Chimiothérapie aux soins intensifs

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Aucun conflit d’intérêt à déclarer

Littérature

- Peu de données disponibles
- Séries et cas cliniques
- Etudes rétrospectives
- Avis d'experts

⮑ Niveau de preuve faible

Chimiothérapie à l’USI
Dans quelle situation?

- Surveillance et administration de soins intensifs

- Chimiothérapie au décours d’une complication motivant l’admission à l’USI

Surveillance et administration de soins intensifs

1. Traitement compliqué
   – Méthotrexate à haute dose
   – Interleukine à haute dose
2. Co-morbidités
   – Pathologie cardiaque
   – Insuffisance hépato-cellulaire…

Surveillance et administration de soins intensifs

3. Risques allergiques majeurs
   - Patient ayant présenté une allergie sévère au produit et devant à nouveau être exposé: taxanes, dérivés du platine
4. Syndrome de lyse tumorale

Chimiothérapie au décours d'une complication motivant l'admission à l'USI

Intensive care in patients with newly diagnosed malignancies and a need for cancer chemotherapy*

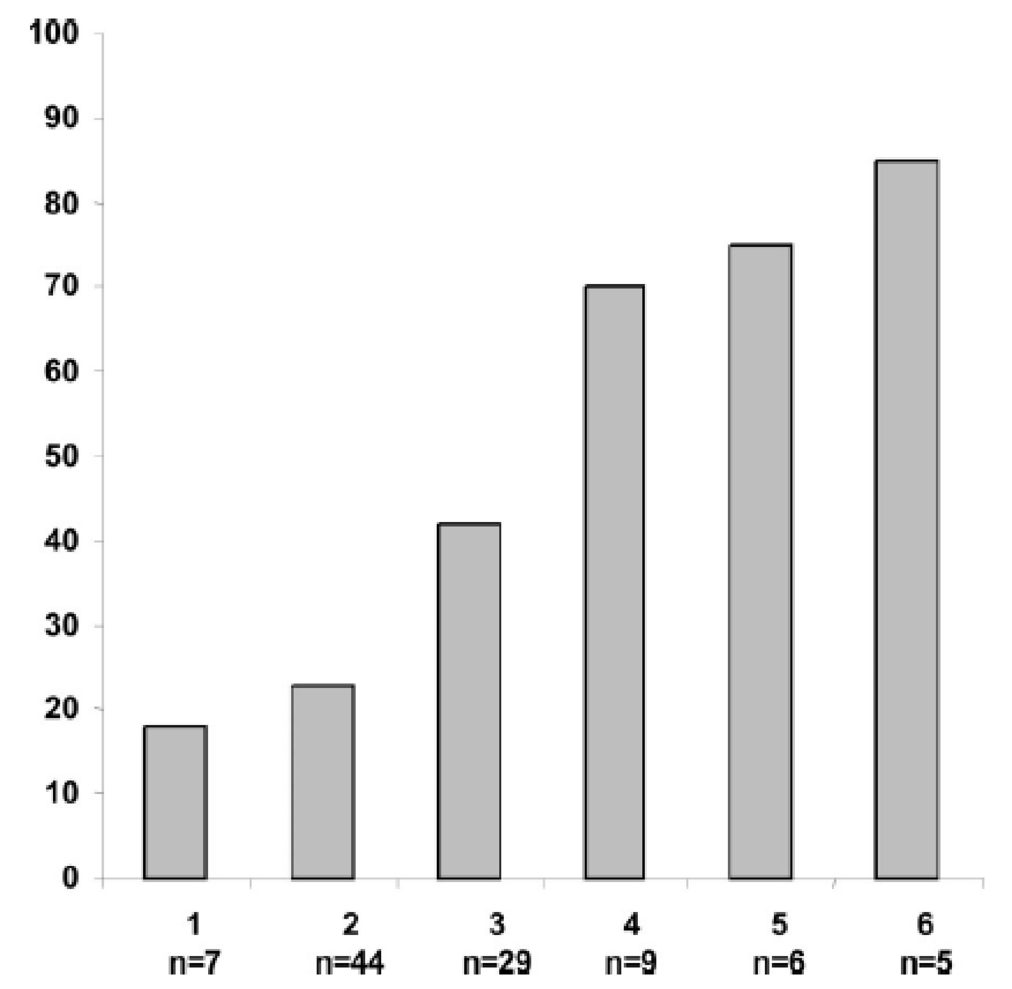
Michael Darmon, MD; Guillaume Thiery, MD; Magali Ciroldi, MD; Sandra de Miranda, MD;
Lionel Galicier, MD; Emmanuel Raffoux, MD; Jean-Roger Le Gall, MD; Benoît Schlemmer, MD;
Élie Azoulay, MD, PhD

		No. (%) or Median (Interquartile Range)	
	All Patients n = 100	Survivors n = 60	Nonsurvivors n = 40
Male gender	64	34 (56.7)	30 (75)
Age, yrs	47 (32–61)	47 (35–61)	46.5 (30–62)
SAPS II score at ICU admission	39 (30–48)	38 (28–47)	44 (35–74)
LOD score at ICU admission	5 (3–7)	4 (2–6)	7 (4–9)
Nature of the underlying malignancy			
Acute leukemia	43	29 (48.3)	14 (35)
Non-Hodgkin's lymphoma	32	18 (30)	14 (35)
Solid tumors	12	7 (11.7)	5 (12.5)
Hodgkin's disease	5	2 (3.3)	3 (7.5)
Miscellaneous malignancies	8	4 (6.7)	4 (10)
Advanced malignancy	84	43 (71.7)	34 (85)
Reasons for ICU admission			
Acute respiratory failure	70	38 (63.3)	32 (80)
Acute renal failure	43	21 (35)	22 (55)
Shock	19	8 (13.3)	11 (27.5)
Coma	21	9 (15)	12 (30)
Hepatic failure	12	3 (5)	9 (22.5)
Hemophagocytosis	15	7 (11.7)	7 (17.5)
Clinically documented infection	54	27 (45)	27 (67.5)
Tumor lysis syndrome	31	20 (33)	11 (27.5)
Treatments in the ICU			
Endotracheal mechanical ventilation	54	19 (31.6)	35 (87.5)
Noninvasive mechanical ventilation	33	20 (33.3)	13 (32.5)
Vasopressive agents	42	12 (20)	30 (75)
Dialysis	30	12 (20)	18 (45)

Crit Care Med 2005 Vol. 33, No. 11

Table 3. Multivariable analysis: Independent predictors of 30-day mortality

	Odds Ratio	95% CI	p Value
Need for vasopressors	6.01	1.86–19.4	.003
Mechanical ventilation	6.36	1.76–22.94	.028
Hepatic failure	7.76	1.25–48.27	.005



Risk factors to predict outcome in critically ill cancer patients receiving chemotherapy in the intensive care unit

Table 1 Baseline characteristics at the time of initiating chemotherapy

Characteristics	No. of patients (%)
Age, median (interquartile range) years	50 (37–63)
Gender ratio, male/female	38:24
Type of malignancy	
Hematologic	49 (79)
Solid	13 (21)

Support Care Cancer (2011) 19:491–495

Prédicteurs mortalité USI

Variables on the day of chemotherapy	Survivors (n=37)	Non-survivors (n=25)	p value
Age, median (interquartile range), years	51 (36–65)	48 (37–62)	0.785
Gender (female)	12 (32%)	12 (48%)	0.217
Status of malignancy			
Hematologic cancer	31 (84%)	18 (72%)	0.264
SPAS II	46 (34–57)	64 (55–74)	<0.001
Severe neutropaenia	3 (8%)	1 (4%)	0.518
Need for mechanical ventilation	16 (43%)	22 (88%)	<0.001
Need for vasopressor support	6 (16%)	10 (40%)	0.036
Need for renal replacement therapy	12 (32%)	7 (28%)	0.710
Concomitant infection	10 (27%)	13 (52%)	0.046

Table 4 Multiple logistic regression analysis for the probability of intensive care unit (ICU) mortality

	Odds ratio	95% CI	p value
SOFA score ≥10	9.66	1.43–65.47	0.020
Need for mechanical ventilation	6.26	1.12–34.95	0.037

Support Care Cancer (2011) 19:491–495

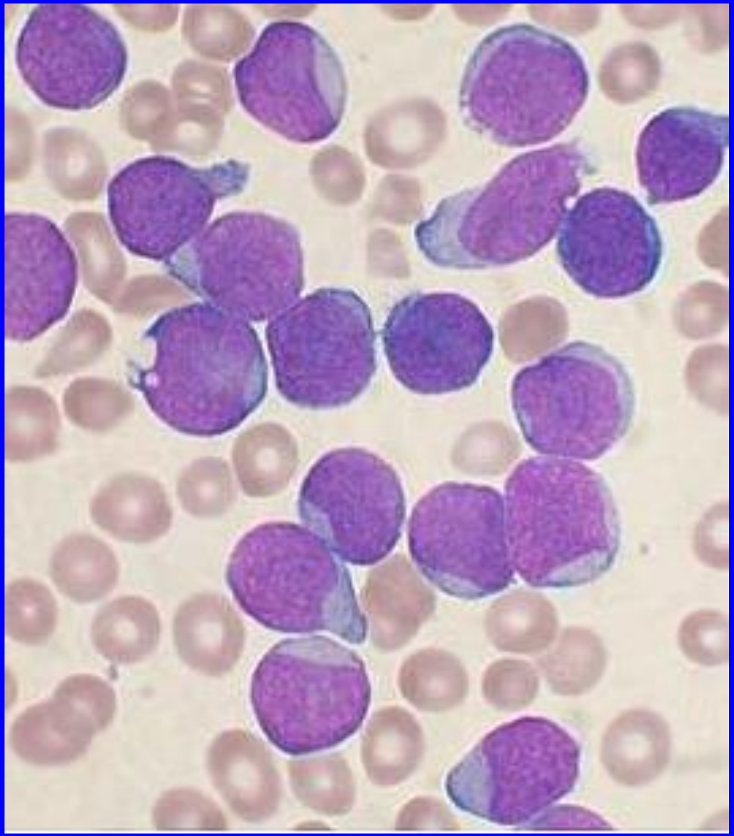
Le pronostic du patient cancéreux admis à l'USI est fonction de la gravité de la complication et pas de l'affection néoplasique sous-jacente

	Résultats des analyses multivariées	
Mortalité USI	ICM scoring system APACHE II	OR = 2.24 (95% CI 1.60-3.13; $p < 0.001$) OR = 1.10 (95% CI 1.04-1.16; $p < 0.001$)
Mortalité hospitalière	ICM scoring system SAPS II	OR = 2.31 (95% CI 1.69-3.16; $p < 0.001$) OR = 1.05 (95% CI 1.02-1.08; $p < 0.001$)
Survie après sortie de l'hôpital	ICM scoring system Phase du cancer Type de cancer	HR = 1.67 (95% CI 1.22-2.30; $p = 0.001$) HR = 3.29 (95% CI 1.58-6.81; $p = 0.001$) HR = 0.35 (95%CI 0.13-0.90; $p = 0.03$)

Berghmans et al; Supp Care Cancer

Faire la distinction

Tumeur hématologique



Tumeur solide

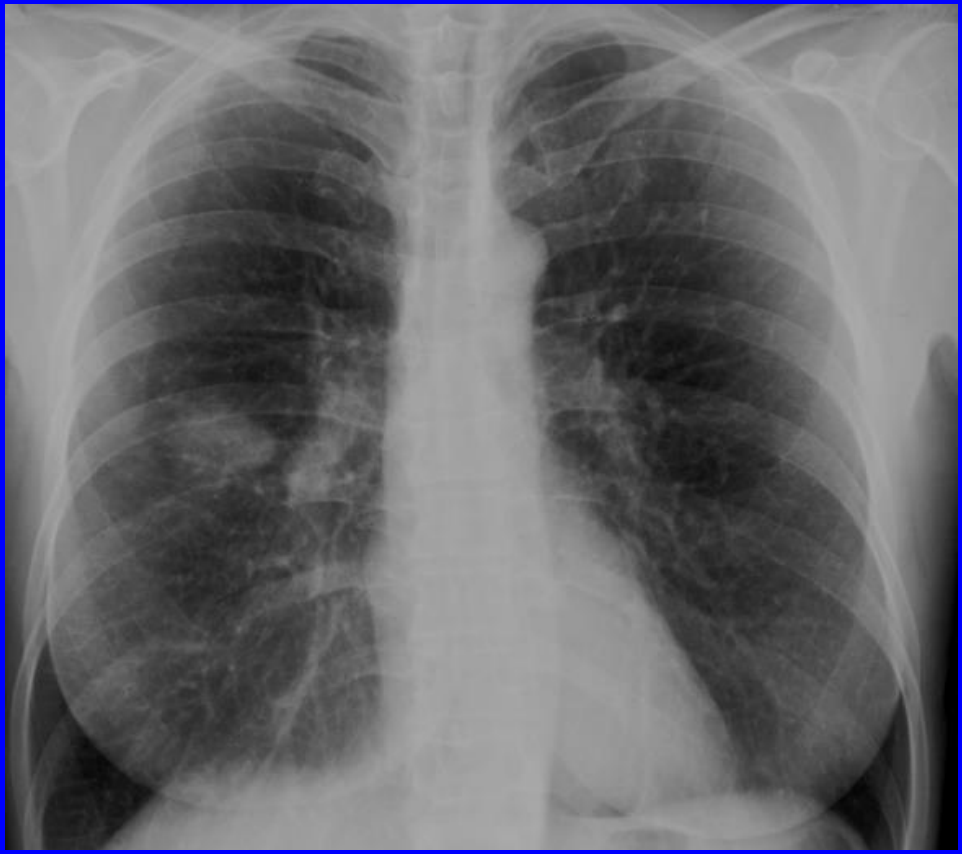


Table 1. Efficacy of chemotherapy in selected advanced malignancies

Disease	Initial Chemotherapy Regimen (Reference)	Complete Response Rate, %	5-Year Disease-Free Survival Rate, %
Solid tumors			
Non-small cell lung cancer	Carboplatin and paclitaxel (6)	1	0
Colorectal cancer	Fluorouracil, oxaliplatin, and leucovorin (7)	1	0
Breast cancer	Doxorubicin and paclitaxel (8)	11	<10
Gastric cancer	Epirubicin, cisplatin, and fluorouracil (9)	4	0
Pancreatic cancer	Gemcitabine and erlotinib (10)	<1	0
Ovarian cancer	Paclitaxel and carboplatin (11)	46	>40
Hematologic malignancies			
Non-Hodgkin's lymphoma	Cyclophosphamide, doxorubicin, vincristine, prednisone, and rituximab (12)	76	>50
Acute myeloid leukemia	Daunorubicin and cytarabine (13)	72	46
Acute lymphoblastic leukemia	Prednisone, vincristine, cyclophosphamide and daunorubicin or idarubicin (14)	72	33
Hodgkin's disease	Bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone (15)	96	91

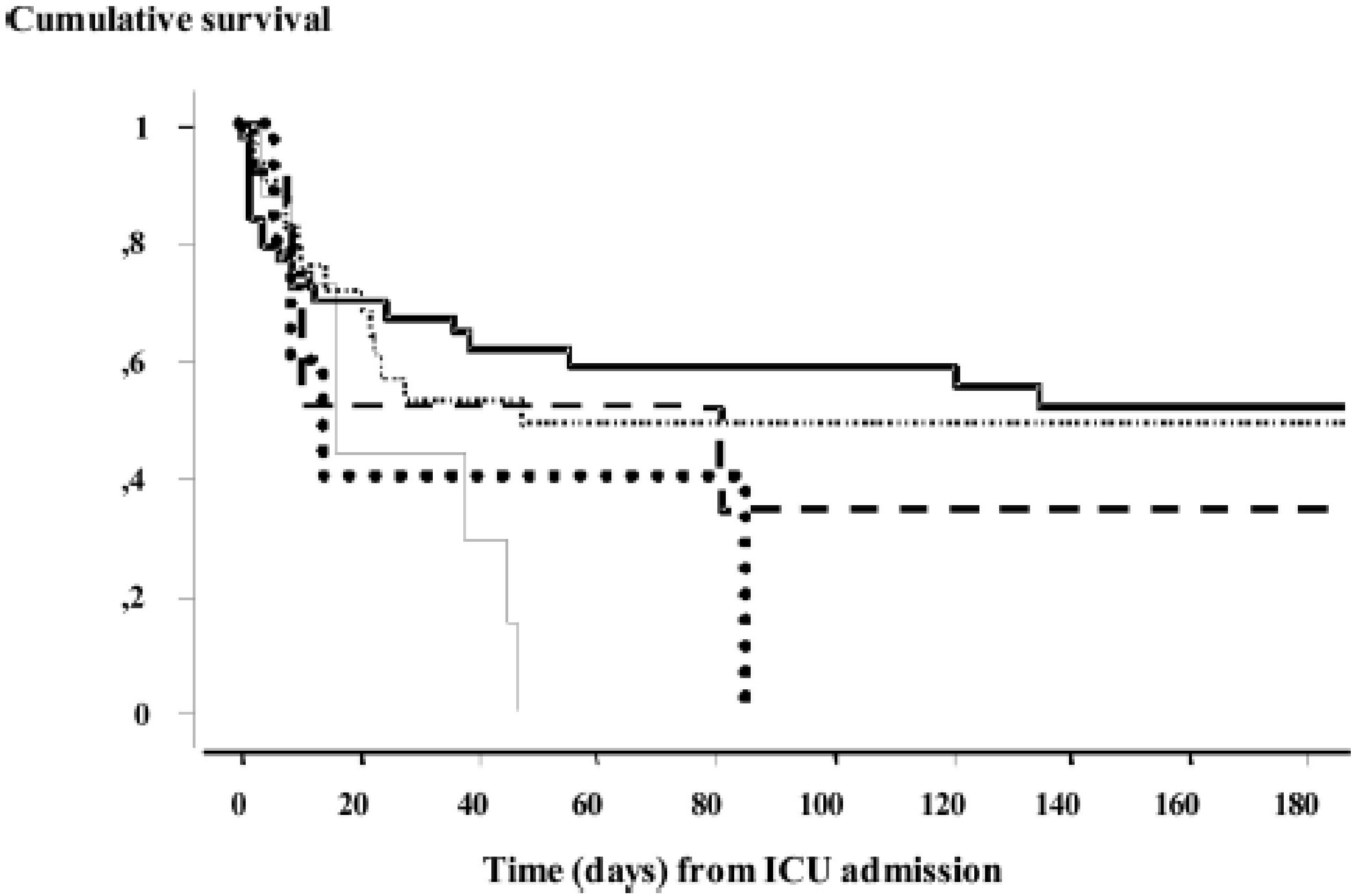


Figure 2. Survival according to the underlying malignancy. *Solid line*, acute leukemia (n = 43); *dotted line*, Hodgkin's disease (n = 5); *thin dotted line*, non-Hodgkin's lymphoma (n = 32); *dashed line*, solid tumors (n = 12); and *thin solid line*, other tumors (n = 8). *ICU*, intensive care unit.

Tumeur hématologique

Cytotoxic chemotherapy administered to two patients with partially refractory leukaemia while receiving intensive care treatment

is an extremely rare event. We report
two patients with partially refractory
acute myel
achieved re
mia after re
the intensiv
were subse
neic bone marrow transplant.

We suspect that the excellent results of cytotoxic chemotherapy occurred because ARDS was the result of combined effects of bronchopneumonia, sepsis and severe leukaemic lung injury. The continued improvement following the critical episodes was sustained by the BMT.

Importance d'avoir des causes réversibles

Support Care Cancer (2004) 12:739–742
DOI 10.1007/s00520-004-0665-7

Outcome in severely ill patients with hematological malignancies who received intravenous chemotherapy in the intensive care unit

Table 1 Main reasons to start chemotherapy in the ICU (n=37)

Extensive disease with major organ involvement	20 (54%)
Pulmonary or airway involvement	13 (35%)
Leukostasis or leukemic infiltration	6[a]
Lymphoma invasion	3
Bulky mediastinum with tracheal compression	3[b]
Upper airway obstruction	1
Nonpulmonary major organ involvement	7 (19%)
Renal invasion	4[c]
Bulky disease with pericardial tamponade	1
Brainstem invasion	1
Hepatic invasion	1
Extensive disease without major organ involvement	7 (19%)
High leukemic burden	4[d]
Stage III or IV lymphoma	3
Other reasons	10 (27%)
Severe disseminated intravascular coagulation (DIC)	4[e]
All trans-retinoic acid syndrome	2
Paraneoplastic polyneuropathy with respiratory failure	1
T-cell lymphoma related hemophagocytic syndrome	2
Acute life-threatening hemolysis	1

Intensive Care Med (2006) 32:93–99
DOI 10.1007/s00134-005-2836-5

	Alive (n=21)	Dead (n=16)	p
Baseline characteristics			
Gender male	10 (48%)	10 (63%)	0.51
Age (years)	45±21	47±16	0.81
Status and type of malignancy			
High (vs. low) grade malignancy	17 (81%)	15 (94%)	0.36
Intravenous chemotherapy <3 weeks	1 (5%)	2 (13%)	0.57
First presentation (vs. relapse)	16 (76%)	10 (63%)	0.47
Chemotherapy within 48 h admission	18 (86%)	9 (56%)	0.07
Reasons to start chemotherapy in the ICU			0.21
Extensive disease with organ invasion	14 (67%)	6 (38%)	
Extensive disease without organ invasion	3 (14%)	4 (25%)	
Other	4 (19%)	6 (38%)	
Severity of illness upon admission			
APACHE II score	22±8	23±6	0.68
APACHE II expected mortality	47±24	46±22	0.92
Mechanical ventilation	6 (29%)	7 (44%)	0.49
Vasopressor use	7 (33%)	5 (31%)	0.99
Severity of illness during ICU stay			
Mechanical ventilation[a]	9 (43%)	14 (88%)	0.007
Duration of mechanical ventilation, median (IQR)[b]	4 (3–5)	9 (4–11)	0.37
Leukopenia during admission	5 (24%)	7 (44%)	0.29
Infection at initiation of chemotherapy	8 (38%)	7 (44%)	0.75
According to the diagnostic certainty[c]			0.99
Documented infection[d]	3 (14%)	2 (13%)	
Clinically suspected infection	5 (24%)	5 (32%)	
According to the severity of infection[c]			0.25
Sepsis	0 (0%)	1 (6%)	
Severe sepsis	3 (14%)	4 (25%)	
Septic shock	5 (24%)	2 (13%)	
According to the site of infection[c]			0.99
Pulmonary	4 (19%)	4 (25%)	
Nonpulmonary	4 (19%)	3 (19%)	
Renal replacement therapy	5 (25%)	4 (25%)	0.99
Length of stay at the ICU, median (days; IQR)	7 (5–11)	12 (7–15)	0.23

Intensive Care Med (2006) 32:93–99
DOI 10.1007/s00134-005-2836-5

Tumeur solide

Sur quelles bases décider de l'administration d'une chimiothérapie à l'USI?

Sensibilité de la néoplasie à la chimiothérapie

Tumeur chimiosensible

- Sarcome Ewing
- CBPC

Sensibilité intermédiaire

- CBNPC
- Sein

Tumeur chimiorésistante

- Rein
- Mélanome

Tenir compte de l'exposition antérieure à une chimiothérapie

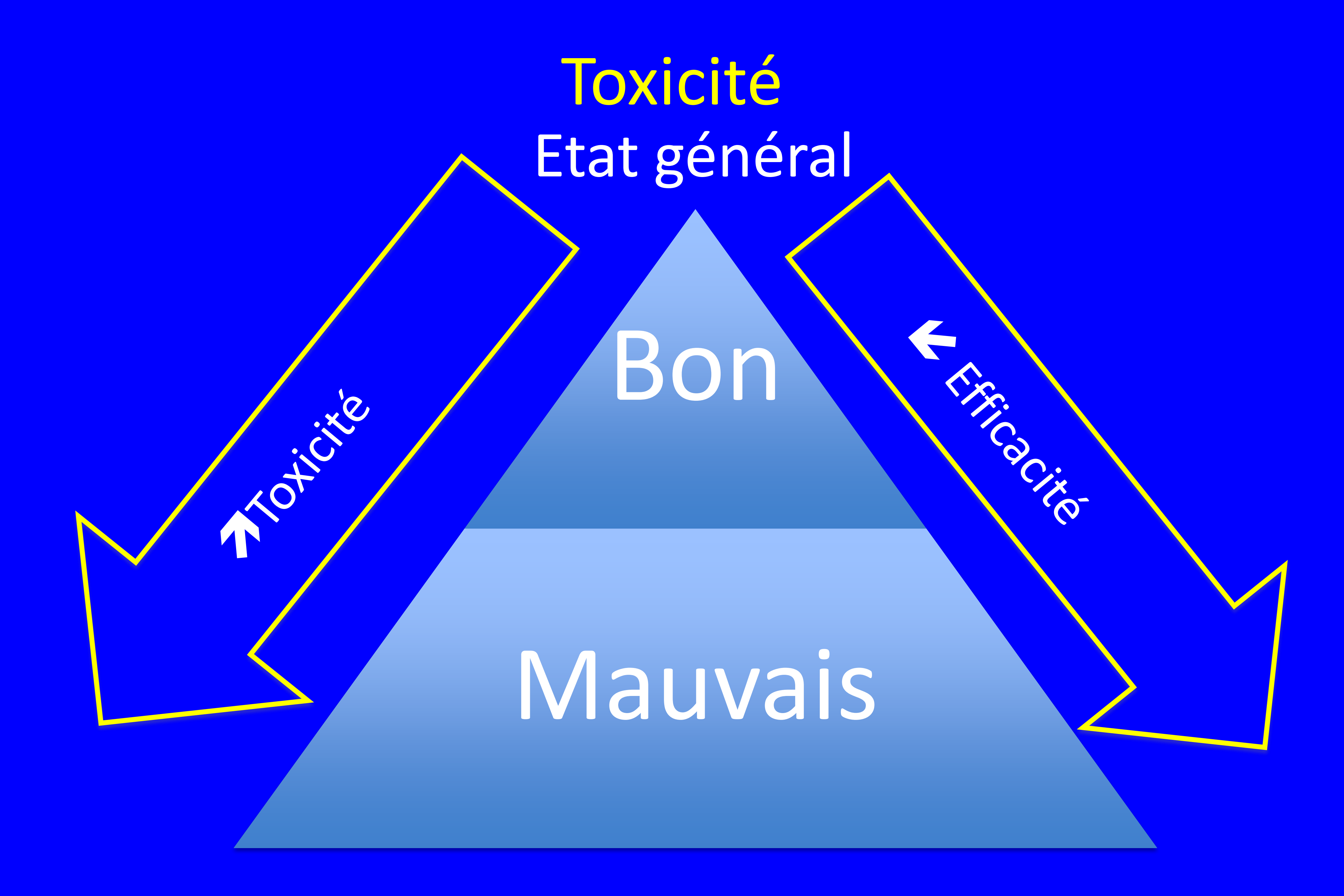
Sur quelles bases décider de l’administration d’une chimiothérapie à l’USI?

- Pronostic intrinsèque de la tumeur
  - CBNPC EGFRm vs wtEGFR
  - Carcinomatose méningée
  - Lymphangite pulmonaire
  - …

Overall Survival (months)			
Mutant	Wild Type	*P*	Reference
30.5	6.6	.001	Han[46]
20.8	8.4	.09	Cappuzzo[47]
14.7	4.7	.046	
13	4.9	.02	
Not reached	7	.0022	
20.4	6.9	.0001	

	EGFR mutant	**Wild type**	***P***
Han et al. (17)			
Response (%)	65	13.7	<0.001
TTP (mo)	22	1.8	<0.001
Median survival (mo)	30.5	6.6	<0.001
Mitsudomi et al. (16)			
Response (%)	83	10	<0.0001
Median survival (mo)	>20	13.0	0.0053
Takano et al. (30)			
Response (%)	82	11	<0.0001
Median survival (mo)	20.0	7.0	0.0001
Cortes-Funes et al. (38)			
Response (%)	60	9	0.001
Median survival (mo)	13.0	4.9	0.02
Taron et al. (39)			
Response (%)	94	13	<0.0001
Median survival (mo)	>20	9.9	0.001

J Clin Oncol 2007: 587
Clin Cancer Res 2006: 4416S


Toxicité
Etat général
Bon
Mauvais
↑Toxicité
← Efficacité

Comment approcher la chimiothérapie pour une tumeur solide? L'exemple du cancer bronchique

Cancer bronchique à petites cellules

Outcome of patients admitted to the intensive care unit with newly diagnosed small cell lung cancer

Ross R. Jennens[a,*], Mark A. Rosenthal[a], Paul Mitchell[b], Jeffrey J. Presneill[c]

Patient demographics

Parameter	$n = 20$
Age, median (range), *y*	67 (38–82)
Male/female ratio	10/10
Disease status limited/extensive	8/12
Intubated, *n* (%)	9 (45)
Duration in ICU, median (range), *d*	2 (1–11)
Treatment with chemotherapy, *n* (%)	16 (80%)
Timing of SCLC diagnosis, n (%)	
Pre ICU	3 (15)
During ICU	7 (35)
Post ICU	10 (50)
Timing of chemotherapy[a]	
Pre ICU	1 (5)
During ICU	5 (25)
Post ICU	11 (55)
Adjusted Manchester score	
0	1 (5)
1	10 (50)
2	4 (20)
3	3 (15)
4	2 (10)

Lung Cancer 38 (2002) 291–296

Score de Manchester

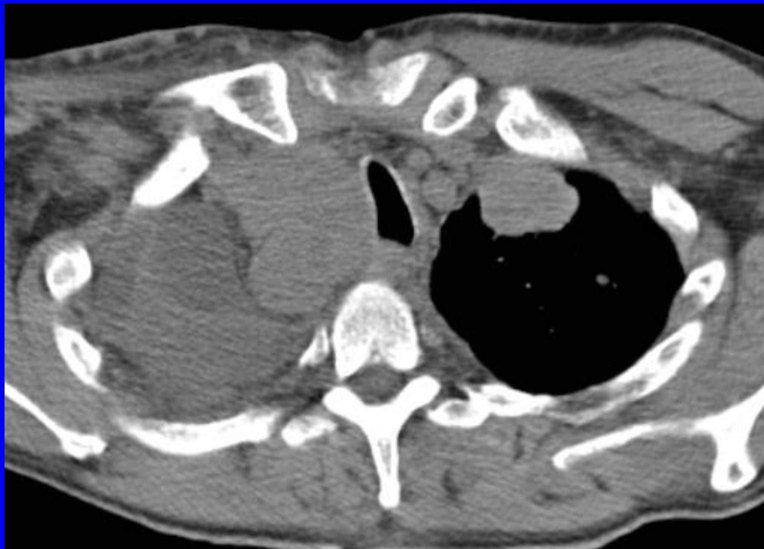
- Indice de performance
- Maladie étendue/Métastatique
- LDH élevé > 550 UI/l
- Natrémie < 132 mEq/l
- Phosphatases alcalines > 165 UI/l

Score 2-3 → survie 1 an de 15%

Score 4-5 → survie 1 an 0%

Data for five patients treated with chemotherapy in ICU

Patient number	Age (years)	Sex	Stage	ICU duration (days)	Intubation duration (days)	Reason for ICU admission	Treatment	Timing of diagnosis[a]	Response	Manchester score (adjusted)	Survival (days)[b]
1	68	F	ED	11	11	Respiratory failure	1 × CE	During	No	2	11
2	55	F	ED	9	6	Respiratory failure	2 × CAV	During	No	2	16
3	64	M	ED	2	0	Respiratory monitoring	1 × Cyclo	Pre	No	3	37
4	38	M	LD	5	5	Respiratory failure	4 × CAV	During	Yes	1	210[c]
5	68	F	LD	9	9	Respiratory failure	4 × CE	During	Yes	1	214[c]



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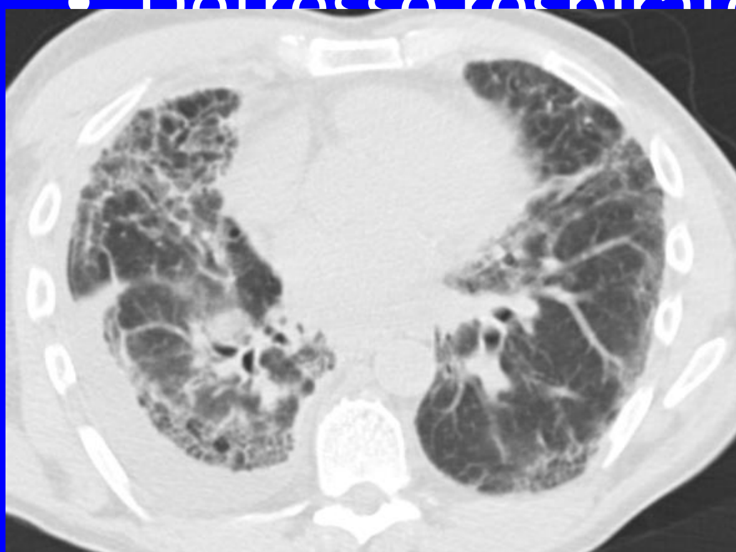
- Détresse respiratoire → intubation et ventilation



ocarcinome p
nnaire massiv
va se marier;
demandeuse de tout tenter ma
sombre

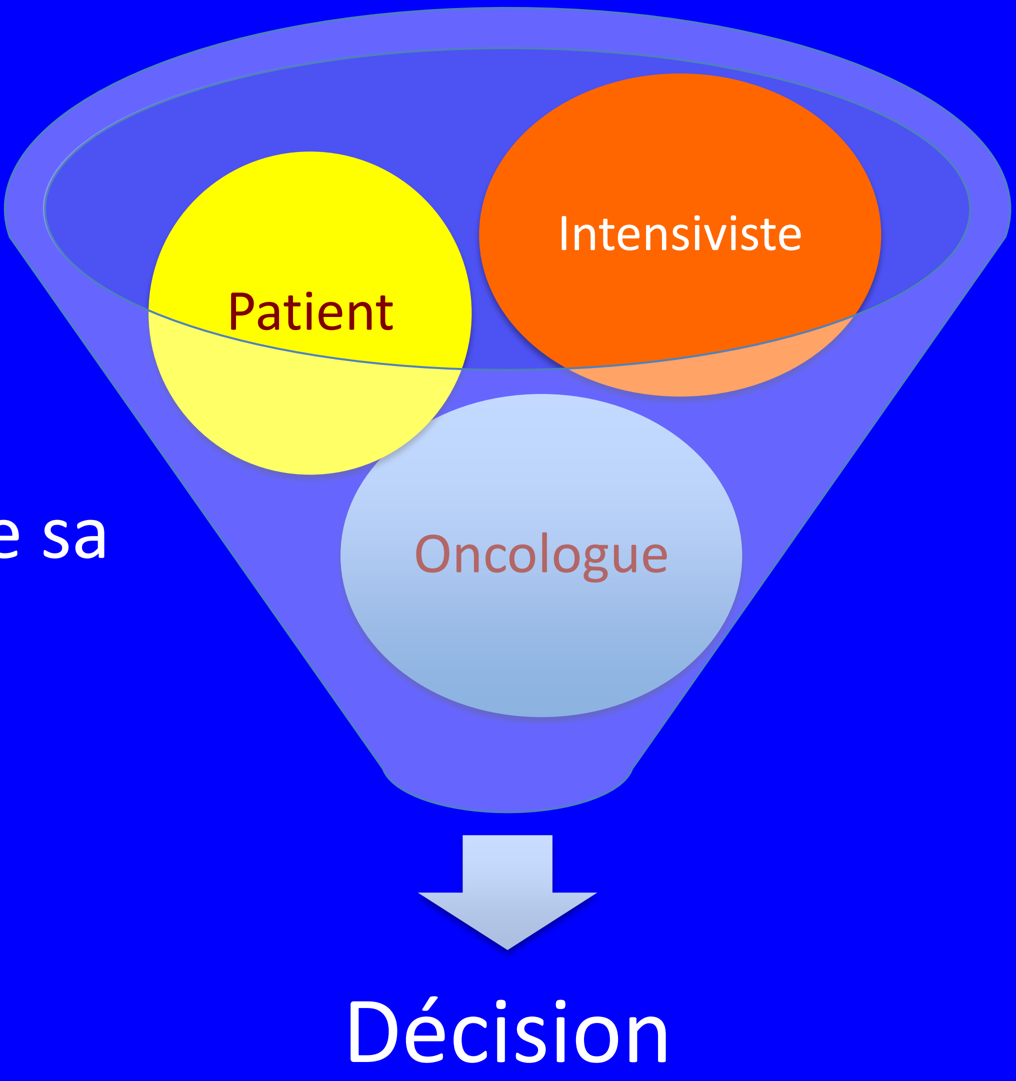
Quelle serait votre attitude thérapeutique?

1. Désescalade thérapeutique
2. Non escalade thérapeutique et soins de confort
3. Essai de sevrage de la VM et demander au patient son avis pour une chimiothérapie palliative
4. Chimiothérapie palliative sous respirateur en accord avec la famille

Evolution

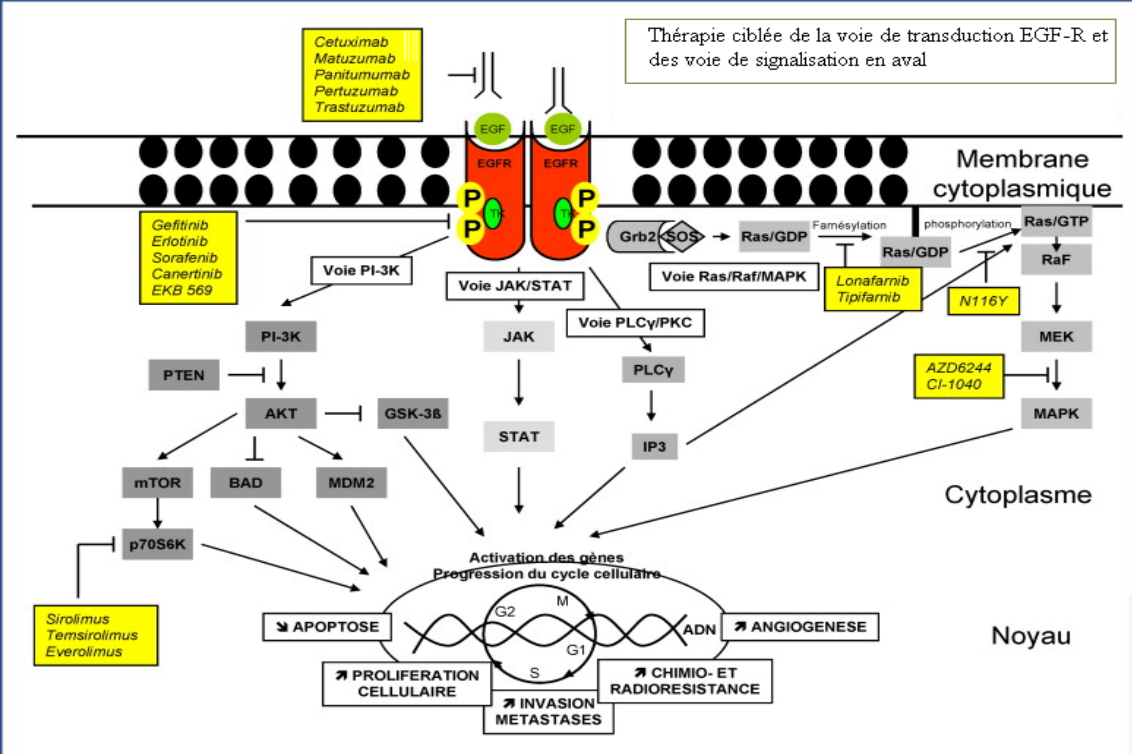
- Trachéotomie
- Chimiothérapie par cisplatine-pémétrexed
- Sevrage du respirateur après la 1ère cure de CT
- Le patient peut régler ses affaires et « dire au revoir »
- Reprise évolutive rapide → décès en insuffisance respiratoire après la 2ème cure

Sur quelles bases décider de l'administration d'une chimiothérapie à l'USI?

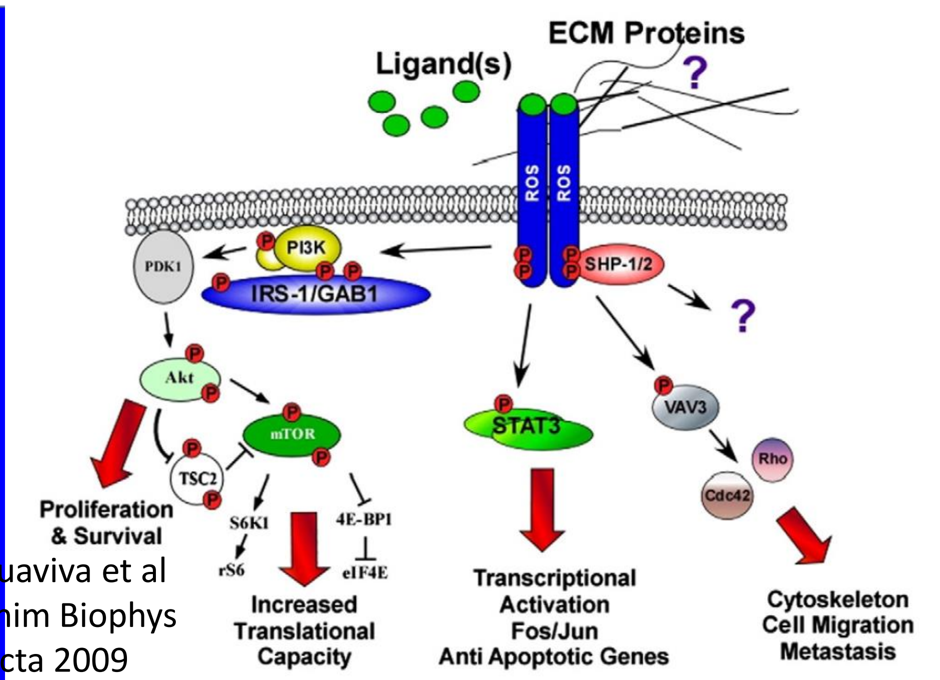


- Désir du patient et de sa famille
- Eviter acharnement thérapeutique

L’arrivée des thérapies ciblées

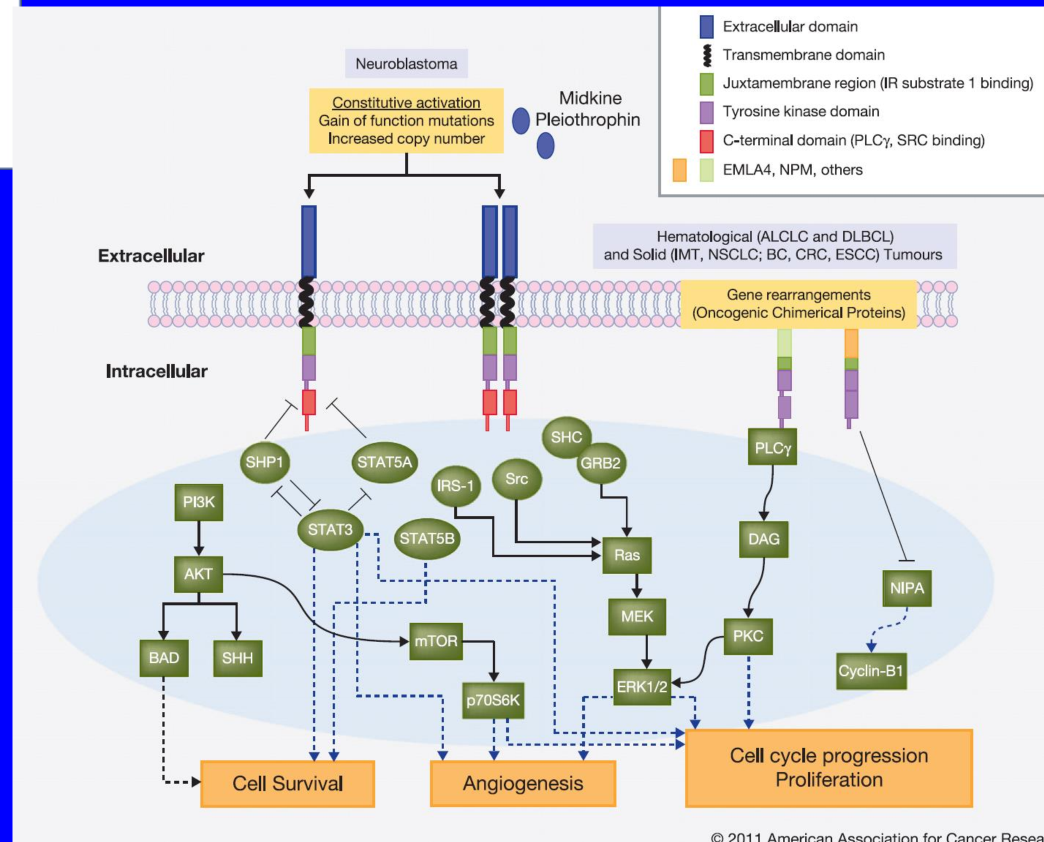


J Clin Oncol 2007: 587
Oncogene 2009: S24



Acquaviva et al Biochim Biophys Acta 2009

Grande et al; Mol Cancer Ther 2011



Maemondo, 2010 Inoue, 2013	Gefitinib	114	73,7%
	CBDCA + Pac	114	30,7%
Rosell, 2012	Erlotinib	86	58 %
	Standard CT	87	15 %
Zhou, 2011 (ASCO 2012)	Erlotinib	83	82 %
	Gem + CBDCA	82	36 %
Sequist, 2013	Afatinib	230	56%
	CDDP-PEM	115	23%
Wu, 2014	Afatinib	242	67%
	CDDP-GEM	122	23%

Taux de réponse très élevés …et rapides

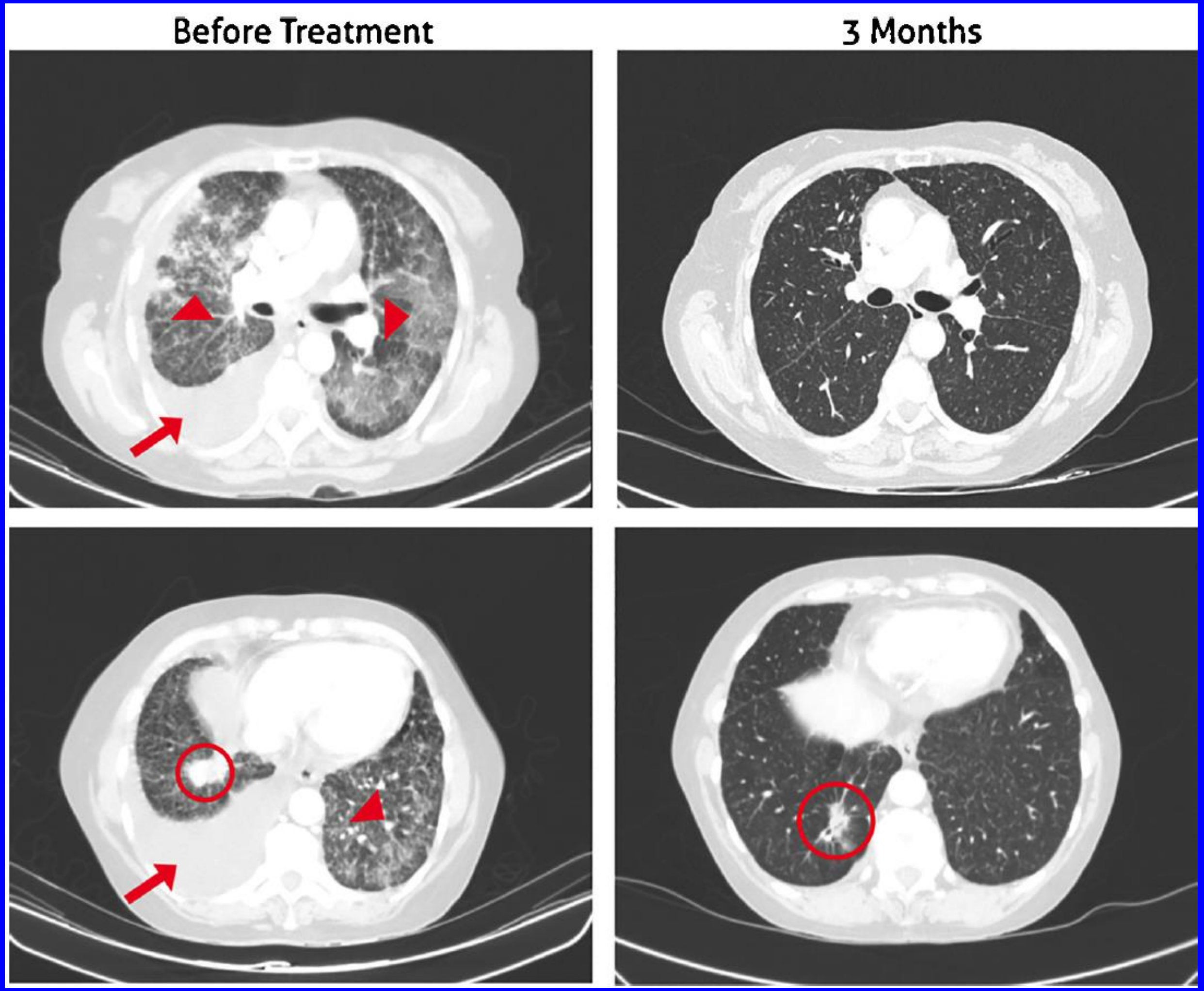
Response	Crizotinib (N=173)	Chemotherapy (N=174)
Type of response — no. (%)		
Complete response	1 (1)	0
Partial response	112 (65)	34 (20)
Stable disease	32 (18)	63 (36)
Progressive disease	11 (6)	60 (34)
Could not be evaluated†	17 (10)	17 (10)

Shaw et al, NEJM 2013

Successful empirical erlotinib treatment of a mechanically ventilated patient newly diagnosed with metastatic lung adenocarcinoma

Joaquim Bosch-Barrera[a,b,c,*,1], Elia Sais[a,1], Carol Lorencio[d], Rut Porta[a,b,c], Angel Izquierdo[a,b], Javier A. Menéndez[b,e], Joan Brunet[a,b,c], Josep Maria Sirvent[d], Rafael Rosell[f,**]

- Insuffisance respiratoire sur infiltration tumorale (avec lymphangite C)
- Détubation à 5j d'erlotinib
- Sortie de l'hôpital à 2 sem
- En vie sans récidive à 6 mois



Lung Cancer 86 (2014) 102–104

Surviving Respiratory Insufficiency with Intensive Care Support in a Pretreated, Extensively Metastasized Patient with an EML4-ALK Translocation

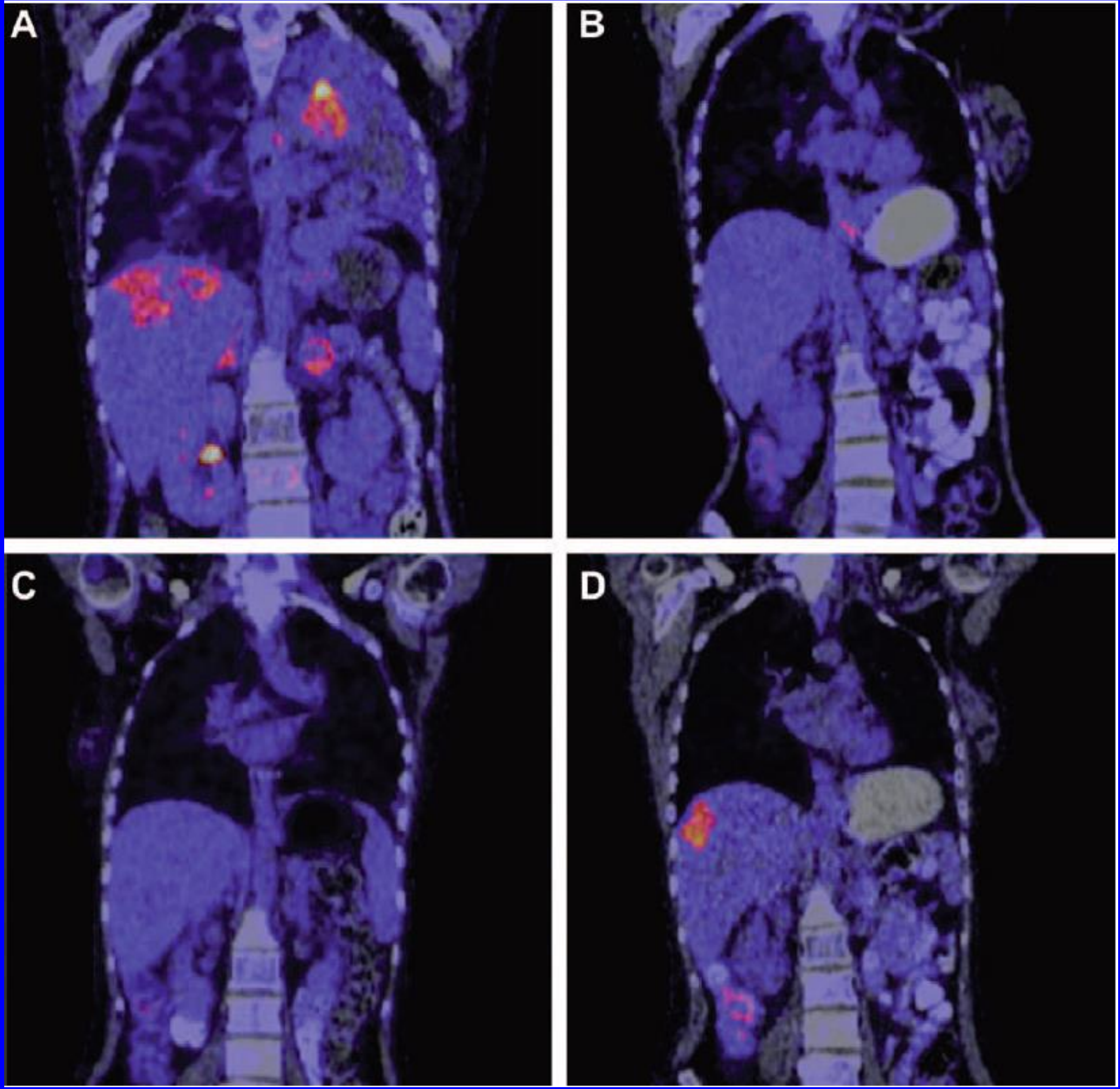


FIGURE 1. Fluorodeoxyglucose positron emission tomography/computed tomography scan showing FDG uptake reflecting disease activity. A, Baseline (October 28, 2011). B, Partial tumor response at 6 weeks (December 8, 2011). C, Partial tumor response at 12 weeks (January 17, 2012). D, Recurrent FDG uptake in the liver at 6 months (April 12, 2012). FDG, fluorodeoxyglucose.

Van Geffen et al, J Thorac Oncol 2013

Successful Treatment with Crizotinib in Mechanically Ventilated Patients with ALK Positive Non–Small-Cell Lung Cancer

	Age	Histology	Number of Previous Chemotherapies	Timing of Crizotinib Initiation from MV Initiation (days)	Weaning from MV/ T-tube (days)	Discharge from Hospital (days)	ECOG PS at Discharge from Hospital	PFS (mo)
1	F/40	Adenoca	2	21	42/57	60	2	3
2	F/44	Adenoca	4	12	20/36	38	2	8
3	F/49	Adenoca	3	10	17/-	92	3	3

						4	2	21	42/57	60	2	3
2	F/44	Adenoca	Positive	Failed FISH test because of tissue insufficiency	WT/WT	13	4	12	20/36	38	2	8
3	F/49	Adenoca	Positive	Failed FISH test because of tissue insufficiency	WT/WT	13	3	10	17/-	92	3	3

(*J Thorac Oncol.* 2013;8: 250–253)

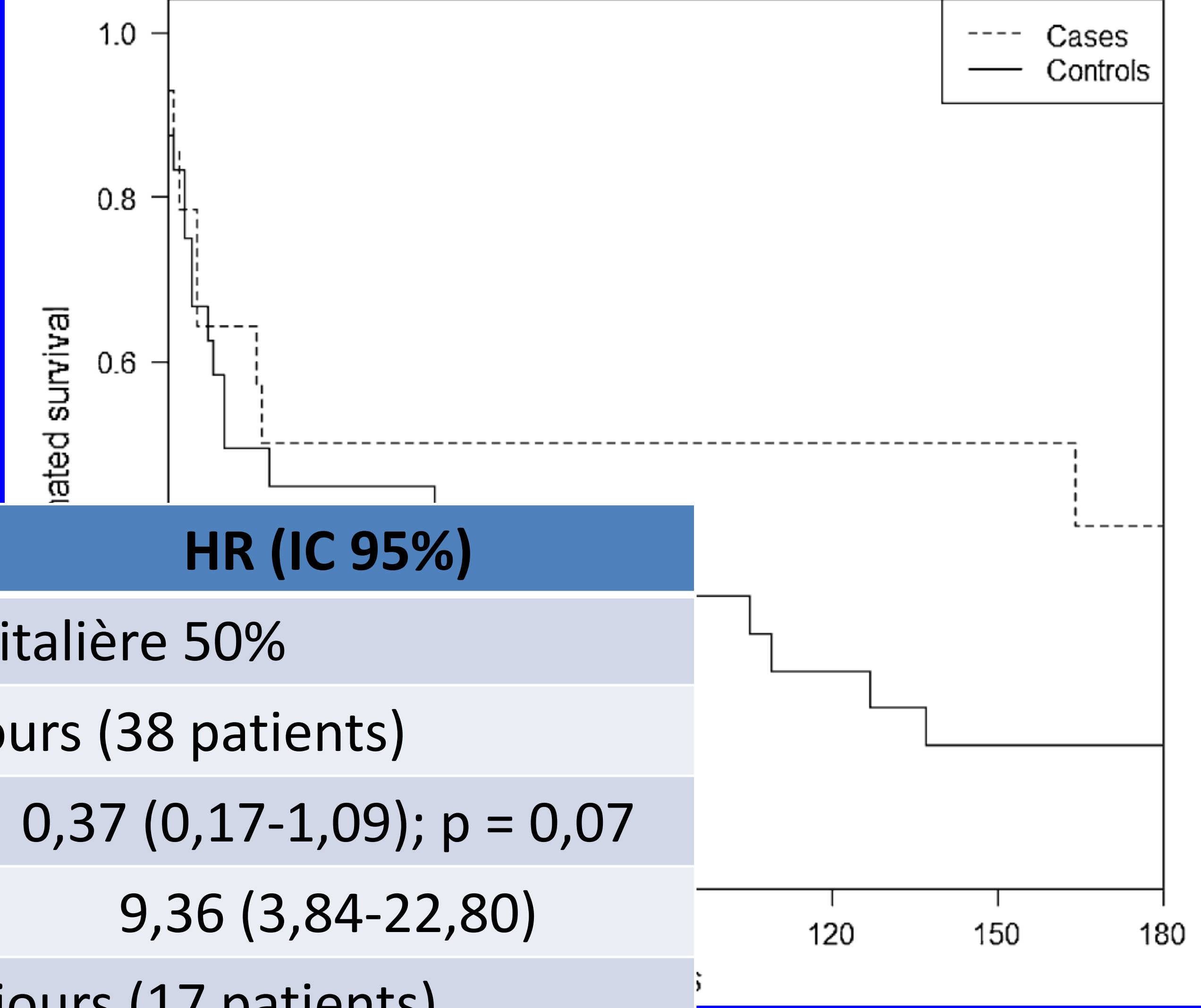
Patients with advanced lung cancer harboring oncogenic mutations should be admitted to intensive care units

- Etude cas (mutation oncogénique) – contrôle (pas de mutation)
- 14 patients = +/- 14% des CB admis à l'USI pour raison médicale
- EGFR (n=5), ALK (n=8), ROS1 (n=1)
- 10 traitement ciblé dont 6 à l'USI et 4 < 1 mois avant USI

Toffart et al, Intensive Care Med 2015

IP ECOG	Traitement	Motif USI	SAPS II	Ventilation	Amines
3	Crizo J-15	IRA < obstruction T*	69	VMI	Non
1	Crizo J-28	IRA < pneumonie	61	VMI	Oui
3	Crizo J+7	IRA < obstruction T*	47	VNI	Non
2	Crizo J-6	IRA < OAP	56	VMI	Non
2	Carbo-Pem USI	IRA < pneumonie	48	VMI	Oui
1	Non	IRA < obstruction T*	94	VMI	Oui
3	Crizo J+5	Tamponnade	22	Non	Non
3	Crizo J+1	IRA < lymphangite	77	VMI	Oui
2	Erlo J-28	IRA < pneumonie	35	VMI	Oui
3	Non	IRA < EP	56	VMI	Oui
2	Erlo J+3	IRA < lymphangite	27	VNI	Non
2	Non	IRA < pleurésie	110	VMI	Oui
3	Gefi J+6	Tamponnade	35	VNI	Non
3	Crizo J+1	Sepsis sévère	50	VNI	Non

Toffart et al, CPLF 2015



Variables	HR (IC 95%)
Mortalité hospitalière 50%	
Décès dans les 30 jours (38 patients)	
Cas	0,37 (0,17-1,09); p = 0,07
Recours à la VM	9,36 (3,84-22,80)
Décès au-delà de 30 jours (17 patients)	
Cas	0,12 (0,03-0,47); p = 0,002
Recours à la VM	2,11 (0,17-26,33)

Toffart et al, Intensive Care Med 2015

Radiotherapy for Intubated Patients with Malignant Airway Obstruction

Futile or Facilitating Extubation?

Alexander V. Louie, MD,† Sophia Lane, MD,* David A. Palma, MD, PhD, MSc,*† Andrew Warner, MSc,† Jeffrey Q. Cao, MD, MBA,*† and George B. Rodrigues, MD, MSC*†‡*

Histology, *n* (%)	
Non–small-cell lung	21 (80.8)
Small-cell lung	4 (15.4)
Lymphoma	1 (3.8)

- 26 patients
- Extubation 27% (n = 7)
- Sorti vivant de l'hôpital n = 6

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Conclusions

- Administrer une chimiothérapie aux soins intensifs nécessite
  - Une intégration entre l'oncologue et l'intensiviste
  - Une évaluation des bénéfices potentiels au vu du pronostic de la néoplasie
- Il convient de distinguer tumeurs hématologiques et solides
- L'évolution des thérapies ciblées peut modifier notre approche du patient cancéreux à l'USI