Les traitements combinés en cancer pulmonaire

La radiothérapie dans le cancer pulmonaire de stade avancé: risques et bénéfices

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Radio-oncologue

19 octobre 2018

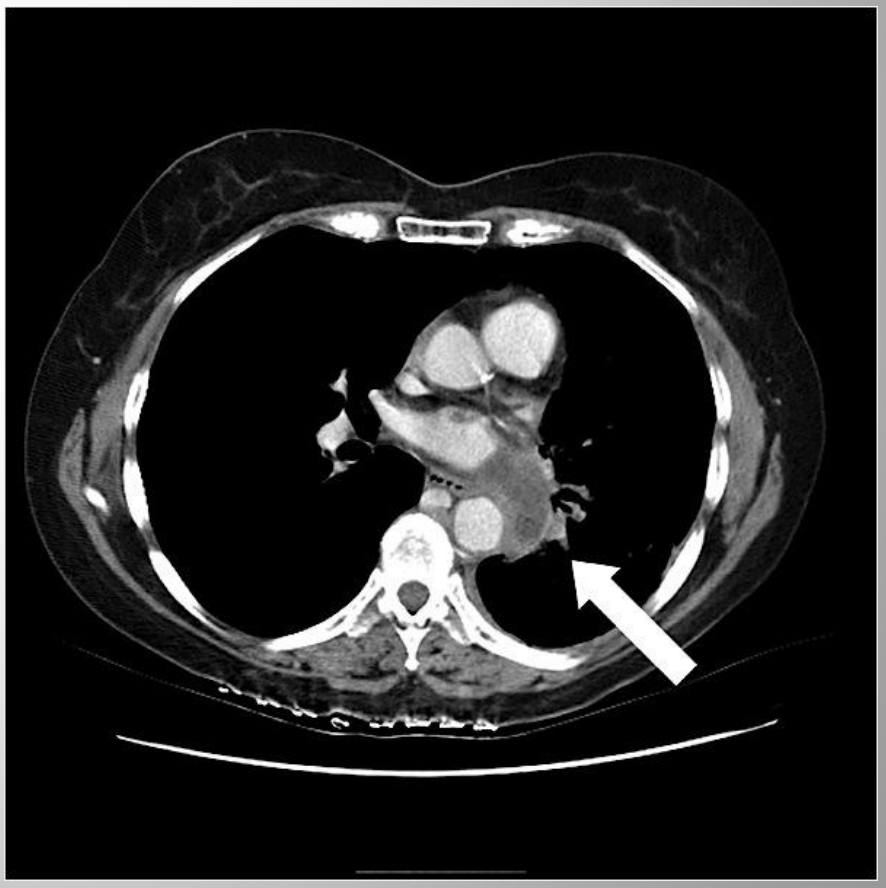
Objectifs

- Définir les indications de radiothérapie dans les cancers pulmonaires
- Réviser les différents fractionnements possibles
- Comprendre les enjeux pronostics selon l'éligibilité à la chimiothérapie
- Discuter des effets secondaires et complications possibles de la radiothérapie
- Aborder les traitements des complications de la radiothérapie

Quiz

1. Si cette patiente est traitée par radiothérapie, de quel effet secondaire est-elle le plus à risque parmi les suivants?

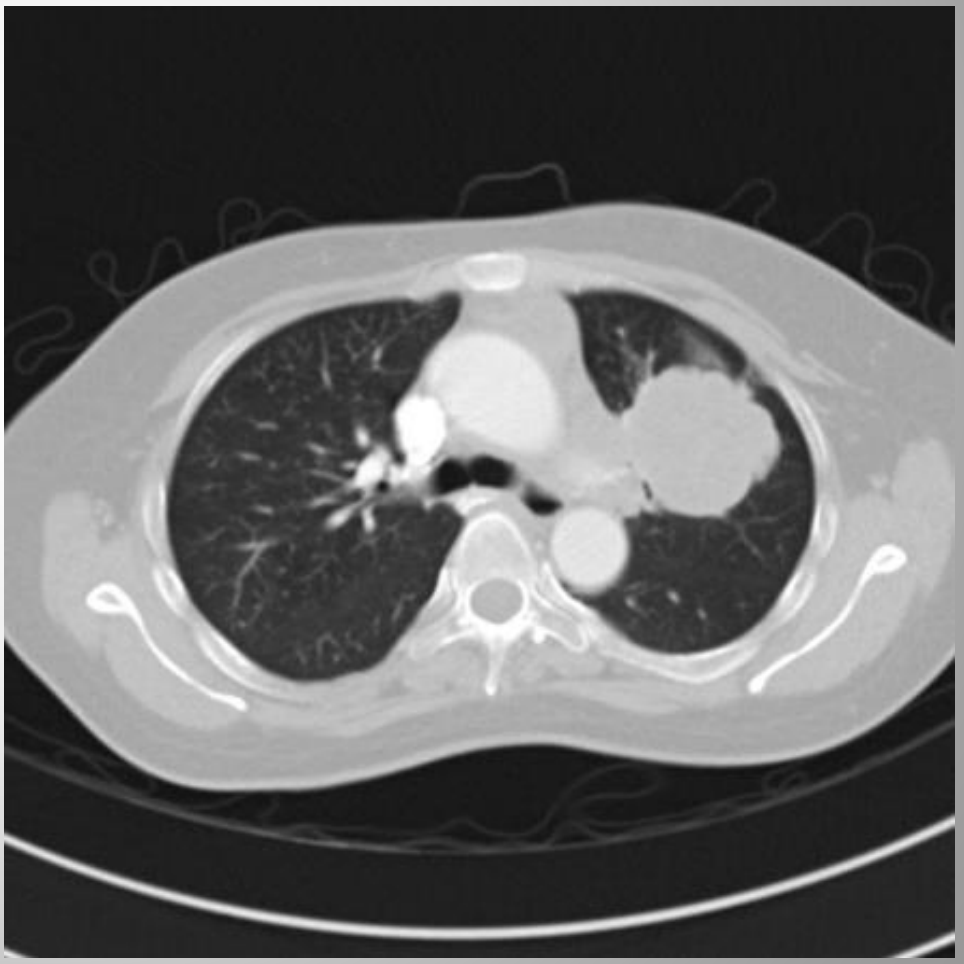
A-Pneumonite
B-Oesophagite
C-Péricardite
D-Myélite



Quiz

2. Si ce patient est traité par radiothérapie, de quel effet secondaire est-il le plus à risque parmi les suivants?

A-Pneumonite
B-Oesophagite
C-Péricardite
D-Myélite



Indications traitement curatif

- Carcinome non à petites cellules
  - Stades précoces non opérables (facteur patient)
  - **Stades avancés non résécables**
  - Post-opératoire si marge + ou N2

- La plupart des carcinomes à petites cellules non métastatique

Table 1. **Definitions for T, N, M**

T		**Primary Tumor**
TX		Primary tumor cannot be assessed, or tumor proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
T0		No evidence of primary tumor
Tis		Carcinoma in situ Squamous cell carcinoma in situ (SCIS) Adenocarcinoma in situ (AIS): adenocarcinoma with pure lepidic pattern, ≤3 cm in greatest dimension
T1		Tumor ≤3 cm in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus)
	T1mi	Minimally invasive adenocarcinoma: adenocarcinoma (≤3 cm in greatest dimension) with a predominantly lepidic pattern and ≤5 mm invasion in greatest dimension
	T1a	Tumor ≤1 cm in greatest dimension. A superficial, spreading tumor of any size whose invasive component is limited to the bronchial wall and may extend proximal to the main bronchus also is classified as T1a, but these tumors are uncommon.
	T1b	Tumor >1 cm but ≤2 cm in greatest dimension
	T1c	Tumor >2 cm but ≤3 cm in greatest dimension
T2		Tumor >3 cm but ≤5 cm or having any of the following features: (1) Involves the main bronchus, regardless of distance to the carina, but without involvement of the carina; (2) Invades visceral pleura (PL1 or PL2); (3) Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, involving part or all of the lung
	T2a	Tumor >3 cm but ≤4 cm in greatest dimension
	T2b	Tumor >4 cm but ≤5 cm in greatest dimension
T3		Tumor >5 cm but ≤7 cm in greatest dimension or directly invading any of the following: parietal pleura (PL3), chest wall (including superior sulcus tumors), phrenic nerve, parietal pericardium; or separate tumor nodule(s) in the same lobe as the primary
T4		Tumor >7 cm or tumor of any size invading one or more of the following: diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina; separate tumor nodule(s) in a ipsilateral lobe different from that of the primary

Table 1. **Definitions for T, N, M (continued)**

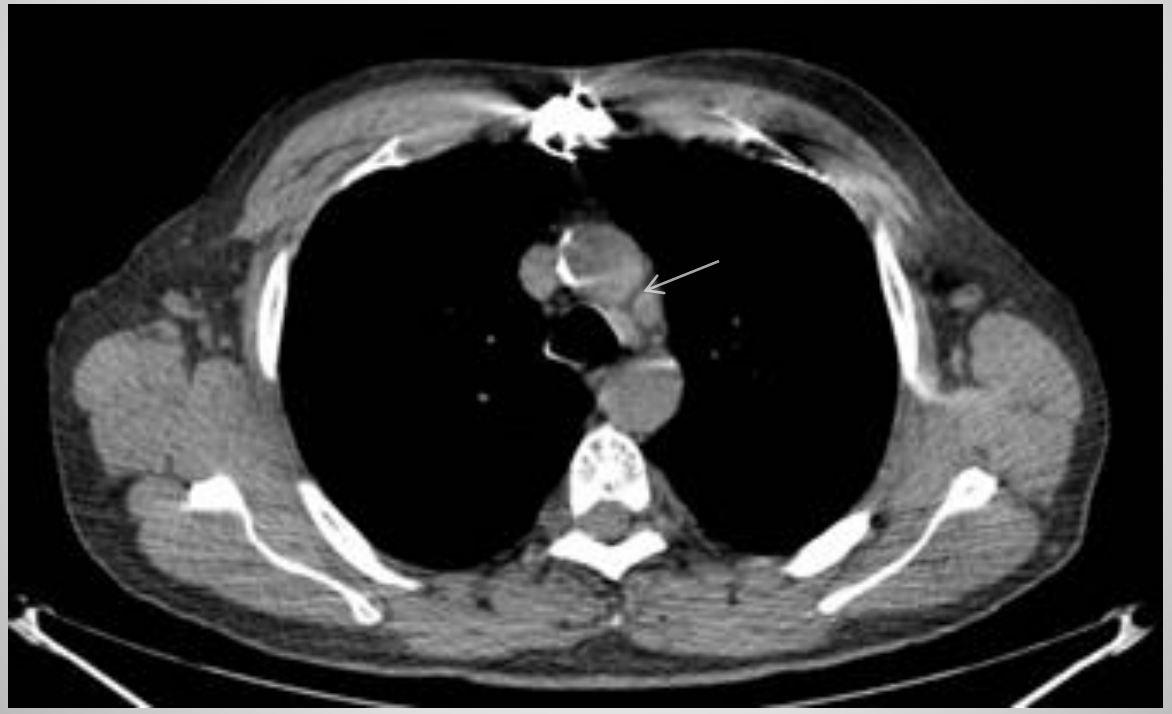
N		**Regional Lymph Nodes**
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1		Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2		Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3		Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)
M		**Distant Metastasis**
MX		Distant metastasis cannot be assessed
M0		No distant metastasis
M1		Distant metastasis
	M1a	Separate tumor nodule(s) in a contralateral lobe; tumor with pleural or pericardial nodules or malignant pleural or pericardial effusion[a]
	M1b	Single extrathoracic metastasis in a single organ (including involvement of a single nonregional node)
	M1c	Multiple extrathoracic metastases in a single organ or in multiple organs

Table 2. **AJCC Prognostic Groups**

	T	N	M
Occult Carcinoma	TX	N0	M0
Stage 0	Tis	N0	M0
Stage IA1	T1mi	N0	M0
	T1a	N0	M0
Stage IA2	T1b	N0	M0
Stage IA3	T1c	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
Stage IIB	T1a	N1	M0
	T1b	N1	M0
	T1c	N1	M0
	T2a	N1	M0
	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1a	N2	M0
	T1b	N2	M0
	T1c	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N1	M0
	T4	N0	M0
	T4	N1	M0
Stage IIIB	T1a	N3	M0
	T1b	N3	M0
	T1c	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N2	M0
	T4	N2	M0
Stage IIIC	T3	N3	M0
	T4	N3	M0
Stage IVA	Any T	Any N	M1a
	Any T	Any N	M1b
Stage IVB	Any T	Any N	M1c

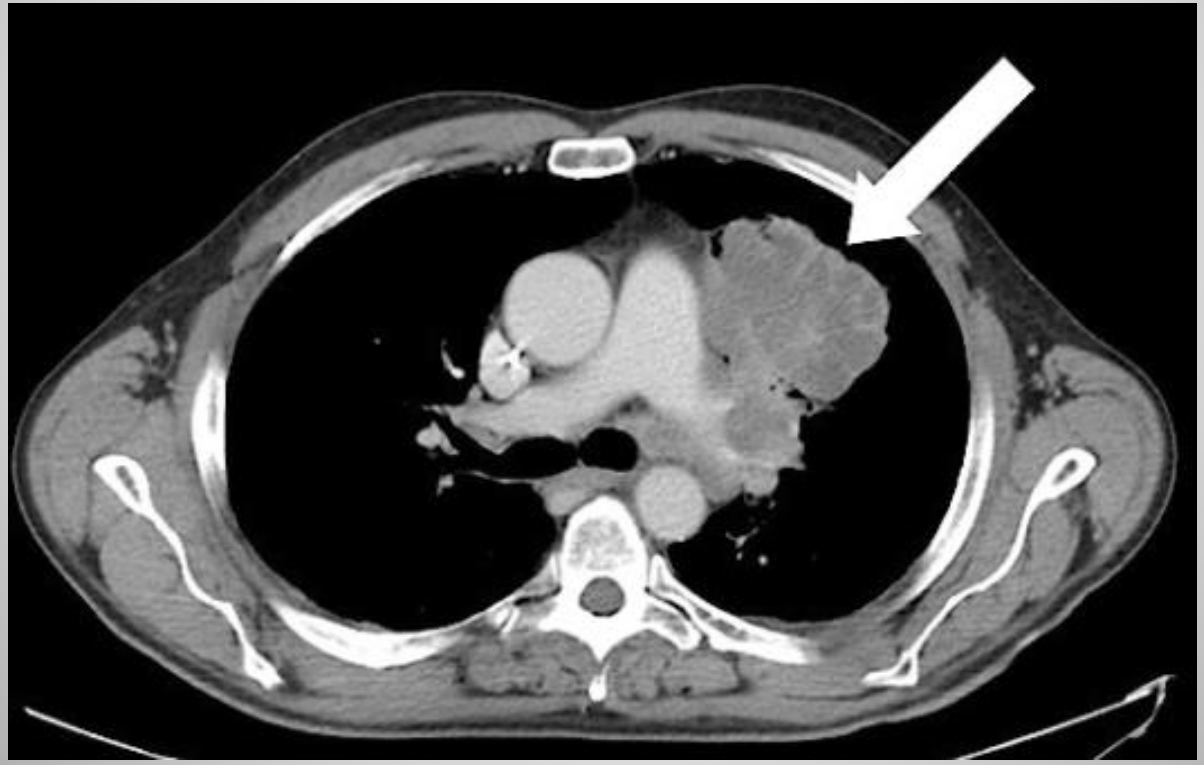
Stades avancés

- N2



Stades avancés

- T4

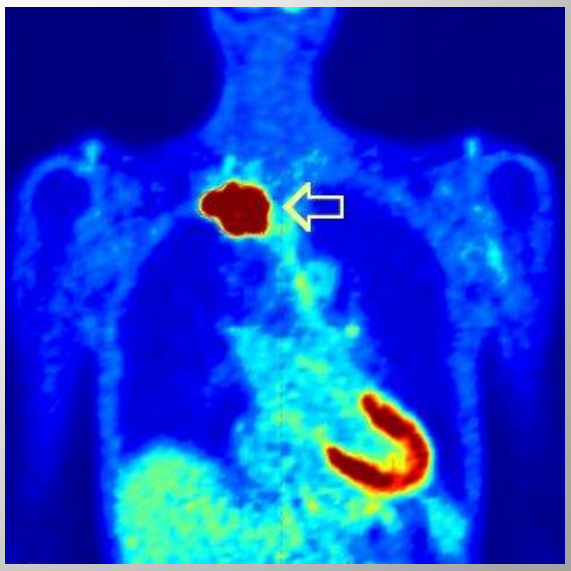


T4	Tumor >7 cm or tumor of any size invading one or more of the following: diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina; separate tumor nodule(s) in a ipsilateral lobe different from that of the primary

Stades avancés

Exceptions

- T3N1
  - Deux lésions dans même lobe vs envahissement du péricarde
- Tumeur Pancoast
  - Par définition T3 ou T4



Bilans

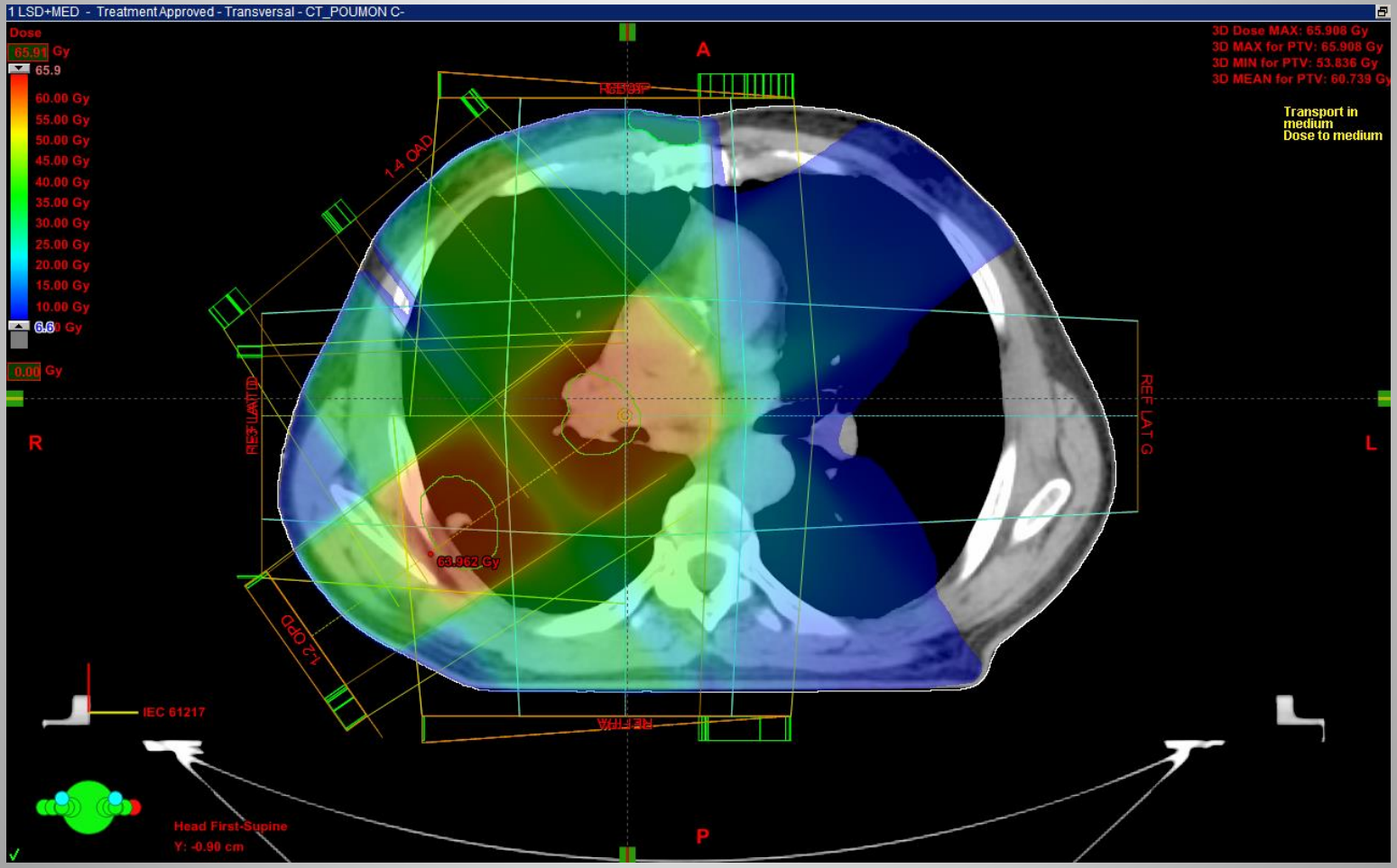
- TFR
- Bronchoscopie
- Biopsie ganglions médiastinaux
- TEP scan
- IRM cerveau

Cheminement du patient

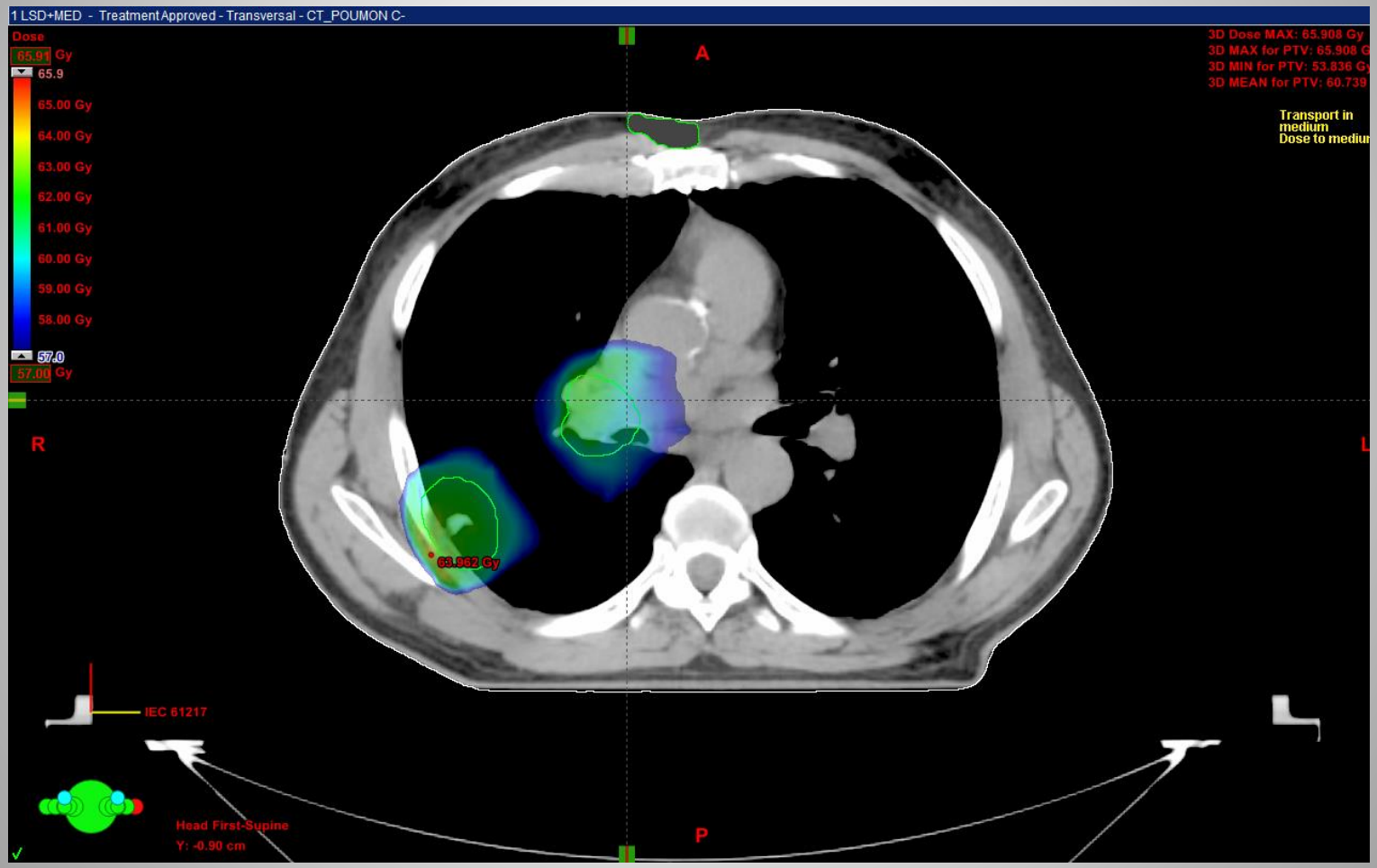
- Consultations
  - Pneumologie
    - Chir thoracique si possibilité chx
  - H-onco + R-onco
  - Cardiologie si pacemakeer/defib
- Planification RT une fois plan tx établi
  - Scan 4D (même jour consultation pour patients éloignés si bilan complet et plan tx certain)
  - Contours, dosimétrie, vérification par physicien en salle: 5-7 jours

*Parfois on ne peut pas être certain qu'un patient est éligible à la radiothérapie avant de faire la dosimétrie

Dosimétrie


1 LSD+MED - Treatment Approved - Transversal - CT_POUMON C-
Dose
65.91 Gy
65.9
60.00 Gy
55.00 Gy
50.00 Gy
45.00 Gy
40.00 Gy
35.00 Gy
30.00 Gy
25.00 Gy
20.00 Gy
15.00 Gy
10.00 Gy
6.6 Gy
0.00 Gy
3D Dose MAX: 65.908 Gy
3D MAX for PTV: 65.908 Gy
3D MIN for PTV: 53.836 Gy
3D MEAN for PTV: 60.739 Gy
Transport in medium
Dose to medium
A
P
R
L
1-4 OAD
REF LAT D
REF LAT G
63.962 Gy
IEC 61217
Head First-Supine
Y: -0.90 cm

Dosimétrie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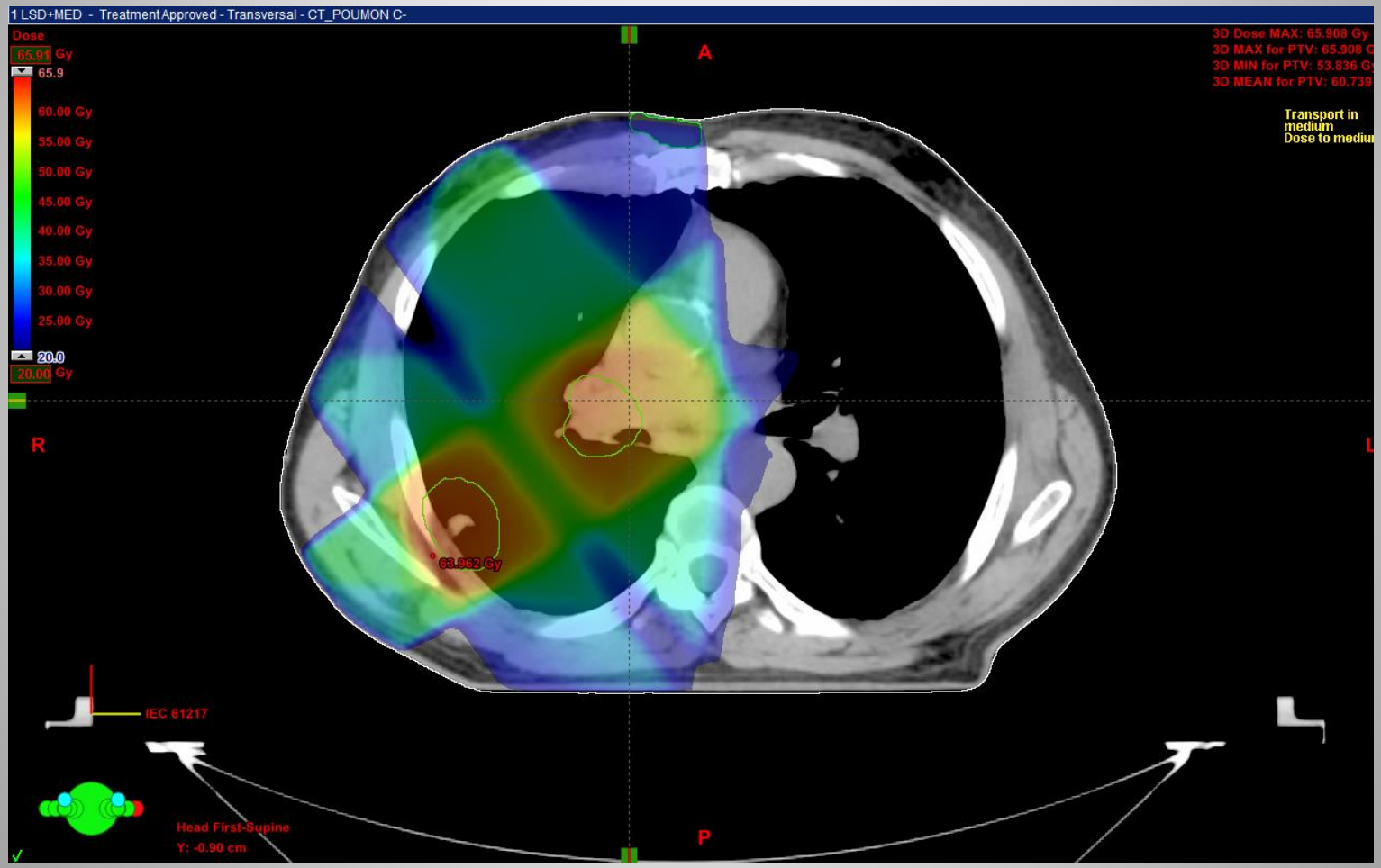
3D MIN for PTV: 53.836 Gy
3D MEAN for PTV: 60.739
Transport in medium
Dose to mediu
63.982 Gy
IEC 61217
Head First-Supine
Y: -0.90 cm

Dosimétrie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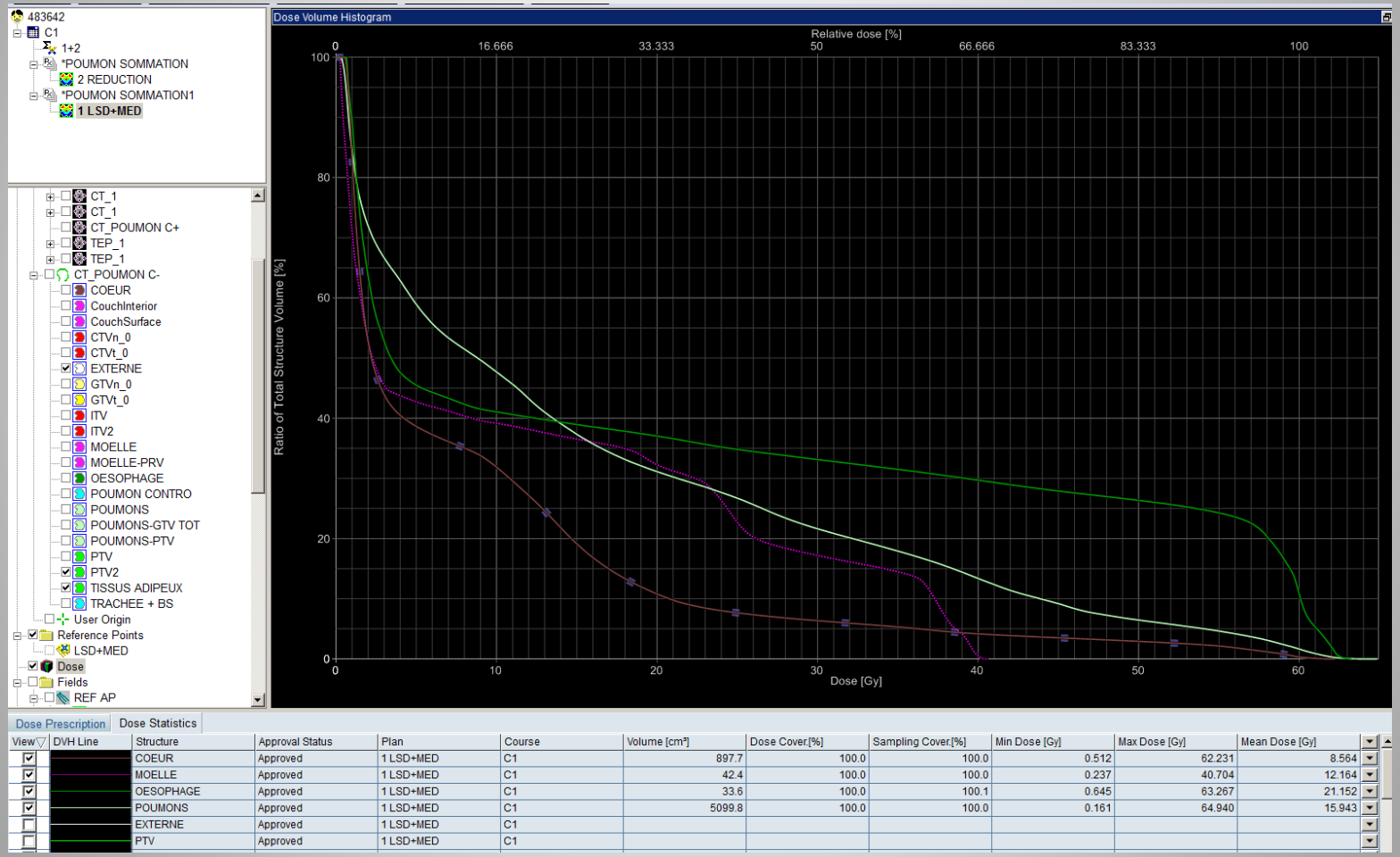
Dosimétrie



Dose Prescription | Dose Statistics

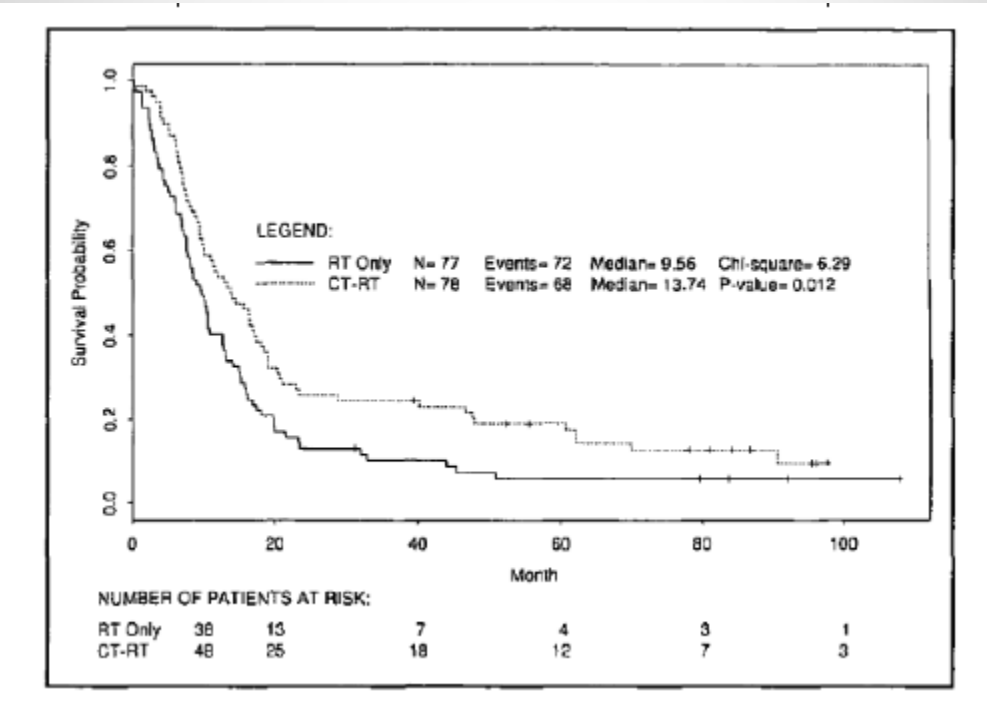
View	DVH Line	Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [Gy]	Max Dose [Gy]	Mean Dose [Gy]
☑		COEUR	Approved	1 LSD+MED	C1	897.7	100.0	100.0	0.512	62.231	8.564
☑		MOELLE	Approved	1 LSD+MED	C1	42.4	100.0	100.0	0.237	40.704	12.164
☑		OESOPHAGE	Approved	1 LSD+MED	C1	33.6	100.0	100.1	0.645	63.267	21.152
☑		POUMONS	Approved	1 LSD+MED	C1	5099.8	100.0	100.0	0.161	64.940	15.943
☐		EXTERNE	Approved	1 LSD+MED	C1						
☐		PTV	Approved	1 LSD+MED	C1						

Fractionnement de la radiothérapie

- 30 à 33 traitements de radiothérapie si chimiothérapie concomitante
  - Donc 6-7 semaines à 5tx/sem
  - 30 vs 33 selon volume à traiter
- Si non éligible à la chimiothérapie
  - Possibilité de donner des plus grosses fractions et réduire le nombre de traitements
  - 20 à 22 traitements
  - Selon proximité OAR

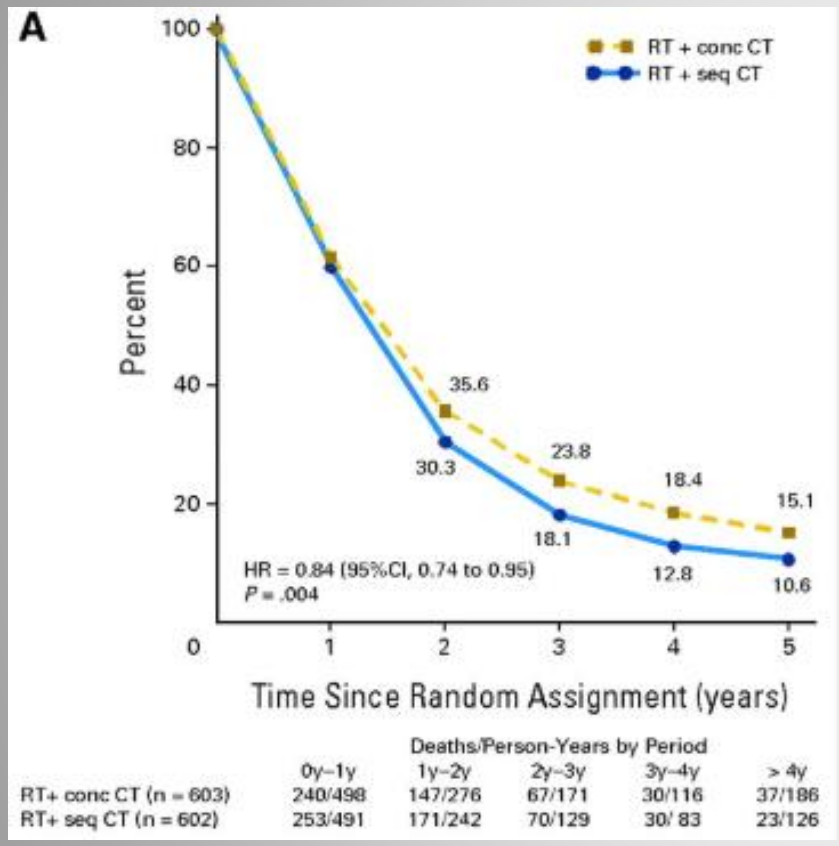
Avec ou sans chimiothérapie

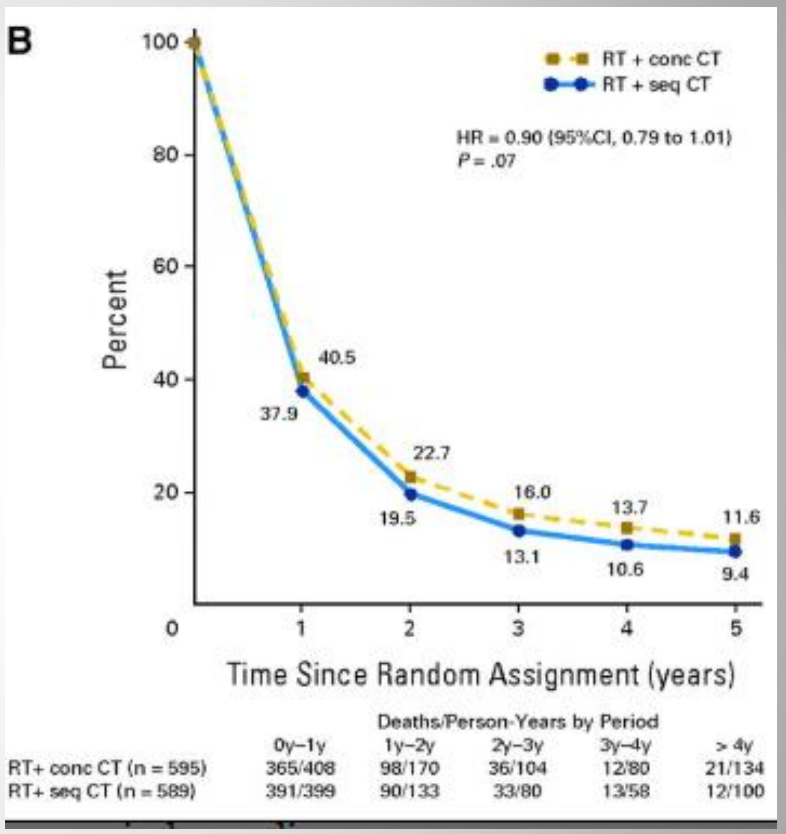
- Survie médiane 29 mois traitements concomitants (Bradley et al)



Dillman et al

RT pendant ou après CT



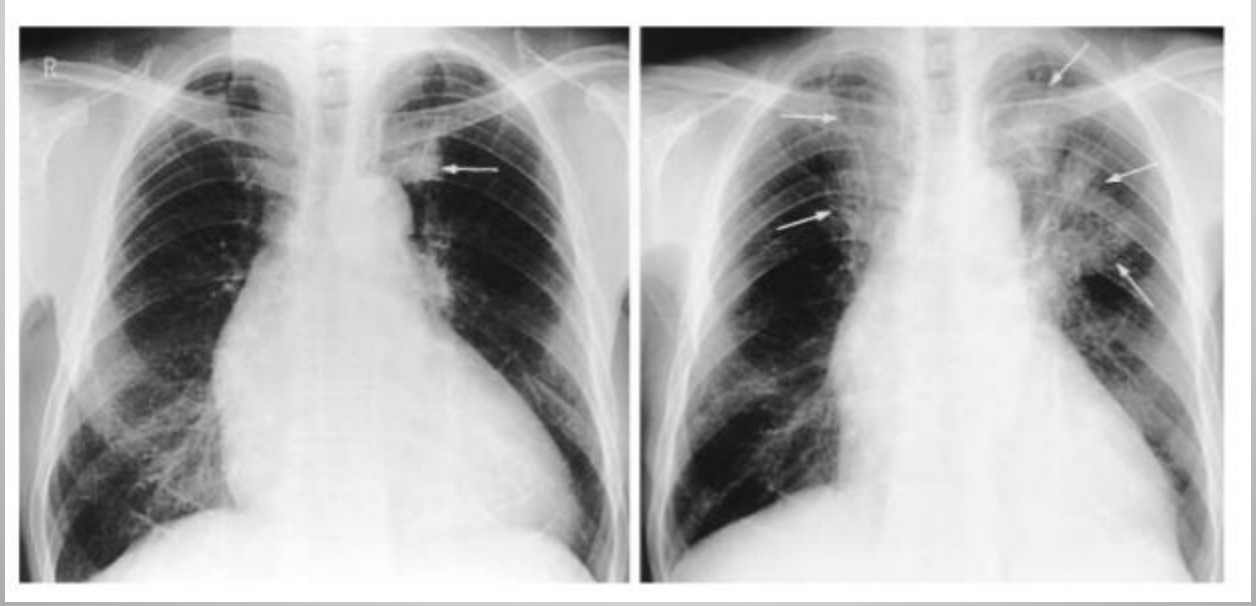


A)Survie B)Survie sans progression
Méta-analyse Aupérin et al

Effets secondaires et complications

Pneumonite

- Toux + dyspnée
- Pendant RT ad qques mois après fin
- 5-10%
- Proportionnel au volume traité
- Conco > Séquentiel > RT seule

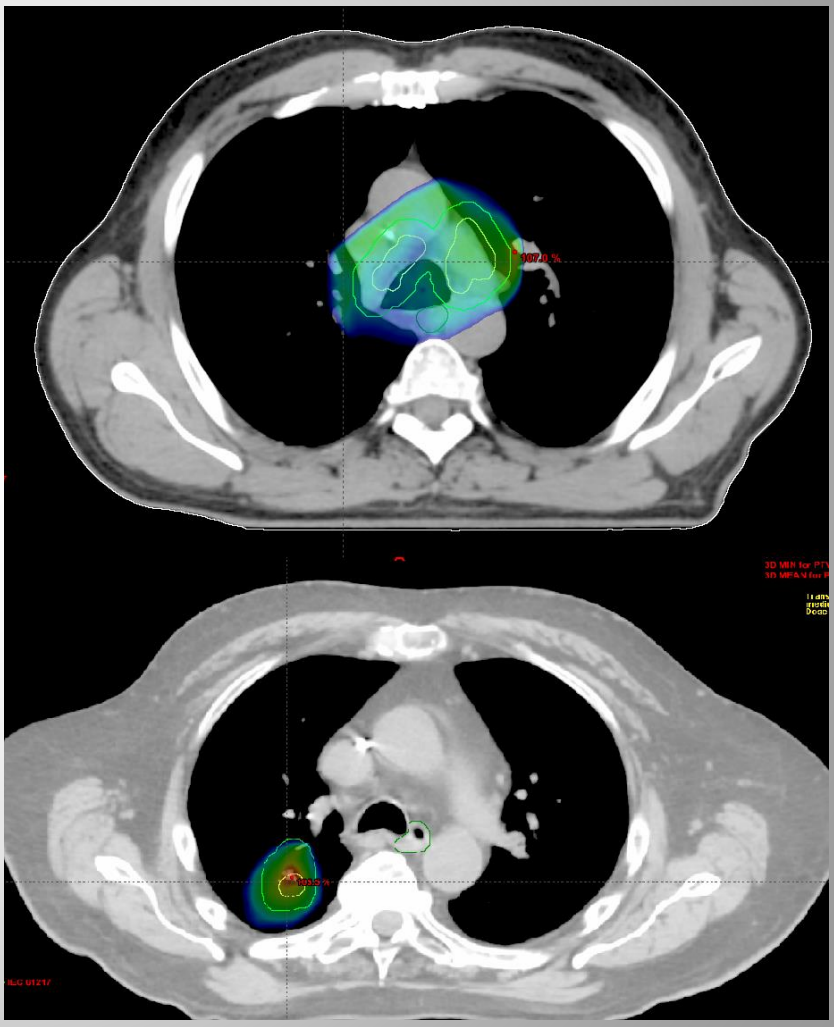


Effets secondaires et complications

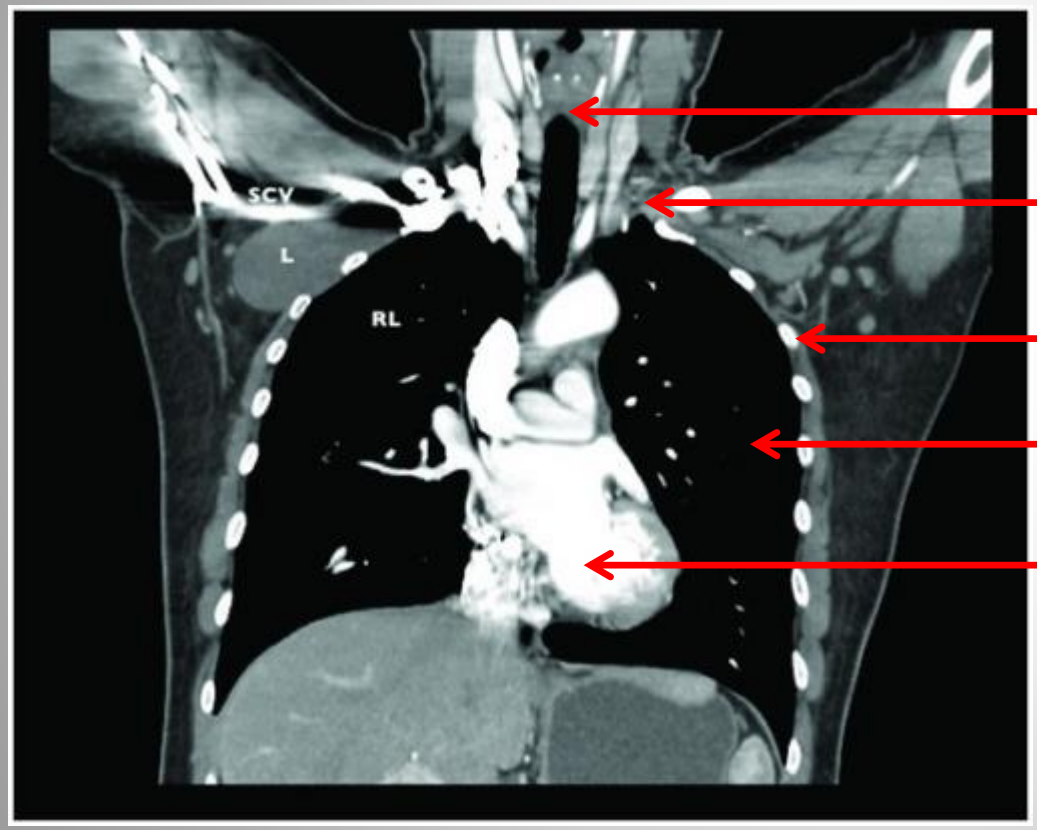
- Pneumonite
  - Radiologique seulement: pas d'intervention
  - Peu ou pas symptomique: observation, cortico inhalé
  - Symptomatique:
    - prednisone 40-60 mg die x2-4 semaines puis sevrage selon évolution
    - r/o embolie, surinfection, décompensation MPOC, IC
  - SDRA rare mais possible

Effets secondaires et complications

- Oesophagite
  - Aiguë
    - Mucite
    - Odynophagie
    - Sensation de brûlure
    - Sulcrate, pantoloc
    - Ajustement des textures
  - Chronique
    - Possibilité de sténose/strictures
    - Dysphagie
    - Dilatation/stent si échec tx conservateur



Effets secondaires et complications



Hypothyroïdie

Plexopathie

Douleurs costales, risque accru de fractures

Fibrose pulmonaire

Péricardite

MCAS

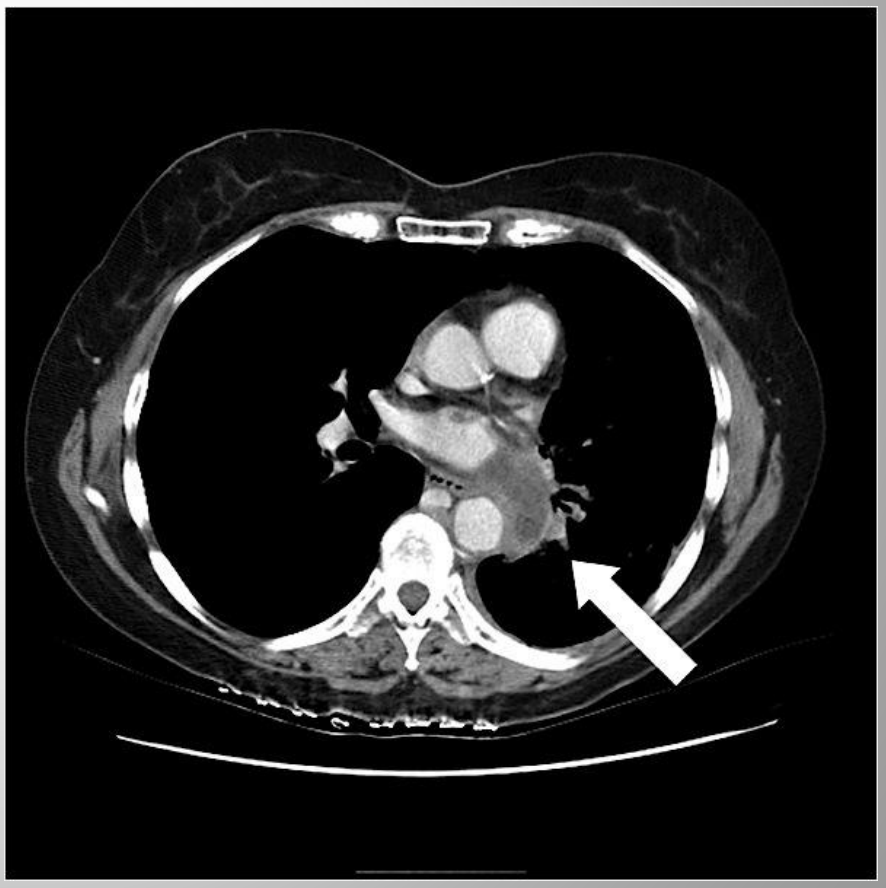
Effets secondaires

- Autres
  - Syndrome de Lhermitte
    - 4 à 12 mois après RT
    - Sensation chocs électriques au tronc et extrémités exacerbée par flexion de la nuque
    - Progression à myélite permanente très rare
    - Résolution spontanée < 6 mois dans plupart des cas
  - Fatigue
  - Dérèglement pacemaker/défib

Quiz

1. Si cette patiente est traitée par radiothérapie, de quel effet secondaire est-elle le plus à risque parmi les suivants?

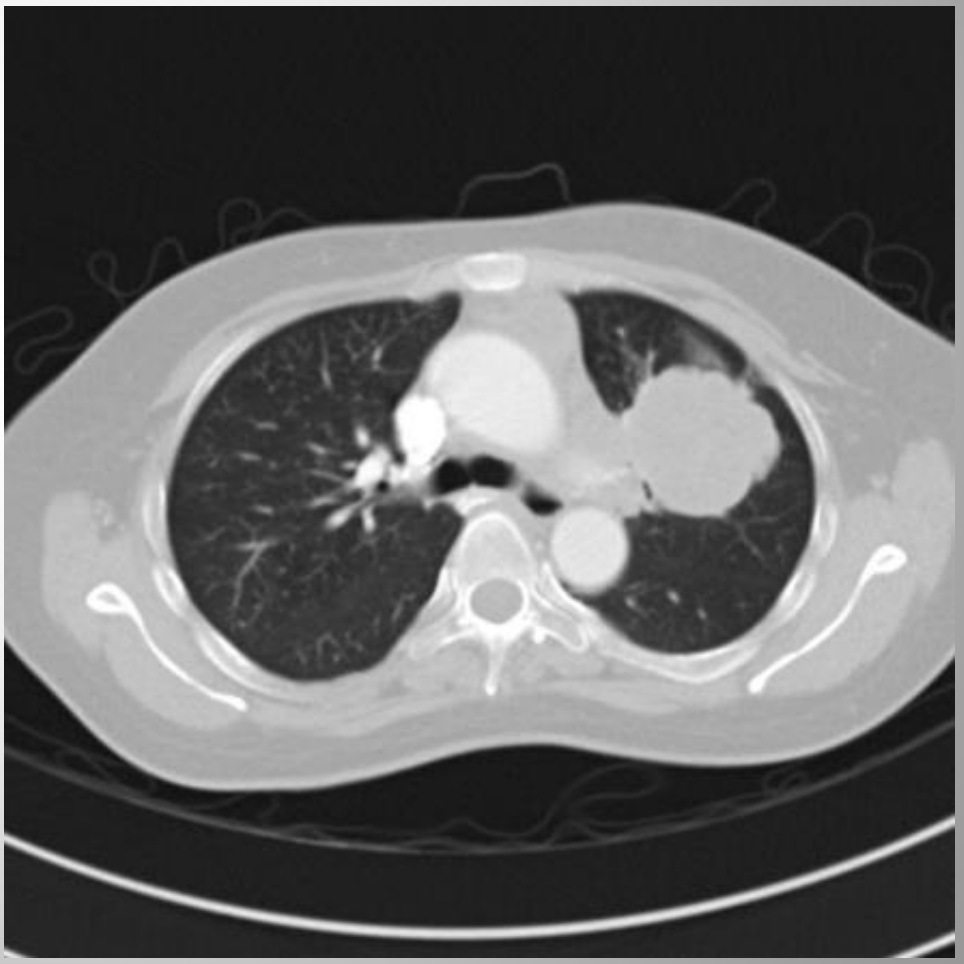
A-Pneumonite
B-Oesophagite
C-Péricardite
D-Myélite



Quiz

2. Si ce patient est traité par radiothérapie, de quel effet secondaire est-il le plus à risque parmi les suivants?

A-Pneumonite
B-Oesophagite
C-Péricardite
D-Myélite



Questions?

Le cancer du poumon stade 3

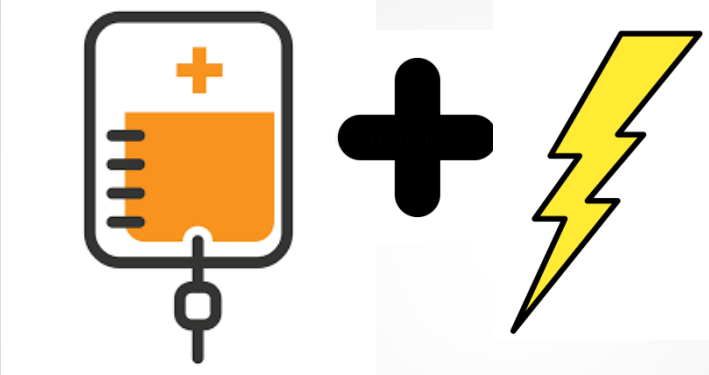
Sophie Savary-Bélanger
Hémato-oncologue
19 octobre 2018

Chimiothérapie

- Traitement standard
- Traitements non standards
- Le petit nouveau

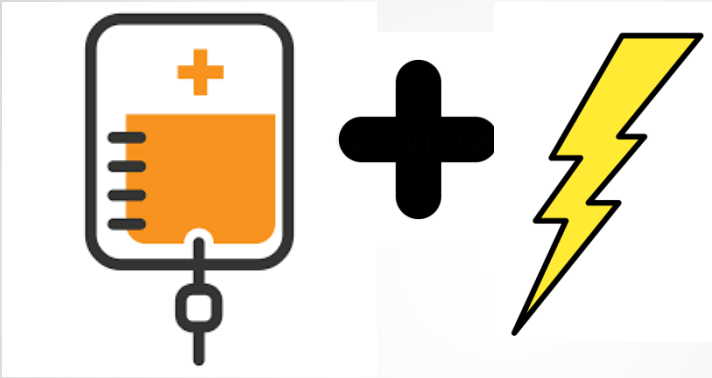
Traitement standard

- Traitement concomitant



Traitement standard

- Traitement concomitant

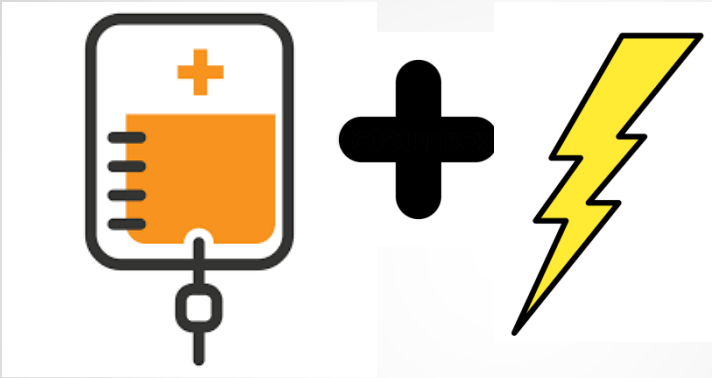


  - Rôles de la chimiothérapie
    - Diminuer les récidives locales

      Radiosensibilisation

Traitement standard

- Traitement concomitant



  - Rôles de la chimiothérapie
    - Diminuer les récidives locales

      Radiosensibilisation
    - Diminuer les récidives à distance

Traitement standard

- Cisplatin +

Traitement standard
Gestion des effets secondaires

- Nausées
  - Emend + Decadron + Stemetil prn
  - Gravol gingembre & Stemetil régulier
  - Hydratation, prolonger Decadron, Zyprexa hs

Traitement standard
Gestion des effets secondaires

- Nausées
  - Emend + Decadron + Stemetil prn
  - Gravol gingembre & Stemetil régulier
  - Hydratation, prolonger Decadron, Zyprexa hs
- IR
  - Hydratation PO/IV
  - Suspendre médicaments néphrotoxiques

Traitement standard
Gestion des effets secondaires

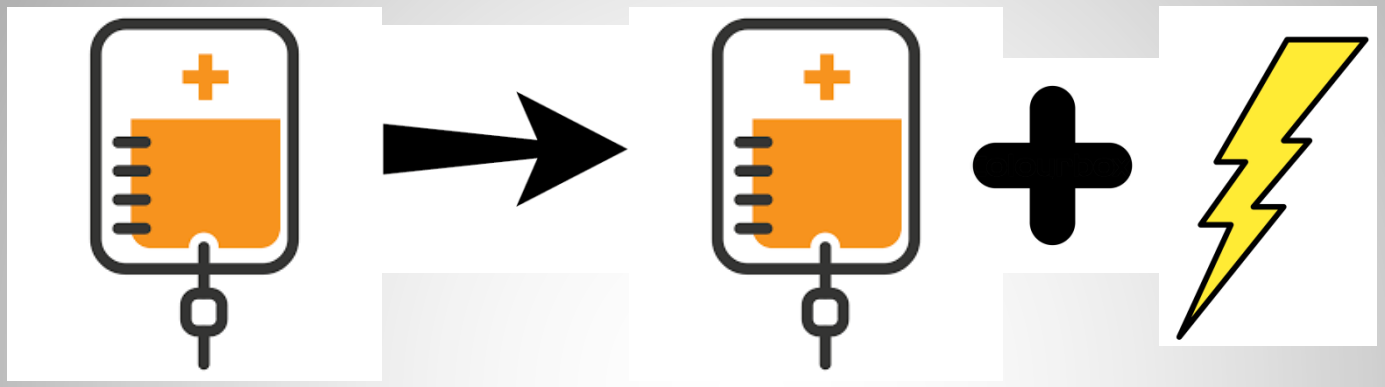
- Nausées
  - Emend + Decadron + Stemetil prn
  - Gravol gingembre & Stemetil régulier
  - Hydratation, prolonger Decadron, Zyprexa hs
- IR
  - Hydratation PO/IV
  - Suspendre médicaments néphrotoxiques

- À surveiller aussi : Ototoxicité, Thrombose, Cytopénies, Neurotoxicité

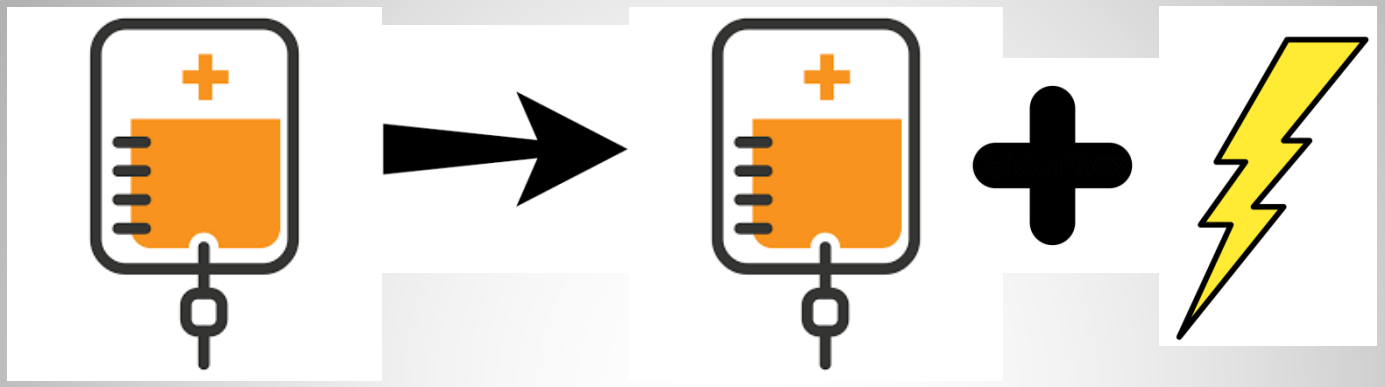
Mon patient n’a pas ce traitement!

Mon patient n’a pas ce traitement!

Traitements non standards
1. Chimiotx avant Radiotx



Traitements non standards
1. Chimiotx avant Radiotx



- Réduire la taille de la tumeur pour radiotx
- (Délai)

Traitements non standards
2.Cisplatin→Carboplatin

- Contre-indication au Cisplatin

Traitements non standards
2.Cisplatin→Carboplatin

- Contre-indication au Cisplatin

Traitements non standards
2.Cisplatin→Carboplatin

- Contre-indication au Cisplatin

- Patient fragile

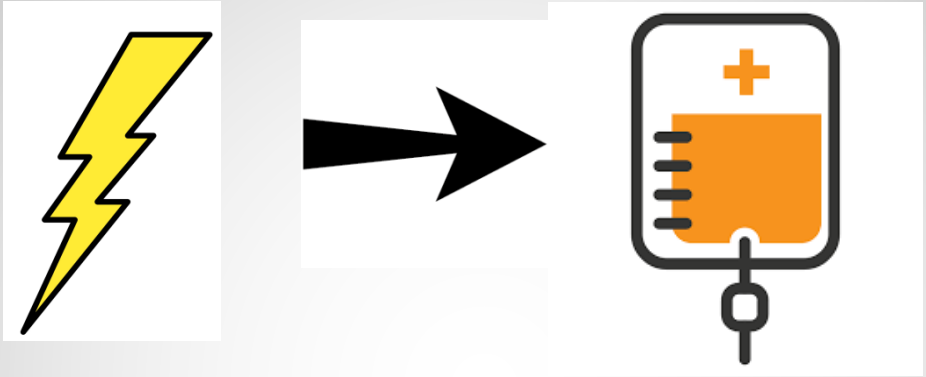
Traitements non standards
2.Cisplatin→Carboplatin

- Contre-indication au Cisplatin

- Patient fragile
  - Carboplatin +
  - Carbo-Taxol

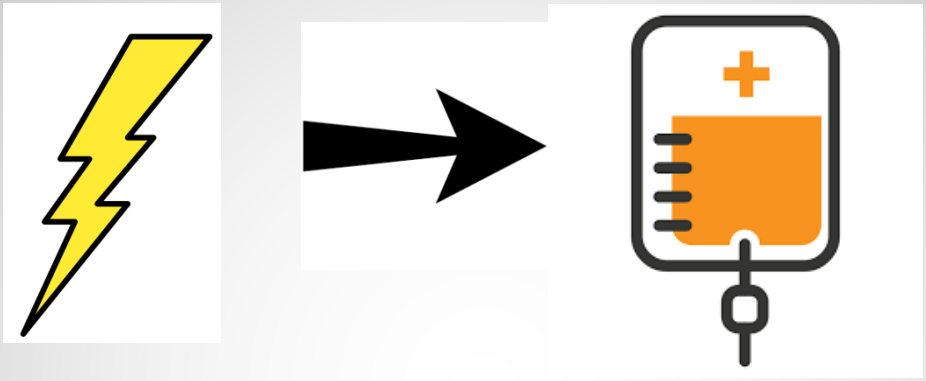
    (Protocole LAMP)

Traitements non standards
3. Radiotx avant Chimiotx



Curran et al. RTOG9401. J Natl Cancer Inst 2011;103:1452–1460.

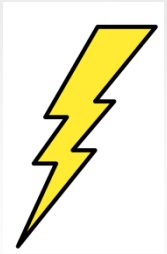
Traitements non standards
3. Radiotx avant Chimiotx



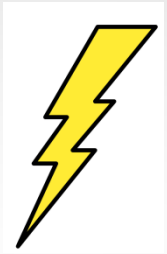
- Diminution des effets secondaires
  - Mucosite
  - Esophagite
  - Nausées/Vomissements

Curran et al. RTOG9401. J Natl Cancer Inst 2011;103:1452–1460.

Traitements non standards
4. Radiotx seule



Traitements non standards
4. Radiotx seule



Primum non nocere

Et le petit nouveau!

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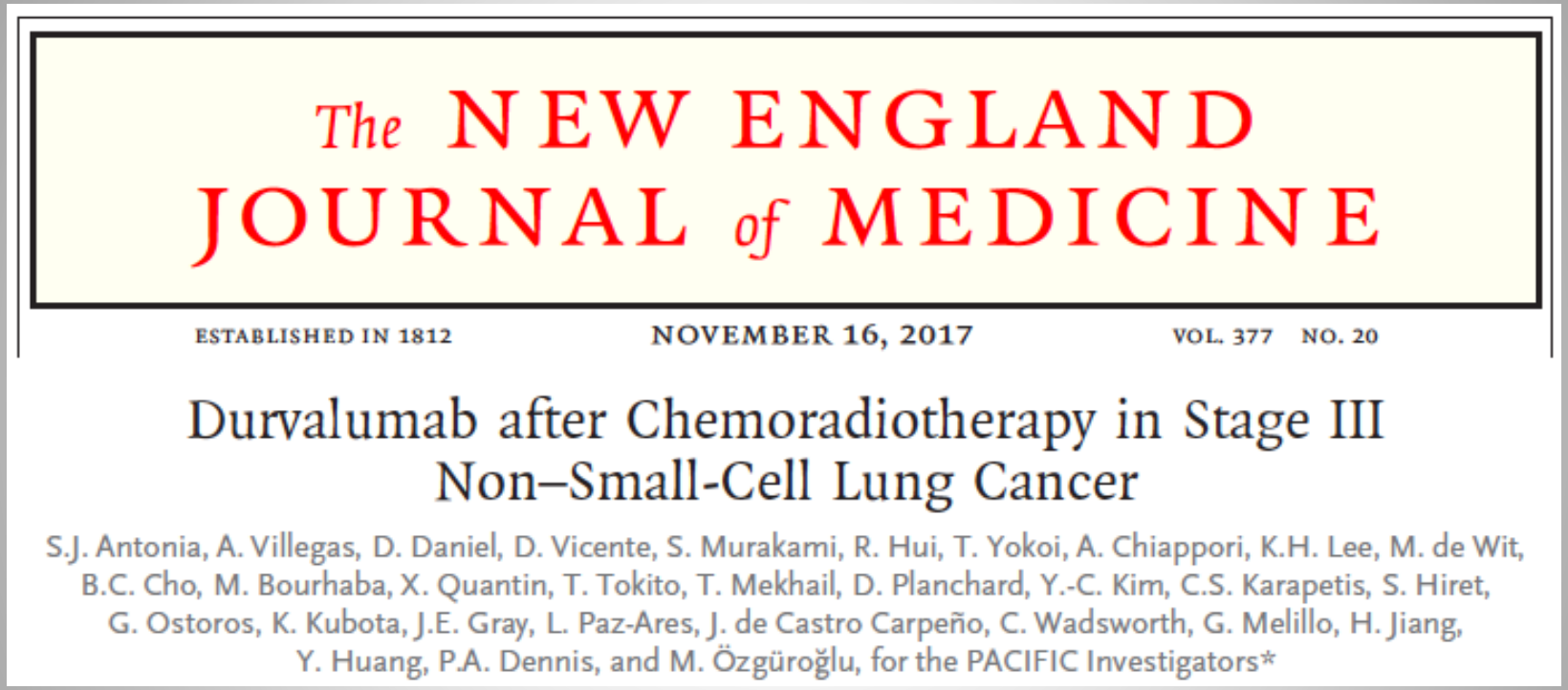

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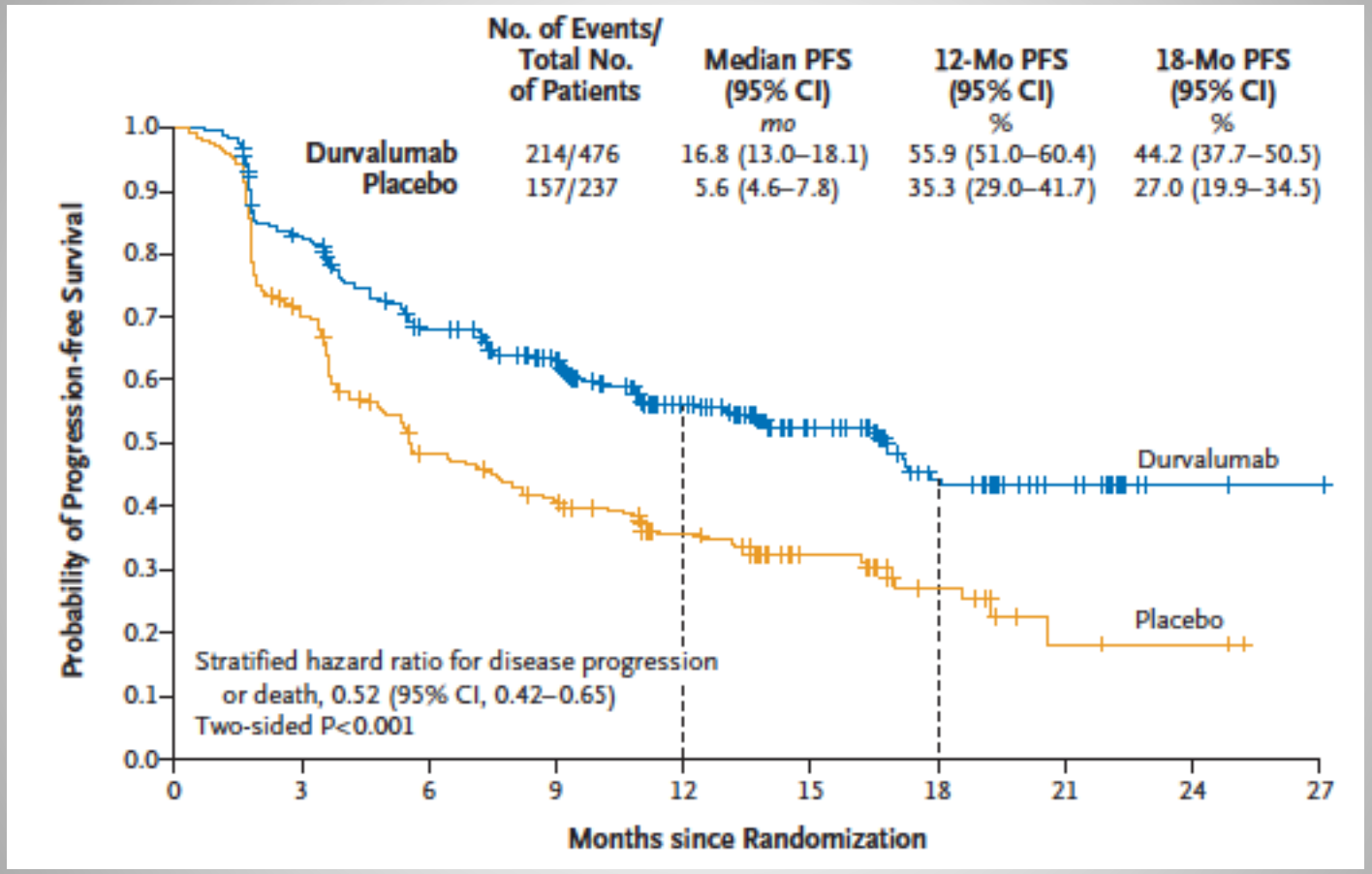
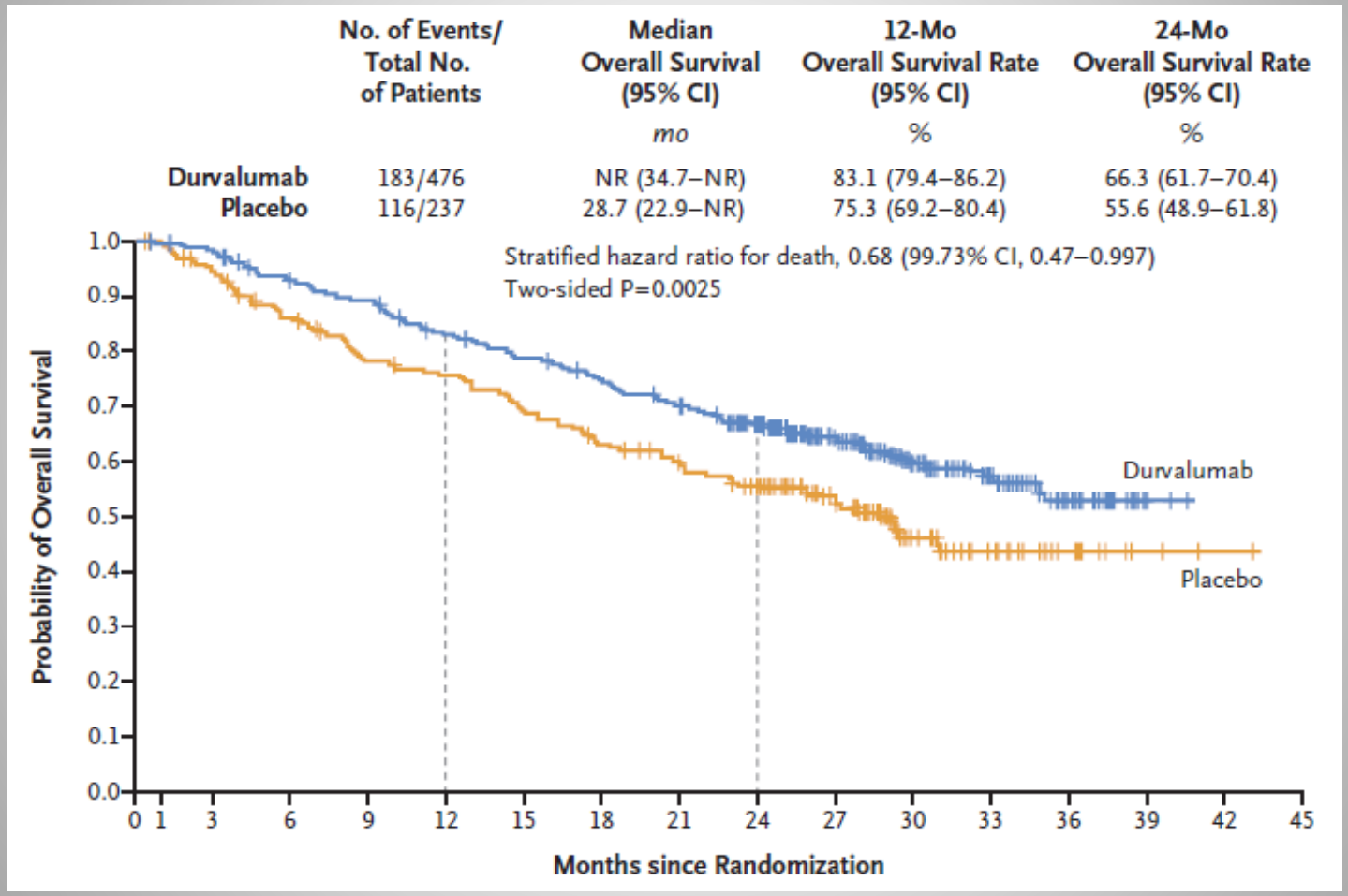
(Parce que ça manquait d'immunothérapie)

Survie sans progression



Antonia et al. N Engl J Med 2017;377:1919-29.

Survie globale



Antonia et al. Published before print 25.9.2018 nejm.org.

Pneumonite

Grading	Management
G1: Asymptomatic, confined to one lobe of the lung or < 25% of lung parenchyma, clinical or diagnostic observations only	Hold ICPi with radiographic evidence of pneumonitis progression May offer one repeat CT in 3-4 weeks; in patients who have had baseline testing, may offer a repeat spirometry/DLCO in 3-4 weeks May resume ICPi with radiographic evidence of improvement or resolution. If no improvement, should treat as G2 Monitor patients weekly with history and physical examination and pulse oximetry; may also offer CXR
G2: Symptomatic, involves more than one lobe of the lung or 25%-50% of lung parenchyma, medical intervention indicated, limiting instrumental ADL	Hold ICPi until resolution to G1 or less Prednisone 1-2 mg/kg/d and taper by 5-10 mg/wk over 4-6 weeks Consider bronchoscopy with BAL Consider empirical antibiotics Monitor every 3 days with history and physical examination and pulse oximetry, consider CXR; no clinical improvement after 48-72 hours of prednisone, treat as G3
G3: Severe symptoms, hospitalization required, involves all lung lobes or > 50% of lung parenchyma, limiting self-care ADL, oxygen indicated G4: Life-threatening respiratory compromise, urgent intervention indicated (intubation)	Permanently discontinue ICPi Empirical antibiotics; (methyl)prednisolone IV 1-2 mg/kg/d; no improvement after 48 hours, may add infliximab 5 mg/kg or mycophenolate mofetil IV 1 g twice a day or IVIG for 5 days or cyclophosphamide; taper corticosteroids over 4-6 weeks Pulmonary and infectious disease consults if necessary Bronchoscopy with BAL ± transbronchial biopsy Patients should be hospitalized for further management

Brahmer et al. JCO. 2018;36(17):1729.