15 Novembre 2021

Cancer bronchique à petites cellules COM 5

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Introduction

- Le CPC est cancer **agressif, Le temps de doublement est extrêmement rapide(30 j).**
- **Un pouvoir métastatique très important, par voie lymphatique et sanguine, 70 %** des cas sont métastatiques au diagnostic initial
- Fortement lié au tabagisme, rôle important de la prévention primaire
- **Très sensible à la chimiothérapie et à la radiothérapie**
- **Risque de rechute importante**
- Pronostic sombre : survie moyenne de 10 à 12 mois, amélioré par l'immunothérapie.

Épidémiologie

- Années 80: 25% de tous les cancers bronchiques
- De nos jours en France : 15%
- Données américaines SEER: 10%
- Fortement lié au tabagisme
- L'âge moyen : 63 ans

Pujol .La Lettre du Cancerologue • Vol. XXIV - n° 1 - janvier 2015

Anatomopathologie

Présentation: médiastinopulmonaire

- **Macroscopie** : tumeurs blanchâtres, très friables

- **IHC** :**Microscopie :** neuroendocrine et la prolifération est faite de cellules de **petites tailles**.

-TTF1 (90%) chromogranine A +, synaptophysine +, CD56 + (N-CAM),

-Marqueurs NE, Ki67 élevé +++

Diagnostic

- Se localise : prés des voies aériennes proximales (centrale, rarement peripheries)
- Les symptomes révélateurs: tumeur et son extension loco-regionale
- **Signes de dissémination métastasiques:**
- syndrome paranéoplasiques

Diagnostic

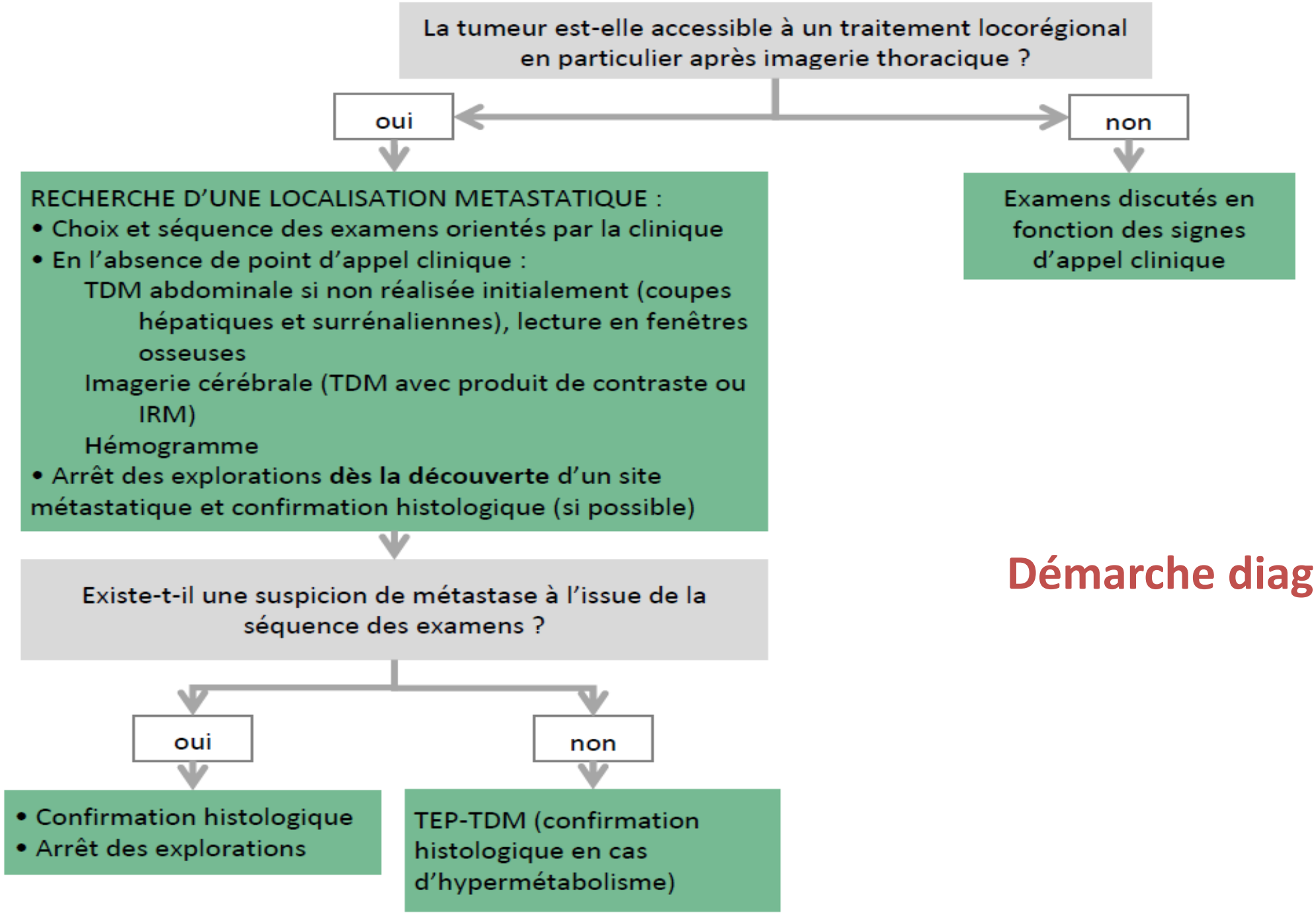
- La radiographie thoracique :
- La TDM thoraco-abdomino-pelvienne : Masse hilaire ou périhilaire avec ADP mediastinales et collapsus lobaire
- La fibroscopie bronchique avec prélèvements biopsiques
- IRM Cérébrale
- Scintigraphie osseuse
- La tomographie par émission de positons au 18-FDG couplée a une tomodensitométrie : si chirurgie

Table 1. Diagnostic and staging work-up of SCLC

History and clinical examination
Medical history (including smoking history and comorbidities)
PS
Physical examination
Assessment of paraneoplastic syndromes (especially when initiating immunotherapy)
Laboratory analysis
CBC, liver enzymes, sodium, potassium, calcium, glucose, LDH and renal functions tests should be carried out
Imaging
CT of the thorax and abdomen should be carried out in all patients; an FDG–PET–CT is optional
In case of a suspicion of bone metastasis and no other metastasis, a bone scintigraphy should be carried out unless FDG–PET is available
Imaging of the brain (preferably MRI) is mandated in patients with stage I-III disease
MRI of the brain is recommended for patients with stage IV disease who are eligible for PCI but who choose not to undergo PCI
Tumour biopsy
A diagnosis of SCLC is preferably assessed based on histological examination of a biopsy
In case of planned surgery, invasive mediastinal staging is required
Functional assessment
Pulmonary function testing (FEV1, VC, DLCO) is required for patients with stage I-III SCLC who are candidates for surgery or RT
VO2 max assessment by cycle ergometry should be carried out if surgery is planned when pulmonary function tests are limited

SCLC ESMO CPG, Ann Oncol 2021

Démarche diagnostique

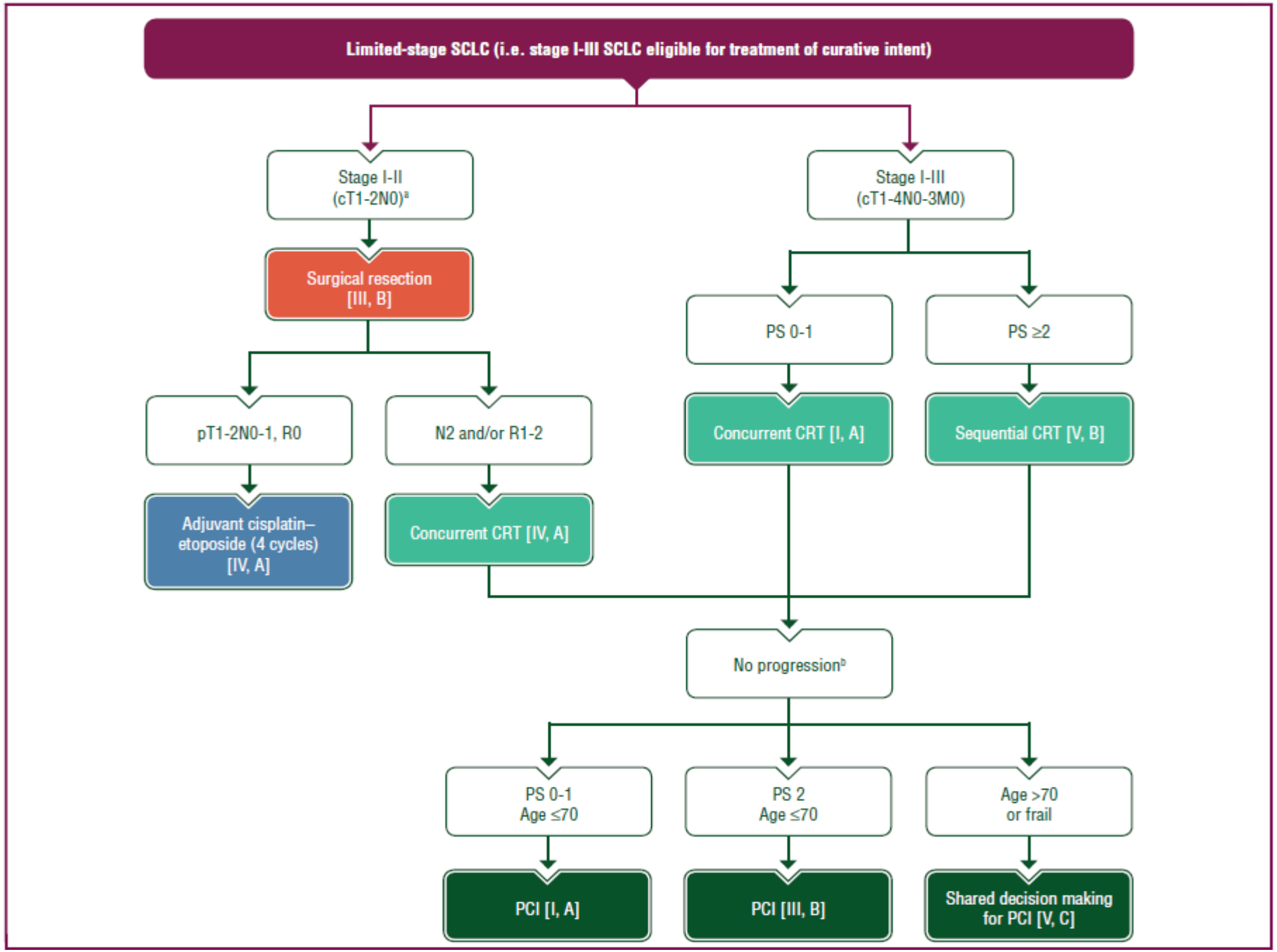


Classification

	N0	N1	N2	N3	M1a-b *Tout N*	M1c *Tout N*
T1a	IA-1	IIB	IIIA	IIIB	IV-A	IV-B
T1b	IA-2	IIB	IIIA	IIIB	IV-A	IV-B
T1c	IA-3	IIB	IIIA	IIIB	IV-A	IV-B
T2a	IB	IIB	IIIA	IIIB	IV-A	IV-B
T2b	IIA	IIB	IIIA	IIIB	IV-A	IV-B
T3	IIB	IIIA	IIIB	IIIC	IV-A	IV-B
T4	IIIA	IIIA	IIIB	IIIC	IV-A	IV-B

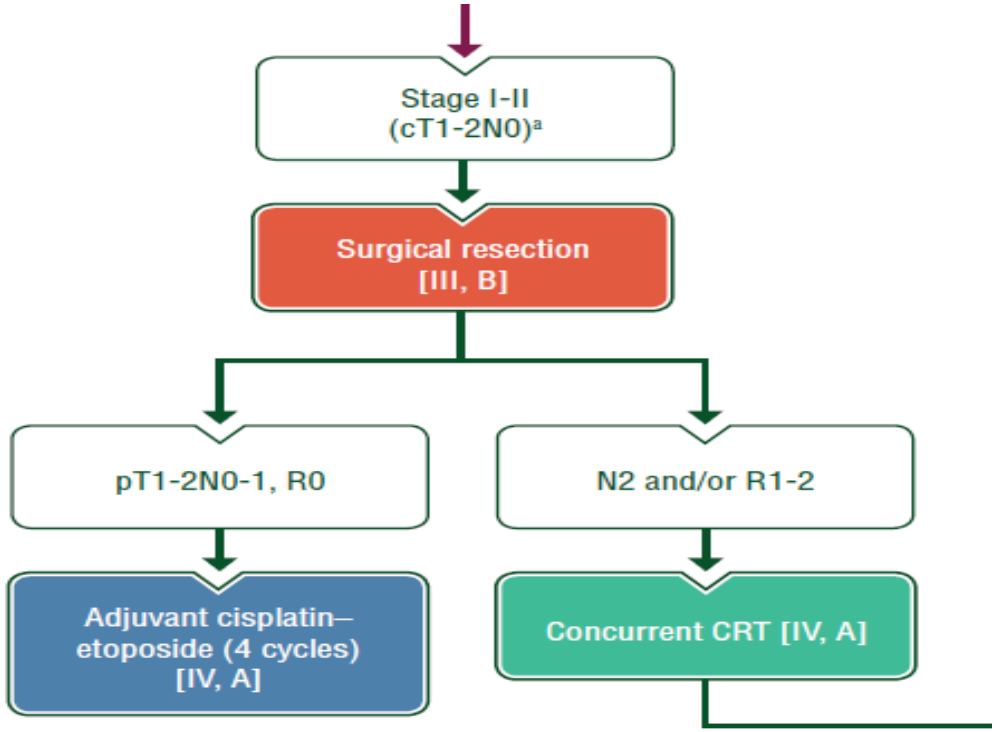
8éme Classification TNM

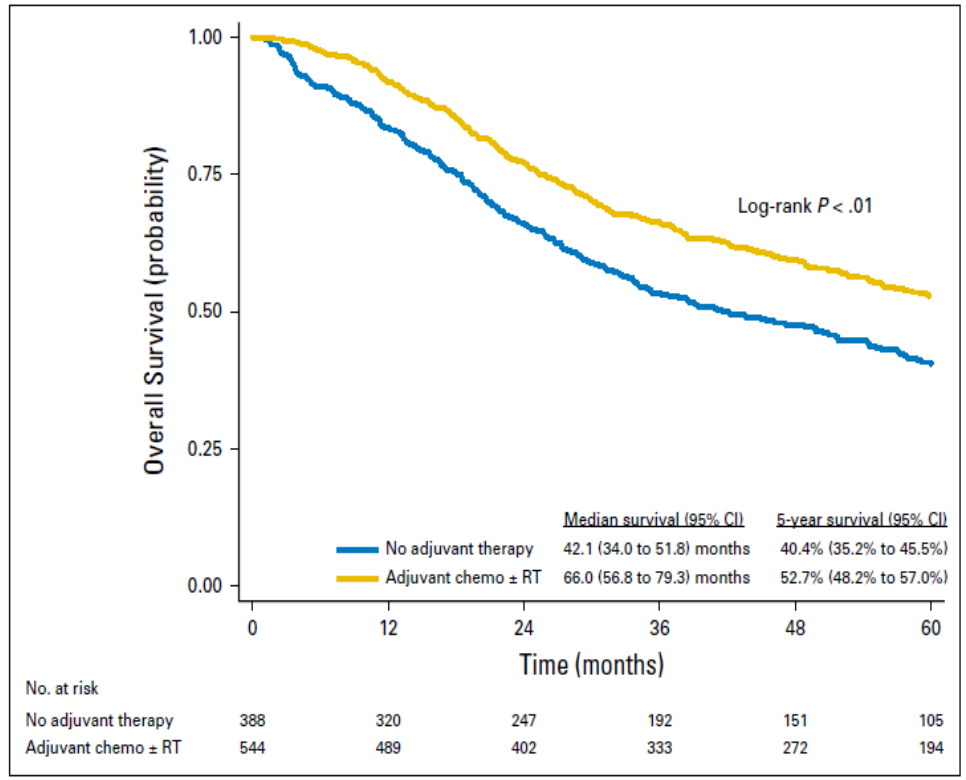
Traitement



SCLC ESMO CPG, Ann Oncol 2021

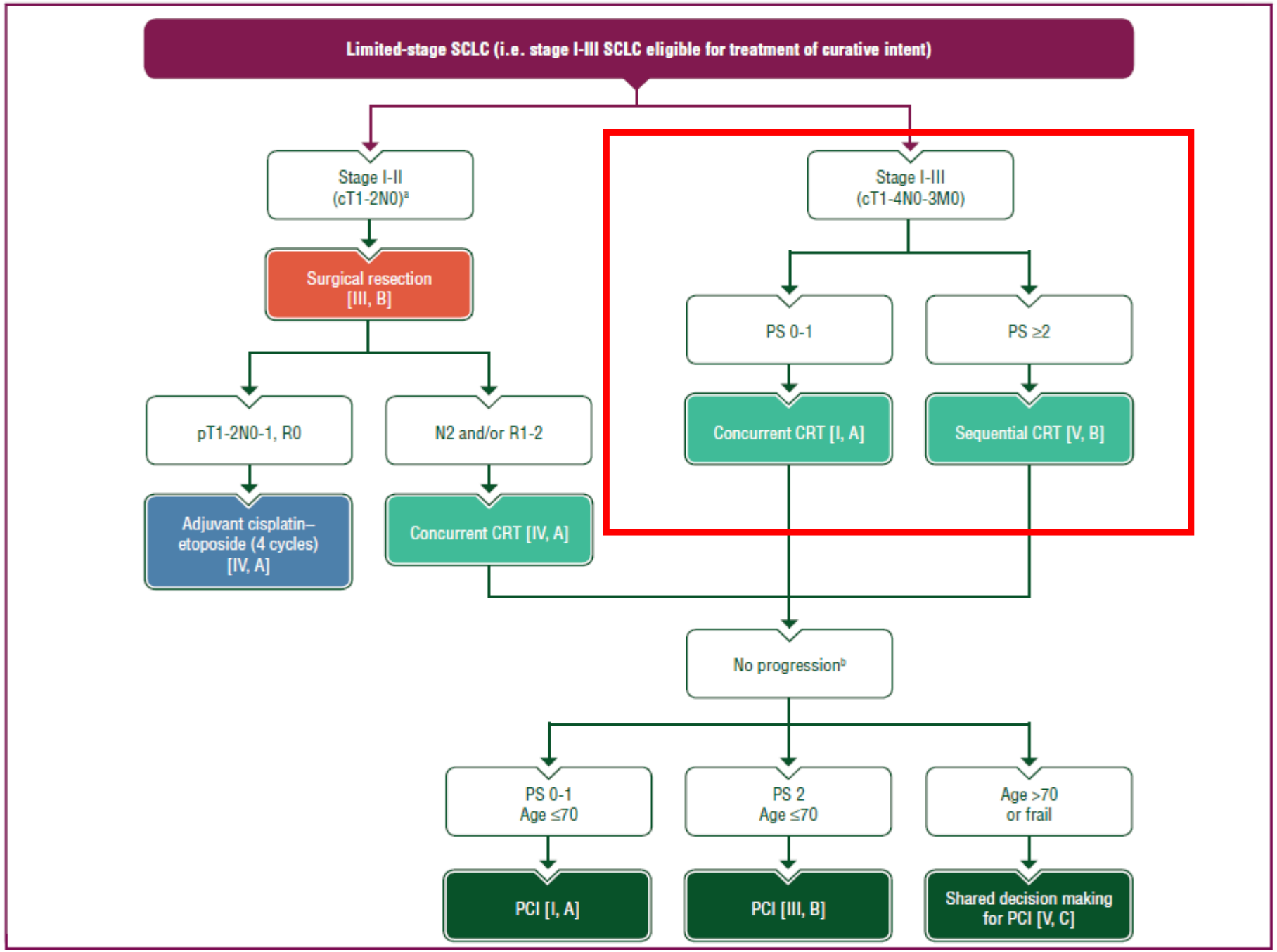
Chirurgie des stades précoces





- CPC = 4%-12% des nodules solitaires réséqués
- Classification pathologique gg médiastinale indispensable
- CT adjuvante améliore la survie

Yang et al, J Clin Oncol, 2016 Apr 1;34(10):1057-64



SCLC ESMO CPG, Ann Oncol 2021

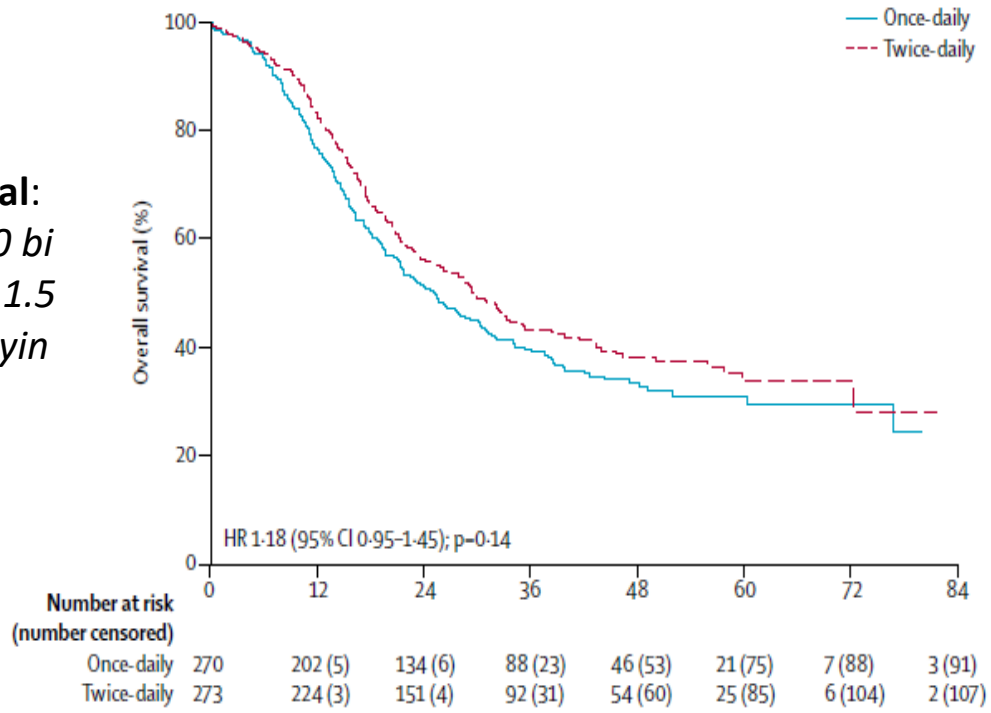
PRINCIPLES OF SYSTEMIC THERAPY

PRIMARY OR ADJUVANT THERAPY FOR LIMITED-STAGE SCLC:
Four cycles of systemic therapy are recommended. Planned cycle length should be every 21–28 days during concurrent RT. During systemic therapy + RT, cisplatin/etoposide is recommended (category 1). The use of myeloid growth factors is not recommended during concurrent systemic therapy plus RT (category 1 for not using GM-CSF).[1]
Preferred Regimens • Cisplatin 75 mg/m² day 1 and etoposide 100 mg/m² days 1, 2, 3[2] • Cisplatin 60 mg/m² day 1 and etoposide 120 mg/m² days 1, 2, 3[3] Other Recommended Regimens • Cisplatin 25 mg/m² days 1, 2, 3 and etoposide 100 mg/m² days 1, 2, 3[2] • Carboplatin AUC 5–6 day 1 and etoposide 100 mg/m² days 1, 2, 3[a,4]

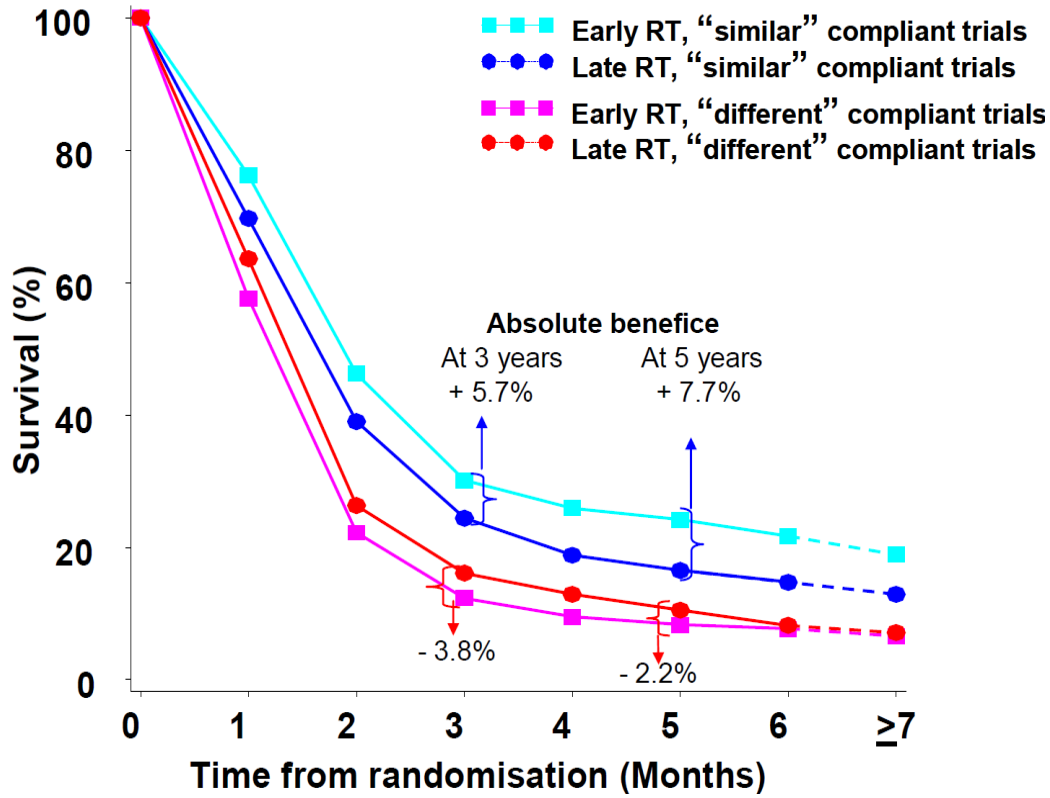
RCC

- Chimioradiothérapie concomitante si PS 0 et 1
- Dose recommandée 45 Gy en B.I.D en 30 fractions
- Commencer le plus tôt possible

Convert trial:
45 Gy en 30 bi fraction /J 1.5 Gy vs. 66 Gyin 33 une fraction/J



Méta-analyse : RCC dans 30 jours après début de la CT



1.Faivre Finn et al, *Lancet Oncol*2017, 18(8):1116-1125

2.De Ruysscheret al, Ann Oncol2016

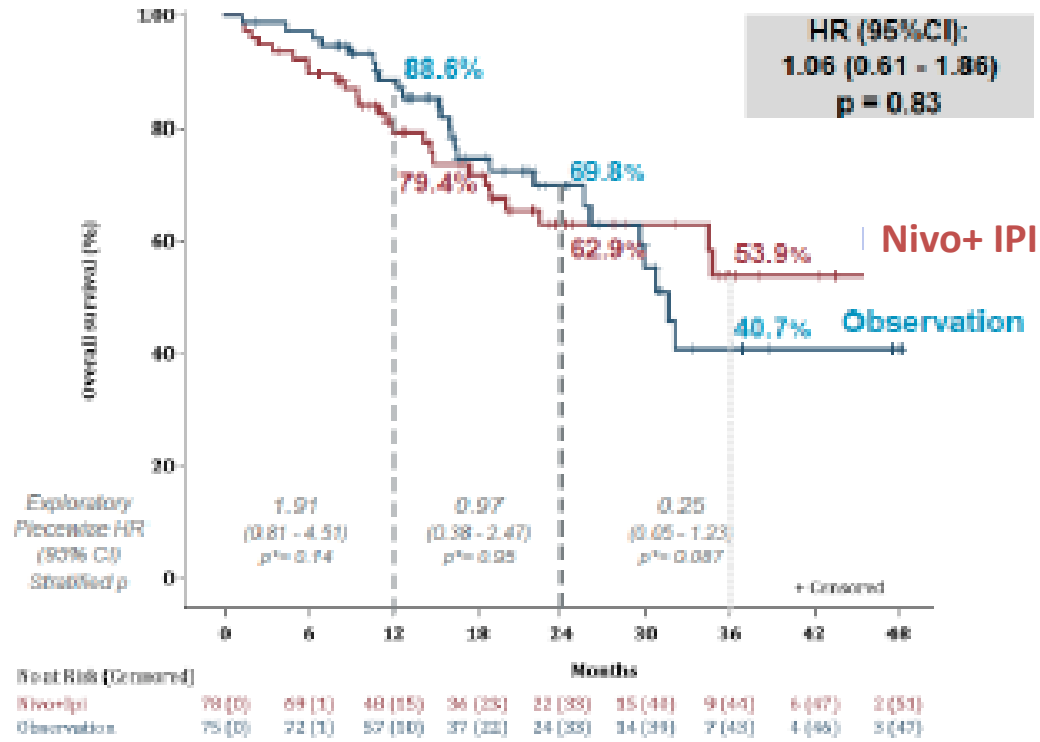
Maintenance par immunothérapie après RCC?

- Cisplatine 60-80 mg/m2 J1
- etoposide 100-120 mg/m2 J 1, 2 et 3,
- Cycle 3 semaines, 4 cycles
- Carboplatine plus etoposide si CI cisplatine

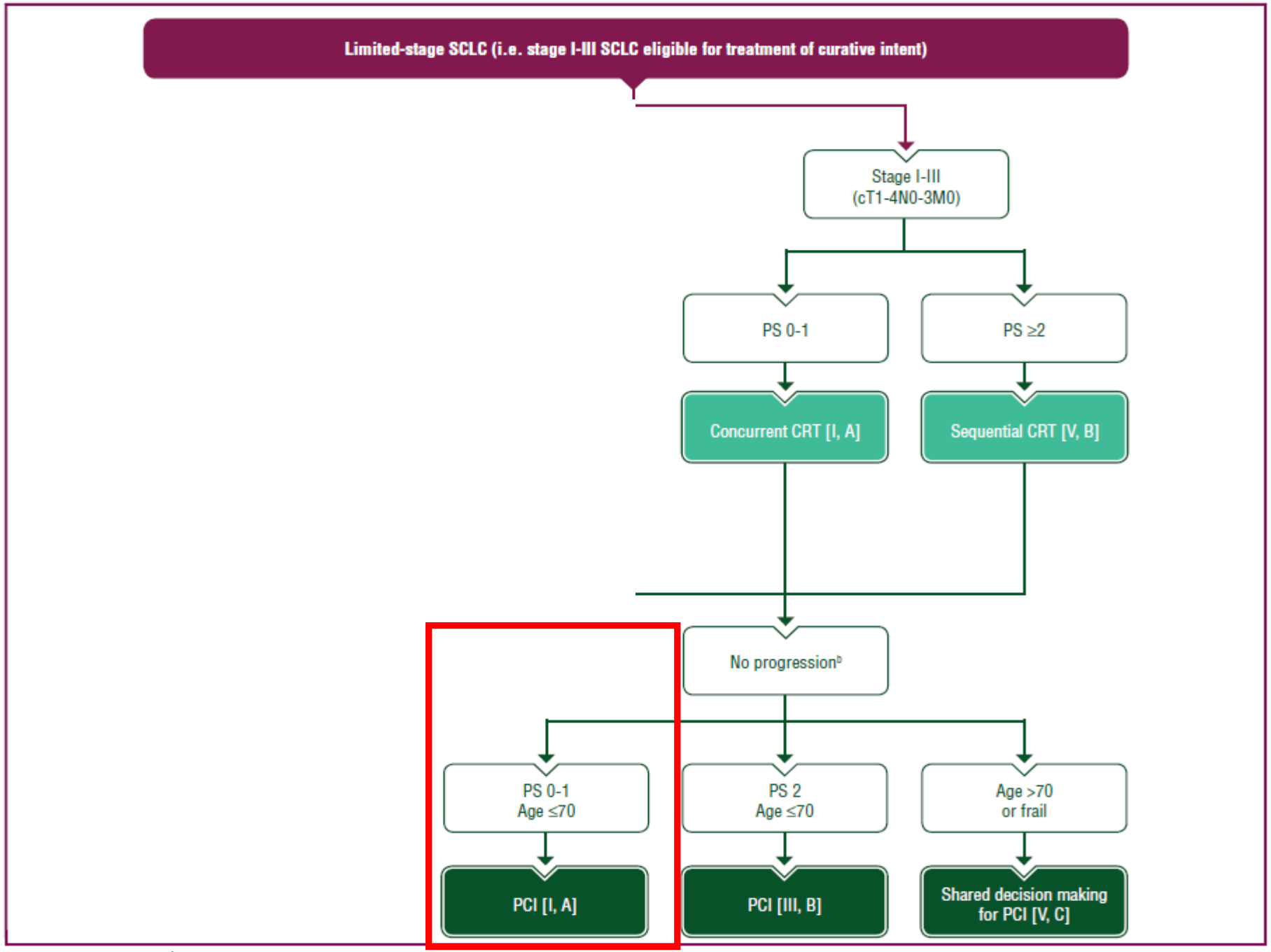
Stimuli trial:

Nivolumab +Ipilimumab pdt 1 an vs **placebo**

Pas de bénéfice SSP ni SG



Peters et al ESMO 2020

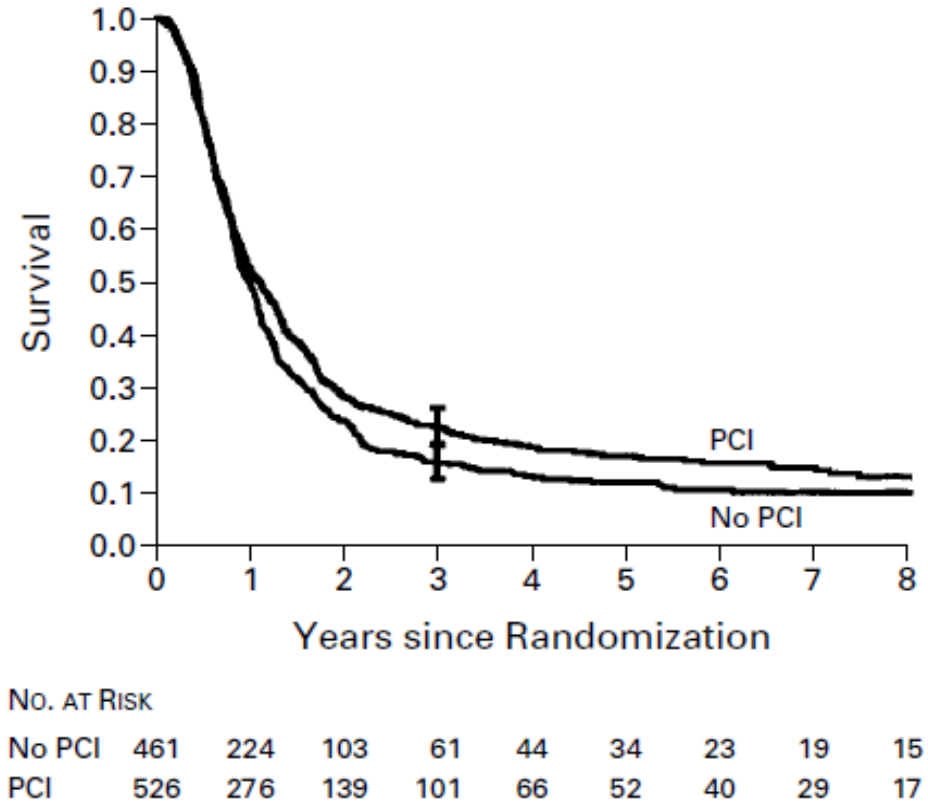


SCLC ESMO CPG, Ann Oncol 2021

Radiothérapie cérébrale prophylactique

- Indiquée au stade III CPC, aprés réponse CRT
- Chez des patients PS of 0-1.
- 3 ans: 33.3% vs 58.6% mets cérèbrale
- Recommandé IPC : 25 Gy/10 fractions

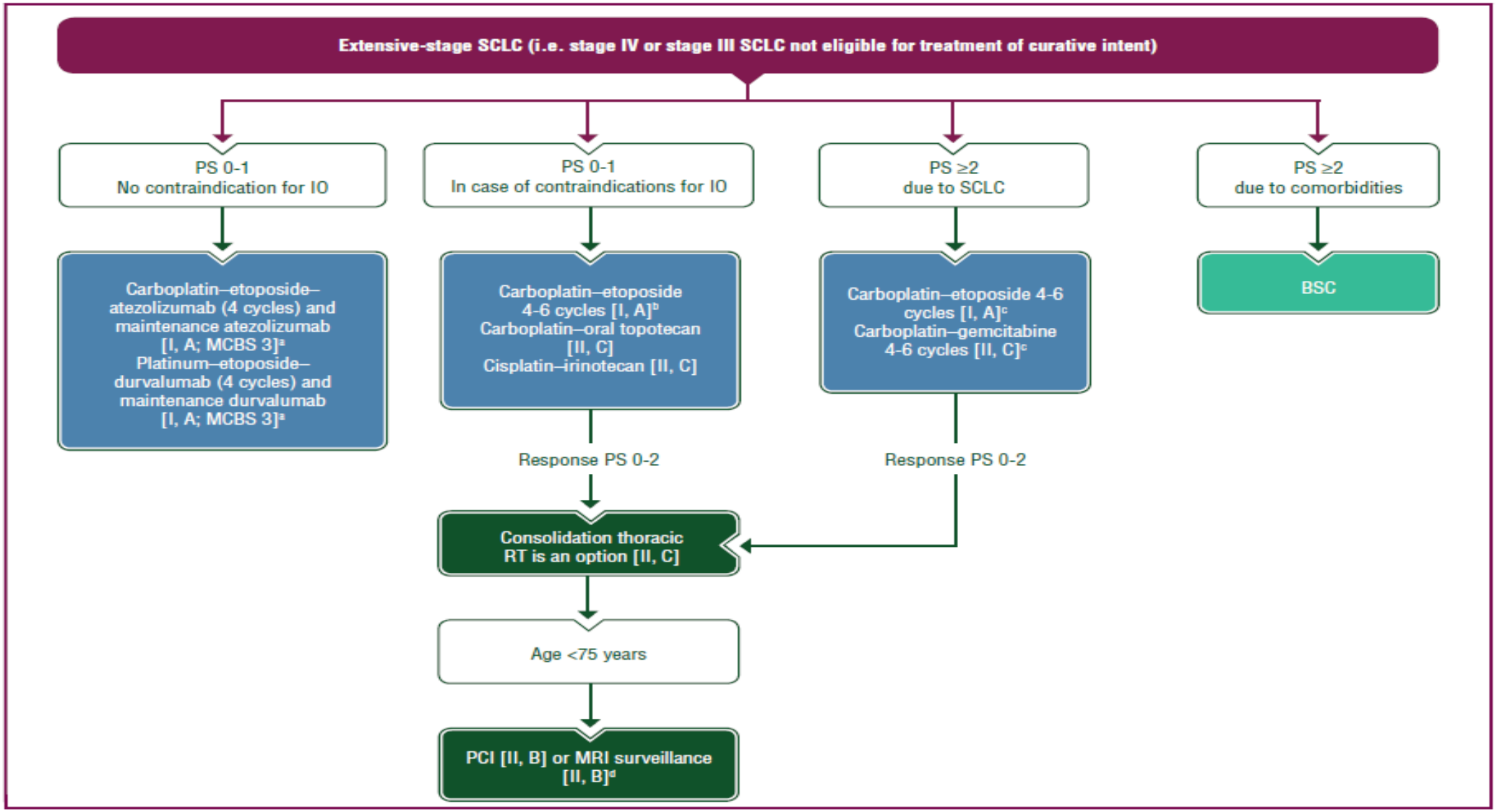
- <u>Méta-analyse</u> IPC Vs pas de IPC



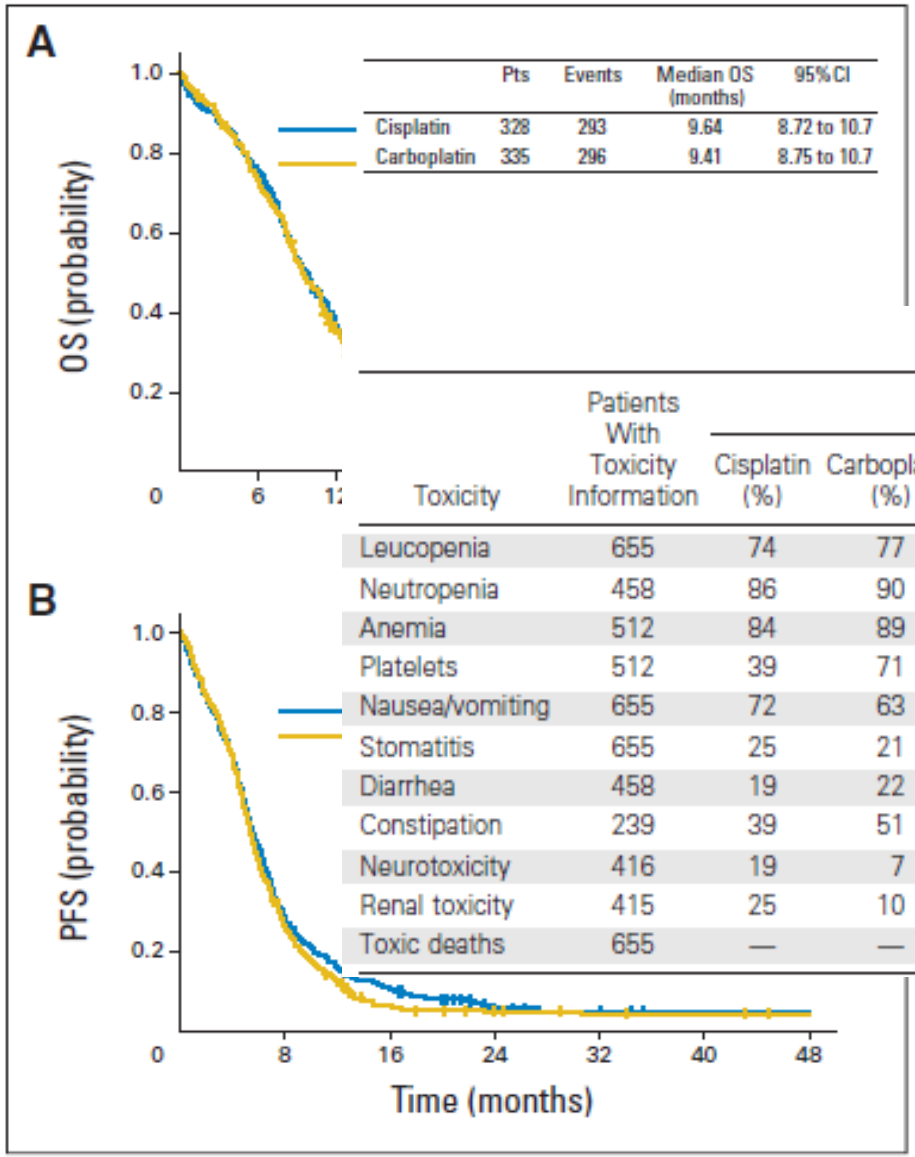
No. at Risk									
No PCI	461	224	103	61	44	34	23	19	15
PCI	526	276	139	101	66	52	40	29	17

Auperinet al, N EnglJ Med 1999, 341(7):476:84

Traitement des stades IV



• Carboplatine VS Cisplatine en 1ére ligne CPC



	Pts	Events	Median OS (months)	95% CI
Cisplatin	328	293	9.64	8.72 to 10.7
Carboplatin	335	296	9.41	8.75 to 10.7

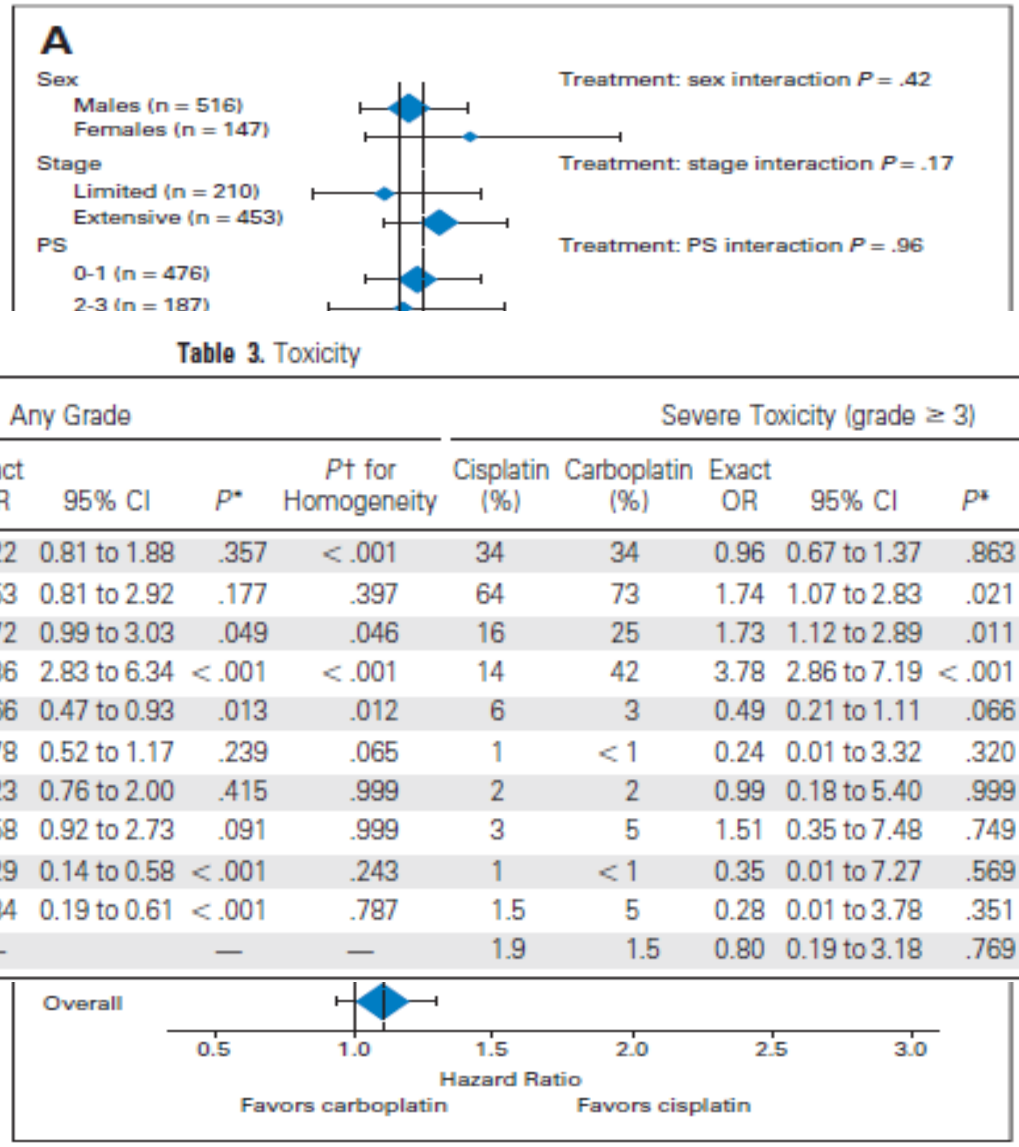


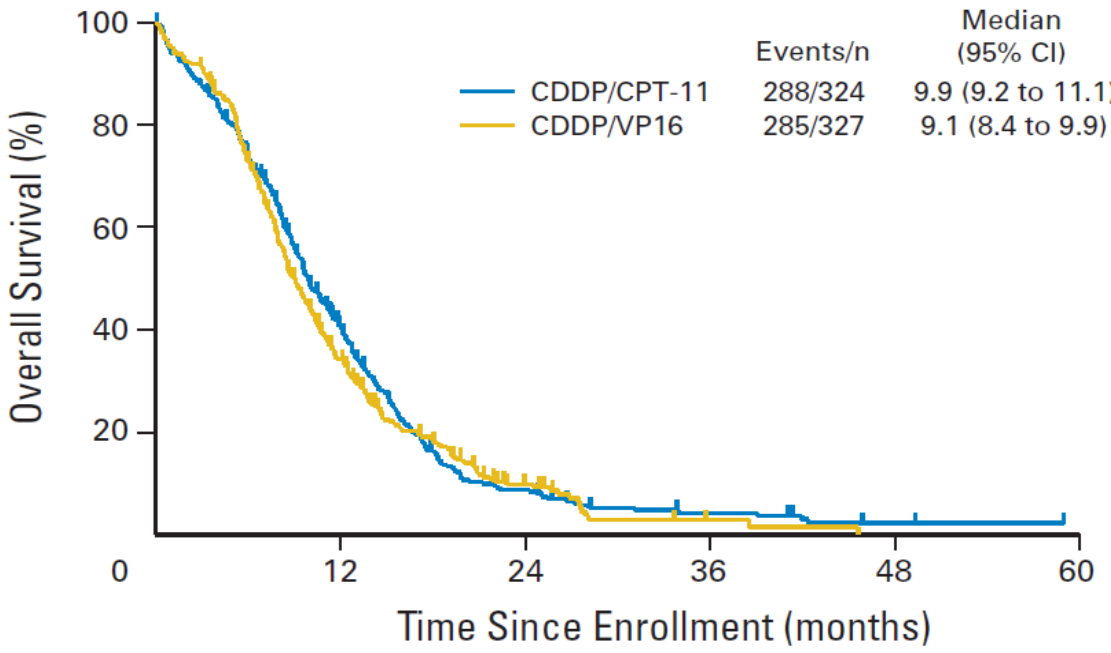
Table 3. Toxicity

Toxicity	Patients With Toxicity Information	Any Grade						Severe Toxicity (grade ≥ 3)					
		Cisplatin (%)	Carboplatin (%)	Exact OR	95% CI	P*	P† for Homogeneity	Cisplatin (%)	Carboplatin (%)	Exact OR	95% CI	P*	P† for Homogeneity
Leucopenia	655	74	77	1.22	0.81 to 1.88	.357	< .001	34	34	0.96	0.67 to 1.37	.863	< .001
Neutropenia	458	86	90	1.53	0.81 to 2.92	.177	.397	64	73	1.74	1.07 to 2.83	.021	.999
Anemia	512	84	89	1.72	0.99 to 3.03	.049	.046	16	25	1.73	1.12 to 2.89	.011	< .001
Platelets	512	39	71	3.36	2.83 to 6.34	< .001	< .001	14	42	3.78	2.86 to 7.19	< .001	< .001
Nausea/vomiting	655	72	63	0.66	0.47 to 0.93	.013	.012	6	3	0.49	0.21 to 1.11	.066	.999
Stomatitis	655	25	21	0.78	0.52 to 1.17	.239	.065	1	< 1	0.24	0.01 to 3.32	.320	.999
Diarrhea	458	19	22	1.23	0.76 to 2.00	.415	.999	2	2	0.99	0.18 to 5.40	.999	.999
Constipation	239	39	51	1.58	0.92 to 2.73	.091	.999	3	5	1.51	0.35 to 7.48	.749	.999
Neurotoxicity	416	19	7	0.29	0.14 to 0.58	< .001	.243	1	< 1	0.35	0.01 to 7.27	.569	.999
Renal toxicity	415	25	10	0.34	0.19 to 0.61	< .001	.787	1.5	5	0.28	0.01 to 3.78	.351	.540
Toxic deaths	655	—	—	—		—	—	1.9	1.5	0.80	0.19 to 3.18	.769	.101

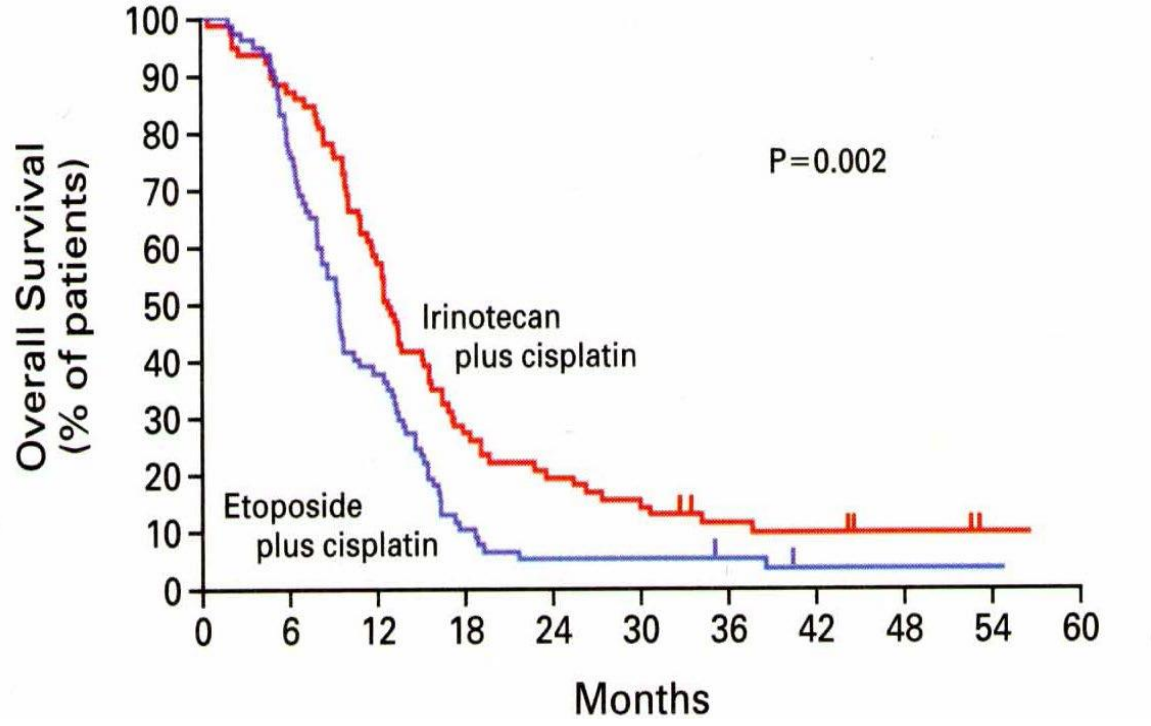
Fig 3. Forest plot of (A) overall survival and (B) progression-free survival by patients' subgroups. PS, performance status.

Rossi et al, *Journal of Clinical Oncology*30, no.14 (May 10, 2012) 1692-1698

CPC Etendu CT ancienne



Lara et al.



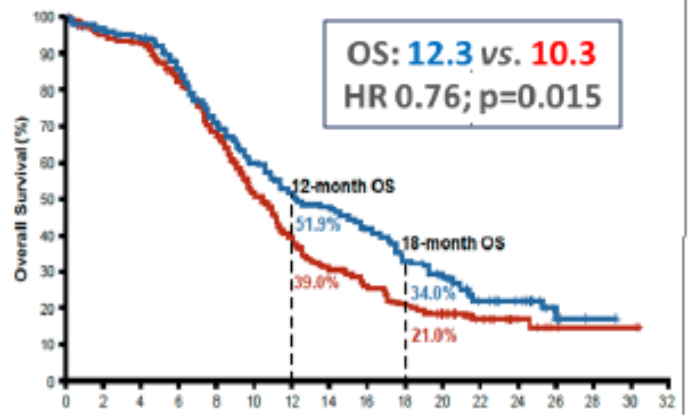
Noda et al.

1. Lara et al *Journal of Clinical Oncology*27, no. 15 (May 20, 2009) 2530-2535.

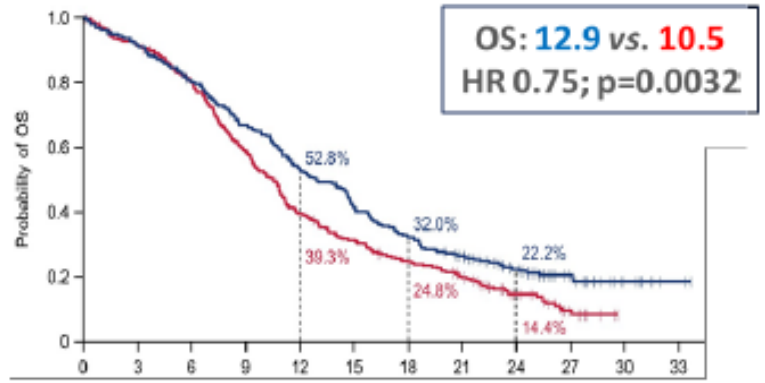
2. Noda et all, *N Engl J Med* 2002; 346:85-9

Immunothérapie en 1ére ligne

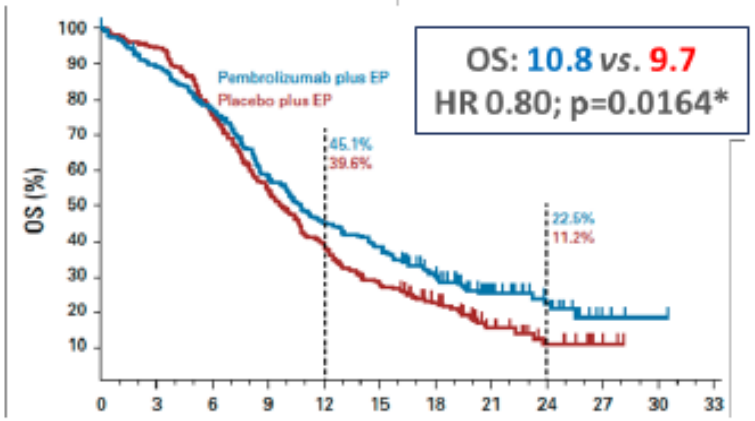
IMpower 133 Atezolizumab



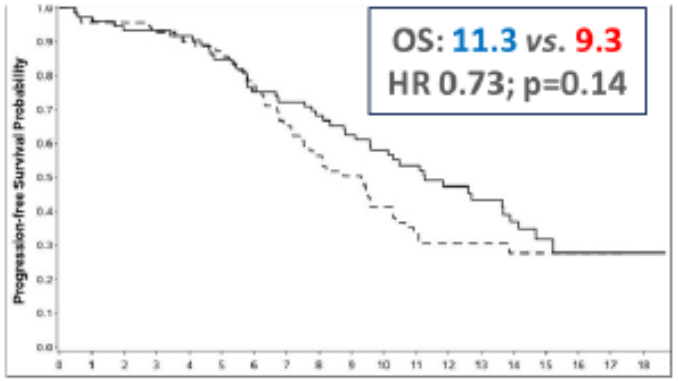
CASPIAN Durvalumab



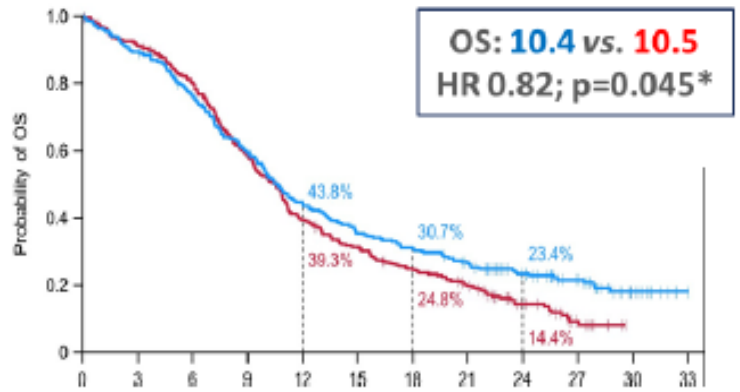
KEYNOTE 604 Pembrolizumab



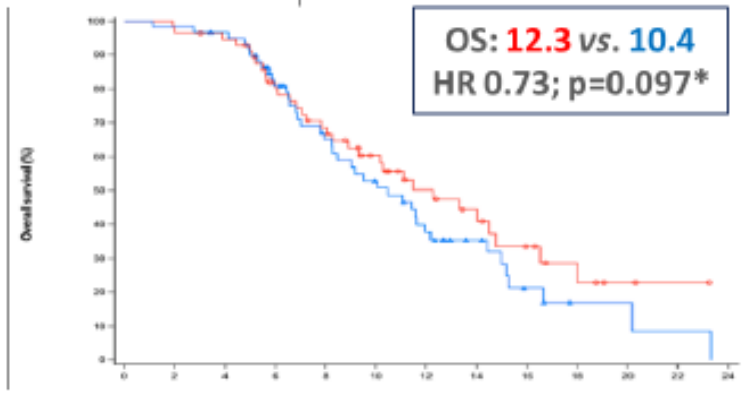
ECOG-ACRIN 5161 Nivolumab



CASPIAN Durvalumab + Tremelimumab

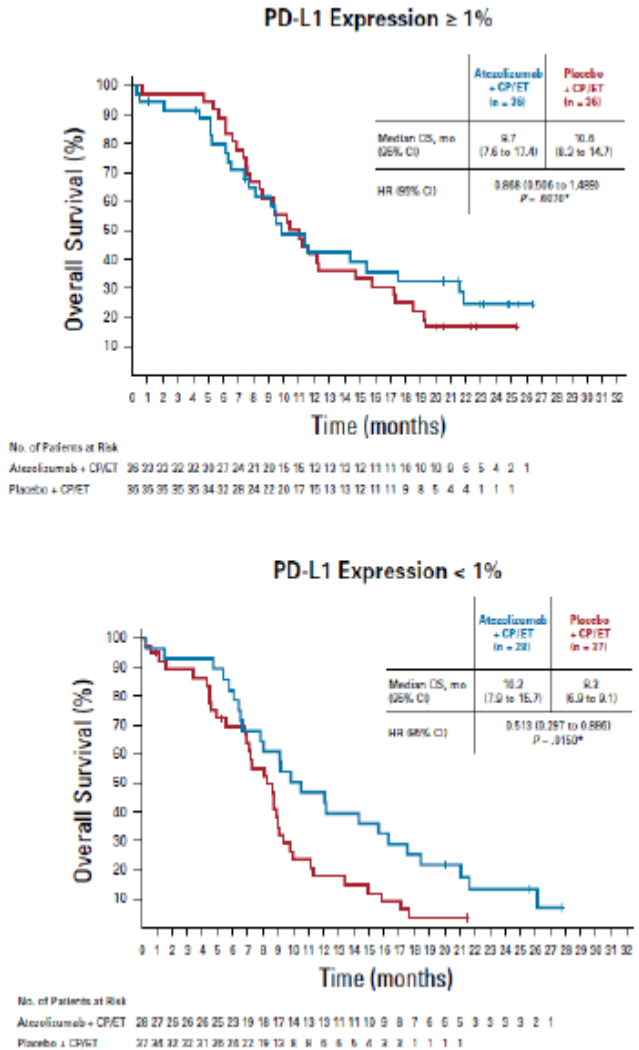


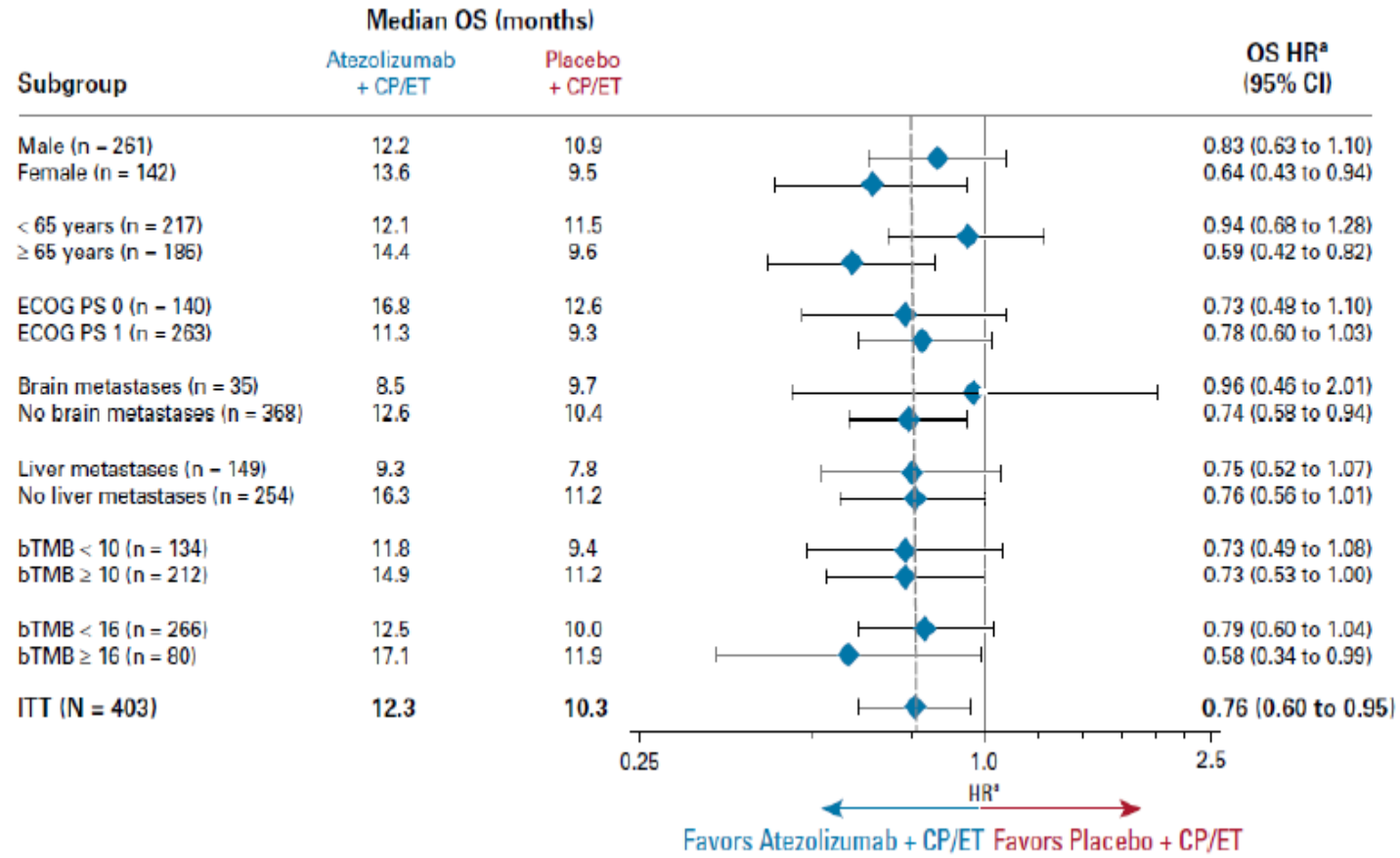
REACTION Pembrolizumab



1.Horn et al, N Engl J Med 2018; 379:2220-2229; **2**.Paz-Ares et al, The Lancet 2019; 394(10212); **3.**Rudin et al, Journal of ClinicalOncology 38, no. 21 (July 20, 2020) 2369-2379.
4.Leal et al, Journal of Clinical Oncology 38, no. 15_suppl (May 20, 2020) 9000-9000; 5.Paz-Ares et al, Journal of Clinical Oncology 38, no. 15_suppl (May 20, 2020) 9002-9002;
6.Besse et al, Annals of Oncology (2020) 31 (suppl_4);

Biomarqueur de réponse à l'Immunothérapie





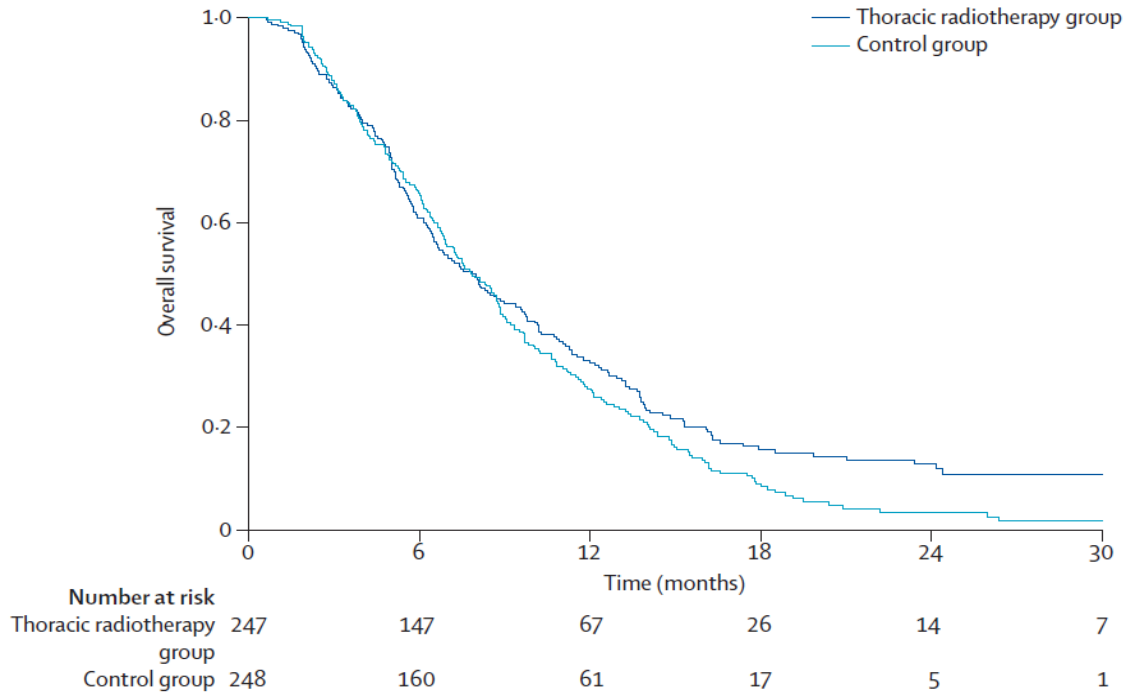
Liu, S et al, *Journal of Clinical Oncology*39, no.6 (February 20, 2021) 619-630

CASPIAN vs IMpower 133

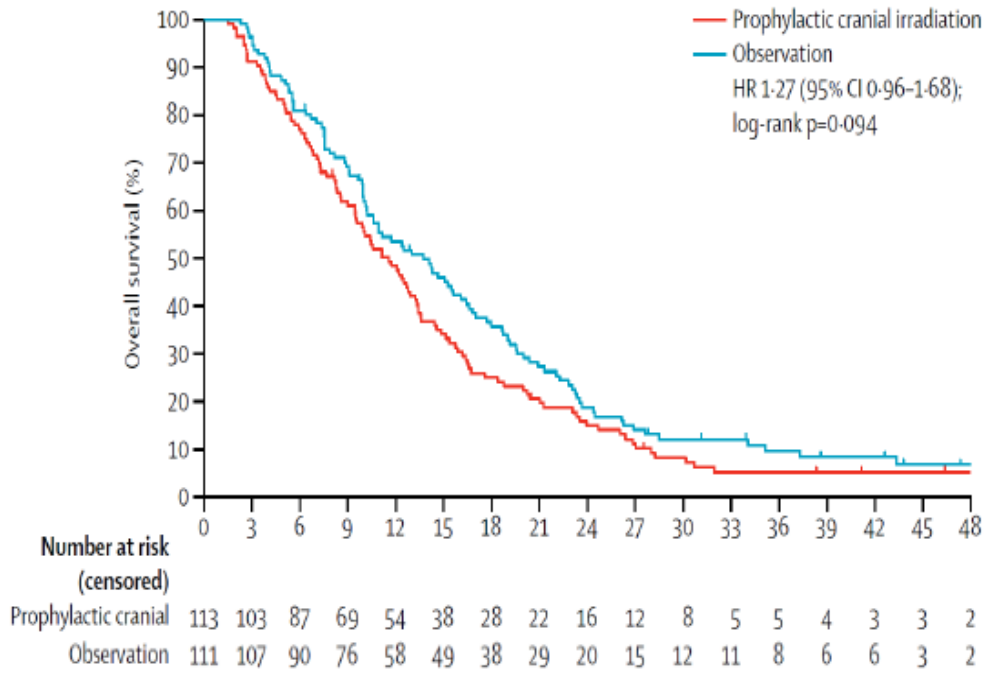
	CASPIAN		IMpower 133	
	Durvalumab+EP (n=268)	EP (n=269)	Atezolizumab +EC (n= 201)	EC + placebo (n=202)
OS,m	**13.0** HR=0.73	10.3	**12.3** HR=0.76	10.3
OS at 12m,%	**53.7**	39.8	**51.7**	38.2
PFS, m	5.1 HR=0.78	5.4	5.2 HR=0.77	4.3
ORR, %	**67.9**	57.6	**60.2**	64.4
DOR, m	5.1	5.1	4.2	3.9
G 3/4 AEs	61.5	62.4	67.2	63.8
irAE	19.6	2.6	39.9	24.5
Biomarker	PDL1	PDL1	PDL1, bTMB available	
Poststudy Tx	42	44	50	57

Radiothérapie des stades étendus

Radiothérapie thoracique



RT Encéphalique prophylactique



SG 1 an : 33% (RT) vs. 28%, p=0.066
SG 2 ans : 13% (RT) vs. 3%, p=0.004
Pas de données sur RT après CT+ Immunothérapie

PCI (20 Gy/5 fractions and 25 Gy/10 fractions)
patient <75 ans, PS of 0-2, réponse CT

Slotman et al, *The Lancet* 2015,385(9962)

Takahashi et al, *The Lancet Oncol* 2017, 18(5):663-671

PRIMARY THERAPY FOR EXTENSIVE-STAGE SCLC:

Four cycles of therapy are recommended, but some patients may receive up to 6 cycles based on response and tolerability after 4 cycles.

Preferred Regimens

- Carboplatin AUC 5 day 1 and etoposide 100 mg/m² days 1, 2, 3 and atezolizumab 1,200 mg day 1 every 21 days x 4 cycles followed by maintenance atezolizumab 1,200 mg day 1, every 21 days (category 1 for all)[b,5]
- Carboplatin AUC 5 day 1 and etoposide 100 mg/m² days 1, 2, 3 and atezolizumab 1,200 mg day 1 every 21 days x 4 cycles followed by maintenance atezolizumab 1,680 mg day 1, every 28 days[b]
- Carboplatin AUC 5–6 day 1 and etoposide 80–100 mg/m² days 1, 2, 3 and durvalumab 1,500 mg day 1 every 21 days x 4 cycles followed by maintenance durvalumab 1,500 mg day 1 every 28 days (category 1 for all)[b,6]
- Cisplatin 75–80 mg/m² day 1 and etoposide 80–100 mg/m² days 1, 2, 3 and durvalumab 1,500 mg day 1 every 21 days x 4 cycles followed by maintenance durvalumab 1,500 mg day 1 every 28 days (category 1 for all)[b,6]

Other Recommended Regimens

- Carboplatin AUC 5–6 day 1 and etoposide 100 mg/m² days 1, 2, 3[7]
- Cisplatin 75 mg/m² day 1 and etoposide 100 mg/m² days 1, 2, 3[8]
- Cisplatin 80 mg/m² day 1 and etoposide 80 mg/m² days 1, 2, 3[9]
- Cisplatin 25 mg/m² days 1, 2, 3 and etoposide 100 mg/m² days 1, 2, 3[10]

Useful In Certain Circumstances

- Carboplatin AUC 5 day 1 and irinotecan 50 mg/m² days 1, 8, 15[11]
- Cisplatin 60 mg/m² day 1 and irinotecan 60 mg/m² days 1, 8, 15[12]
- Cisplatin 30 mg/m² days 1, 8 and irinotecan 65 mg/m² days 1, 8[13]

Subsequent Systemic Therapy (SCL-E 2 of 5)
Response Assessment (SCL-E 3 of 5)
References (SCL-E 4 of 5)

[a] Cisplatin contraindicated or not tolerated.
[b] Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or concurrent use of immunosuppressive agents.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

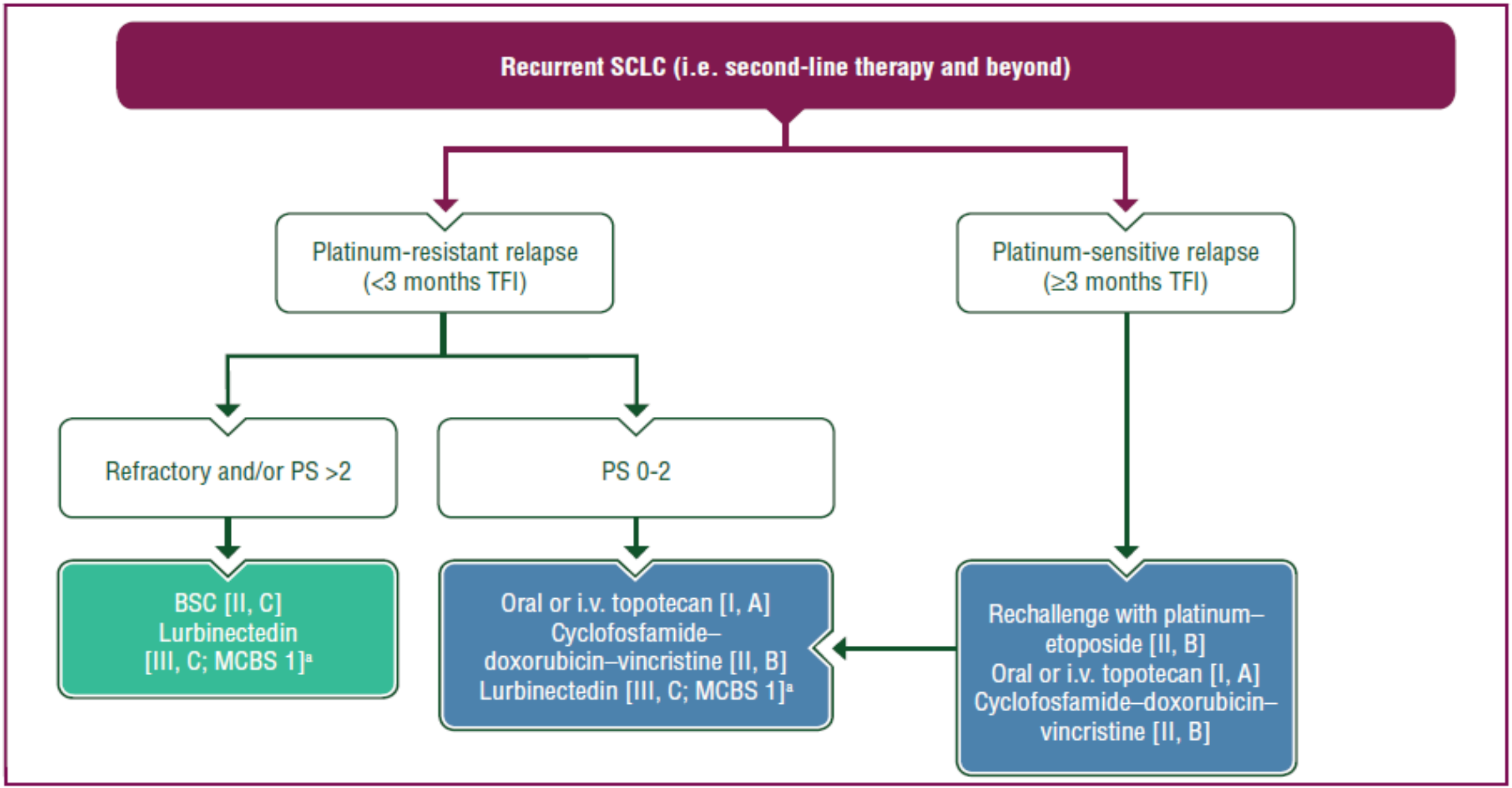


Figure 3. Treatment algorithm for SCLC in patients with recurrent SCLC (i.e. second-line therapy and beyond).

GFPC 13-01 : Study Design

Sensitive relapsed SCLC
(> 90 days from D1 of the last cycle of chemotherapy)

ECOG PS 0-2, age > 18 years

Stratification :
PS
Institution
Response to first line

R

Carboplatin Etoposide

Carboplatin AUC 5 Day 1
Etoposide 100 mg/m2 on day 1-3 IV
Q 3wX6 courses

GCSF is recommended in primary prevention

Topotecan (oral)

2.3 mg/m2 on day 1-5 oral
Q 3wX6 courses

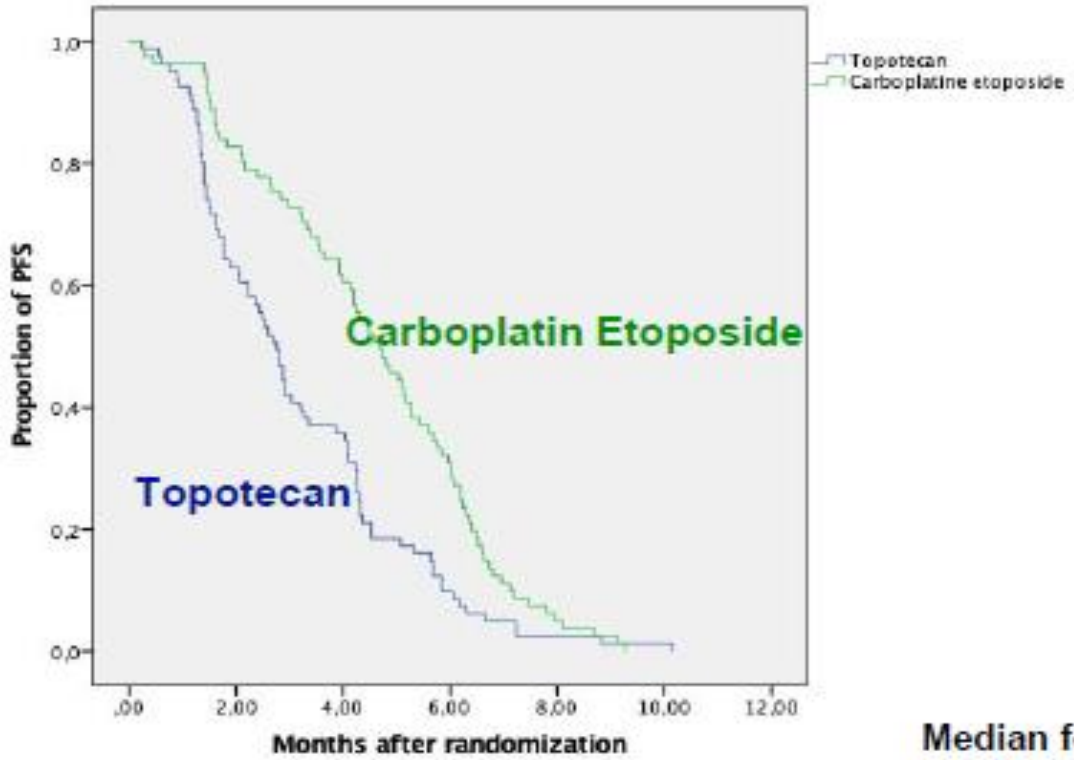
Primary endpoint: PFS
Secondary endpoints: OS, ORR (RECIST v1.1, central review), Safety, Quality of Life

Monnet. I, et al, IASLC 2019

Secondary Endpoint :Tumor Response

Tumor assessment	Topotecan (n=81)	Carboplatin Etoposide (n=81)
Complete Response	1,2%	14%
Partial Response	24%	35,5%
ORR	25%	49% *p=0,002*
Stable Disease	37,4%	37,4%
Disease Progression	37,4%	21,5%

Primary Endpoint : Progression-Free Survival



	Topotecan	Carboplatine Etoposide
Events	81	81
mPFS	2.7 mo	4.7 mo
(95%CI)	(2.3-3.2)	(3.9-5.5)

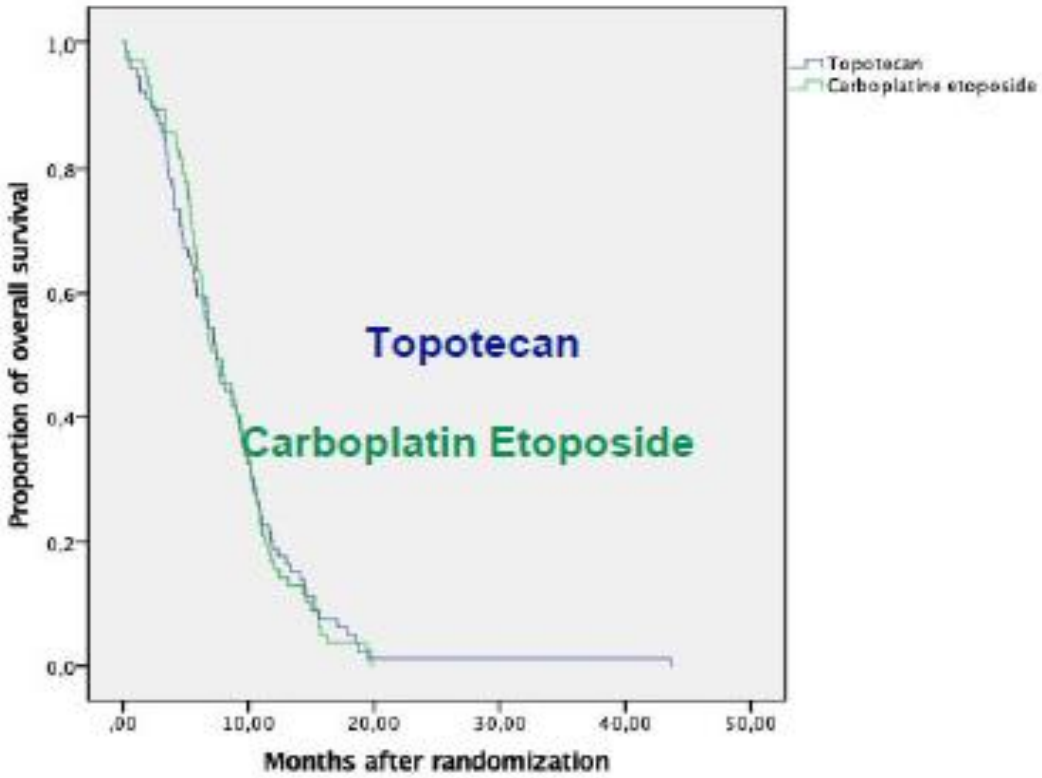
One sided p< 0.001

By stratified log-rank test

Hazard ratio, 0.6; 95% CI 0.4-0.8

Median follow-up: 16 months

Secondary Endpoint : Overall Survival



	Topotecan	Carboplatine Etoposide
Events	81	81
mOS	7.4 mo	7.5 mo
(95%CI)	(6.0-8.7)	(5.4-9.5)

One sided p< 0.936

By stratified log-rank test

Hazard ratio, 0.987; 95% CI 0.7-1.3

Chimiothérapie de 2éme ligne

- Lurinectidine : Analogue trabectidine

	Lurbinectedin (n=105)	Von Pawel 2014: Topotecan (n=213)[1]	Von Pawel 2014: Amrubicin (n=424)[1]
ORR (%)	**35.2**	**16.9**	**31.1**
ORR sens (%)	45.0	23.1	40.9
ORR res (%)	22.2	9.4	20.1
mPFS	**3.9 m**	**3.5 m**	**4.1 m**
mPFS sens	4.6 m	4.3 m	5.5 m
mPFS res	2.6 m	2.6 m	2.8 m
mOS	**9.3 m** 95% CI 6.3-11.8	**7.8 m** 95% CI 6.6-8.5	**7.5 m** 95% CI 6.8-8.5
mOS sens	11.9 m	9.9 m	9.2 m
mOS res	5.0 m	6.2 m	5.7 m

- Lurbinectidine: a une efficacité comparable aux autres molécules.

1.Von Pawel et al, JCO 2014
Paz Ares L et al, ASCO 2019

LURBINECTEDIN

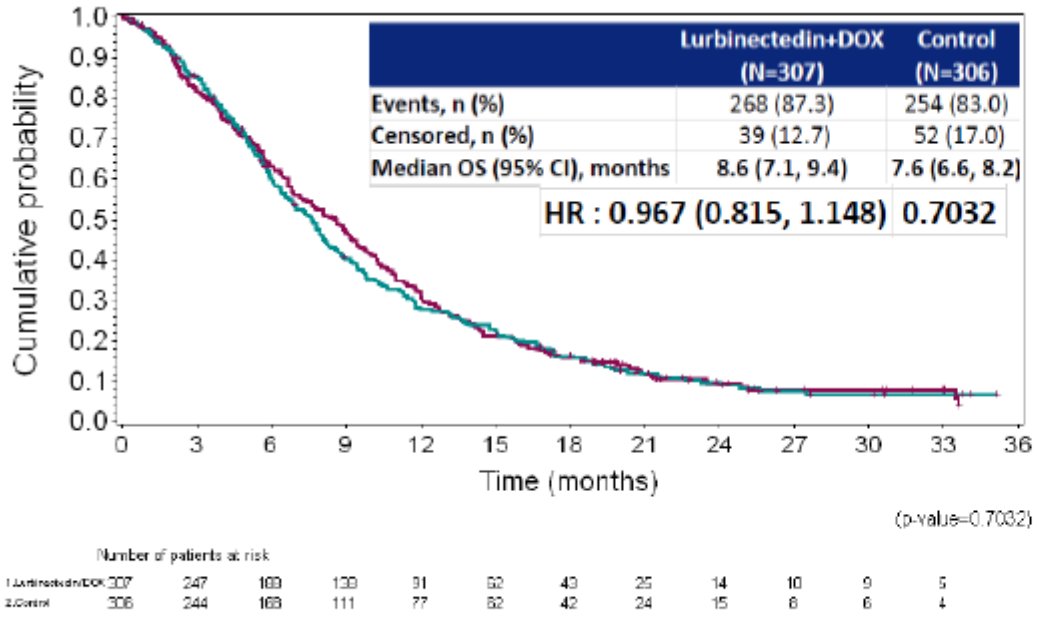
Sensitive or refractory relapse SCLC
(> 30 days from D1 of the last cycle of chemotherapy)

R

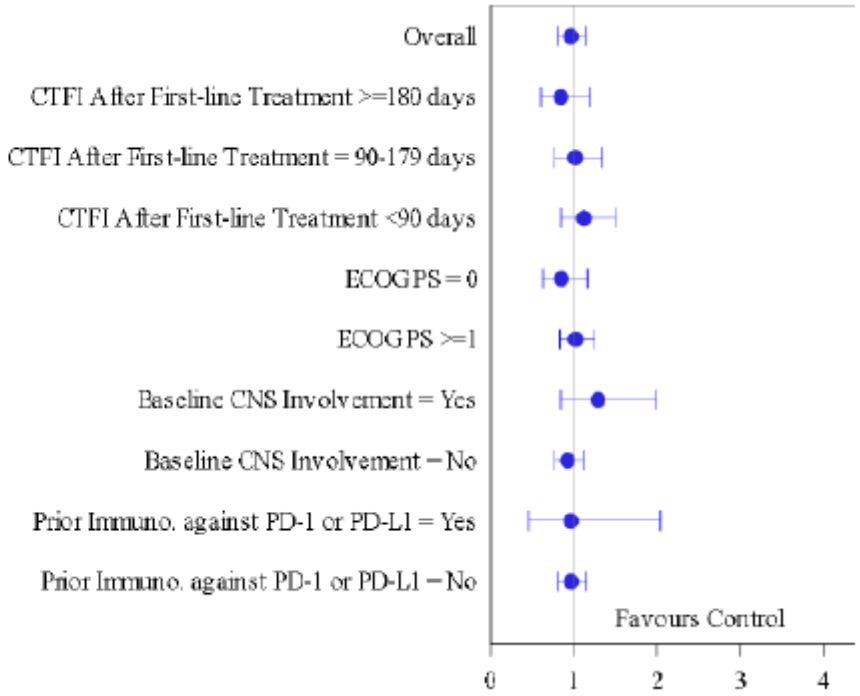
- **Doxorubicine 40 mg/m²**
  Lurbinectedin 2 mg/m²
- **Topotecan I.V.**
  Or CAV

OS

Primary endpoint



	Lurbinectedin+DOX (N=307)	Control (N=306)
Events, n (%)	268 (87.3)	254 (83.0)
Censored, n (%)	39 (12.7)	52 (17.0)
Median OS (95% CI), months	8.6 (7.1, 9.4)	7.6 (6.6, 8.2)
HR : 0.967 (0.815, 1.148)		0.7032



Pas-Arez et al, ESMO 2021

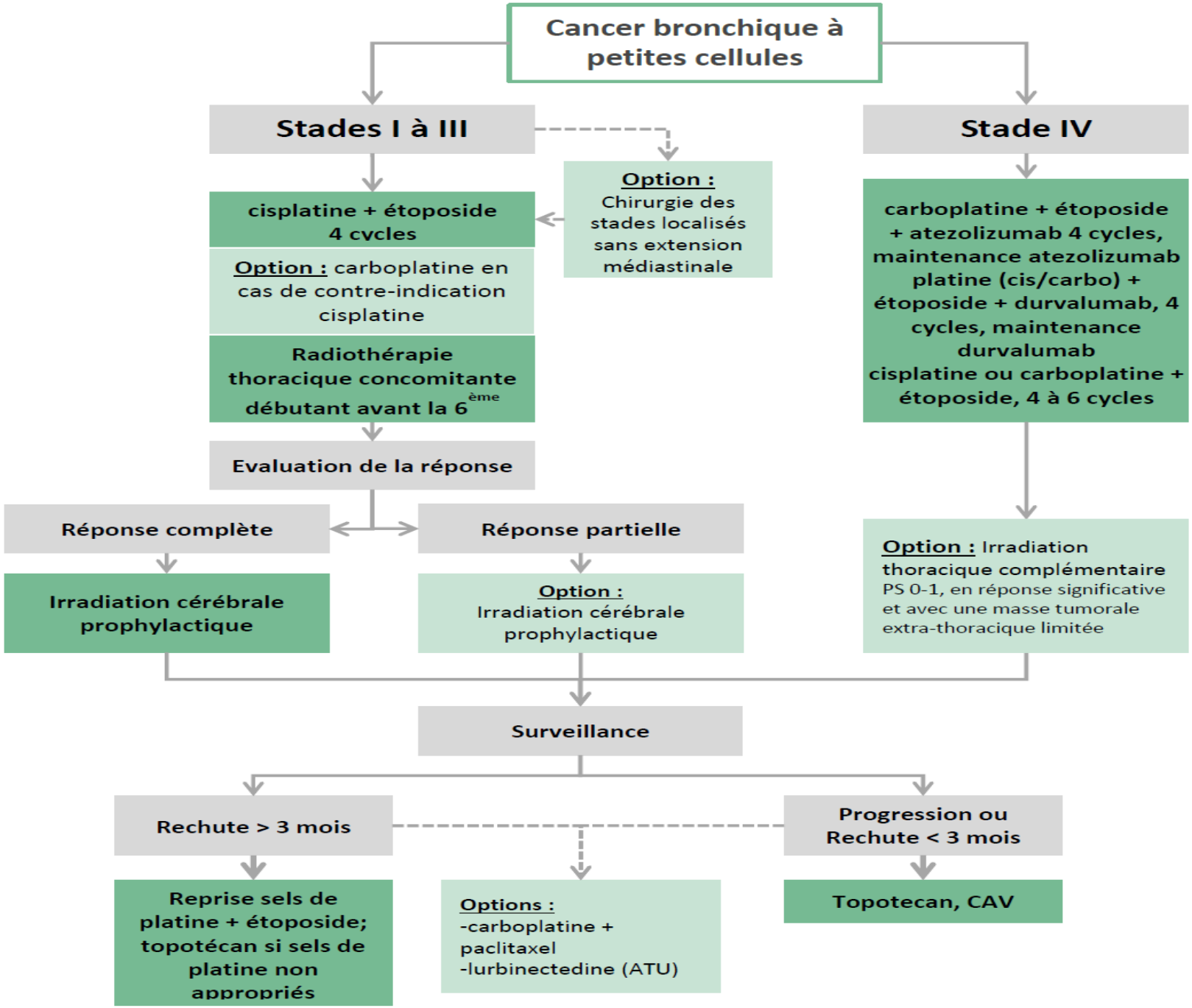
PRINCIPLES OF SYSTEMIC THERAPY

SCLC SUBSEQUENT SYSTEMIC THERAPY (PS 0–2)[c] Consider dose reduction or growth factor support for patients with PS 2.	
Relapse ≤6 months	Relapse >6 months
Preferred Regimens • Topotecan PO or IV[14-16] • Lurbinectedin[17] • Clinical trial Other Recommended Regimens • Paclitaxel[18,19] • Docetaxel[20] • Irinotecan[21] • Temozolomide[22,23] • Cyclophosphamide/doxorubicin/vincristine (CAV)[14] • Oral etoposide[24,25] • Vinorelbine[26,27] • Gemcitabine[28,29] • Nivolumab[b,d,30,31] • Pembrolizumab[b,d,32-34] • Bendamustine (category 2B)[35]	Preferred Regimens • Original regimen[d,36,37] Other Recommended Regimens • Topotecan PO or IV[14-16] • Paclitaxel[18,19] • Docetaxel[20] • Irinotecan[21] • Temozolomide[22,23] • CAV[14] • Oral etoposide[24,25] • Vinorelbine[26,27] • Gemcitabine[28,29] • Nivolumab[b,d,30,31] • Pembrolizumab[b,d,32-34] • Lurbinectedin[38] • Bendamustine (category 2B)[35]

Response Assessment (SCL-E 3 of 5)
References (SCL-E 4 of 5)

[b] Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or concurrent use of immunosuppressive agents.
[c] Subsequent systemic therapy refers to second-line and beyond therapy.
[d] The use of immune checkpoint inhibitors is discouraged if there is progression on maintenance atezolizumab or durvalumab at time of relapse.

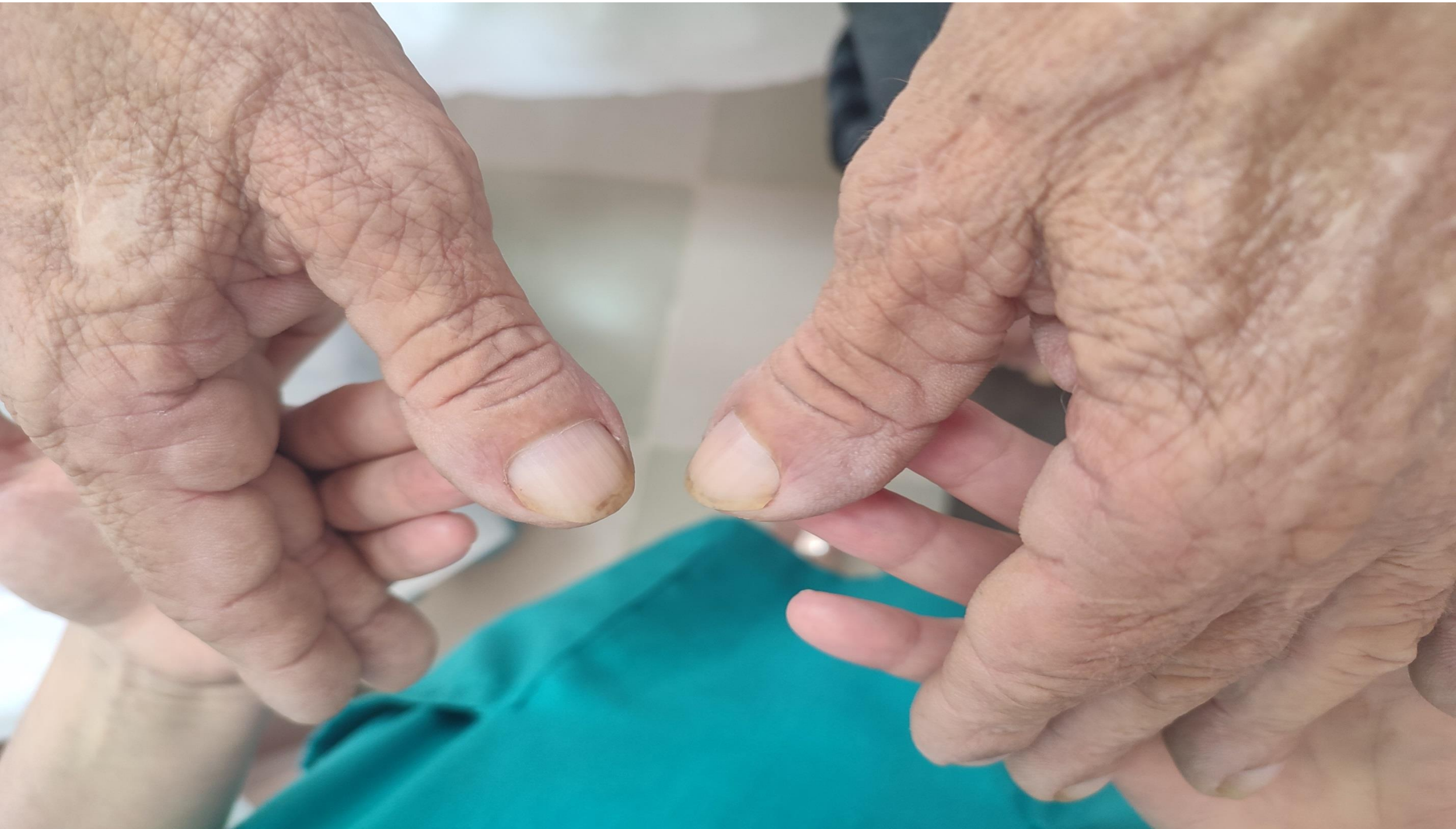
Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

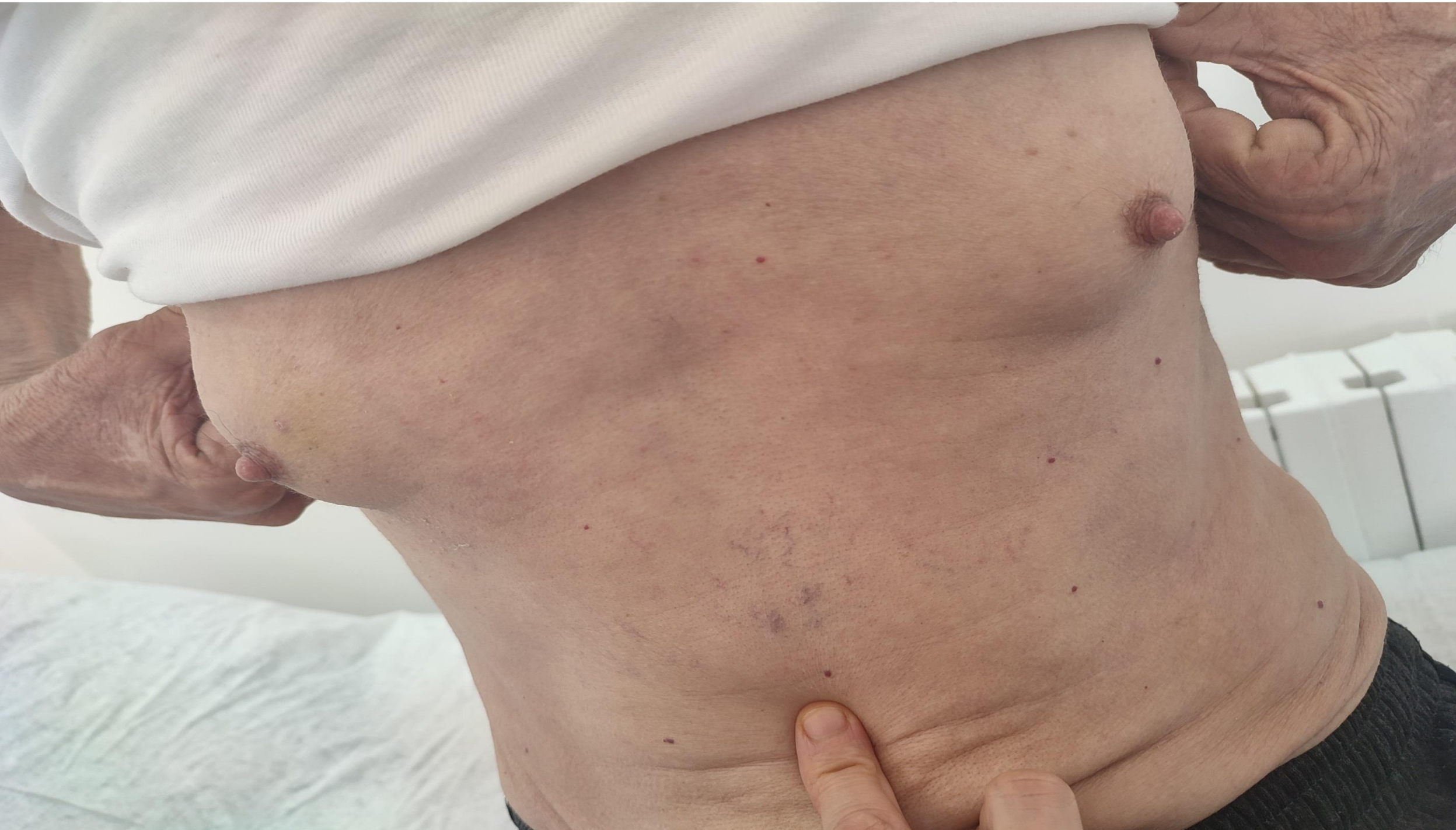

Cancer bronchique à petites cellules
Stades I à III
Stade IV
Option : Chirurgie des stades localisés sans extension médiastinale
cisplatine + étoposide 4 cycles
Option : carboplatine en cas de contre-indication cisplatine
Radiothérapie thoracique concomitante débutant avant la 6ème
Evaluation de la réponse
carboplatine + étoposide + atezolizumab 4 cycles, maintenance atezolizumab
platine (cis/carbo) + étoposide + durvalumab, 4 cycles, maintenance durvalumab
cisplatine ou carboplatine + étoposide, 4 à 6 cycles
Réponse complète
Réponse partielle
Irradiation cérébrale prophylactique
Option : Irradiation cérébrale prophylactique
Option : Irradiation thoracique complémentaire PS 0-1, en réponse significative et avec une masse tumorale extra-thoracique limitée
Surveillance
Rechute > 3 mois
Progression ou Rechute < 3 mois
Reprise sels de platine + étoposide; topotécan si sels de platine non appropriés
Options : -carboplatine + paclitaxel -lurbinectedine (ATU)
Topotecan, CAV

Cas clinique

- Monsieur SA âgé de 57 ans originaire et demeurant à Hadjout, plombier de profession, tabagique chronique à raison de 120 P/A sevré depuis 1 mois, consulte pour des douleurs articulaires associées à changement de la texture des mains.
- L’examen clinique :
- OMS I , poids 61 Kg, T: 1.67 m TA 14/7
- Perte pondérale de 3 kg en 3 mois
- L’examen clinique:
- Kératodermie jaunatre avec accentuation des dermatoglyphes palmaires
- L'examen ostéoarticulaire négatif sauf des ongles bombés.


Kératodermie palmaire
Ongle Bombé

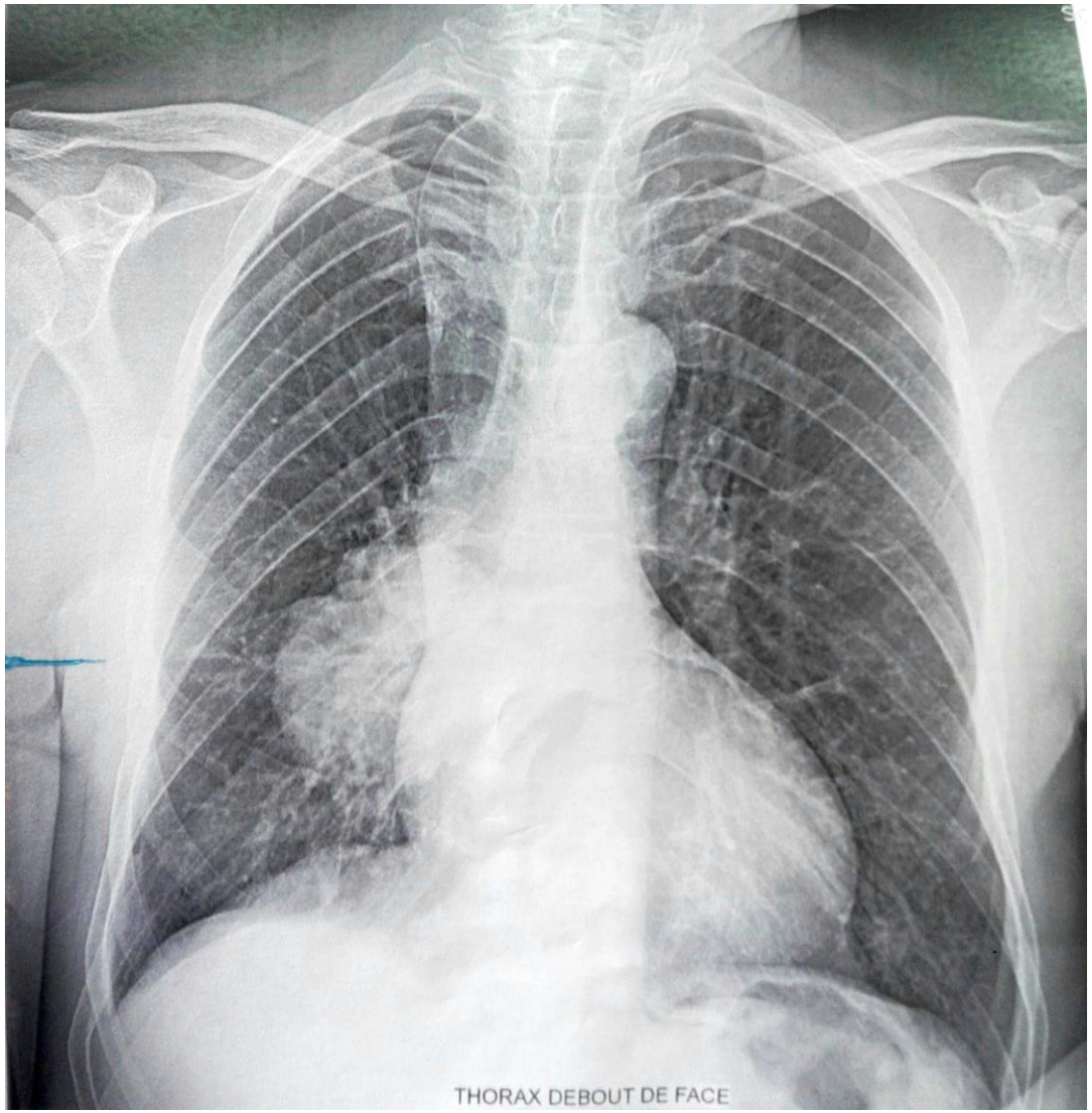




- Devant ce tableau clinique quels diagnostics évoquez vous ?

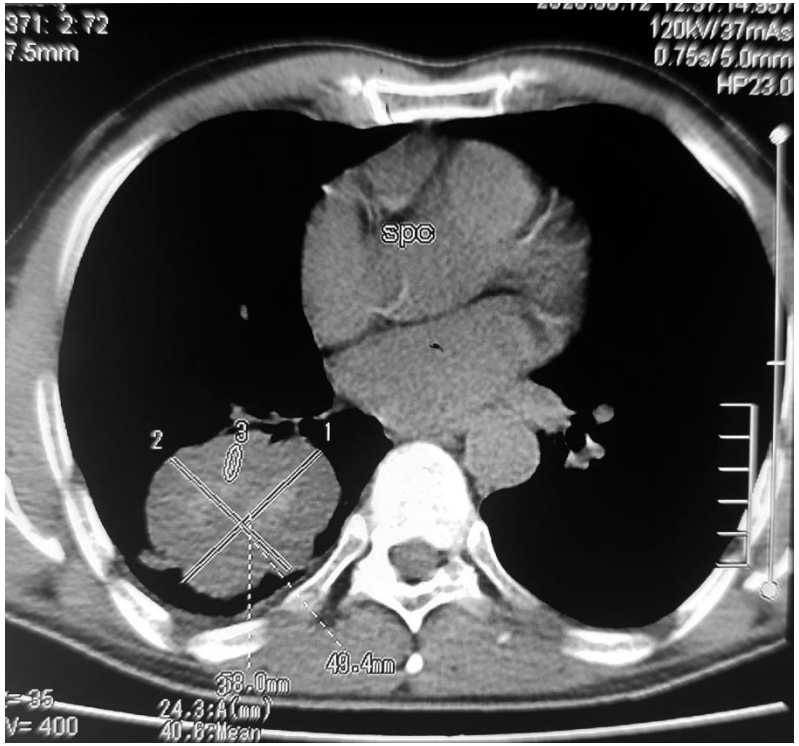
- L’examen clinique de Mr SA retrouve une gynécomastie bilatérale associée avec pachydermatoglyphie
-  **SYNDROME PARANÉOPLASIQUE**

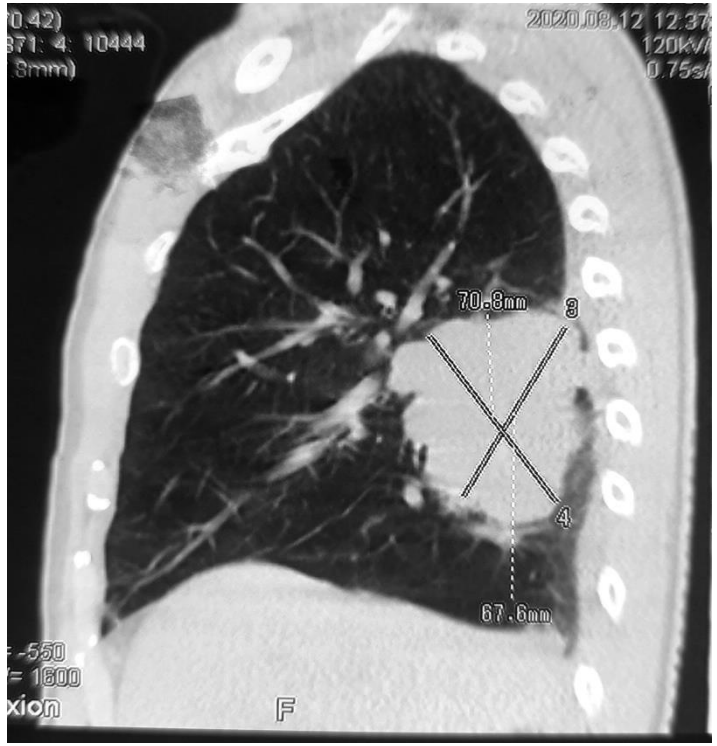
Radiographie thoracique

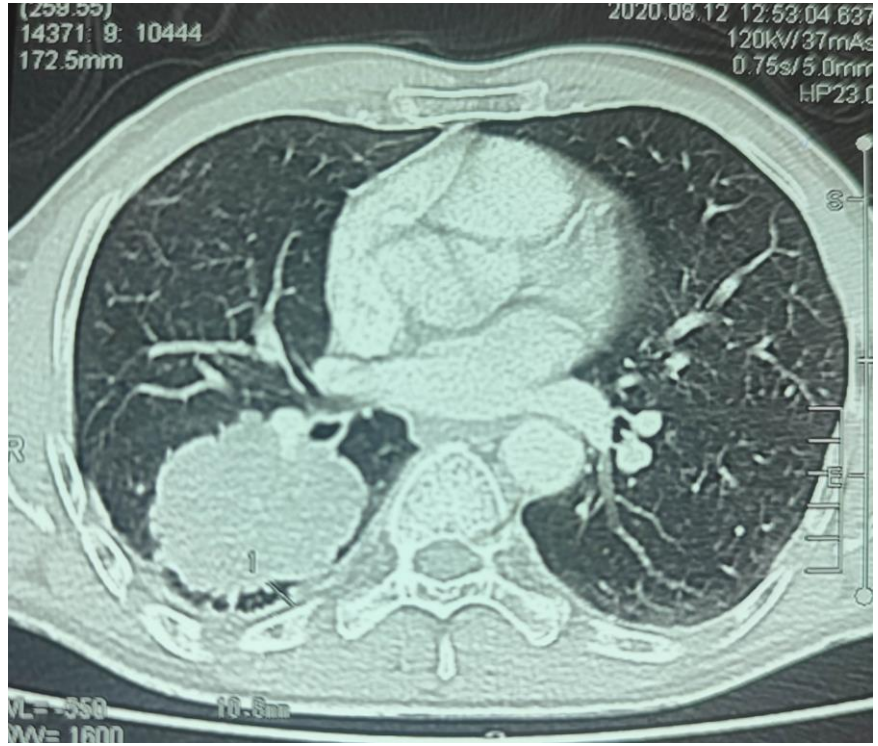


Échographie abdominopelvienne : RAS

1er TDM thoracique 12/08/2020



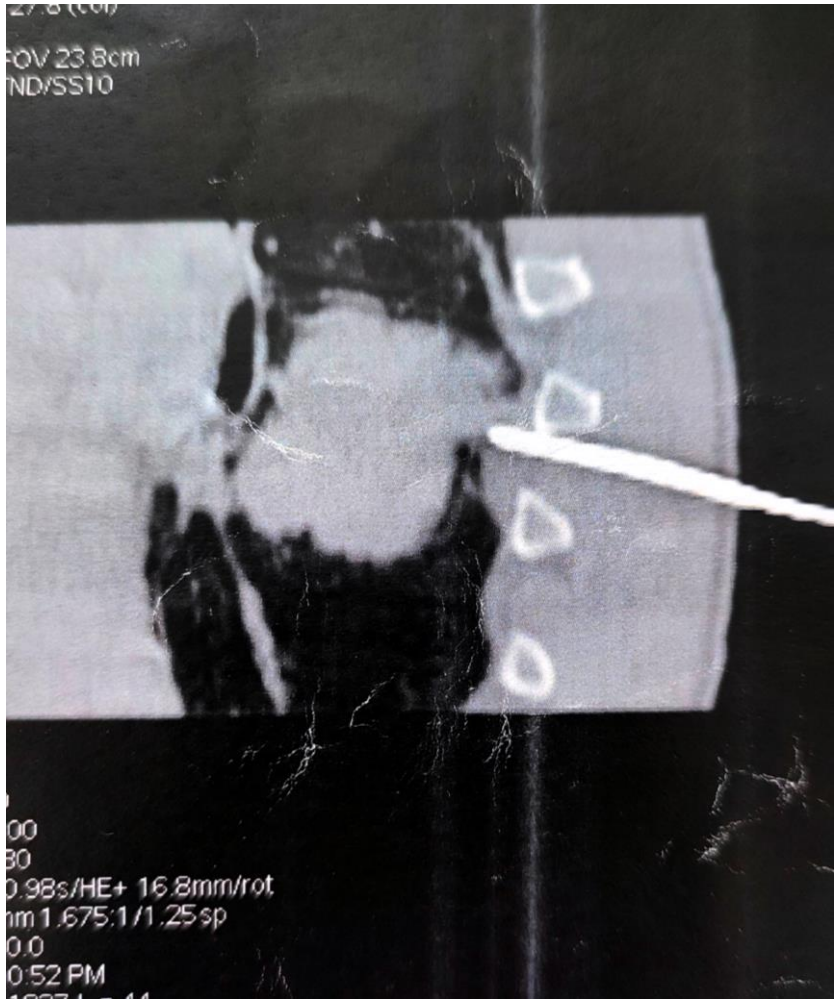


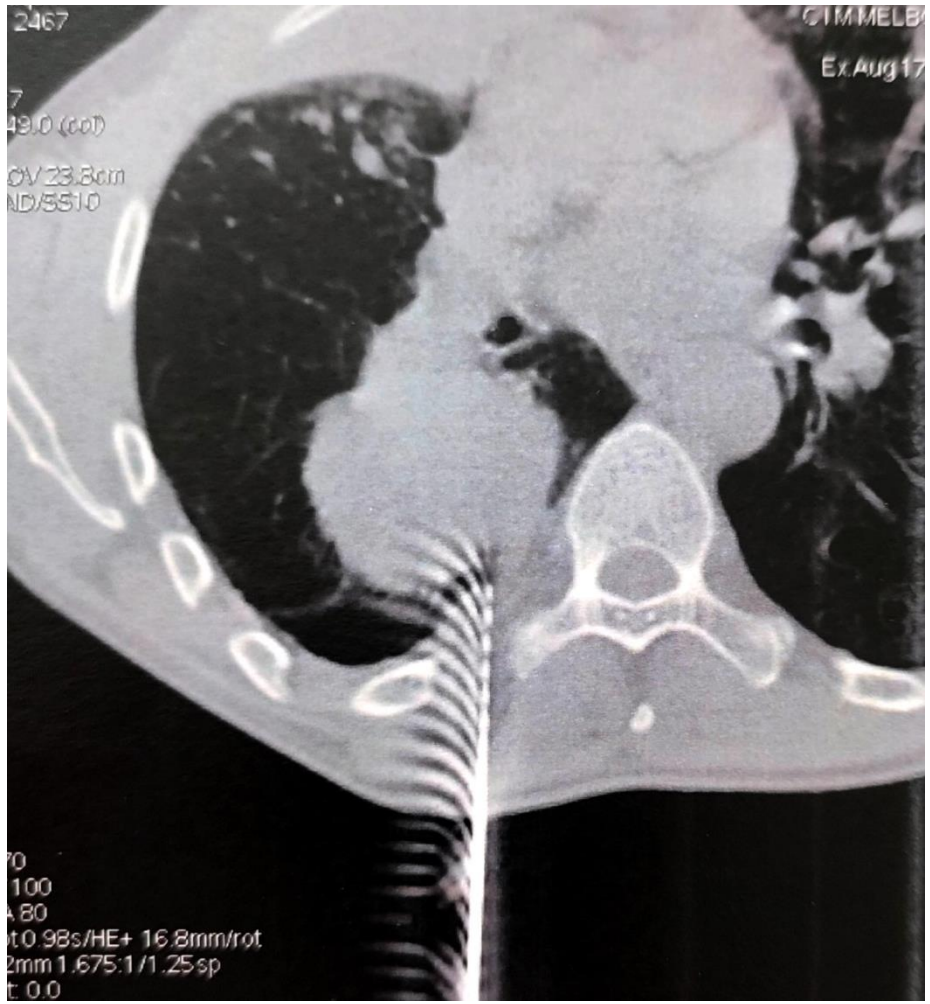


Masse tissulaire para hilaire du LID mesurant 66 × 68 mm engainant la branche artérielle LID + multiples ADP médiastino-hilaires homolatérales, la plus volumineuse = 23,5mm × 17,5 mm

- Fibroscopie bronchique: inflammation de l’arbre bronchique droit avec compression extrinsèque de LID, biopsie +++
- Résultat anapath: biopsie négative, cytologie du liquide d’aspiration positive.

BIOPSIE SCANNO-GUIDEE faite le 25/08/2020





- **Résultats de la biopsie :**

Carcinome bronchique à petite cellule(CPC)

- **Immunohistochimie** :

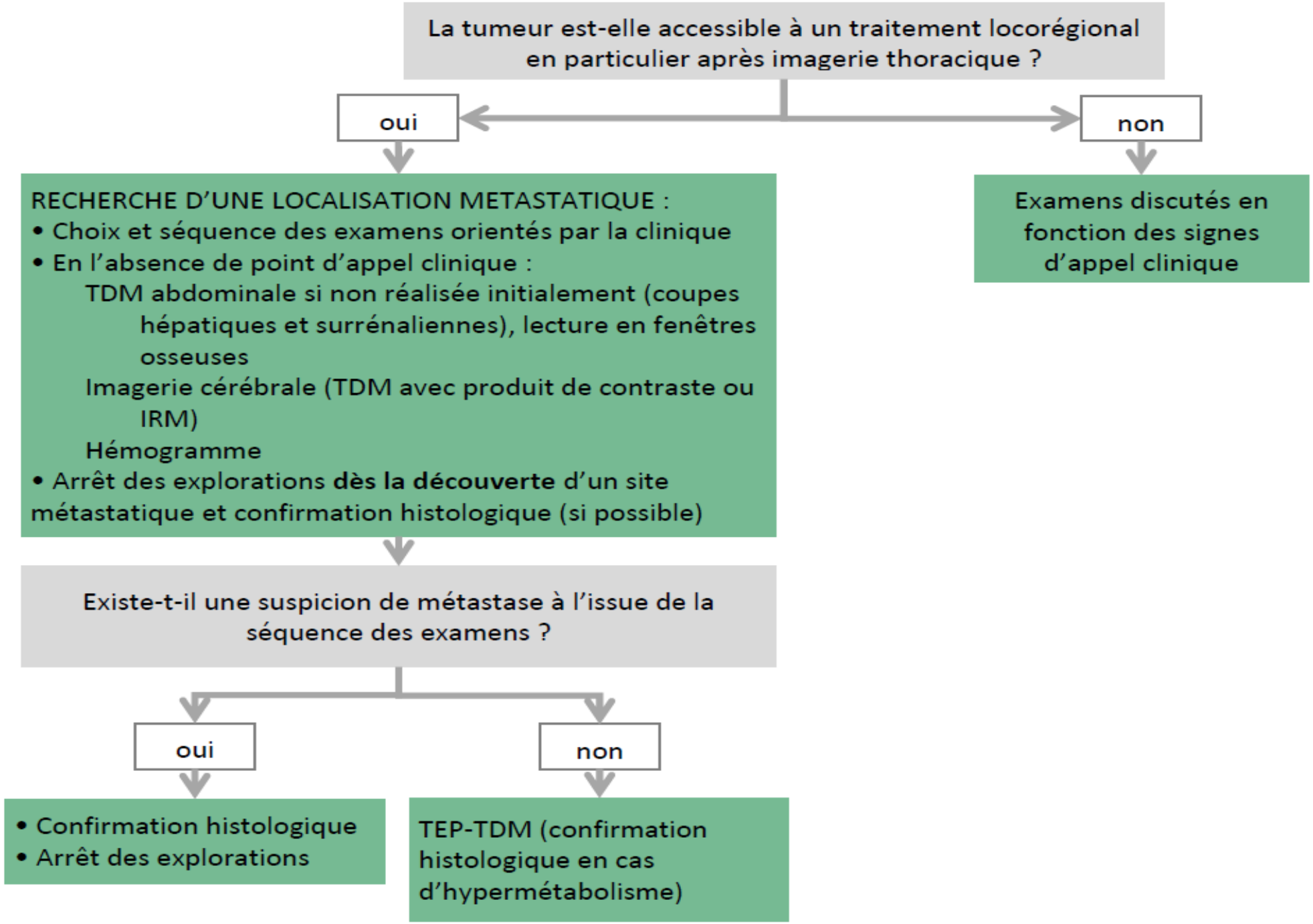
-CD 56: expression membranaire intense et diffuse

-Anti chromogranine : expression focale, Synaptophysine +

-TTF1: expression nucléaire des cellules néoplasiques

-P40 : négatif

-Ki 67 : 95 %

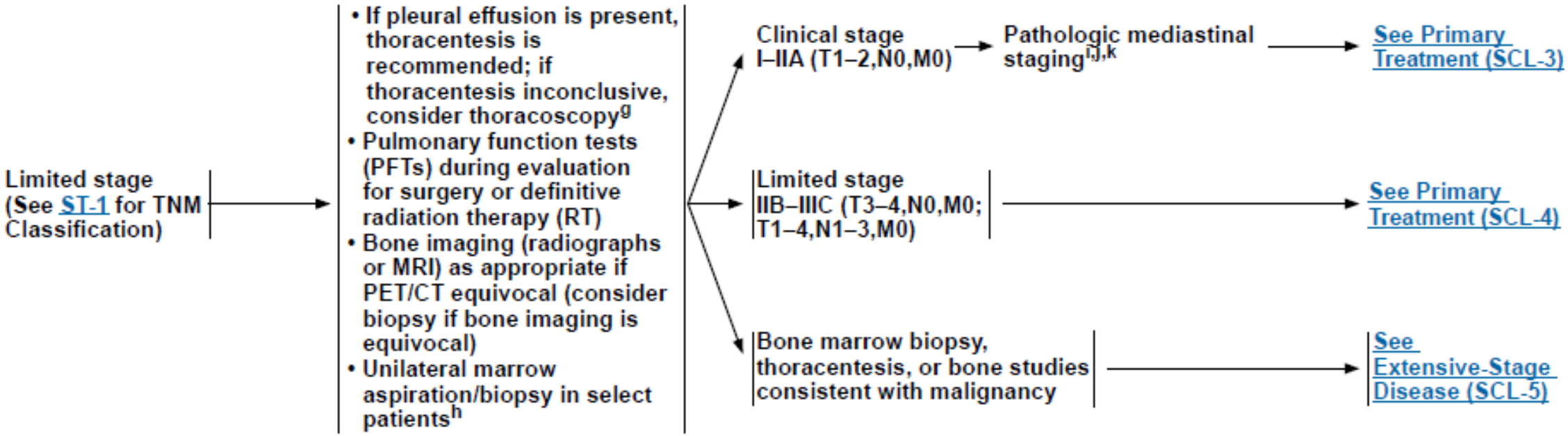

La tumeur est-elle accessible à un traitement locorégional en particulier après imagerie thoracique ?
oui
non
RECHERCHE D'UNE LOCALISATION METASTATIQUE :
• Choix et séquence des examens orientés par la clinique
• En l'absence de point d'appel clinique :
TDM abdominale si non réalisée initialement (coupes hépatiques et surrénaliennes), lecture en fenêtres osseuses
Imagerie cérébrale (TDM avec produit de contraste ou IRM)
Hémogramme
• Arrêt des explorations dès la découverte d'un site métastatique et confirmation histologique (si possible)
Examens discutés en fonction des signes d'appel clinique
Existe-t-il une suspicion de métastase à l'issue de la séquence des examens ?
oui
non
• Confirmation histologique
• Arrêt des explorations
TEP-TDM (confirmation histologique en cas d'hypermétabolisme)

Examens indispensables pour traiter notre patient ?

- Scintigraphie osseuse
- IRM Cérébrale
- PET Scanner
- FNS
- BR
- BH
- LDH
- EFR

Examens indispensables pour traiter notre patient ?

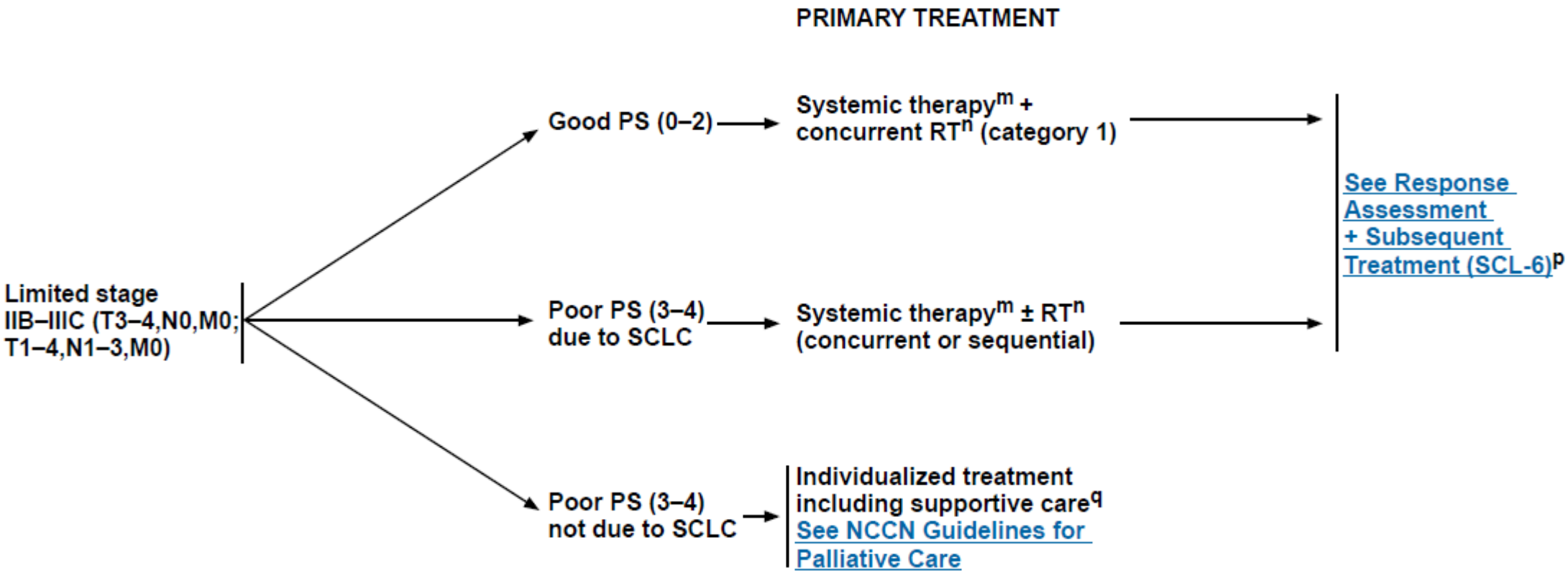
- Scintigraphie osseuse :RAS
- IRM Cérébrale : RAS
- PET Scanner Non fait
- FNS: GR: 4.5 M, GB: 15000, plaquettes: 500 milles
- BR: urée sg : 8, créatinine sg: 0.6
- BH: Nx
- LDH: 500 UI/ml
- EFR: syndrome restrictif VEMS 70%

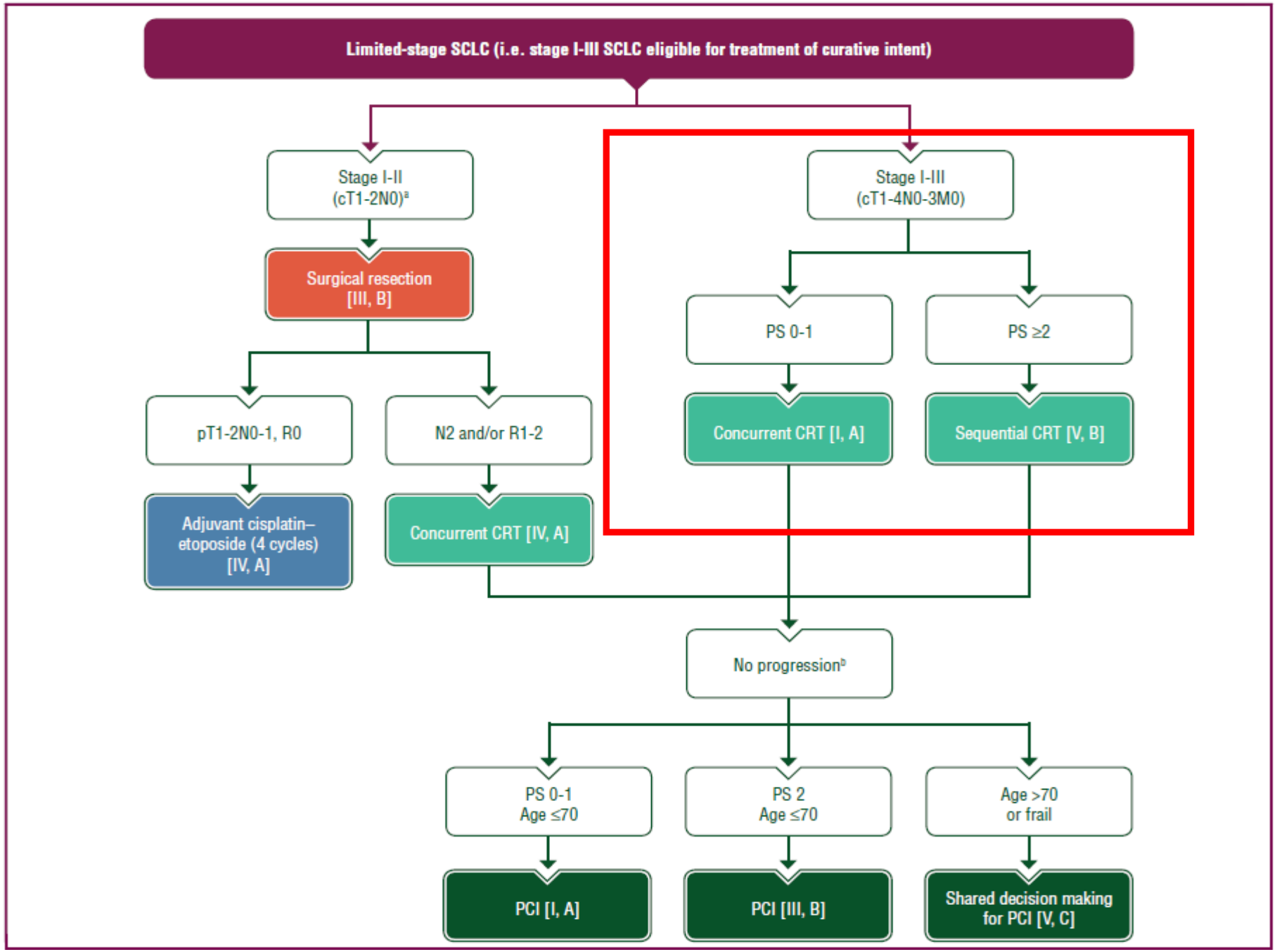

STAGE
ADDITIONAL WORKUP
Limited stage (See ST-1 for TNM Classification)
• If pleural effusion is present, thoracentesis is recommended; if thoracentesis inconclusive, consider thoracoscopy[g]
• Pulmonary function tests (PFTs) during evaluation for surgery or definitive radiation therapy (RT)
• Bone imaging (radiographs or MRI) as appropriate if PET/CT equivocal (consider biopsy if bone imaging is equivocal)
• Unilateral marrow aspiration/biopsy in select patients[h]
Clinical stage I–IIA (T1–2,N0,M0)
Pathologic mediastinal staging[i,j,k]
See Primary Treatment (SCL-3)
Limited stage IIB–IIIC (T3–4,N0,M0; T1–4,N1–3,M0)
See Primary Treatment (SCL-4)
Bone marrow biopsy, thoracentesis, or bone studies consistent with malignancy
See Extensive-Stage Disease (SCL-5)

Mr SA présente un carcinome à petites cellules.

- Comment classez vous la maladie ?

- T3N2M0 stade IIIB
- T4N1M0 stade IIIA
- T3N1M0 stade IIIA
- T3N2M0 stade IIIA
- T3N3M0 stade IIIC
- T2N2M0 stade IIB

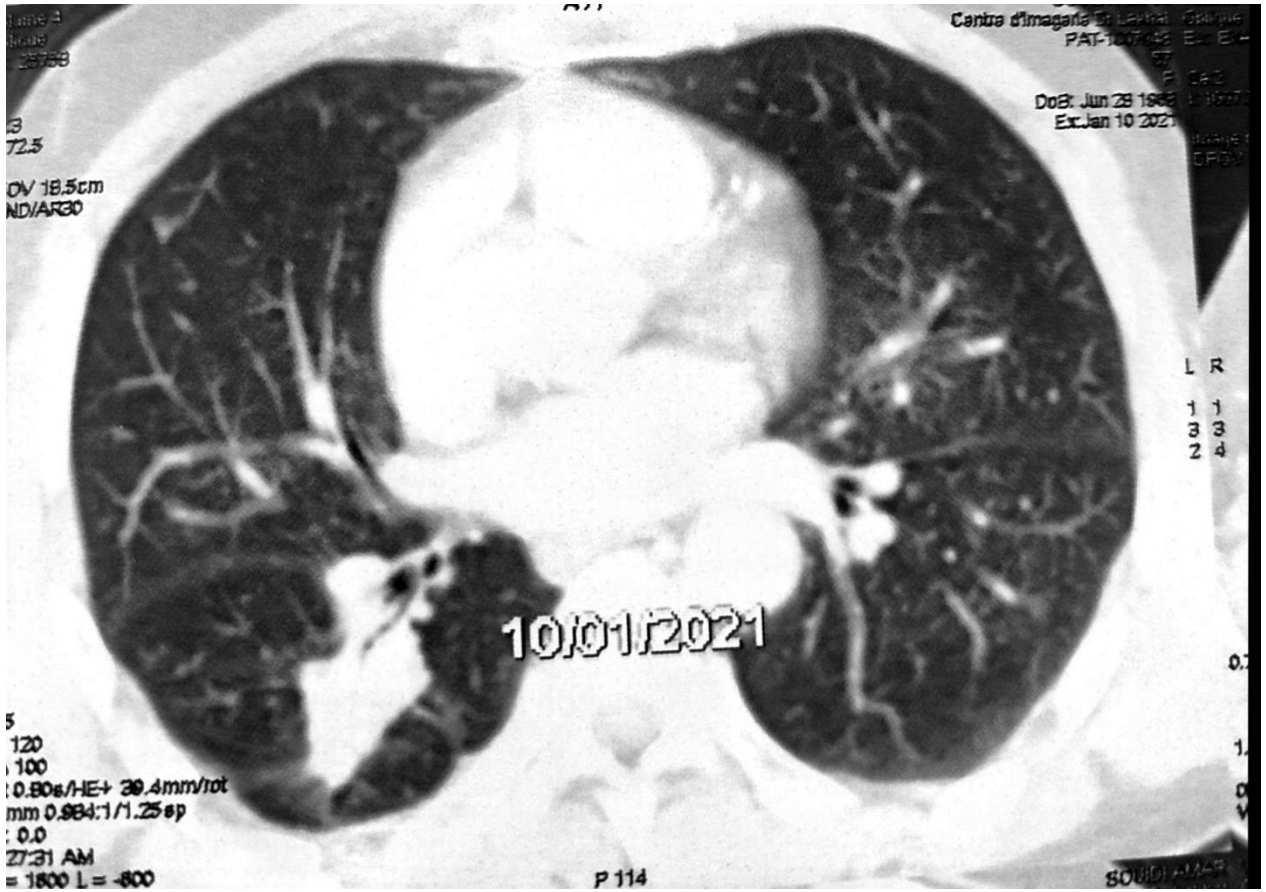

PRIMARY TREATMENT
Limited stage IIB–IIIC (T3–4,N0,M0; T1–4,N1–3,M0)
Good PS (0–2)
Systemic therapy[m] + concurrent RT[n] (category 1)
Poor PS (3–4) due to SCLC
Systemic therapy[m] ± RT[n] (concurrent or sequential)
Poor PS (3–4) not due to SCLC
Individualized treatment including supportive care[q]
See NCCN Guidelines for Palliative Care
See Response Assessment + Subsequent Treatment (SCL-6)[p]



SCLC ESMO CPG, Ann Oncol 2021

- Une chimiothérapie néo-adjuvante protocole CDDP Etoposide a été indiquée, l'évaluation après 3 cures de chimiothérapie on note une réponse partielle.

Après 03 autres cures
TDM thoracique 10/01/2021



Masse tumorale mesurant 28*40mm réponse partielle

ADP médiastino-hilaires la plus vol = 10mm

- Nombre de cures de chimiothérapie?

- 3 cures
- 4 cures
- 5 cures
- 6 cures

- Après fin de chimioradiothérapie médiastinopulmonaire, quelle suite de traitement préconisez vous?

- Durvalumab en maintenance pendant 1 an
- Durvalumab en maintenance pendant 1 an si PDL1+
- Radiothérapie encéphalique prophylactique
- 2 autres cures de chimiothérapie CDDP Etoposide
- Suivi régulier sans TRT

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2022
Small Cell Lung Cancer

NCCN Guidelines Index
Table of Contents
Discussion

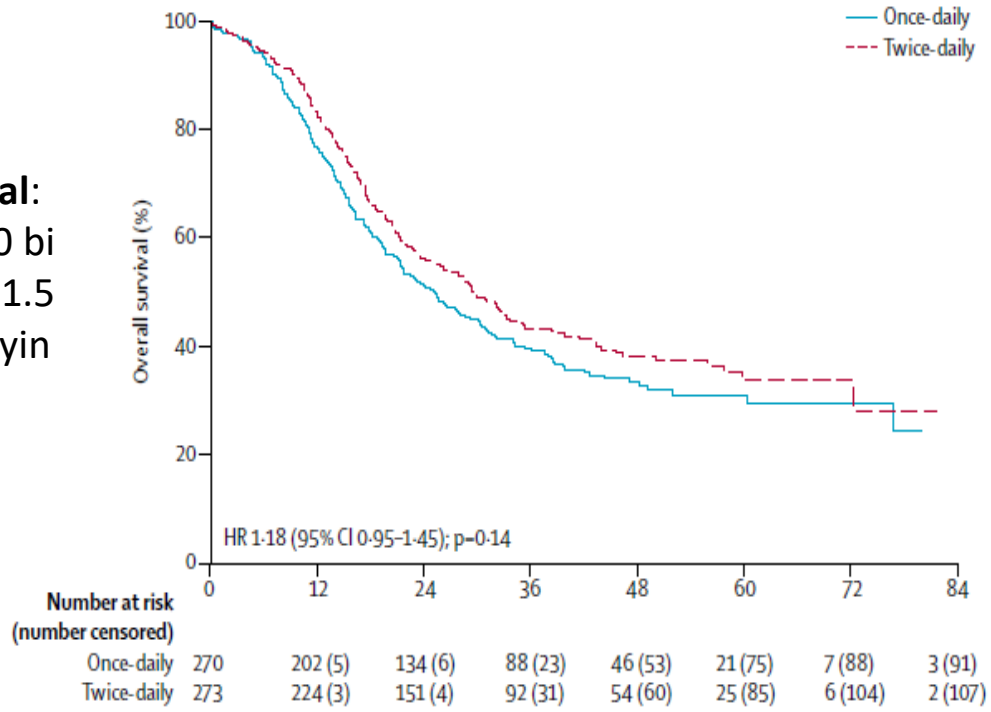
PRINCIPLES OF SYSTEMIC THERAPY

PRIMARY OR ADJUVANT THERAPY FOR LIMITED-STAGE SCLC:
Four cycles of systemic therapy are recommended. Planned cycle length should be every 21–28 days during concurrent RT. During systemic therapy + RT, cisplatin/etoposide is recommended (category 1). The use of myeloid growth factors is not recommended during concurrent systemic therapy plus RT (category 1 for not using GM-CSF).[1]
Preferred Regimens • Cisplatin 75 mg/m² day 1 and etoposide 100 mg/m² days 1, 2, 3[2] • Cisplatin 60 mg/m² day 1 and etoposide 120 mg/m² days 1, 2, 3[3] Other Recommended Regimens • Cisplatin 25 mg/m² days 1, 2, 3 and etoposide 100 mg/m² days 1, 2, 3[2] • Carboplatin AUC 5–6 day 1 and etoposide 100 mg/m² days 1, 2, 3[a,4]

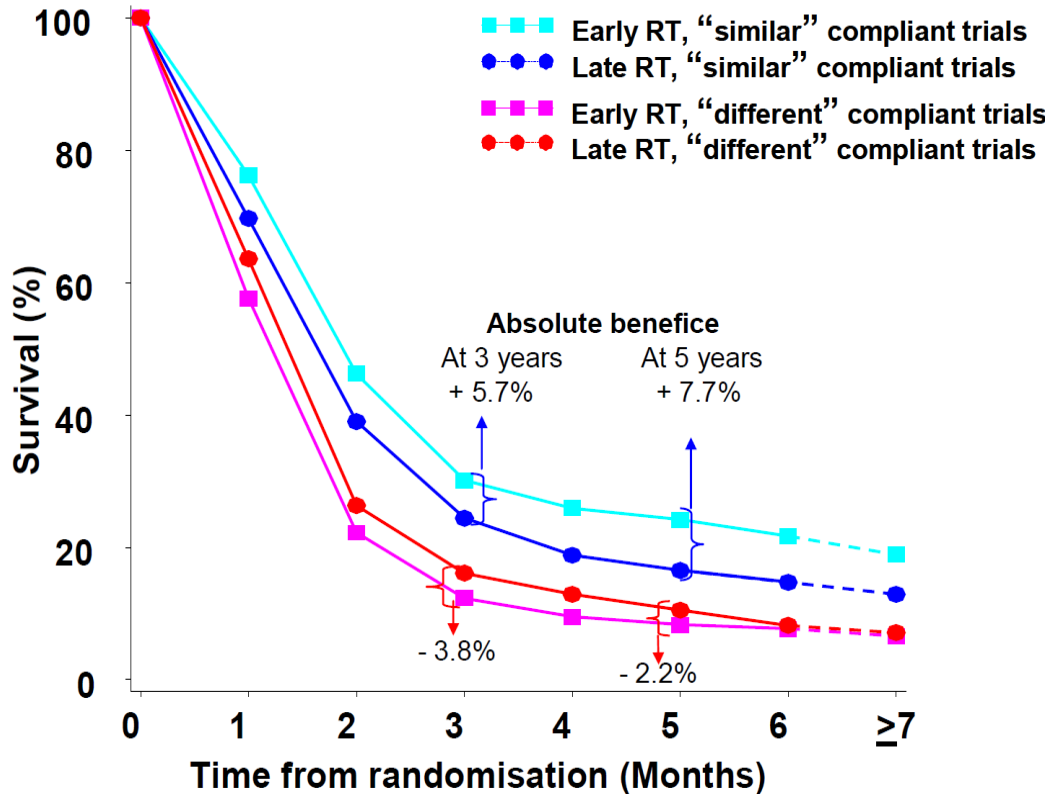
RCC

- Chimioradiothérapie concomitante si PS 0 et 1
- Dose recommandée 45 Gy en B.I.D en 30 fractions
- Commencer le plus tôt possible

Convert trial:
45 Gy en 30 bi fraction /J 1.5 Gy vs. 66 Gyin 33 une fraction/J



Méta-analyse : RCC dans 30 jours après début de la CT



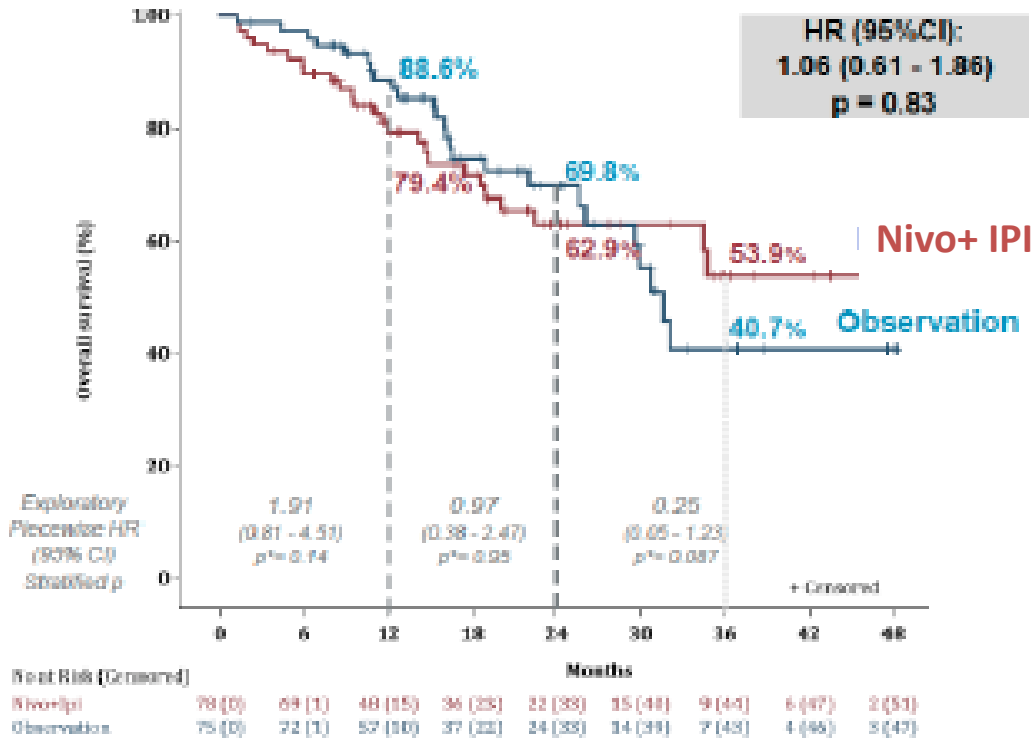
1.Faivre Finn et al, *Lancet Oncol*2017, 18(8):1116-1125

2.De Ruysscheret al, Ann Oncol2016

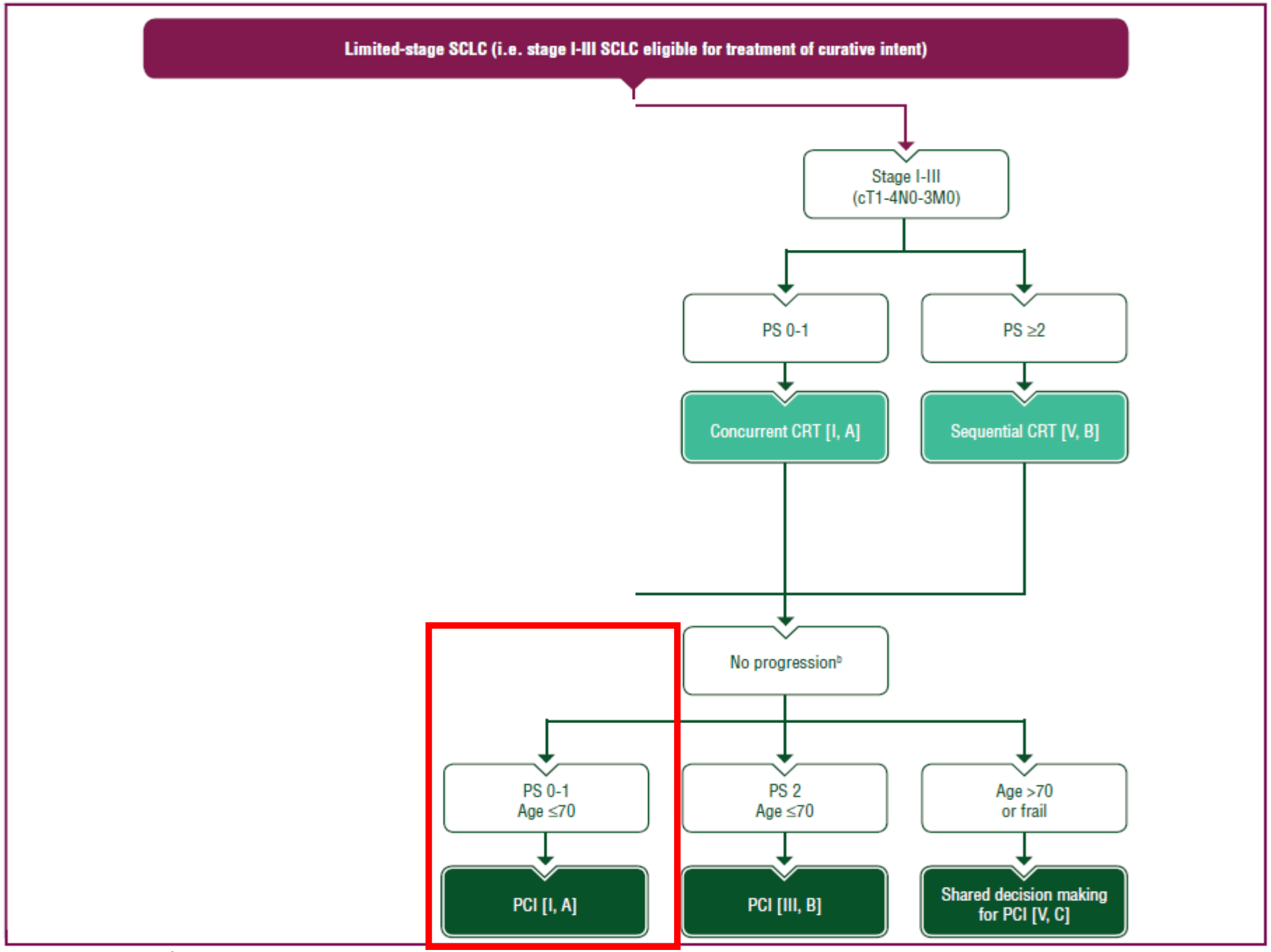
Maintenance par immunothérapie après RCC

- Cisplatine 60-80 mg/m2 J1
- etoposide 100-120 mg/m2 J 1, 2 et 3,
- Cycle 3 semaines, 4 cycles
- Carboplatine plus etoposide si CI cisplatine

Stimuli trial:
Nivolumab +Ipilimumab pdt 1 an vs **placebo**
Pas de bénéfice SSP ni SG



Peters et al ESMO 2020

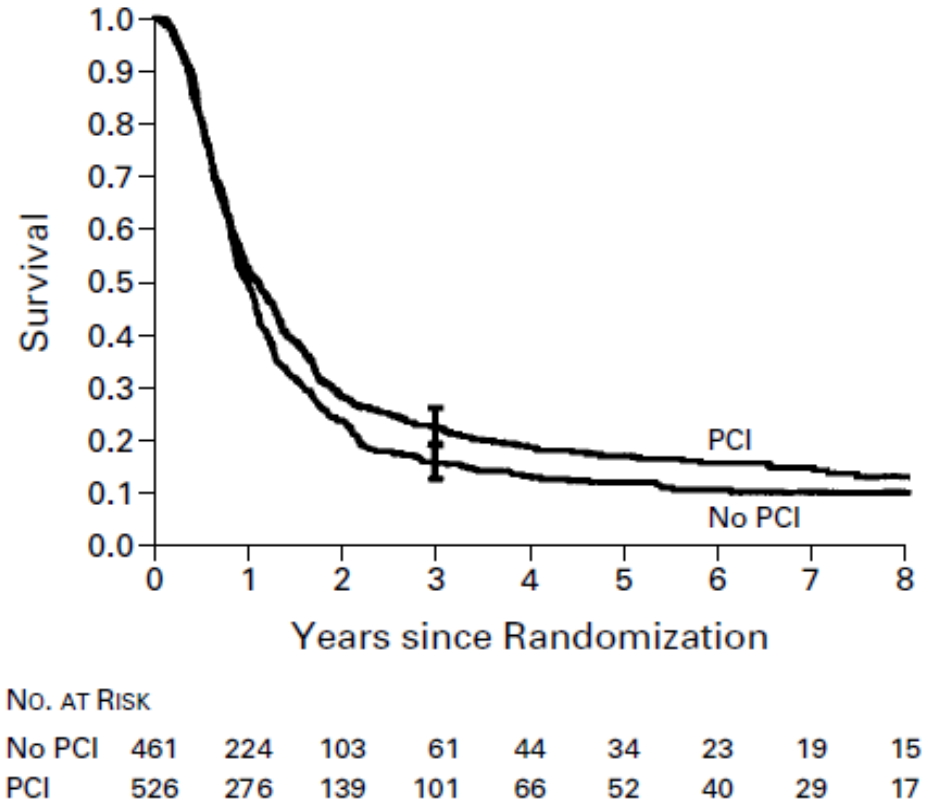


SCLC ESMO CPG, Ann Oncol 2021

Radiothérapie cérébrale prophylactique

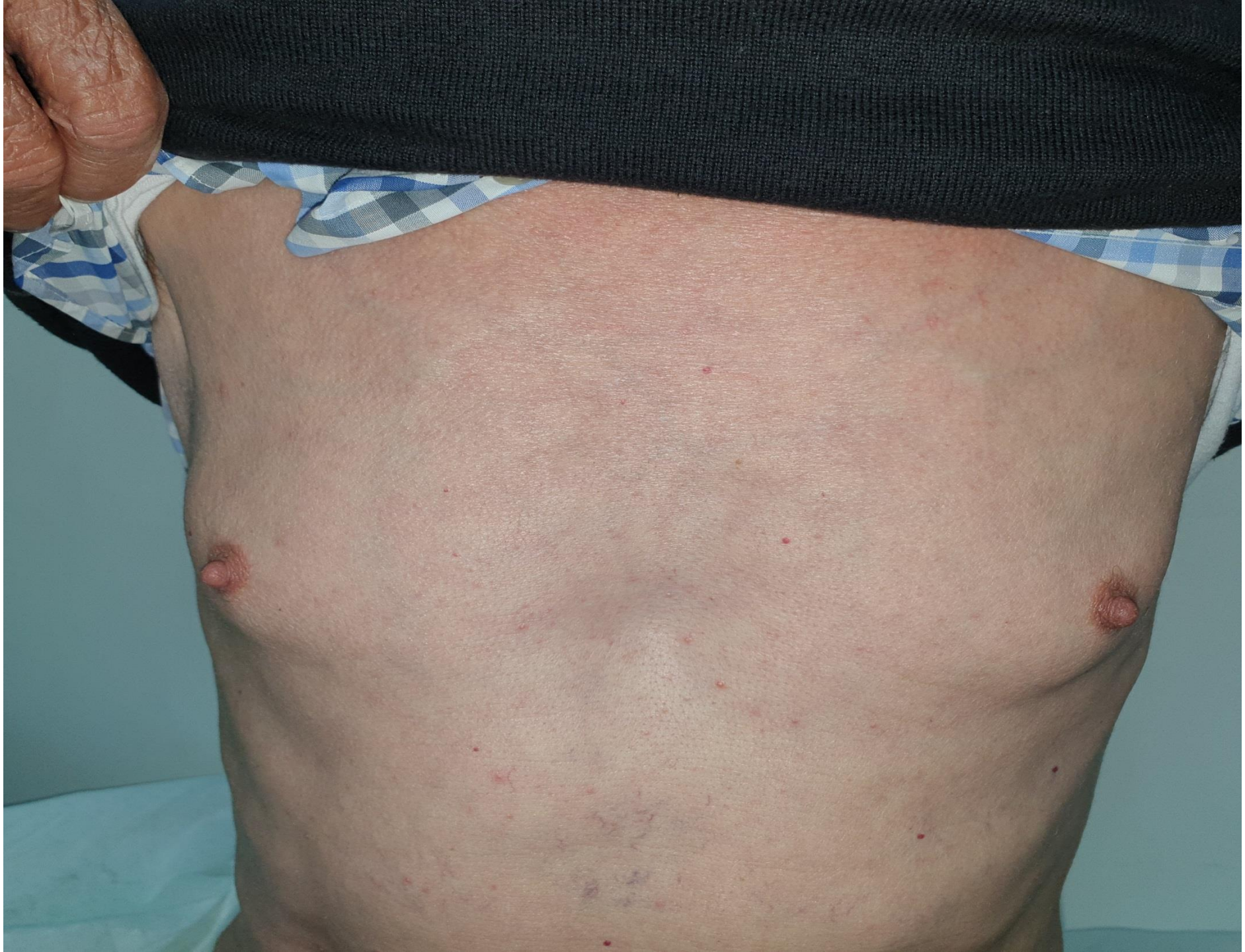
- Indiquée au stade III CPC, aprés réponse CRT
- Chez des patients PS of 0-1.
- 3 ans: 33.3% vs 58.6% mets cérèbrale
- Recommandé IPC : 25 Gy/10 fractions

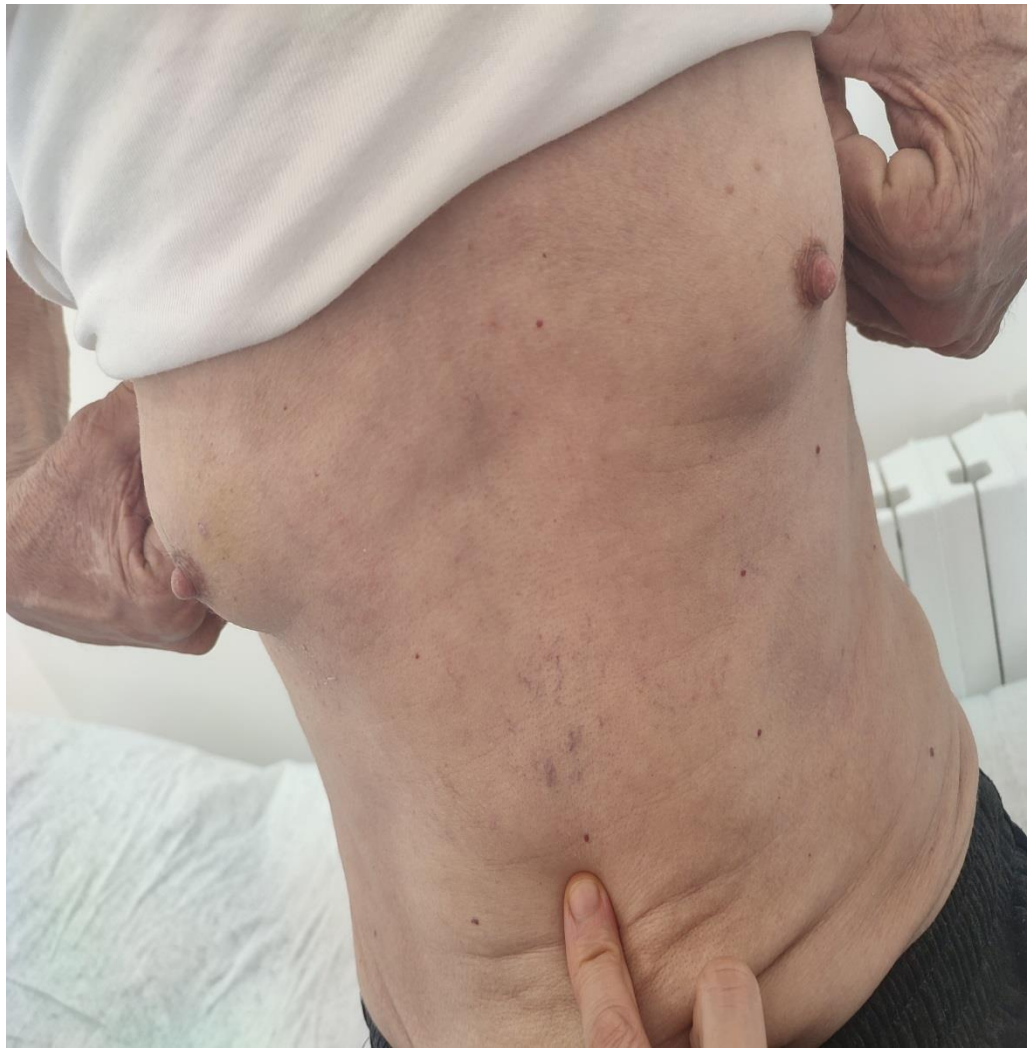
- <u>Méta-analyse</u> IPC Vs pas de IPC



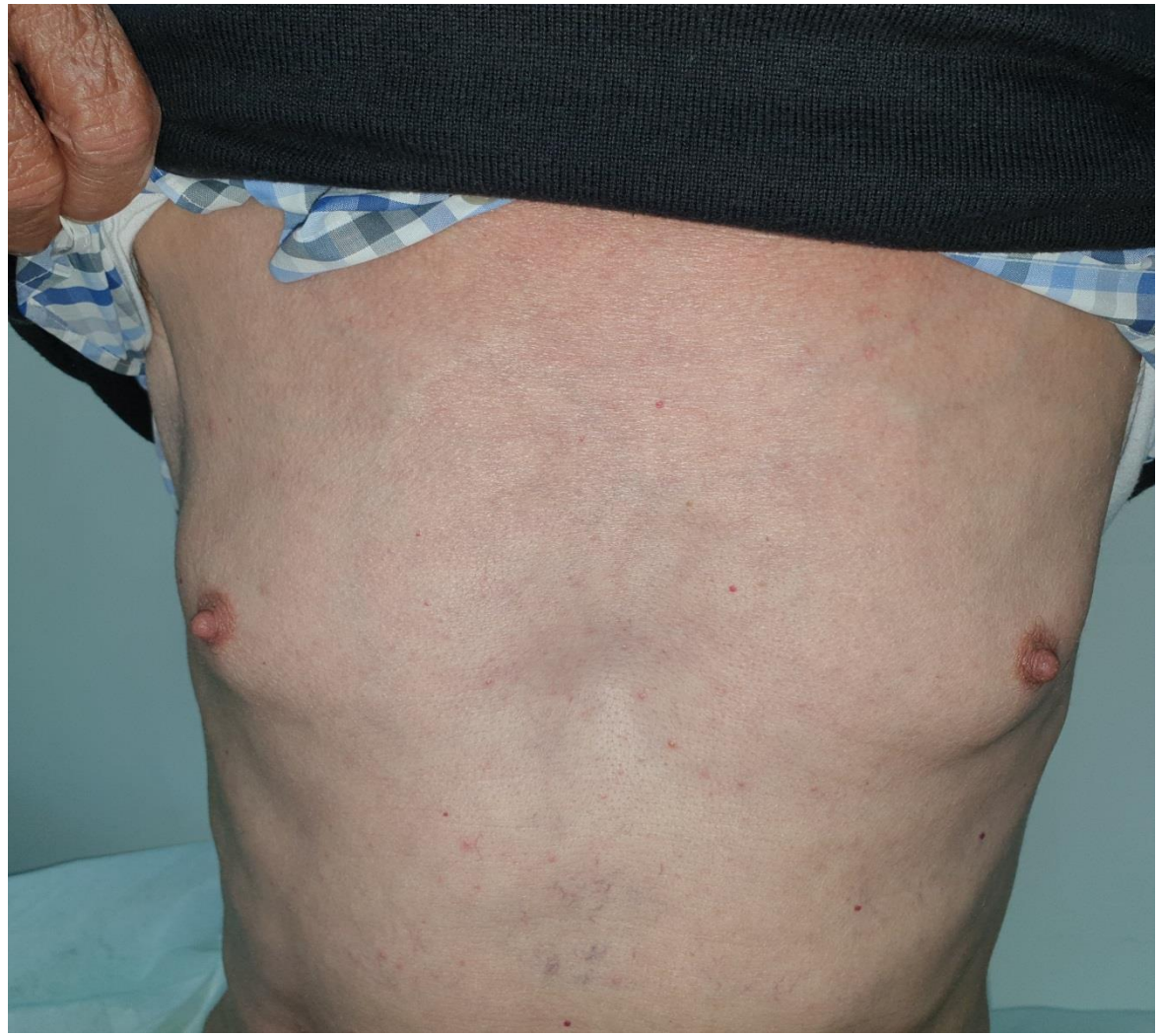
Auperinet al, N EnglJ Med 1999, 341(7):476:84

- Notre patient a reçu une radiothérapie séquentielle du 14/02/2021 au 02/03/2021 dose 54 Gy au niveau masse tumorale + aires gg sur 27 séances
- Radiothérapie encéphalique prophylactique à la dose de 25 Gy en 10 séances.
- Dernière cure de CT Décembre 2020.

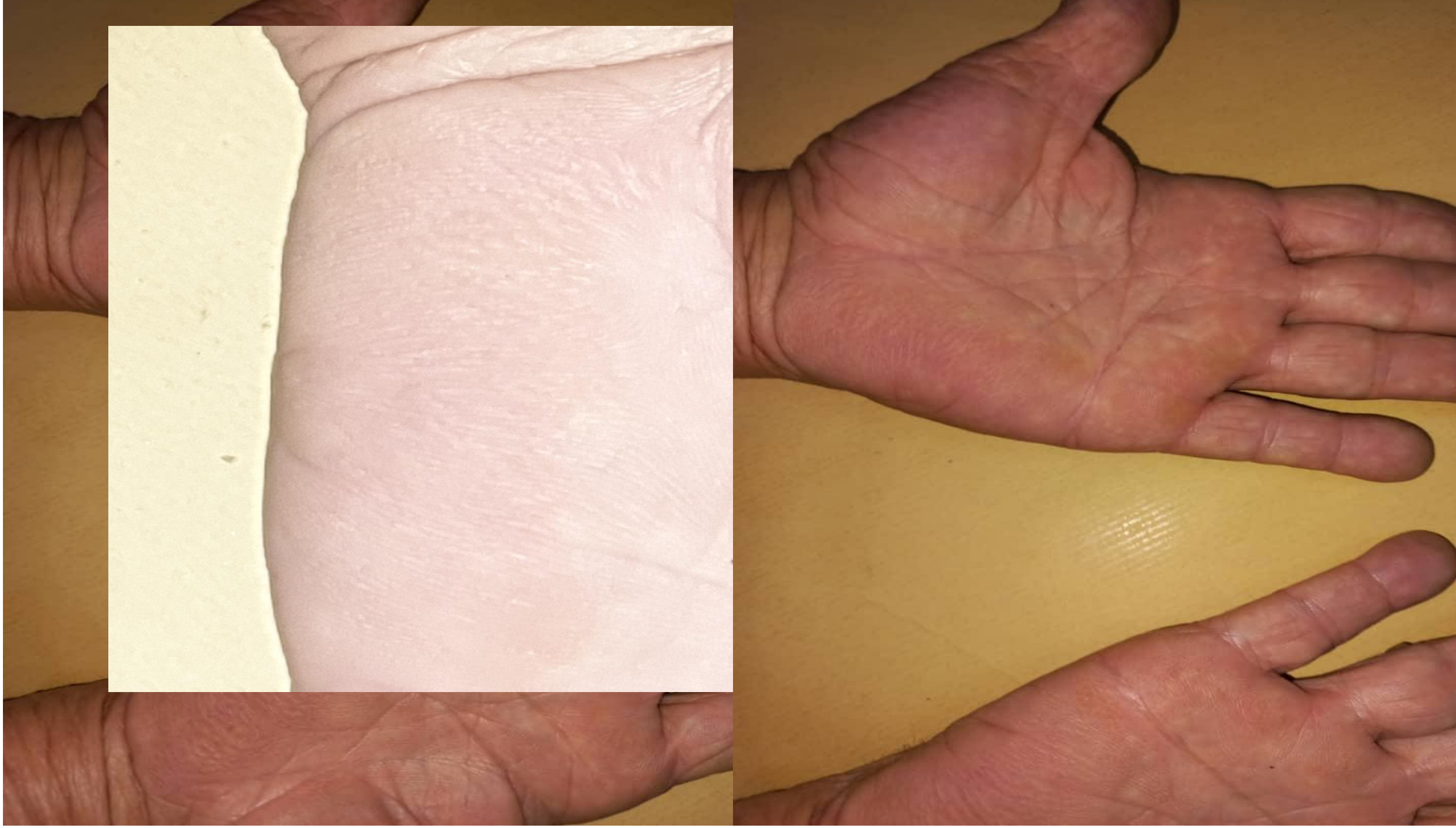


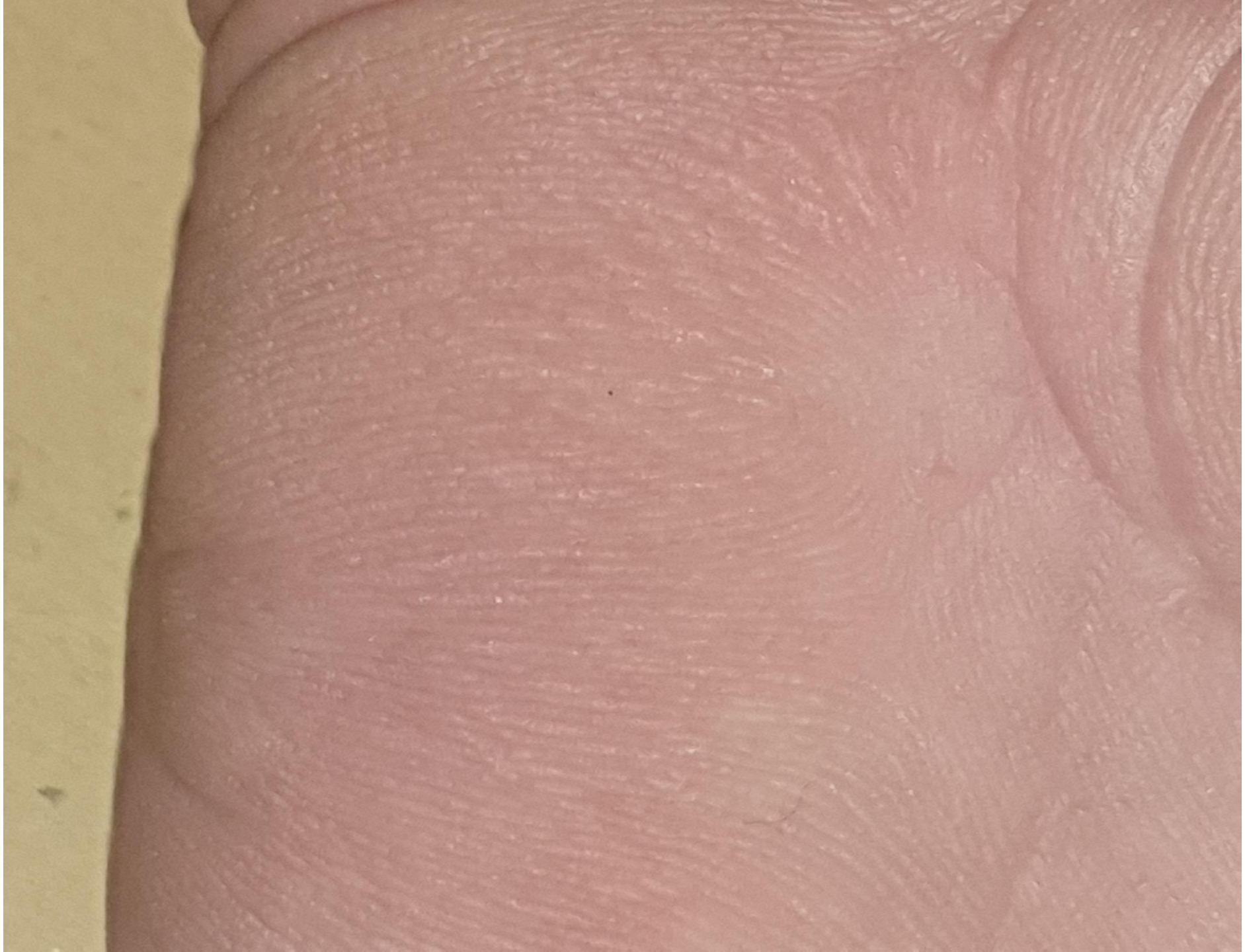


Avant TRT

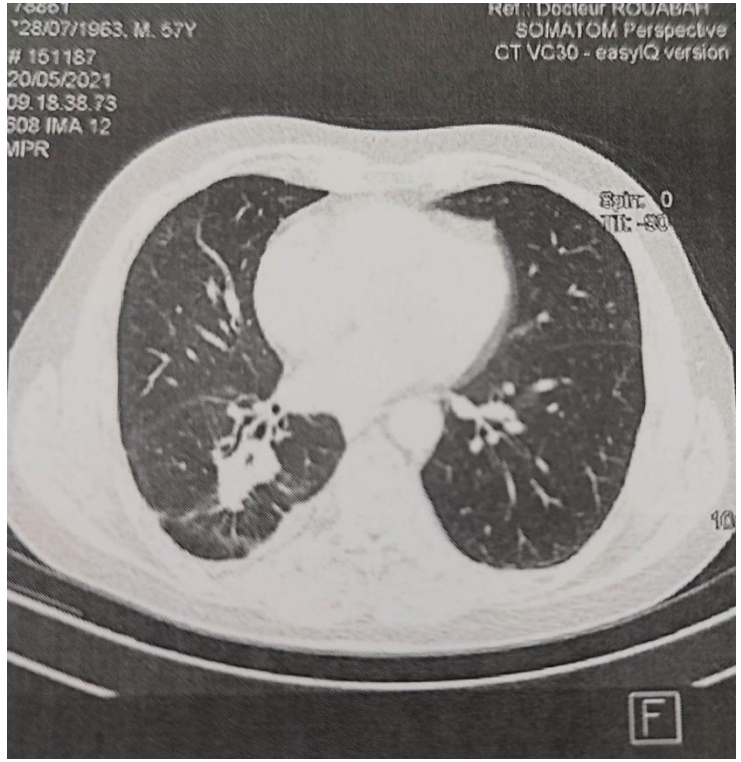


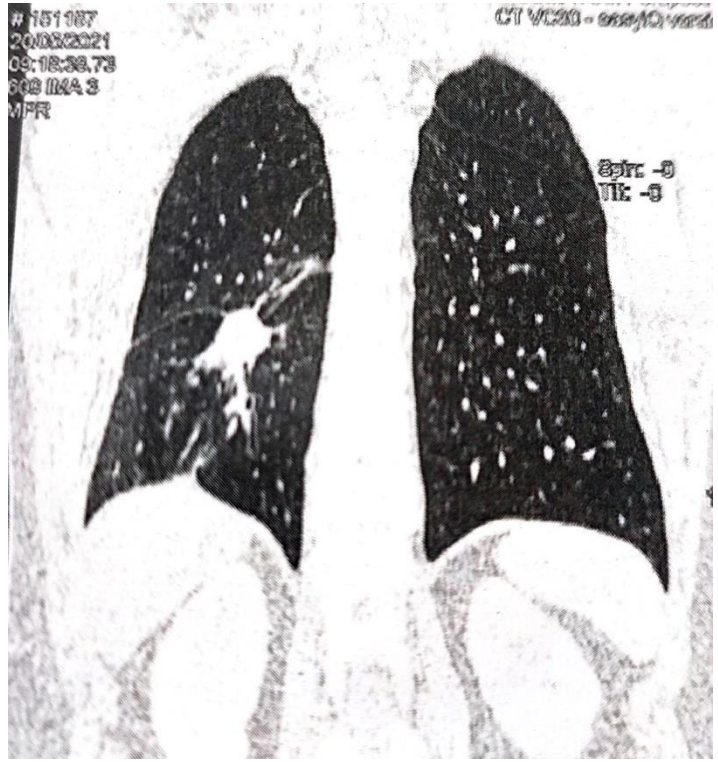
Après TRT





TDM Thoracique 2 mois après RT 20/05/2021





Masse tumorale : 19*26mm et disparition des ADPs médiastino-hilaires

- Quel est le rythme de surveillance ?

- TDM TAP +/- TDM ou IRM cérébrale, tous les 3 à 4 pendant 3 ans.
- Examen clinique mensuelle, TDM TAP/ 6 mois et sevrage tabagique
- Examen clinique/3 Mois et TDM TAP +/- TDM ou IRM cérébrale/6 Mois
- Examen clinique TDM TAP +/- TDM ou IRM cérébrale et sevrage tabagique, 3 à 4 mois pdt 3 ans.

- Le patient a été suivit régulièrement en consultation, en juillet 2021, il consulte dans le cadre de l'urgence pour une dyspnée d'apparition progressive (qlq jours) toux sèche avec douleur pariétale.
- **L'examen clinique:**
- **L'inspection** : une tachypnée superficielle sans tirage intercostal
- **Palpation** reproduit et majore les douleurs thoraciques pariétales diffuses
- **Percussion** est normale
- **L'auscultation**: retrouve des fins crépitants de siège basal postérieur.
- TA: 140/70, T° 37°8, la saturation en oxygène SaO2: 85%

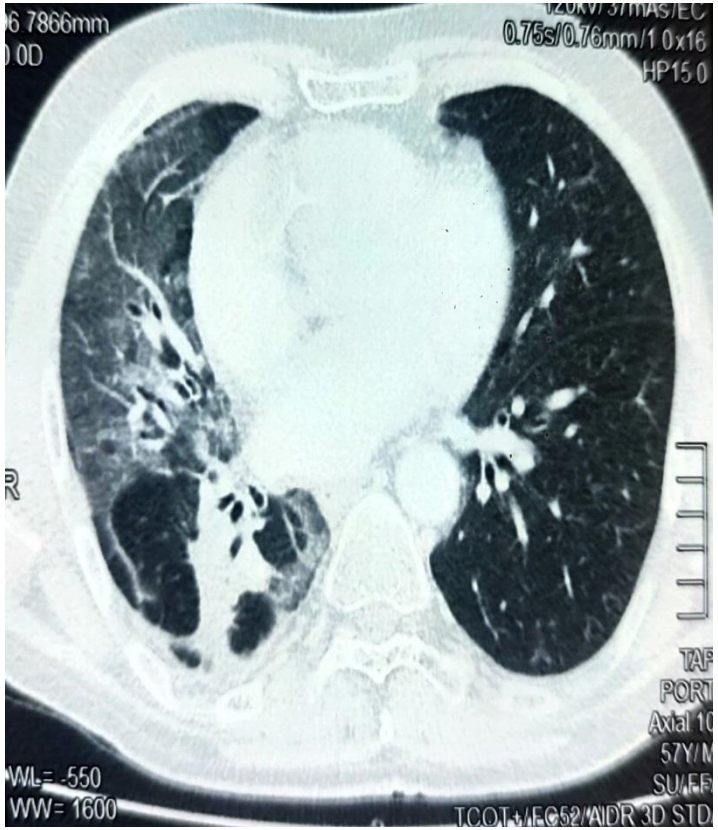
- Devant ce tableau clinique quels sont les diagnostics à évoquer?

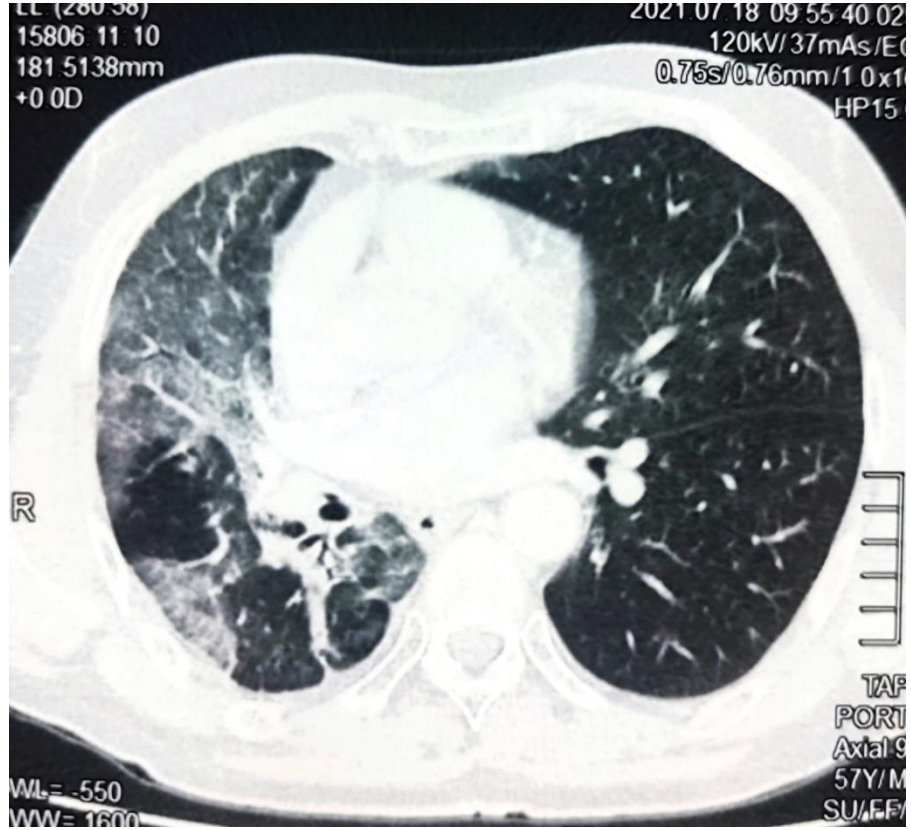
- Reprise évolutive
- Embolie pulmonaire
- Infection bronchique

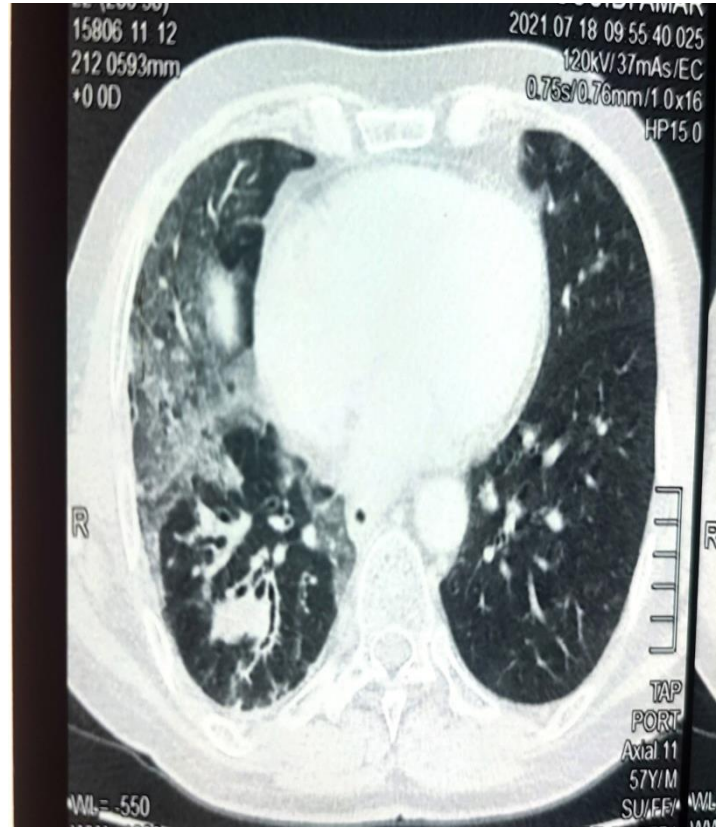
- De quels examens avez-vous besoin pour étayer le diagnostic?

- FNS, VS, CRP, D-dimères, scanner thoracique
- FNS, VS, CRP, PCR, D-dimères, scanner thoracique
- FNS, VS, CRP, urée sg, créatinine Sg, scanner thoracique.
- FNS, VS, CRP, PCR, D-dimeres, urée sg, créatinine Sg, scanner thoracique.

TDM thoracique: 18/07/2021







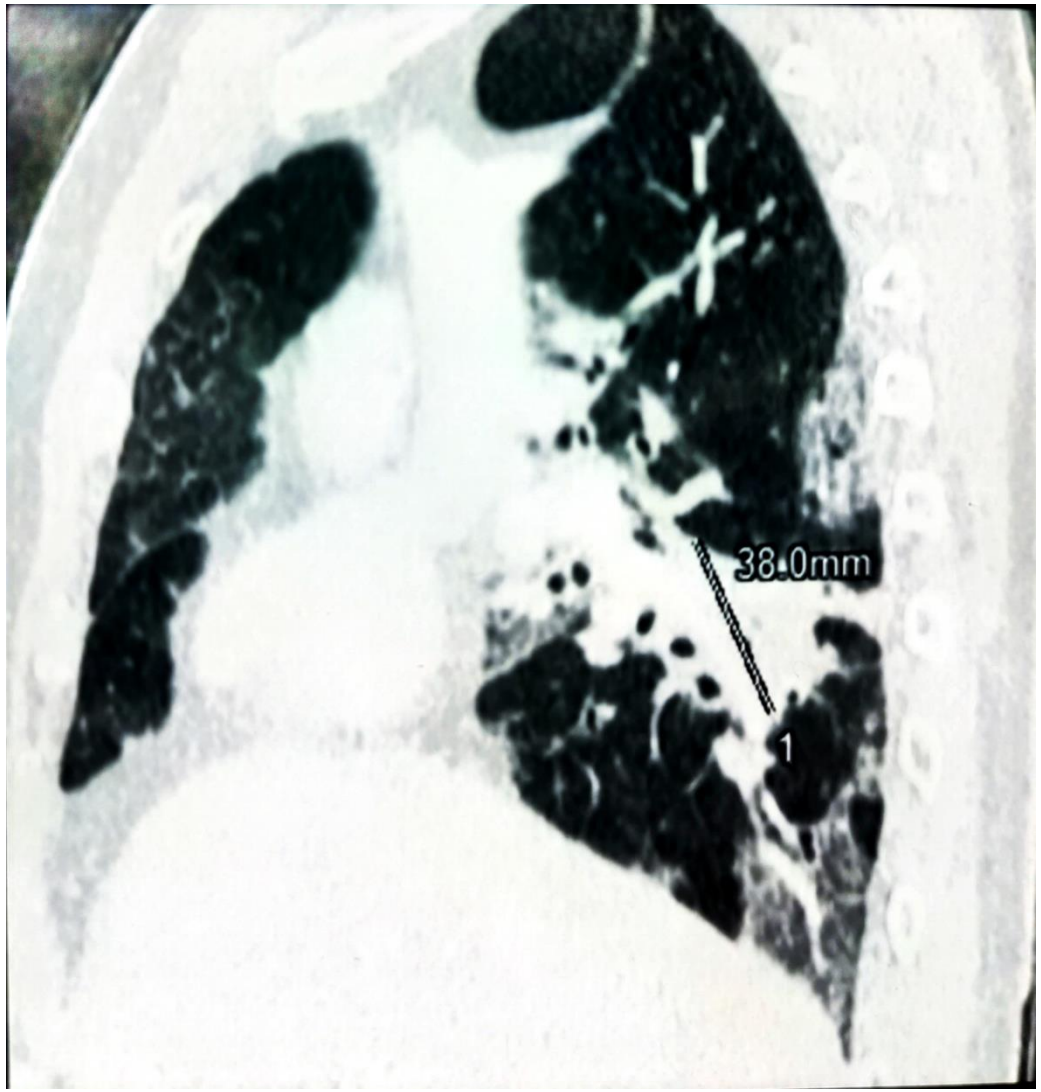
Aspect d'une atteinte COVID dans sa forme sévère

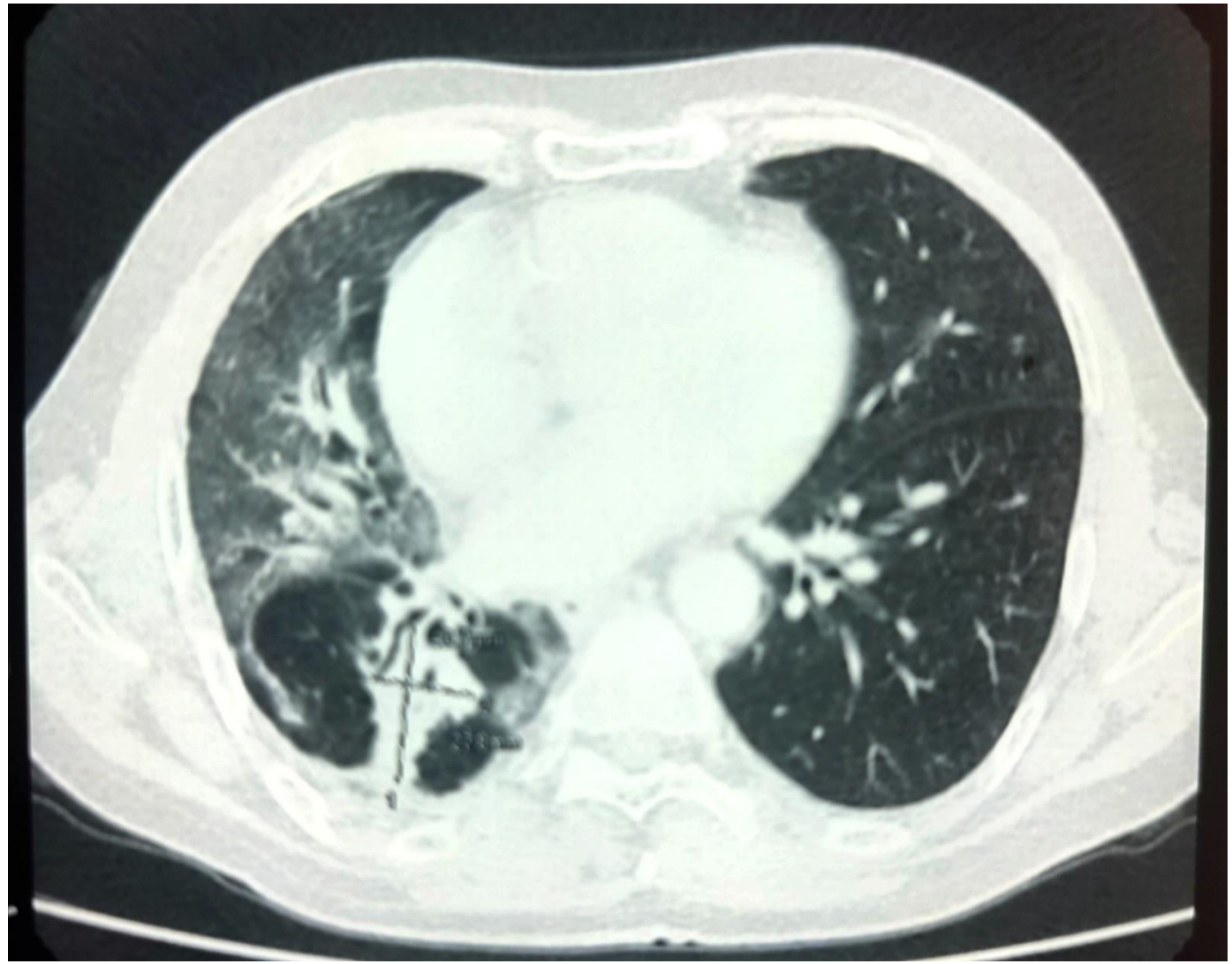
PCR –, D-diméres: 4556, CRP: 157, FNS: hyperleucocytose à polynucléaire.

VS1: 70 VS2: 125 Urée sg: 0.45 g/l, Créatinine sg: 8 mg/l

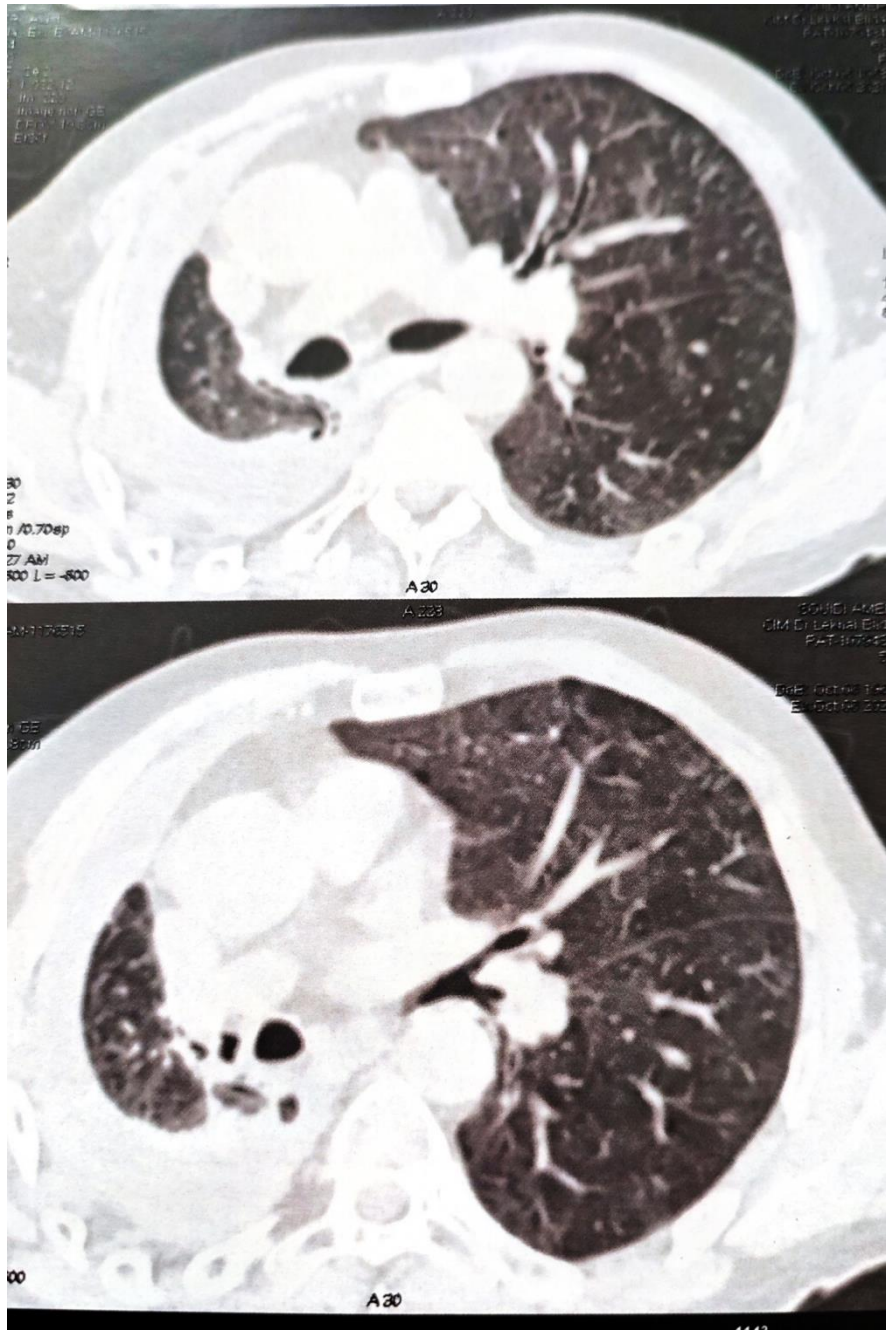
- Le patient a été hospitalisé et traité pour une infection covid pendant 14 jours
- lors d'une consultation de contrôle et après un intervalle libre de 10 mois, il se présente avec une TDM.

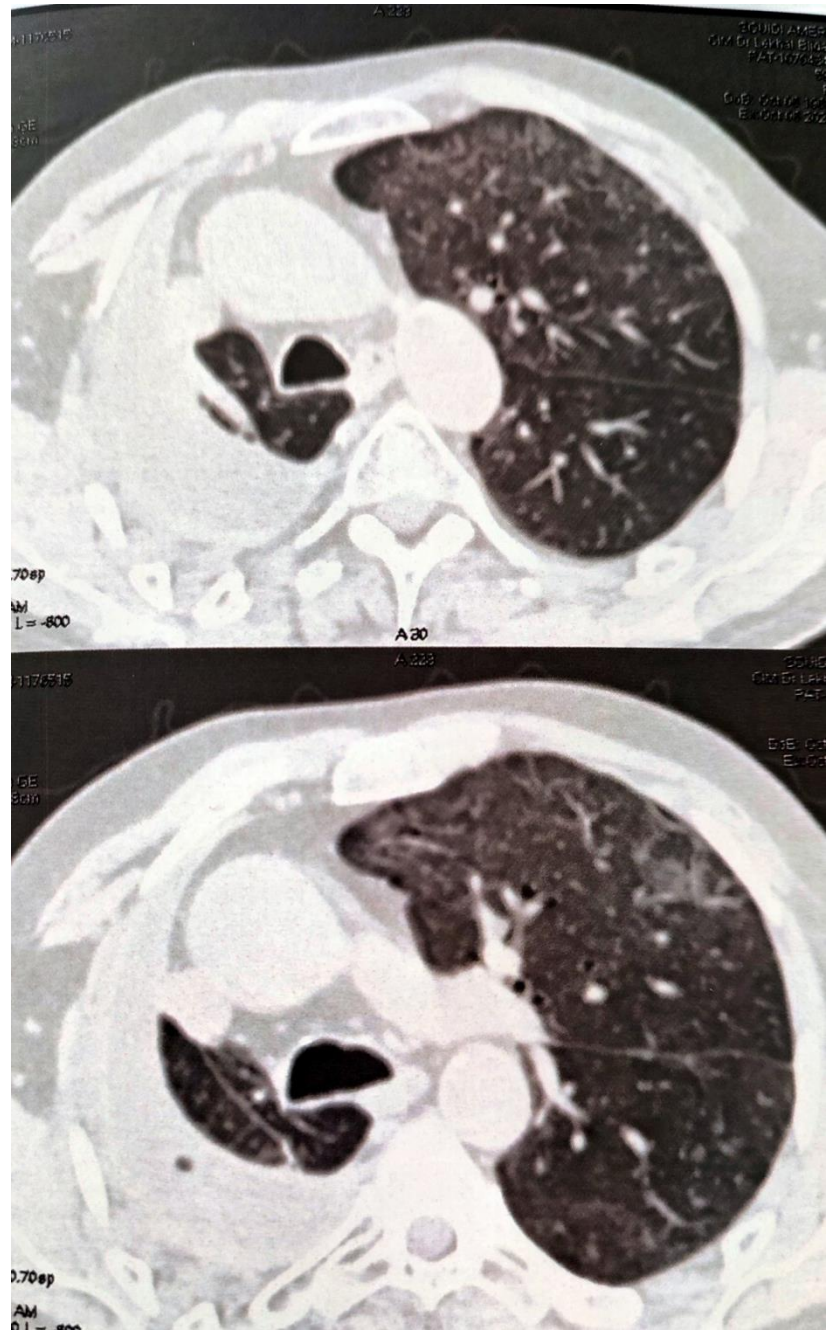
- **TDM Octobre 2021**: Asymétrie du volume des poumons avec atrophie globale du poumon droit
- Apparition de multiples condensations rétractiles pulmonaires droites, épanchement pleural liquidien de moyenne abondance
- Présence d'un pneumothorax partiel apical homolatéral minime
- Présence de stigmates d'un COVID 19 dans sa forme sévère en phase résolutive, métastase hépatique au niveau du segt IV 30 mm.


38.0mm
1



TDM Octobre 2021





- Mr SA est toujours en OMS1, quel protocole de traitement est indiqué chez notre patient ?

- Etoposide carboplatine
- Etoposide cisplatine atezolizumab
- Etoposide cisplatine durvalumab
- Etoposide carboplatine atezolizumab
- Cyclophosphamide-Adriamycine- Vincristine
- Topotecan
- Soins de support

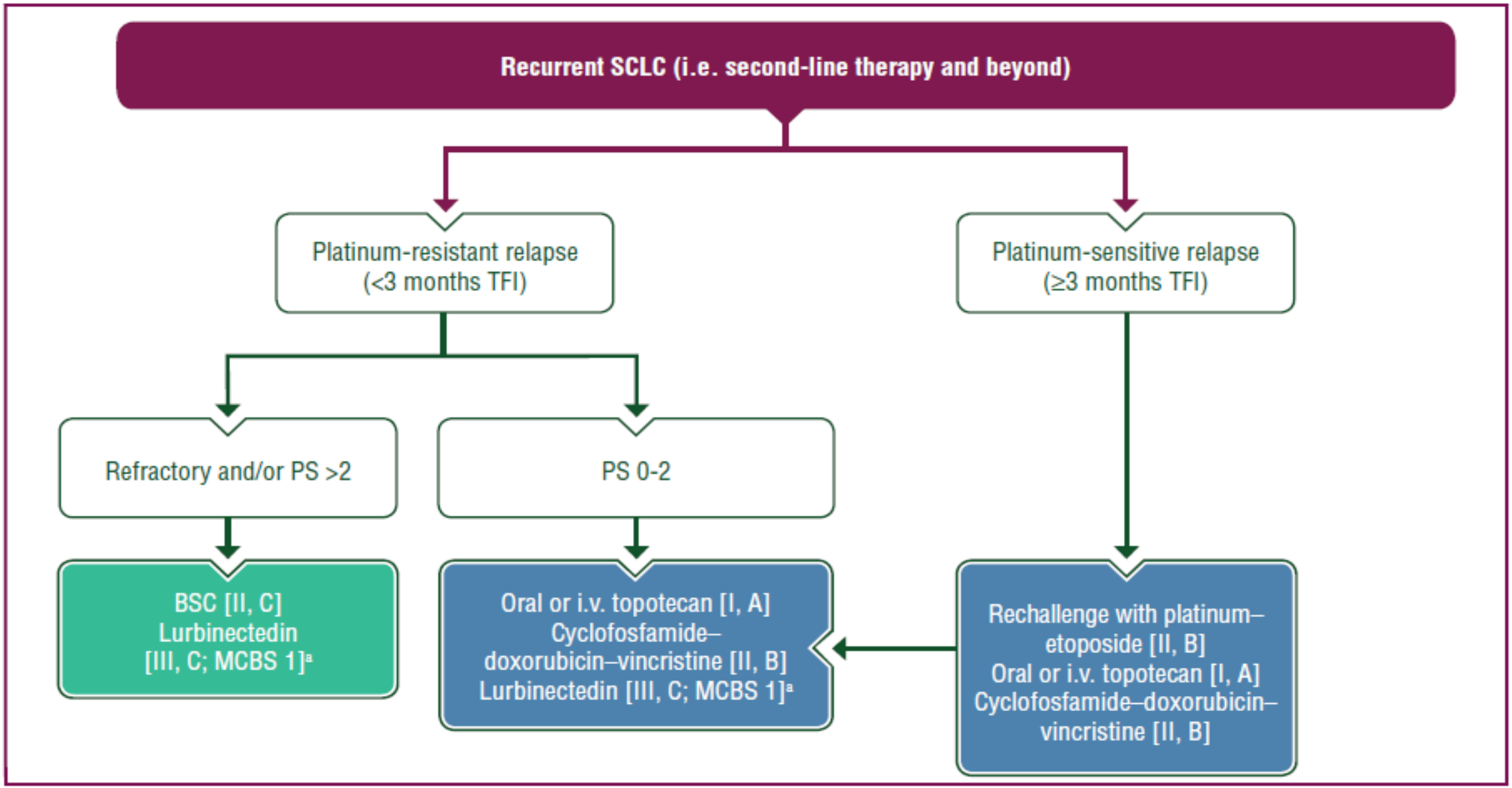


Figure 3. Treatment algorithm for SCLC in patients with recurrent SCLC (i.e. second-line therapy and beyond).

GFPC 13-01 : Study Design

Sensitive relapsed SCLC
(> 90 days from D1 of the last cycle of chemotherapy)

ECOG PS 0-2, age > 18 years

Stratification :
PS
Institution
Response to first line

R

Carboplatin Etoposide

Carboplatin AUC 5 Day 1
Etoposide 100 mg/m2 on day 1-3 IV
Q 3wX6 courses

GCSF is recommended in primary prevention

Topotecan (oral)

2.3 mg/m2 on day 1-5 oral
Q 3wX6 courses

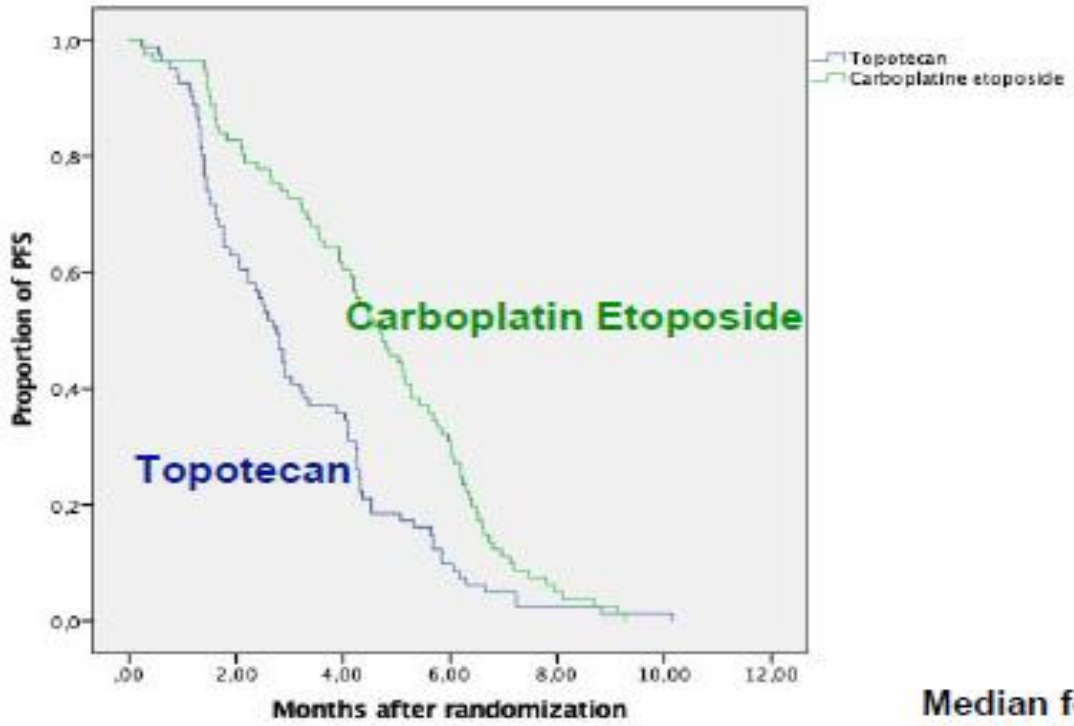
Primary endpoint: PFS
Secondary endpoints: OS, ORR (RECIST v1.1, central review), Safety, Quality of Life

Monnet. I, et al, IASLC 2019

Secondary Endpoint :Tumor Response

Tumor assessment	Topotecan (n=81)	Carboplatin Etoposide (n=81)
Complete Response	1,2%	14%
Partial Response	24%	35,5%
ORR	25%	49% *p=0,002*
Stable Disease	37,4%	37,4%
Disease Progression	37,4%	21,5%

Primary Endpoint : Progression-Free Survival



	Topotecan	Carboplatine Etoposide
Events	81	81
mPFS	2.7 mo	4.7 mo
(95%CI)	(2.3-3.2)	(3.9-5.5)

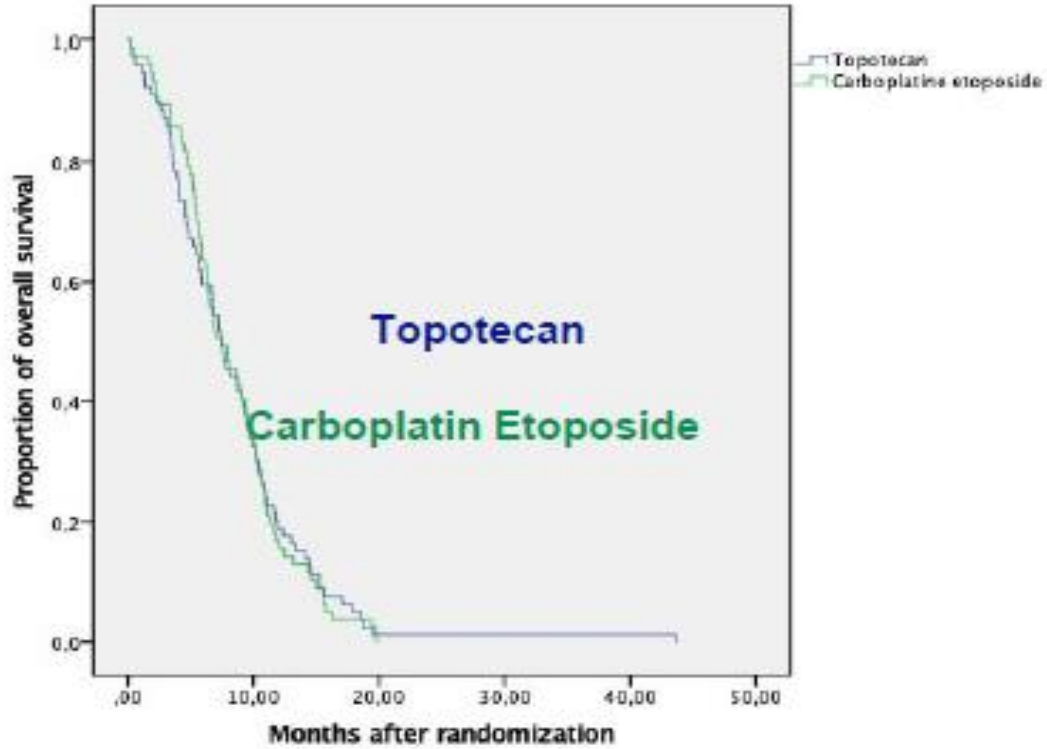
One sided p< 0.001

By stratified log-rank test

Hazard ratio, 0.6; 95% CI 0.4-0.8

Median follow-up: 16 months

Secondary Endpoint : Overall Survival



	Topotecan	Carboplatine Etoposide
Events	81	81
mOS	7.4 mo	7.5 mo
(95%CI)	(6.0-8.7)	(5.4-9.5)

One sided p< 0.936

By stratified log-rank test

Hazard ratio, 0.987; 95% CI 0.7-1.3

PRINCIPLES OF SYSTEMIC THERAPY

SCLC SUBSEQUENT SYSTEMIC THERAPY (PS 0–2)[c] Consider dose reduction or growth factor support for patients with PS 2.	
Relapse ≤6 months	Relapse >6 months
Preferred Regimens • Topotecan PO or IV[14-16] • Lurbinectedin[17] • Clinical trial Other Recommended Regimens • Paclitaxel[18,19] • Docetaxel[20] • Irinotecan[21] • Temozolomide[22,23] • Cyclophosphamide/doxorubicin/vincristine (CAV)[14] • Oral etoposide[24,25] • Vinorelbine[26,27] • Gemcitabine[28,29] • Nivolumab[b,d,30,31] • Pembrolizumab[b,d,32-34] • Bendamustine (category 2B)[35]	Preferred Regimens • Original regimen[d,36,37] Other Recommended Regimens • Topotecan PO or IV[14-16] • Paclitaxel[18,19] • Docetaxel[20] • Irinotecan[21] • Temozolomide[22,23] • CAV[14] • Oral etoposide[24,25] • Vinorelbine[26,27] • Gemcitabine[28,29] • Nivolumab[b,d,30,31] • Pembrolizumab[b,d,32-34] • Lurbinectedin[38] • Bendamustine (category 2B)[35]

Response Assessment (SCL-E 3 of 5)
References (SCL-E 4 of 5)

[b] Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or concurrent use of immunosuppressive agents.
[c] Subsequent systemic therapy refers to second-line and beyond therapy.
[d] The use of immune checkpoint inhibitors is discouraged if there is progression on maintenance atezolizumab or durvalumab at time of relapse.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

- Mr SA est sous chimiothérapie de 1ére ligne protocole carboplatine étoposide