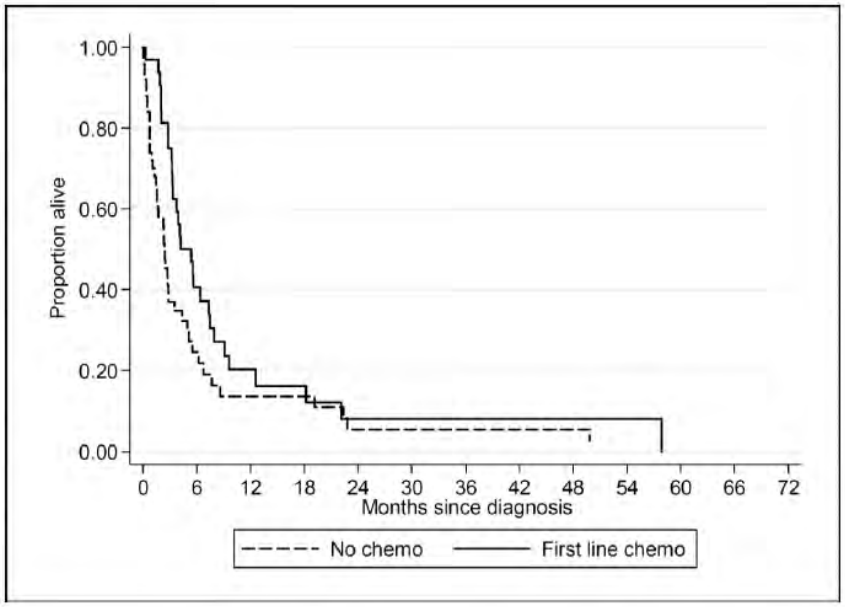


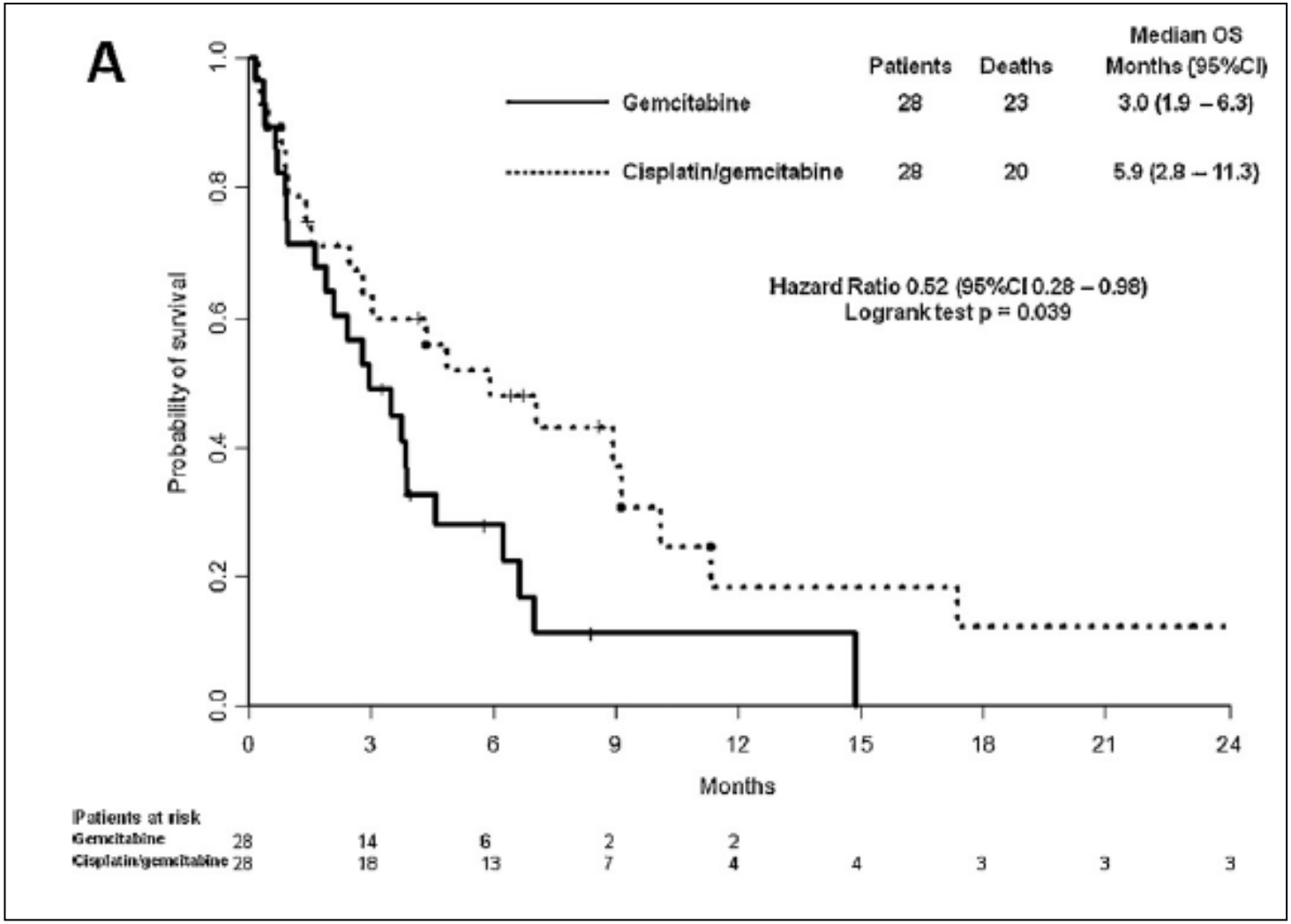
Figure 2.
Survival of advanced non-small cell lung cancer patients, ECOG performance status 3–4, with first line chemotherapy (solid line) vs. no chemotherapy (dashed line).

Lung Cancer. 2012 September ; 77(3): 545–549.

La chimiothérapie conventionnelle
Les études prospectives

Randomized phase III trial of gemcitabine and cisplatin vs. gemcitabine alone in patients with advanced non-small cell lung cancer and a performance status of 2: The CAPPA-2 study

Alessandro Morabito[a], Vittorio Gebbia[b], Massimo Di Maio[a], Saverio Cinieri[c,d], Maria Grazia Viganò[e],



Lung Cancer 81 (2013) 77–83

Randomized Phase III Trial of Single-Agent Pemetrexed Versus Carboplatin and Pemetrexed in Patients With Advanced Non–Small-Cell Lung Cancer and Eastern Cooperative Oncology Group Performance Status of 2

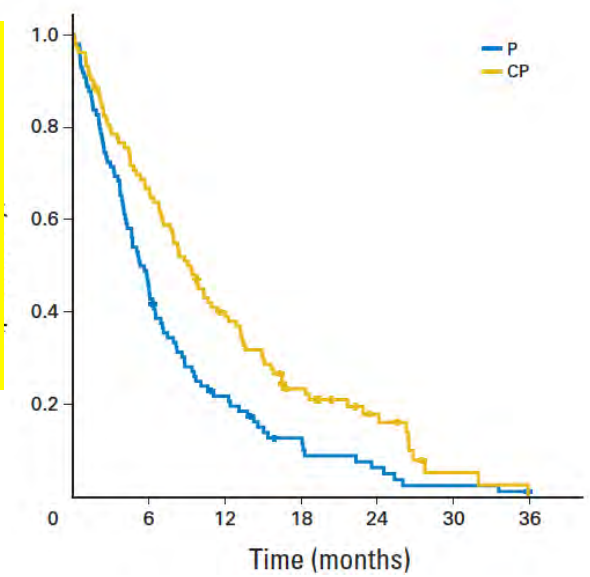
Table 3. Toxicity

Grade 3 or 4 Toxicity	P (n = 102)		CP (n = 103)		
	No.	%	No.	%	*P*
Anemia	4	3.9	12	11.7	.07*
Thrombocytopenia	0	0.0	1	1.0	1.00*
Neutropenia	1	1.0	7	6.8	.06*
Febrile neutropenia	3	2.9	1	1.0	.37*
Nausea/emesis	1	1.0	5	4.9	.21*
Diarrhea	2	2.0	1	1.0	.62*
Dyspnea	11	10.8	6	5.8	.19†
Grade 5 event‡	0	0.0	4	3.9	.12*

Table 4. Efficacy Outcomes

Outcome	P (n = 102)	CP (n = 103)	*P*
ORR, %	10.5	24	.032*
PFS			< .001†
Median, months	2.8	5.8	
Range, months	2.5-3.2	4.7-6.9	
1 year, %	2	17	
OS			.001†
Median, months	5.3	9.3	
Range, months	4.1-6.5	7.2-11.2	
1 year, %	21.9	40.1	

"First, at the main center in Brazil—Instituto Nacional de Cancer—where 60% of patients were enrolled, two independent investigators had to agree on the ECOG PS 2 assignment before the patient was enrolled.

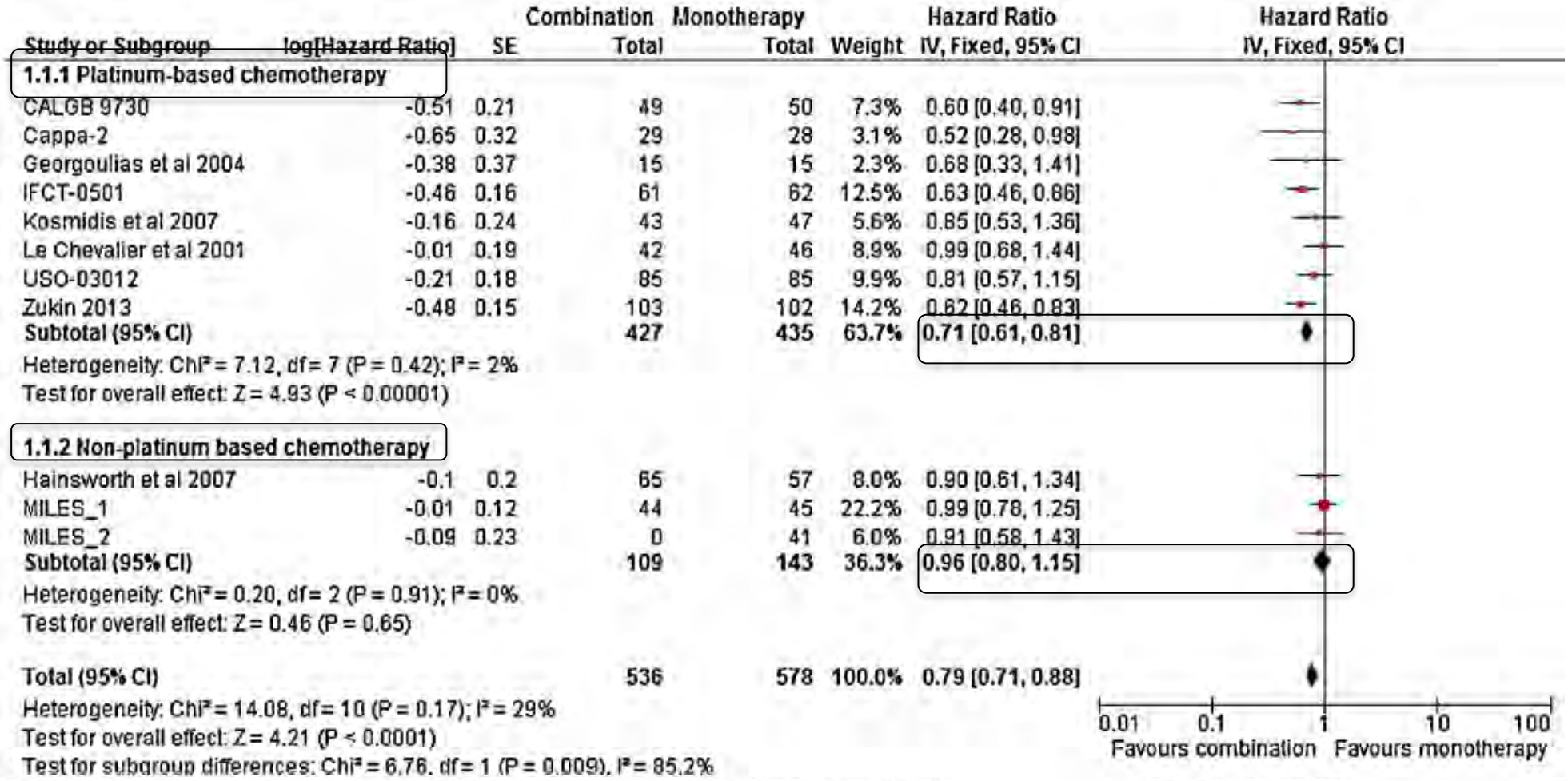


J Clin Oncol 31:2849-2853.

Single-agent versus combination chemotherapy as first-line treatment for patients with advanced non-small cell lung cancer and performance status 2: A literature-based meta-analysis of randomized studies

Author [trial name] (ref)	Study phase	Treatment arms	Dose and schedule of chemotherapy	PS analysis	No of patients
Kosmidis [8]	II	Gemcitabine	1250 mg/m^2 day 1 + 14, q4w	Dedicated to PS 2	47
		Carboplatin-Gemcitabine	3 AUC – 1250 mg/m^2 day 1 + 14, q4w		43
Morabito [CAPPA-2] [9]	III	Gemcitabine	1200 mg/m^2 day 1 + 8, q3w	Dedicated to PS 2	28
		Cisplatin-Gemcitabine	60–1200 mg/m2 day 1 + 8, q3w		29
Reynolds [USO-03012] [10]	III	Gemcitabine	1250 mg/m^2 day 1+ 8, q3w	Dedicated to PS 2	85
		Carboplatin-Gemcitabine	5 AUC – 1000 mg/m^2 day 1 + 8, q3w		85
Zukin [11]	III	Pemetrexed	500 mg/m^2 day 1, q3w	Dedicated to PS 2	102
		Carboplatin-Pemetrexed	5 AUC – 500 mg/m^2 day 1, q3w		103
Comella [SICOG 9909] [14]	III	Gemcitabine	1200 mg/m^2 day 1 + 8 + 15, q4w	Subset analysis	19
		Paclitaxel	100 mg/m^2 day 1 + 8 + 15, q4w		22
		Gemcitabine-Paclitaxel	1000 mg/m^2–80 mg/m2 day 1 + 8, q3w		15
		Gemcitabine-Vinorelbine	1000 mg/m^2–25 mg/m^2 day 1 + 8, q3w		21
Georgoulias [15]	III	Docetaxel	100 mg/m^2 day 1, q3w	Subset analysis	15
		Cisplatin-Docetaxel	80 mg/m^2 day 2–100 mg/m^2 day 1, q3w		15
Hainsworth [16]	III	Docetaxel	36 mg/m2 day 1 + 8 + 15, q4w	Subset analysis	57
		Docetaxel-Gemcitabine	30 mg/m^2–800 mg/m^2 day 1 + 8 + 15, q4w		65
Le Chevalier [17]	III	Vinorelbine	30 mg/m^2 weekly	Subset analysis	46
		Cisplatin-Vinorelbine	120 mg/m^2 day 1 + 29 => q6w, 30 mg/m^2 weekly		42
		Cisplatin-Vindesine	120 mg/m^2 day 1 + 29 => q6w, 3 mg/m^2 weekly for 6 wk => q2w		33
Lilenbaum [CALGB 9730] [18]	III	Paclitaxel	225 mg/m^2 day 1, q3w	Subset analysis	50
		Carboplatin-Paclitaxel	6 AUC–225 mg/m2 day 1, q3w		49
Perrone [MILES] [19]	III	Vinorelbine	30 mg/m^2 day 1 + 8, q3w	Subset analysis	45
		Gemcitabine	1200 mg/m^2 day 1 + 8, q3w		41
		Vinorelbine-Gemcitabine	25–1000 mg/m^2 day 1 + 8, q3w		44
Quoix [IFCT-0501] [20]	III	Gemcitabine or Vinorelbine	1150 mg/m^2 day 1 + 8, q3w or 25 mg/m^2 day 1 + 8, q3w	Subset analysis	62
		Carboplatin-Paclitaxel	6 AUC day 1–90 mg/m^2 day 1 + 8 + 15, q4w		61
Sederholm [21]	III	Gemcitabine	1250 mg/m^2 day 1 + 8, q3w	Subset analysis	20
		Carboplatin-Gemcitabine	5 AUC day 1–1250 mg/m^2 day 1 + 8, q3w		24

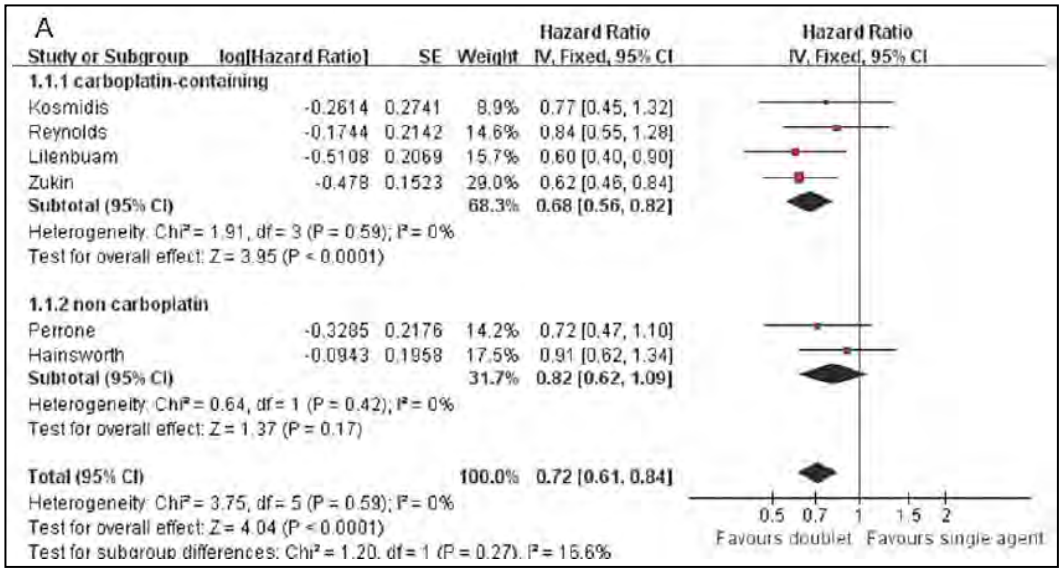
Lung Cancer 84 (2014) 209–214



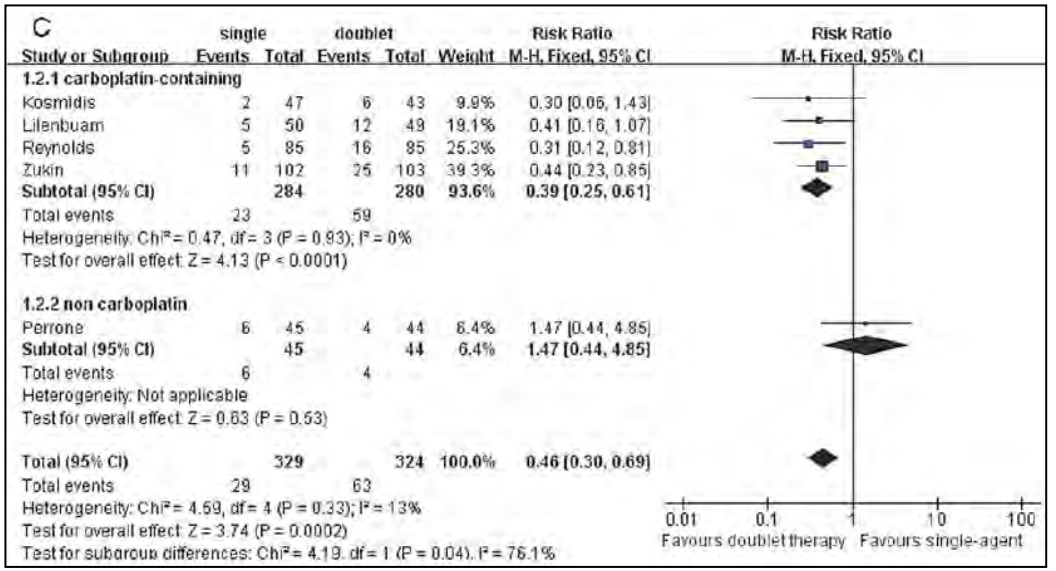
Toxicity grade III–IV	No of studies	No of patients analyzed	Pooled OR (95% CI)	*p*-Value
Hematologic				
Anemia	4	519	3.12 (1.55–6.27)	0.001
Trombocytopenia	4	519	12.81 (4.65–33.10)	<0.001
Neutropenia	4	519	7.91 (3.97–15.78)	<0.001
Non-hematologic				
Febrile neutropenia	3	432	0.32 (0.05–2.06)	0.23
Fatigue	3	349	0.75 (0.40–1.40)	0.36
Nausea	3	432	1.21 (0.05–29.34)	0.91

Comparing single-agent with doublet chemotherapy in first-line treatment of advanced non-small cell lung cancer with performance status 2: A meta-analysis

Survie



Taux de réponse



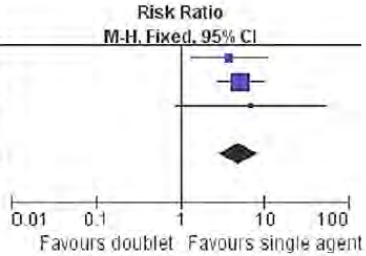
Asia-Pacific Journal of Clinical Oncology 2015; 11: 253–261

Neutropénie et thrombopénie

B

Study or Subgroup	doublet Events	Total	single agent Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Kosmidis	14	43	4	47	27.9%	3.83 [1.36, 10.73]
Reynolds	46	79	9	81	64.8%	5.24 [2.75, 9.97]
Zukin	7	103	1	102	7.3%	6.93 [0.87, 55.34]
Total (95% CI)		225		230	100.0%	**4.97 [2.93, 8.43]**
Total events	67		14			

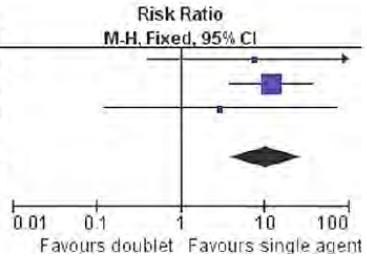
Heterogeneity: Chi² = 0.37, df = 2 (P = 0.83); I² = 0%
Test for overall effect: Z = 5.95 (P < 0.00001)



C

Study or Subgroup	doublet Events	Total	single agent Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Kosmidis	3	43	0	47	12.1%	7.64 [0.41, 143.70]
Reynolds	35	79	3	81	75.1%	11.96 [3.83, 37.31]
Zukin	1	103	0	102	12.7%	2.97 [0.12, 72.09]
Total (95% CI)		225		230	100.0%	**10.29 [3.80, 27.85]**
Total events	39		3			

Heterogeneity: Chi² = 0.69, df = 2 (P = 0.71); I² = 0%
Test for overall effect: Z = 4.59 (P < 0.00001)

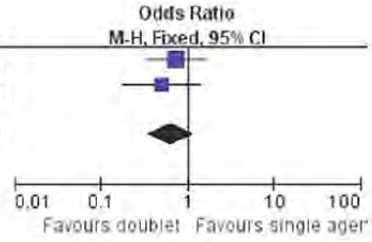


Dyspnée et fatigue

A

or Subgroup	doublet Events	Total	single agent Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Reynolds	13	81	16	79	56.6%	0.75 [0.34, 1.69]
Zukin	6	103	11	102	43.4%	0.51 [0.18, 1.44]
Total (95% CI)		184		181	100.0%	**0.65 [0.34, 1.22]**
Total events	19		27			

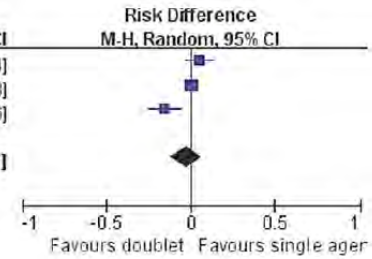
Heterogeneity: Chi² = 0.33, df = 1 (P = 0.56); I² = 0%
Test for overall effect: Z = 1.34 (P = 0.18)



B

or Subgroup	doublet Events	Total	single agent Events	Total	Weight	Risk Difference M-H, Random, 95% CI
Hainsworth	39	174	29	171	31.0%	0.05 [-0.03, 0.14]
Lilenbuam	7	284	5	277	40.1%	0.01 [-0.02, 0.03]
Reynolds	3	81	15	79	28.8%	-0.15 [-0.25, -0.06]
Total (95% CI)		539		527	100.0%	**-0.02 [-0.12, 0.07]**
Total events	49		49			

Heterogeneity: Tau² = 0.01; Chi² = 11.77, df = 2 (P = 0.003); I² = 83%
Test for overall effect: Z = 0.51 (P = 0.61)



Asia-Pacific Journal of Clinical Oncology 2015; 11: 253–261

What can platinum offer yet in the treatment of PS2 NSCLC patients? A systematic review and meta-analysis

Taux de réponse

Citation	Arms	Odds Ratio	95% CI
Zukin, JCO 2013	CPm vs Pm	2,71	1,06-6,93
Lilembaum, JCO 2005	CPa vs Pa	2.91	0,94-9,03
Kosmidis, JTO 2007	CG vs G	3.64	0,69-19,15
Reynolds, JCO 2009	CG vs G	3.71	1,29-10,65
Morabito, LC 2013	CisG vs G	5.86	0,63-53,92
Random combined		**3.24**	**1,88-5,58**

Survie à 1 an

Citation	Arms	Odds Ratio	95% CI
Le Chevalier, The O. 2001	CisV vs V	0.95	0,34-2,67
Kosmidis, JTO 2007	CG vs G	1,29	0,44-3,71
Reynolds, JCO 2009	CG vs G	1,64	0,81-3,28
Lilembaum, JCO 2005	CPa vs Pa	2,02	0,62-6,54
Zukin, JCO 2013	CPm vs Pm	2,4	1,30-4,44
Random combined		**1,74**	**1,20-2,52**

Summary of the pooled odds ratios and 95% CI for each outcome examined in all included trials.

Outcomes	Pooled odds ratios	95% CI
ORR	3.24	1.88–5.58
1-year-OS-rate	1.74	1.20–2.52
G3–4 Anemia	2.74	1.35–5.53
G3–4 Neutropenia	7.23	3.72–14.07
G3–4 Thrombocytopenia	12.88	4.9–33.85

Critical Reviews in Oncology/Hematology 95 (2015) 306–317

Les Traitements ciblés

Randomized phase II trial of gefitinib or gemcitabine or docetaxel chemotherapy in patients with advanced non-small-cell lung cancer and a performance status of 2 or 3 (IFCT-0301 study)

Criterion	Gefitinib ($n=43$)		Gemcitabine ($n=41$)		Docetaxel ($n=41$)	
	No.	%	No.	%	No.	%
Response of first line treatment						
Partial response	0	0	1	2	3	7
Stable disease	9	21	13	32	13	32
Progressive disease	19	44	14	34	11	27
Unable to determine, Premature death/not evaluable	15	35	13	32	14	34
PFS (months)						
Median	1.9		2.0		2.0	
95%CI	1.1–2.2		1.1–3.1		1.5–2.7	
6 months	2.3%		12.2%		17.1%	
95%CI	[0.2%; 10.6%]		[4.5%; 24.1%]		[7.5%; 29.9%]	
12 months	0%		4.9%		2.9%	
95%CI	–		[0.9%; 14.5%]		[0.2%; 12.7%]	
Overall survival						
Median	2.2		2.4		3.5	
95%CI	1.9–3.4		1.6–4.4		1.8–6.6	
6 months	11.2%		34.1%		36.6%	
95%CI	[3.9%; 22.8%]		[20.3%; 48.5%]		[22.3%; 51.0%]	
12 months	5.6%		13.3%		13.1%	
95%CI	[1.1%; 15.9%]		[4.6%; 26.6%]		[4.8%; 25.5%]	

Common treatment-related adverse events (incidence ≥10% in either arm).

	Gefitinib				Gemcitabine				Docetaxel			
	All		Grade 3–4		All		Grade 3–4		All		Grade 3–4	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
All	31	72	10	23	30	73	12	29	32	78	23	56

Lung Cancer 70 (2010) 301–307

Randomized Phase II Trial of Erlotinib or Standard Chemotherapy in Patients With Advanced Non–Small-Cell Lung Cancer and a Performance Status of 2

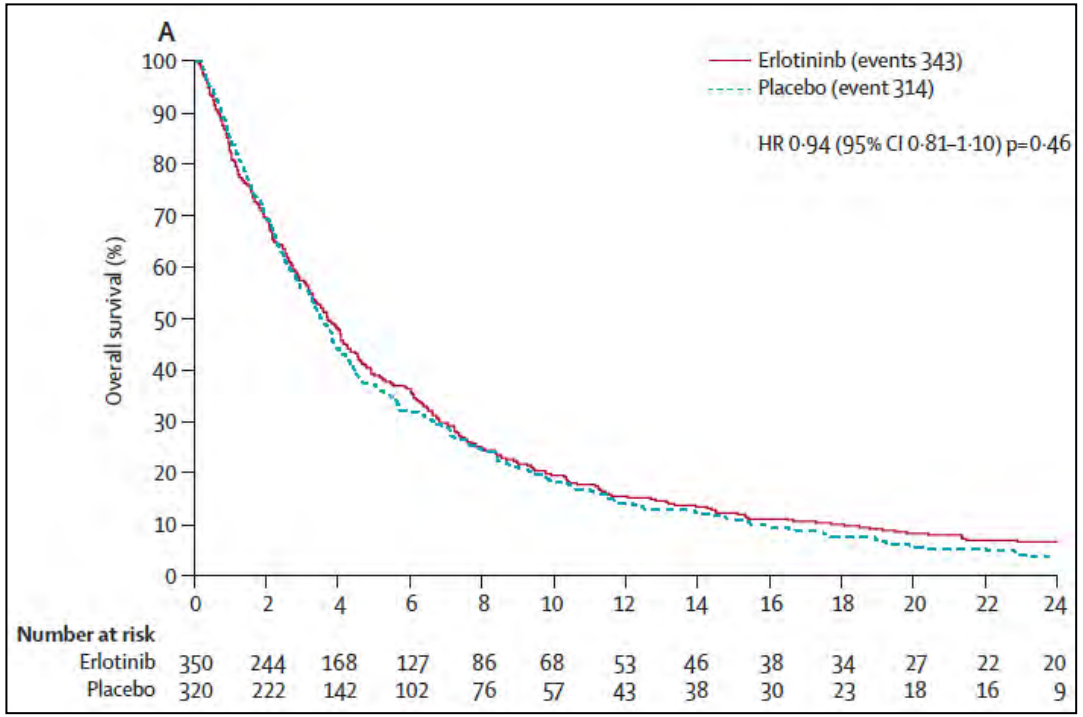
Table 3. Efficacy Results

Criterion	Erlotinib (n = 52)		Paclitaxel + Carboplatin (n = 51)		Crossover to Erlotinib (n = 29)	
	No.	%	No.	%	No.	%
Response						
Complete response	0	0	0	0	1	3
Partial response	2	4	6	12	2	7
Stable disease	19	37	22	43	5	17
Progressive disease	23	44	10	20	14	48
Unable to determine/not evaluable	8	15	13	25	7	24
PFS, months						
Median	1.9		3.5			
95% CI	1.28 to 2.69		1.48 to 4.73			
Survival, months						
Median	6.6		9.5		14.9	
95% CI	3.78 to 8.25		1.94 to 12.45		8.64 to 19.25	

J Clin Oncol 26:863-869. © 2008

First-line erlotinib in patients with advanced non-small-cell lung cancer unsuitable for chemotherapy (TOPICAL): a double-blind, placebo-controlled, phase 3 trial

Adenocarcinoma	133 (38%)	123 (38%)
Squamous	136 (39%)	127 (40%)
Large cell	15 (4%)	15 (5%)
Other	66 (19%)	55 (17%)

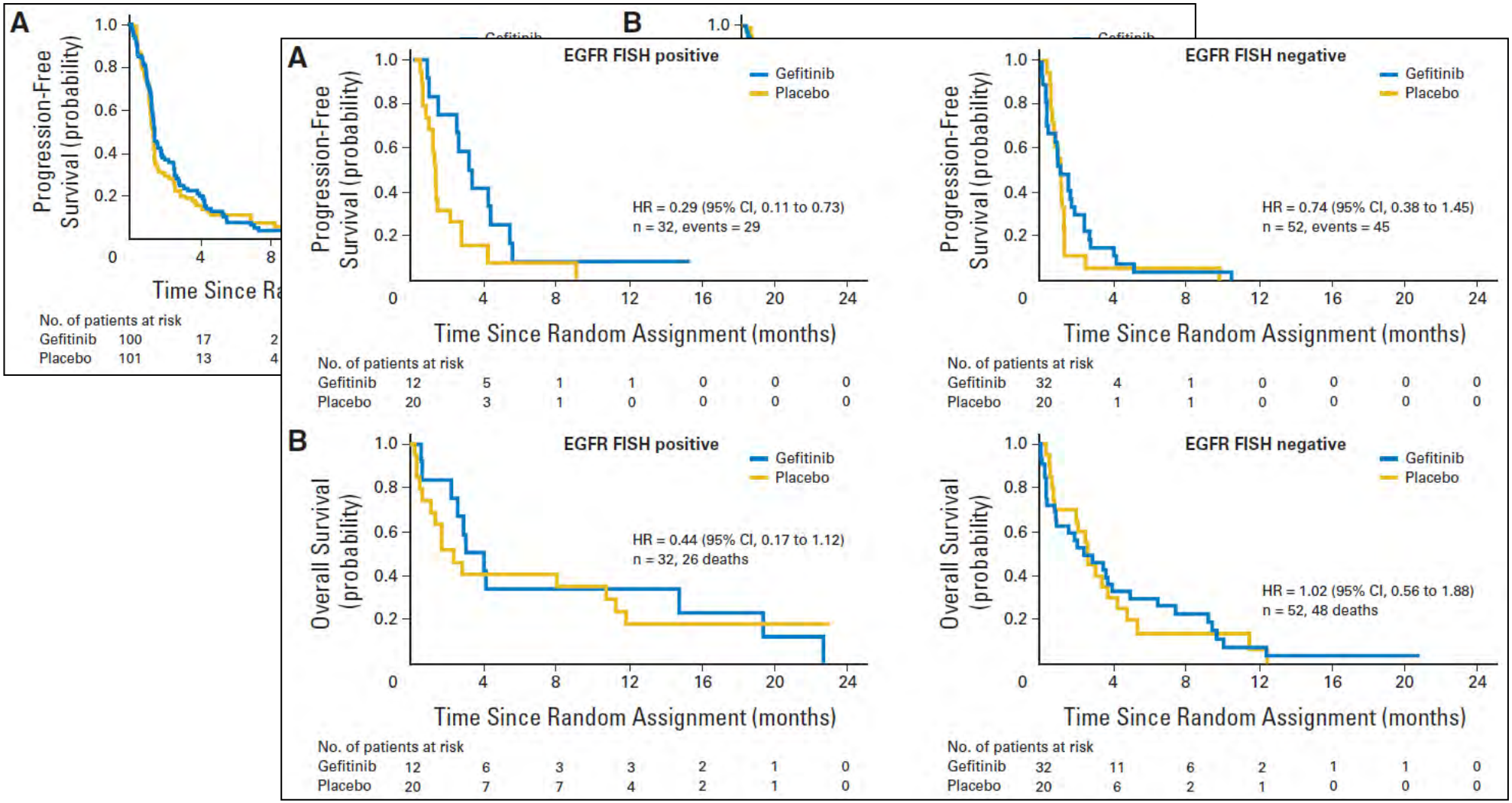


28 *EGFR* mutés (11 del 19, 10 L858R, 7 autres)
MST erlotinib (n=17) 10,4 mois (IC 95% CI 5,5–15,1)
placebo (n=11): 3,7 mois (IC 95% 0,3–49,3)
PFS erlotinib 4,8 mois (IC 95% 1,6–8,8)
placebo 2,9 mois (IC 95% 0,3–10,1)

Lancet Oncol 2012; 13: 1161–70

Randomized Phase II Study of Gefitinib Compared With Placebo in Chemotherapy-Naive Patients With Advanced Non–Small-Cell Lung Cancer and Poor Performance Status

Glenwood Goss, David Ferry, Rafal Wierzbicki, Scott A. Laurie, Joyce Thompson, Bonne Biesma, Fred R. Hirsch, Marileila Varella-Garcia, Emma Duffield, Ozlem U. Ataman, Marc Zarenda, and Alison A. Armour



J Clin Oncol 27:2253-2260. © 2009

The safety and efficacy of EGFR TKIs monotherapy versus single-agent chemotherapy using third-generation cytotoxics as the first-line treatment for patients with advanced non-small cell lung cancer and poor performance status

Characteristics and efficacy outcomes of EGFR TKIs monotherapy trials.

Author	Arm	Median age (years)	Female (%)	PS ≥ 3 (%)
Goss G	G(250)	74	39	45
Inoue A[a]	G(250)	72	79	76
Spigel DR	G(250)	75	41	17
Hesketh PJ	E(150)	74	53	0
Lilenbaum R	E(150)	NA	56	0

Response rates and disease control rates of EGFR TKIs monotherapy and single-agent therapy using third-generation cytotoxics in all included studies and in subgroups of patients with certain characteristics.

Regimens	Groups	No	Response rate		Disease control rate	
			Pooled estimate (%)	95% CI (%)	Pooled estimate (%)	95% CI (%)
EGFR TKIs	Unselected population	300	6	3–8	40	33–47
	EGFR mutation	30	66	46–81	90	75–99
	Including PS 3 to 4	172	5	2–9	38	31–46
	PS 2 targeted	128	6	2–10	41	33–50
	all included Studies	330	18	2–34	50	34–66
Single-agent	Poor PS targeted	498	9	6–13	30	20–41
	Together with elderly	597	13	11–16	41	36–46
	Including PS 3 to 4	353	13	7–18	32	22–43
	PS 2 targeted	742	12	10–14	40	34–47
	all included studies	1095	12	9–14	36	30–43

Lung Cancer 73 (2011) 203–210

Activity of gefitinib in advanced non-small-cell lung cancer with very poor performance status

Table 2. Response to treatment

	No. of patients	%
Complete response	0	0%
Partial response	13	25.0%
Stable disease	11	21.2%
Progressive disease	28	53.8%
Overall response rate	13	25.0%

Table 3. Summary of drug-related adverse events ($n = 52$)

	None (%)	Grade 1 (%)	Grade 2 (%)	Grade 3 (%)	Grade 4 (%)
Skin toxicity	16 (30.8)	28 (53.8)	6 (11.5)	2 (3.9)	0 (0)
Paronychia	42 (80.7)	3 (5.8)	3 (5.8)	4 (7.7)	0 (0)
Diarrhea	34 (65.4)	14 (26.9)	4 (7.7)	0 (0)	0 (0)
Nausea	51 (98.1)	1 (1.9)	0 (0)	0 (0)	0 (0)
Vomiting	51 (98.1)	1 (1.9)	0 (0)	0 (0)	0 (0)
Anorexia	51 (98.1)	1 (1.9)	0 (0)	0 (0)	0 (0)
Elevated LFTs	51 (98.1)	1 (1.9)	0 (0)	0 (0)	0 (0)

Taiwan

Pas de données sur mutation EGFR

mais taux attendu > 30-40%

Investigational New Drugs **23:** 73–77, 2005

First-Line Gefitinib for Patients With Advanced Non–Small-Cell Lung Cancer Harboring Epidermal Growth Factor Receptor Mutations Without Indication for Chemotherapy

Akira Inoue, Kunihiko Kobayashi, Kazuhiro Usui, Makoto Maemondo, Shoji Okinaga, Iwao Mikami, Masahiro Ando, Koichi Yamazaki, Yasuo Saijo, Akihiko Gemma, Hitoshi Miyazawa, Tomoaki Tanaka, Kenji Ikebuchi, Toshihiro Nukiwa, Satoshi Morita, and Koichi Hagiwara

J Clin Oncol 27:1394-1400. © 2009

Performance status	
1	3†
2	4†
3	17
4	5

Table 2. Response to Treatment

Response	No. of Patients	Response Rate (%)	90% CI
Complete response	1	3	—
Partial response	18	62	—
Stable disease	7	24	—
Progressive disease	2	7	—
Not assessable	1	3	—
Overall response	19	66	51 to 80
Disease control rate	26	90	80 to 99

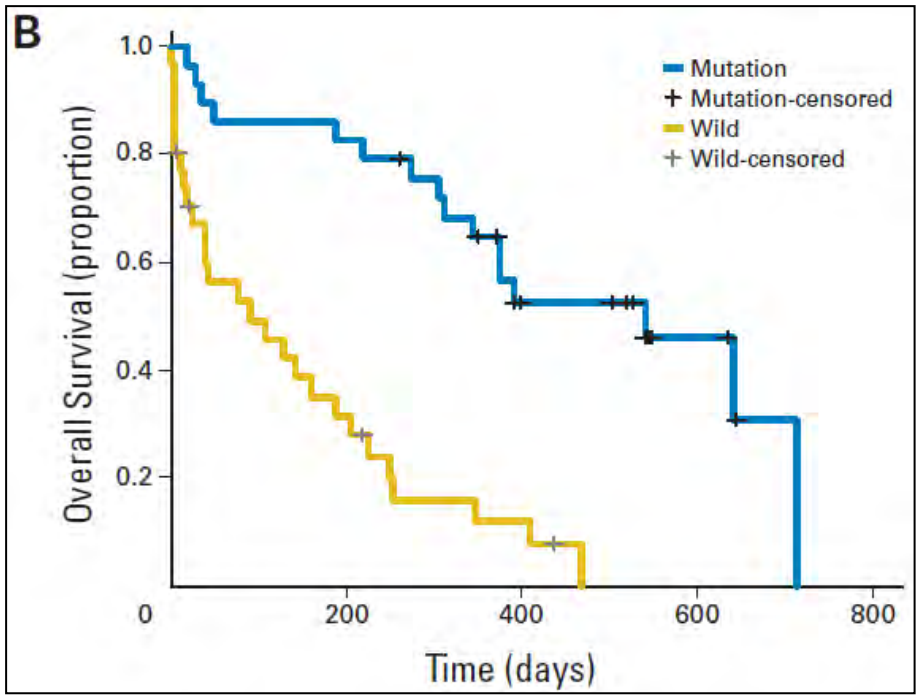
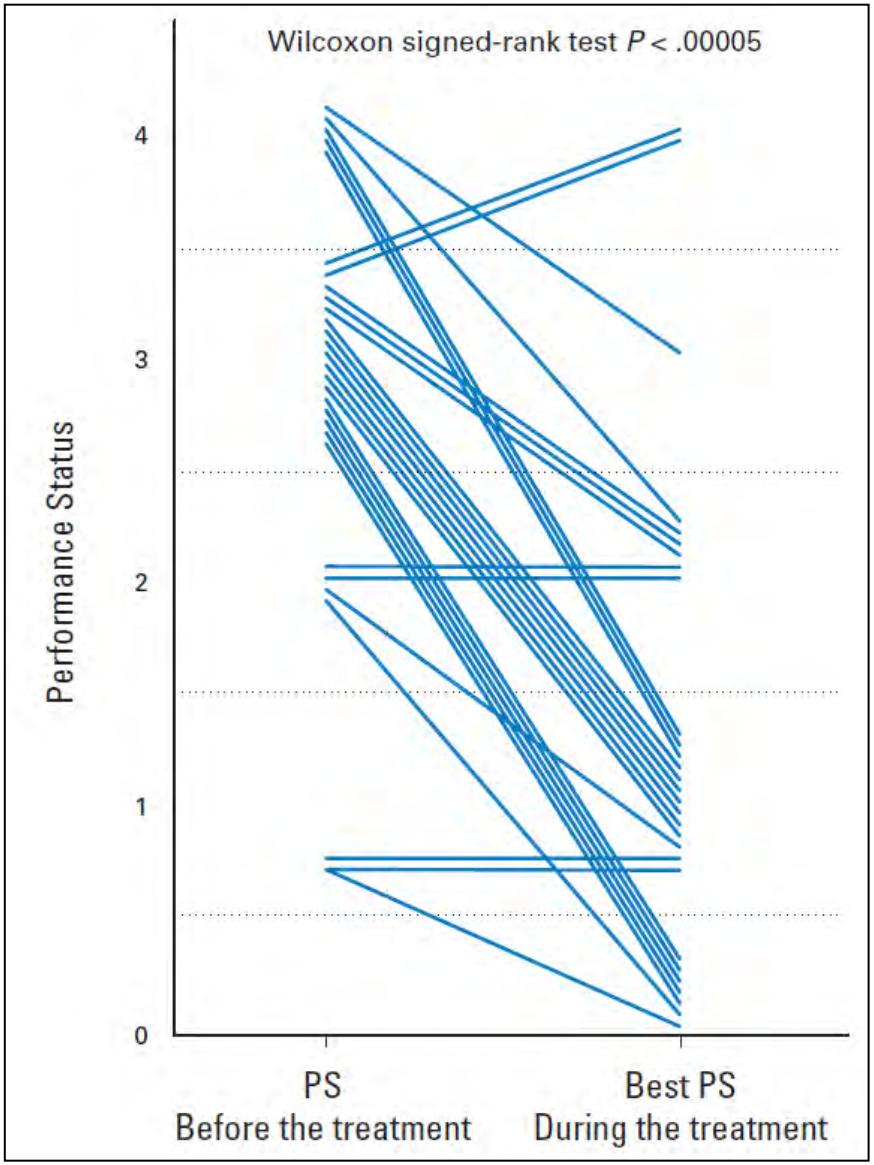


Table 3. Grade 2 or Worse Adverse Events

Toxicity	No. of Patients				
	Grade 2	Grade 3	Grade 4	Total With ≥ Grade 3 Toxicity	
				No.	%
Hematologic					
Anemia	3	2	0	2	7
Neutropenia	2	0	0	0	
Nonhematologic					
Pneumonitis	0	0	1	1	3
AST/ALT	4	3	0	3	10
Anorexia	0	1	0	1	3
Rash	4	0	0	0	
Diarrhea	2	0	0	0	
Hypoalbuminemia	2	0	0	0	
Vomiting	1	0	0	0	
Pain	1	0	0	0	
Hyperkalemia	1	0	0	0	

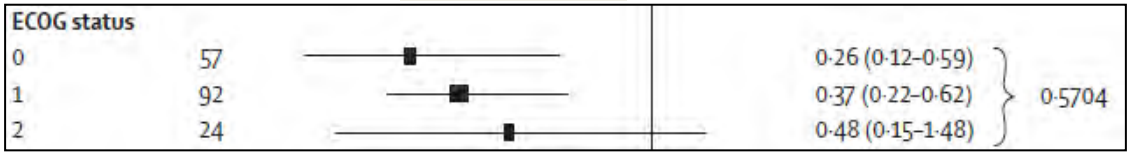


J Clin Oncol 27:1394-1400. © 2009

Erlotinib versus standard chemotherapy as first-line treatment for European patients with advanced EGFR mutation-positive non-small-cell lung cancer (EURTAC): a multicentre, open-label, randomised phase 3 trial

Lancet Oncol 2012; 13: 239–46

PFS



First-line erlotinib versus gemcitabine/cisplatin in patients with advanced *EGFR* mutation-positive non-small-cell lung cancer: analyses from the phase III, randomized, open-label, ENSURE study†

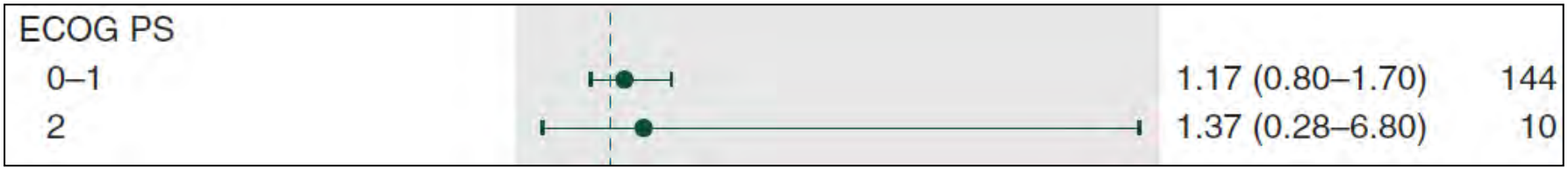
Annals of Oncology 26: 1883–1889, 2015

PFS

Final overall survival results from a randomised, phase III study of erlotinib versus chemotherapy as first-line treatment of EGFR mutation-positive advanced non-small-cell lung cancer (OPTIMAL, CTONG-0802)

Annals of Oncology 26: 1877–1883, 2015

Survie



First-Line Crizotinib versus Chemotherapy in *ALK*-Positive Lung Cancer

N Engl J Med 2014;371:2167-77.

PFS

Crizotinib versus Chemotherapy in Advanced *ALK*-Positive Lung Cancer

N Engl J Med 2013;368:2385-94

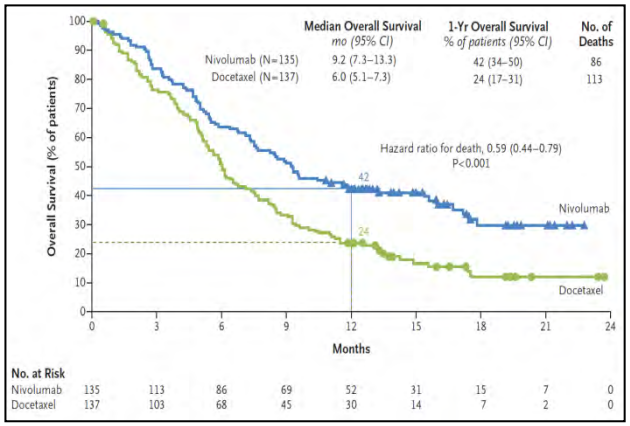
PFS

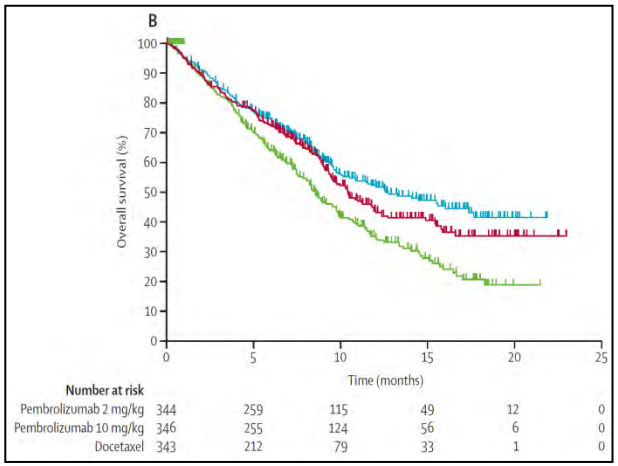
L’immunothérapie

ORIGINAL ARTICLE

Nivolumab versus Docetaxel in Advanced Squamous-Cell Non–Small-Cell Lung Cancer

Julie Brahmer, M.D., Karen L. Reckamp, M.D., Paul Baas, M.D.,





Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial

Roy S Herbst, Paul Baas, Dong-Wan Kim, Enriqueta Felip, José L Pérez-Gracia, Ji-Youn Han, Julian Molina, Joo-Hang Kim, Catherine Dubos Arvis,

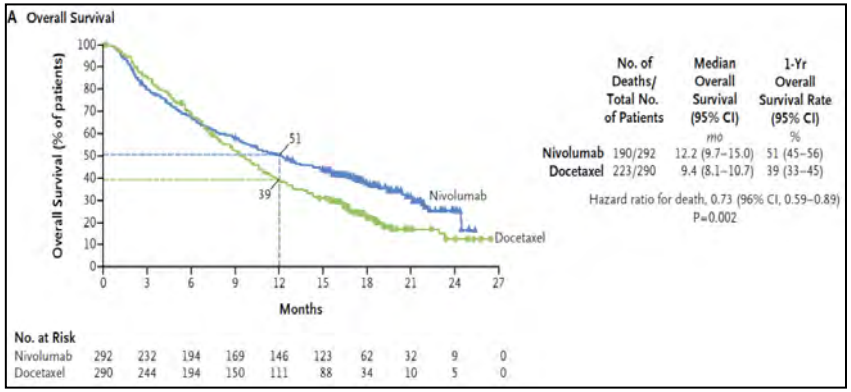
Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial

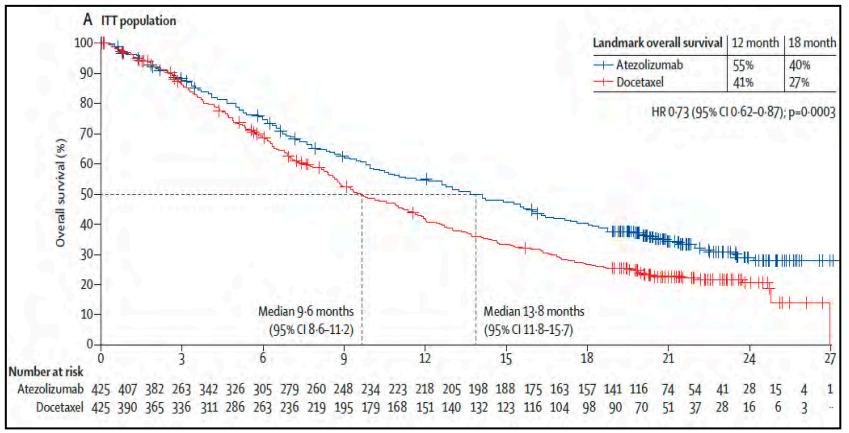
Achim Rittmeyer, Fabrice Barlesi, Daniel Waterkamp, Keunchil Park, Fortunato Ciardiello, Joachim von Pawel, Shirish M Gadgeel, Toyoaki Hida, Dariusz M Kowalski, Manuel Cobo Dols, Diego L Cortinovis, Joseph Leach, Jonathan Polikoff, Carlos Barrios, Fairooz Kabbinavar, Osvaldo Arén Frontera, Filippo De Marinis, Hande Turna, Jong-Seok Lee, Marcus Ballinger, Marcin Kowanetz, Pei He, Daniel S Chen, Alan Sandler, David R Gandara, for the OAK Study Group*

ORIGINAL ARTICLE

Nivolumab versus Docetaxel in Advanced Nonsquamous Non–Small-Cell Lung Cancer

H. Borghaei, L. Paz-Ares, L. Horn, D.R. Spigel, M. Steins, N.E. Ready, L.Q. Chow,

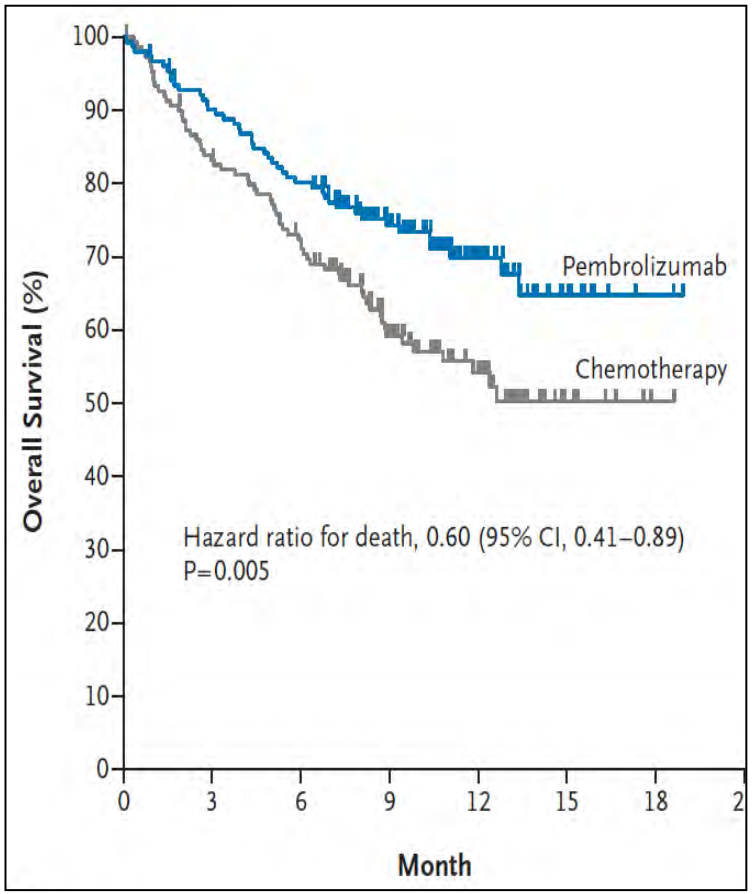




NEJM 2015: 123; NEJM 2015: 1627; Lancet 2016: 1540; Lancet 2017: 255

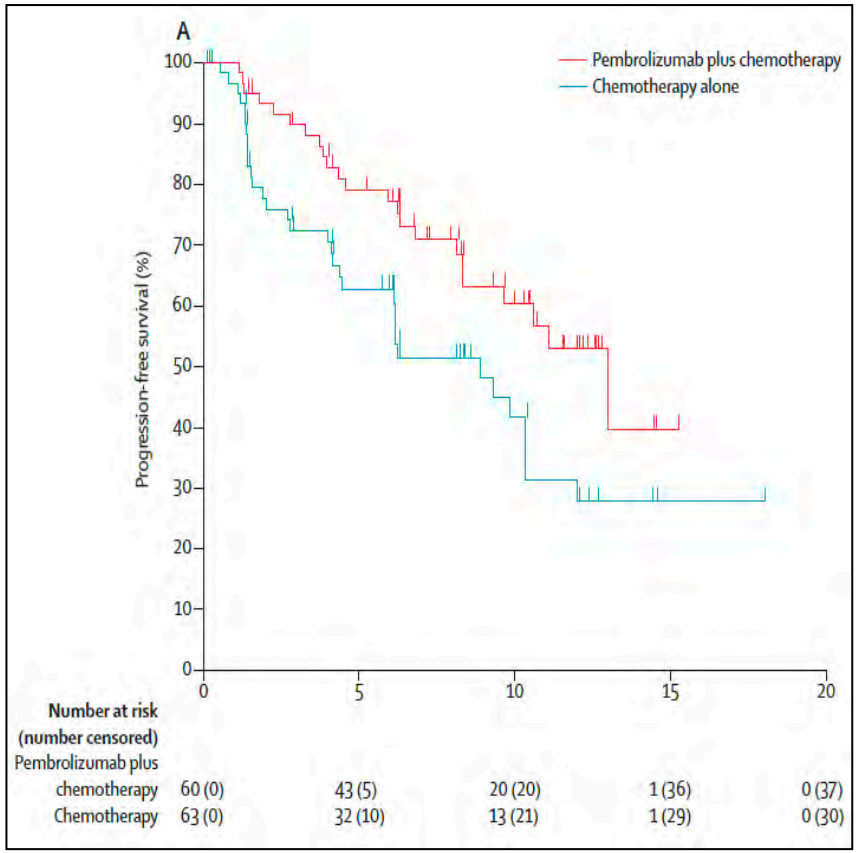
Pembrolizumab versus Chemotherapy for PD-L1–Positive Non–Small-Cell Lung Cancer

Martin Reck, M.D., Ph.D., Delvys Rodríguez-Abreu, M.D.,



Carboplatin and pemetrexed with or without pembrolizumab for advanced, non-squamous non-small-cell lung cancer: a randomised, phase 2 cohort of the open-label KEYNOTE-021 study

Corey J Langer, Shirish M Gadgeel, Hossein Borghaei, Vassiliki A Papadimitrakopoulou, Amita Patnaik, Steven F Powell, Ryan D Gentzler,



NEJM 2016: 1823; Lancet Oncol 2016: 1497

Immunothérapie pour PS ≥ 2?

PATIENTS

Eligible patients had documented stage IIIB or IV or recurrent nonsquamous NSCLC after radiation therapy or surgical resection and had also had disease recurrence or progression during or after one prior platinum-based doublet chemotherapy regimen. Patients with known *EGFR* mutation or *ALK* translocation were allowed to have received or be receiving an additional line of tyrosine kinase inhibitor therapy, and a continuation of or switch to maintenance therapy with pemetrexed, bevacizumab, or erlotinib was allowed in all patients.

have an Eastern Cooperative Oncology Group (ECOG) performance-status score of 0 or 1 (on a

Pas d'information si PS 2!!!

Patients had to be 18 years of age or older, have an Eastern Cooperative Oncology Group (ECOG) performance-status score of 0 or 1 (on a scale from 0 to 5, with higher numbers indicating greater tumor-related disability; a score of 0 indicates no symptoms, and 1 mild symptoms), and have adequate hematologic, hepatic, and renal function; patients with central nervous system metastases were eligible if the metastases had been treated and were stable. Tumor tissue obtained before treatment was required for use in biomarker analyses but was not used in the selection of patients. Exclusion criteria were autoimmune disease, symptomatic interstitial lung disease, systemic immunosuppression, prior treatment with immune-stimulatory antitumor agents including checkpoint-targeted agents, and prior use of docetaxel. Complete eligibility criteria are provided in the study protocol, available with the full text of this article at NEJM.org.

N Engl J Med 2015;373:1627-39.

Severe exacerbation or manifestation of primary disease related to nivolumab in non-small-cell lung cancer patients with poor performance status or brain metastases

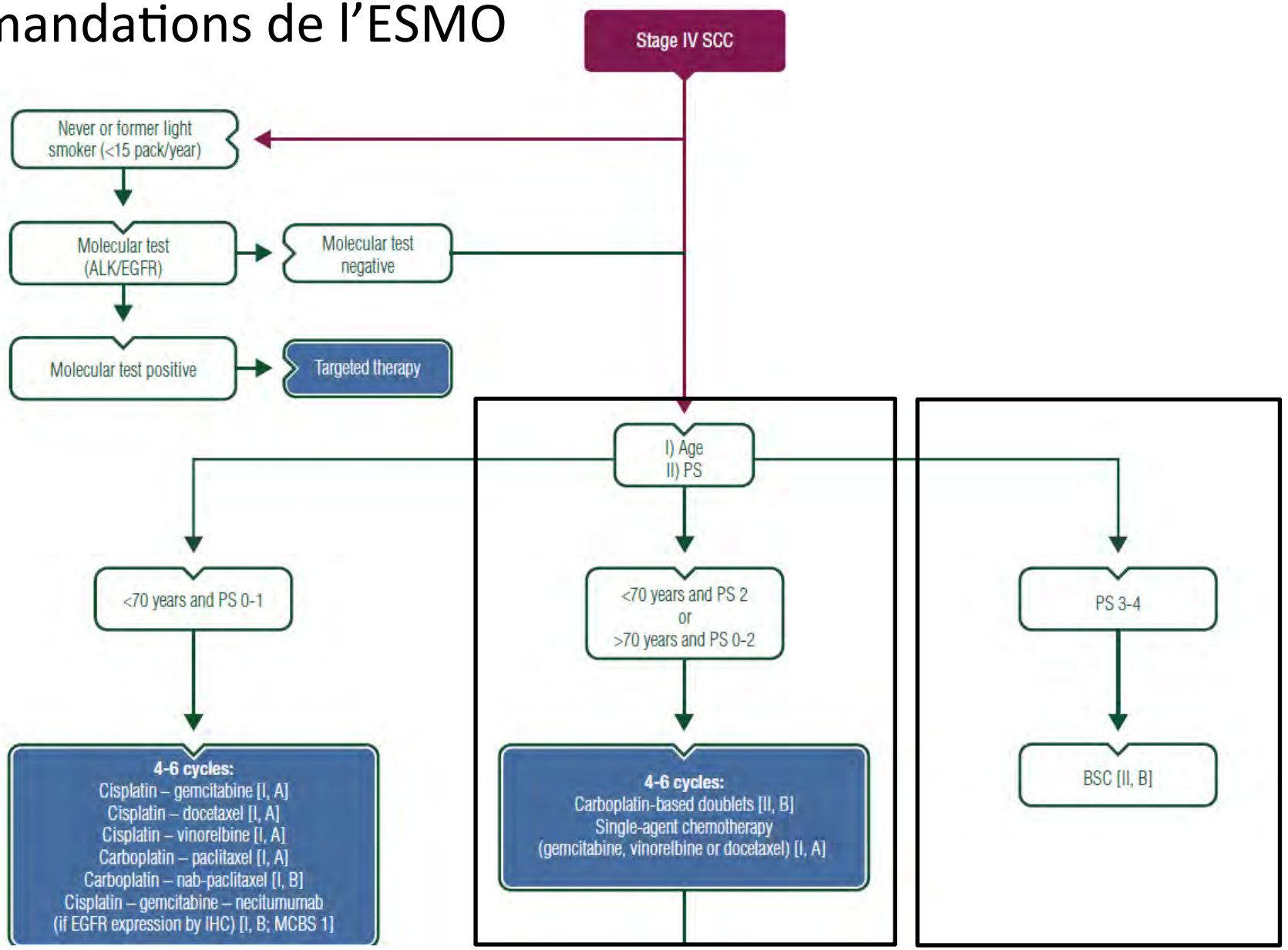
Table 1. Baseline characteristics, stratification factors, prior therapy, and distant metastases

Characteristic	Discontinued patients ($N = 12$)	Consecutive patients ($N = 20$)	Total ($N = 32$)
Age (years), median (range)	73 (46–85)	70 (53–83)	71 (46–85)
Male sex, no. (%)	7 (58)	14 (70)	21 (66)
ECOG PS, no. (%)			
0	0	5 (25)	5 (16)
1	4 (33)	14 (70)	18 (56)
2	2 (17)	1 (5)	3 (9)
3	6 (50)	0	6 (19)

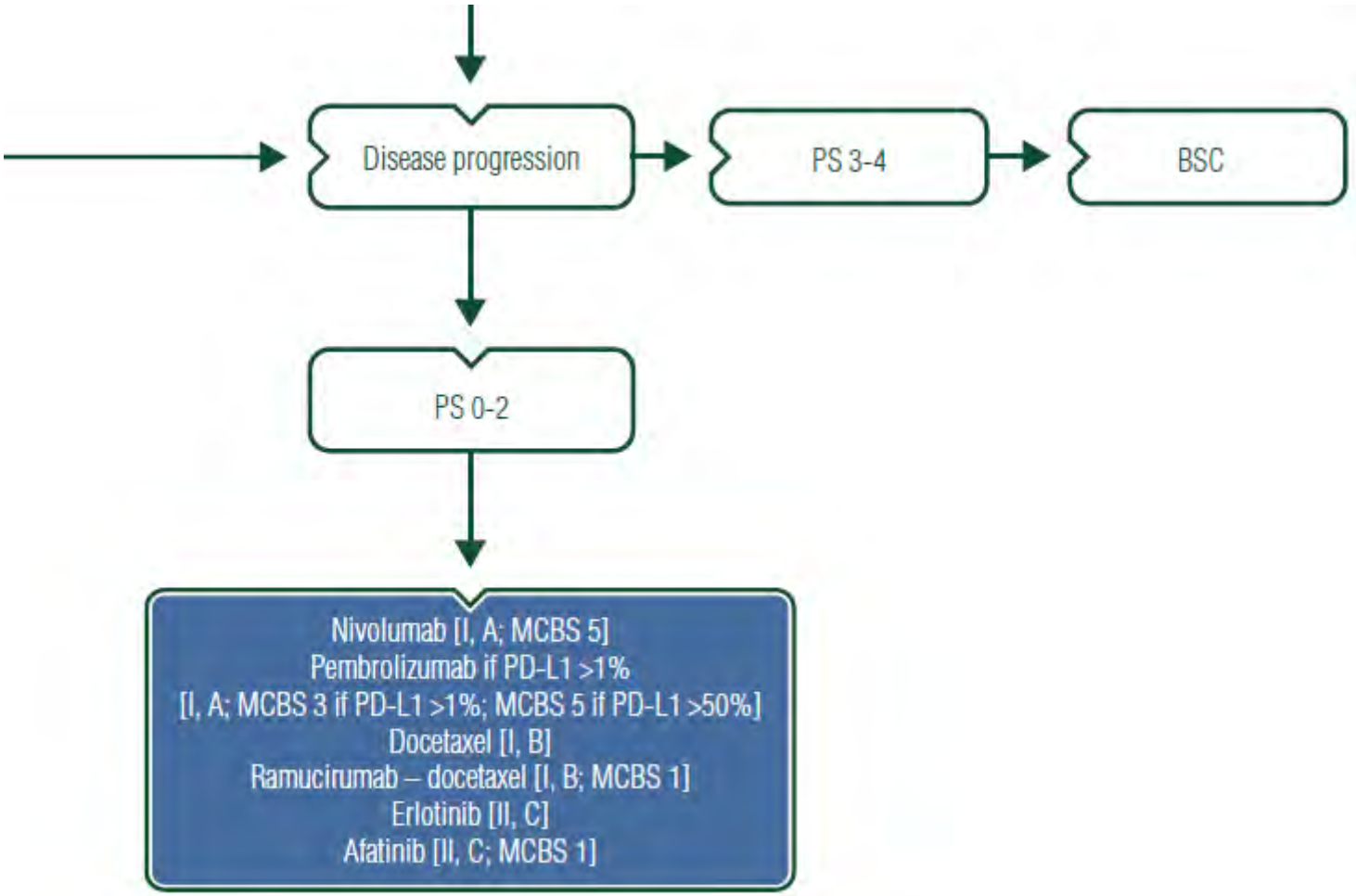
The following characteristics were noted more frequently in discontinued patients than in consecutive patients: female, Eastern Cooperative Oncology Group performance status (ECOG PS) score of 2 or 3, adenocarcinoma histology, CNS metastasis and bone metastasis. In particular, discontinued patients more frequently exhibited an ECOG PS score of 3 or CNS metastasis. All 6 patients with an ECOG PS score of 3 and 8 of the 10 patients with CNS metastases discontinued treatment due to severe exacerbation or manifestation.

Ann Oncol 2016: 1354

Recommandations de l'ESMO



Annals of Oncology 27 (Supplement 5): v1–v27, 2016


Disease progression
PS 3-4
BSC
PS 0-2
Nivolumab [I, A; MCBS 5]
Pembrolizumab if PD-L1 >1%
[I, A; MCBS 3 if PD-L1 >1%; MCBS 5 if PD-L1 >50%]
Docetaxel [I, B]
Ramucirumab – docetaxel [I, B; MCBS 1]
Erlotinib [II, C]
Afatinib [II, C; MCBS 1]

Et les cancers à petites cellules?

Chemoradiotherapy duration correlates with overall survival in limited disease SCLC patients with poor initial performance status who successfully completed multimodality treatment

Tab. 1 Patients' characteristics according to the type of CRT

Characteristic	CRT type		Significance
	Concurrent (n = 51)	Sequential (n = 74)	
Age, years	61.5	64.3	n.s.
Sex, %	58 men, 42 women	68 men, 37 women	n.s.
PS	2 (range 2–3)	2 (range 2–3)	n.s.

Tab. 2 Treatment outcome according to the type of CRT

Treatment outcome	CRT type		Significance
	Concurrent (*n* = 51)	Sequential (*n* = 74)	
Objective response, %	80	75	n.s.
Complete response, %	45	41	n.s.
Median PFS, months	12 (95% CI 7.9–16.2)	11.6 (95% CI 9.8–13.4)	n.s.
Median OS, months	14.9 (95% CI 11.7–18.2)	16.1 (95% CI 12.1–20)	n.s.
1-year survival, %	62.1	67.1	n.s.
2-year survival, %	37.9	22.4	n.s.
3-year survival, %	22.7	15.2	n.s.

Tab. 4 Factors associated with overall survival according to the univariate and multivariate analysis

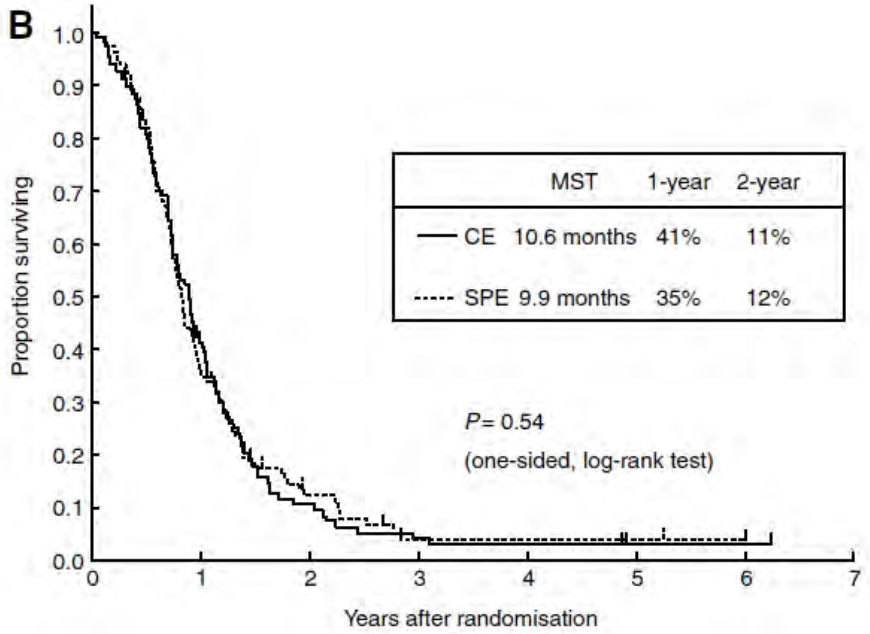
Patient and treatment characteristics	Univariate analysis (p value)	Multivariate analysis (p value)
Age	n.s.	n.s.
Sex	n.s.	–
Time from diagnosis to start of TRT	n.s.	n.s.
PCI	n.s.	n.s.
Occurrence of BM	n.s.	<0.042*
Number of chemotherapy cycles (≥4 versus <4)	n.s.	–
Type of CRT	n.s.	n.s. (0.072)
CRT duration	<0.014*	<0.025*

Randomised phase III trial of carboplatin plus etoposide *vs* split doses of cisplatin plus etoposide in elderly or poor-risk patients with extensive disease small-cell lung cancer: JCOG 9702

Table 2 Compliance and drug delivery

	CE ($n = 110$)	SPE ($n = 109$[a])	*P*-value
Median interval of each chemotherapy (days) (range)			
1–2	27 (14–35)	23 (20–37)	0.02[b]
2–3	25 (21–56)	22 (20–35)	0.07[b]
3–4	27 (21–36)	24 (21–38)	0.05[b]
Total delivered courses/projected courses	353/440 (80%)	360/436 (83%)	
Dose reduction	32 (29%)	11 (10%)	<0.01[c]
Course delay	45 (41%)	40 (37%)	0.58[c]
G-CSF delivery	81 (74%)	84 (77%)	0.64[c]
No. of courses with G-CSF delivery/number of total courses	183/354 (52%)	203/362 (56%)	

	CE	SPE	Total
CR	5	5	10
PR	75	75	150
NC	17	11	28
PD	11	16	27
NE	2	3	5
Total	110	110	220
Response rate	73%	73%	
95% CI	63–81%	63–81%	



British Journal of Cancer (2007) 97, 162–169

Conclusions (1)

- L'indice de performance est une mesure globale de l'état de santé du patient
- Deux échelles sont couramment utilisées: ECOG et Karnofsky
- Mais
  - L'évaluation de l'indice de performance est en partie opérateur dépendant.

Conclusions (2)

- Il existe peu de données pour les traitements à visée curative pour lesquels, l'impact des comorbidités plutôt que l'indice de performance, va influer sur le choix thérapeutique

Conclusions (3)

- Pour les maladies avancées et métastatiques et PS2
  - Un doublet de platine, même s'il est plus toxique, est supérieur à une monothérapie en 1ère ligne
  - Il n'y a pas de données factuelles avec haut niveau de preuve permettant un choix entre cis- et carboplatine
- En cas d'altération moléculaire ciblable (EGFR/ALK), un traitement ciblé peut être proposé en cas de PS 2-3
- Les données actuelles ne permettent pas de positionner l'immunothérapie pour les PS > 1