

15. Autres altérations oncogéniques cliniquement pertinentes

Les dossiers des patients présentant une altération oncogénique cliniquement pertinente (autres altérations de *MET*, réarrangements *NRG1*) doivent être discutés dans des RCP intégrant des biologistes moléculaires en vue d'inclusion en essais cliniques notamment.

Concernant les amplifications de *MET* (≥ 6 copies), 25 patients ont été traités par crizotinib dans la cohorte ACSé. Les résultats étaient décevants avec un taux de réponse objective à deux cycles de 16%, un taux de contrôle de la maladie à 4 cycles de 52% et une médiane de survie sans progression de 3,2 mois (169).

Plusieurs inhibiteurs des mutations G12D ou G12X (toutes mutations G12) de *KRAS* sont en cours de développement et il est conseillé d'identifier ces patients et de les orienter vers des essais cliniques.

16. Inhibiteurs des Tyrosines Kinases utilisés dans les CBNPC

Le tableau 11 reprend les principales modalités de prescription et de surveillance des ITK qui peuvent être utilisés dans les CBNPC.

Le site internet de l'Intergroupe Francophone de Cancérologie Thoracique (IFCT) référence en temps « réel » l'évolution des différents types d'autorisation d'accès des médicaments innovants⁴¹.

⁴¹ <https://www.ifct.fr/publications-ifct/acces-derogatoire-aux-medicaments>

TKI	Posologie	Forme	Dosages	Adaptation (/prise)	Cible(s)	Autorisation	Repas	Surveillance biologique	Surveillance Clinique (Appareils)	Autres surveillances
Adagrasib MRTX849 (Mirati)	600mg x 2/j				KRAS G12C			BH, créat	Cardiaque - Digestif - Général (asthénie, perte appétit) - Hépatique - Hémato	ECG (QT)
Afatinib GIOTRIF (Boehringer Ingelheim)	40mg x1/j	⊕	20mg 30mg 40mg 50mg	/ 10 à 20mg	EGFR	AMM		BH, Créat, iono (K)	Cutané - Digestif - Général, (déshydratation) - Oculaire ORL (épistaxis, rhinorrhée) - Pulmonaire	FEVG / 3 mois
Alectinib ALECENSA (Chugai/Roche)	600mg x2/j	⊖	150mg	/ 150mg	ALK	AMM		BH, CPK, NFS	Anémie - Cardiaque (bradycardie) - Cutané - Digestif Général (oedemes) - Myalgie - Oculaire - Pulmonaire	Suivi tensionnel
Brigatinib ALUNBRIG (Takeda)	90mg x1/j 7j puis 180mg x1/j	⊕	30mg 90mg 180mg	Voir notice	ALK	AMM		Amylase, BH, CPK, créat, Lipase, Gly, iono, Lipase, NFS	Cardiaque (HTA, bradycardie, oedemes) - Céphalées, neuropathies périphériques - Cutané - Digestif (pancréatique) - Général – Métabolique hyperglycémie) - Musculaire - Oculaire - Pulmonaire	ECG (QT), suivi tensionnel
Capmatinib TABRECTA (Novartis)	400mg x2/j	⊕	150mg 200mg	/ 100mg	MET (ex14)	AMM, non disponible		Albumine, Amylase, BH, créat, iono, Lipase, NFS	Cutané - Digestif - Général - Œdèmes	ECG (QT)
Ceritinib ZYKADIA (Novartis)	450mg x1/j	⊖	150mg	/ 150mg	ALK	AMM		Amylase, BH, créat, Gly, Iono (K), Lipase, , NFS	Anémie Cardiaque (bradycardie, péricardite, QT) - Cutané Digestif (pancréatite) - Général - Métabolique (hyperglycémie, hypophosphatémie) - Oculaire - Pulmonaire	ECG (QT), suivi tensionnel
Crizotinib XALKORI (Pfizer)	250mg x2/j	⊖	200mg 250mg	A 200mgx2 ou à 250mgx1	ALK, ROS1	AMM		BH, créat, iono (K), NFS	Cardiaque (bradycardie, QT) - Cutané - Digestif - Hématologique - Oculaire - Pulmonaire	ECG (QT), suivi tensionnel
Dabrafenib ¹ TAFINLAR (Novartis)	150mg x2/j	⊖	50mg 75mg	/ 50mg	BRAF	AMM		BH, créat	Céphalées - Cutané - Digestif - Général - Métabolique (hypophosphatémie, hyperglycémie) - Musculaire - Oculaire – Pulmonaire	Examen dermato /mois, jusqu'à 6 mois après arrêt (cancers cutanés)
Entrectinib ROZLYTREK (Roche)	600mg x1/j	⊖	200mg	/ 200mg	ROS1 NTRK	AMM (non remboursé)		Albumine, Amylase, BH, créat, Gly, iono, Lipase, NFS, , , , Uricémie	Cardiaque (QT, insuffisance cardiaque, hypotension) - Cutané - Digestif – Général (déshydratation) – Hématologique (anémie, neutropénie) - Musculo-squelettique - Neurologique - Oculaire - Pulmonaire	FEVG, ECG (QT)
Erlotinib TARCEVA (Roche & génériques)	150mg x1/j	⊕	25mg 100mg 150mg	/ 50mg	EGFR	AMM		BH, créat, iono	Cutané -Digestif - GénéralOculaire - Pulmonaire	

Gefitinib IRESSA (Astra Zeneca & génériques)	250mg x1/j		250mg	Aucune	EGFR	AMM		BH, créat, iono (K)	Cutané - Digestif - Epistaxis - Oculaire - Pulmonaire	
Larotrectinib VITRAKVI (Bayer)	100mg x2/j		25mg 100mg Sol. Buv. 20mg/ml	/ 25mg	NTRK	AMM (non remboursé chez l'adulte), disponible chez l'enfant		BH, NFS	Digestif - Général - Musculo-squelettique - Neurologique (vertige, trouble de la marche, paresthésies)	
Lorlatinib LORVIQUA (Pfizer)	100mg x1/j		25mg 100mg	/ 25mg	ALK, ROS1	ALK : AMM ROS1 : Pas d'AMM		Amylase, Cholesterol, iono, Lipase, NFS, , , Triglycérides	Cutané - Digestif (pancréatique) – Général- Musculo-squelettique -Neurologique - Oculaire – Oedèmes - Psychiatrique	ECG (PR), FEVG
Mobocertinib EXKIVITY (Takeda)	160mg/j		40mg	Aucune	EGFR ins 20	Accès Compassionnel	(pauvre en matière grasse) Avec 240mL d'eau.	amylase, BH, créat, lipase, ionocomplet (avant, J1C1, J15C1, puis au J1 de chaque cycle), NFS	Cardiaque (HTA, torsades de pointes) – Céphalées - Cutané (xerose, éruptions, infections, onychopathies) – Digestif (pancréatique) - Général (fatigue, perte de poids, déshydratation) - Hématologique (anémie) - Musculo-squelettique (douleurs dorsale)- Mucite (buccale) céphalée - HTA – Pulmonaire (dyspnée, toux)	ECG avant, J1C1, J1C2, puis au J1 tous les 4 cycles. Echo cœur avant, J1C2, J1C5 et J1C9
Osimertinib TAGRISSO (Astra-Zeneca)	80mg x1/j		40mg 80mg	/ 40mg	EGFR	AMM AAP post-AMM (adjuvant)		BH, créat, iono, NFS	Cutané - Digestif - Hématologique - Pulmonaire	ECG (QT)
Pozotinib (Spectrum Pharm.)	16mg/j		2mg 8mg	/ 2mg	EGFR ins 20	Accès Compassionnel		iono, NFS	Cutané – Digestif - Général	NC
Pralsetinib GAVRETO (Roche)	400mg x1/j		100mg	/100mg	RET	AMM Non disponible		BH, iono, NFS	Cardiaque (HTA) – Digestif – Hémato - Pulmonaire	ECG, suivi tensionnel
Repotrectinib (Turning Point Therapeutics Inc)	160mg x1/j J1-14 puis 160mg x2/j		40mg		ROS1	AAC		Idem étude TRIDENT-1	Idem étude TRIDENT-1	
Selpercatinib RETSEVMO (Lilly)	160mg x2/j		40mg 80mg	/40mg	RET	AMM Non disponible	si IPP → au cours repas	BH, créat	Cardiaque (HTA) - Céphalées - Digestif - Général - Œdèmes	ECG
Sotorasib LUMYKRAS (Amgen)	960mg x 1/j (N'est pas un TKI)		120mg	/240mg	KRAS G12C	AAP post AMM		Cholestérol, créat au J1 de chaque cure Coag, Iono, NFS, TG au J1C1, TSH	Digestif - Hématologique (cytopénies) - Hépatique Rénale	ECG avant, J1C1,
Tepotinib TEPMETKO	2 x 225mg x 1/j		225mg	/ 225mg	MET (Ex 14)	AMM, non disponible.		BH, créat, iono, NFS	Digestifs - Généraux - Hématologique - Hépatique – Musculaires – Oedemes - Pulmonaire - Rénal (créatinine)	NC

(Merck)										
Trametinib² MEKINIST (Novartis)	2mg x1/j	⊕	0,5mg 2mg	/ 0,5mg	MEK	AMM		BH, CPK, NFS	Cardiaque (HTA, Altération FEVG) - Cutané - Digestif – Général - Hématologique - Musculaire - Oculaire – Oedemes - Pulmonaire	Examen dermato /mois, jusque 6mois après arrêt FEVG /3 mois, suivi tensionnel
Vemurafenib ZELBORAF (Roche)	960mg x2/j	⊕	240mg	/ 240mg	BRAF	Hors AMM ³	Eviter le jeun	BH, iono (K), NFS, Créat	Digestif – Cutané – Musculaire – Générale - Cardiaque (Trouble du rythme, QT) – Œdème - Oculaire	Examen dermato /mois, jusque 6mois après arrêt (cancer cutané, photosensibilité) ECG (QT)

Tableau 10 - Principales modalités d'utilisation des thérapies ciblées orales dans les CBNPC.

Sources : Société Française de Pharmacie Oncologique, Oncolien®, Fiches et vidéos d'aide au bon usage des traitements anticancéreux oraux, <https://oncolien.sfpo.com/> - Centre National Hospitalier d'Information sur le Médicament, Base de données THERIAQUE, v4.2.4 déployé le 29/08/2017 et mise à jour le 16/02/2022, <http://www.theriaque.org/apps/contenu/accueil.php> - & Site de l'Agence Nationale de Sécurité des Médicaments, Résumé des Caractéristiques du Produit. - Données de la littérature.

Notes : 1. Utilisé en association au tramétinib pour cibler les BRAF V600E. 2. Utilisé en association au Dabrafénib pour cibler les BRAF V600E. 3. Le vemurafenib ne dispose pas d'AMM dans le cancer du poumon..

Repas : ROUGE : A prendre en dehors des repas (pas de prise entre 1h avant et 3h après le repas) - VERT : A prendre au cours des repas - JAUNE : Pendant ou au cours des repas - GRIS : Inconnu.

Abréviations : BH : Bilan Hépatique, Iono : Ionogramme Sanguin, K : Kaliémie, NFS : Numération Formule Sanguine (+Plaquettes), Créat : Créatinine, CPK : Créatine Kinase, ECG : Electrocardiogramme, FEVG : Fraction d'Ejection du Ventricule Gauche, QT : Espace QT corrigé, PR : Espace PR.

NC : Non connu

REFERENCES

- Goldstraw P, Chansky K, Crowley J, Rami-Porta R, Asamura H, Eberhardt WEE, et al. The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. *J Thorac Oncol.* janv 2016;11(1):39-51.
- Eberhardt WEE, Mitchell A, Crowley J, Kondo H, Kim YT, Turrisi A, et al. The IASLC Lung Cancer Staging Project: Proposals for the Revision of the M Descriptors in the Forthcoming Eighth Edition of the TNM Classification of Lung Cancer. *J Thorac Oncol.* nov 2015;10(11):1515-22.
- Rusch VW, Asamura H, Watanabe H, Giroux DJ, Rami-Porta R, Goldstraw P. The IASLC Lung Cancer Staging Project: A Proposal for a New International Lymph Node Map in the Forthcoming Seventh Edition of the TNM Classification for Lung Cancer. *Journal of Thoracic Oncology.* mai 2009;4(5):568-77.
- Dietel M, Bubendorf L, Dingemans AMC, Doooms C, Elmberger G, García RC, et al. Diagnostic procedures for non-small-cell lung cancer (NSCLC): recommendations of the European Expert Group. *Thorax.* févr 2016;71(2):177-84.
- Nicholson AG, Tsao MS, Beasley MB, Borczuk AC, Brambilla E, Cooper WA, et al. The 2021 WHO Classification of Lung Tumors: Impact of advances since 2015. *Journal of Thoracic Oncology.* nov 2021;S1556086421033165.
- Couraud S, Souquet PJ, Paris C, Dô P, Doubre H, Pichon E, et al. BioCAST/IFCT-1002: epidemiological and molecular features of lung cancer in never-smokers. *Eur Respir J.* 5 févr 2015;
- Cancer du poumon, Bilan initial [Internet]. INCa; 2011 juin [cité 19 déc 2014]. (Recommandations et référentiels). Disponible sur: <http://www.e-cancer.fr/publications/55-recommandations-de-pratique-clinique/516-cancer-du-poumon-bilan-initial-abrege>
- Utilisation des marqueurs tumoraux sériques dans le cancer bronchique primitif. Recommandations de la Société de Pneumologie de Langue Française. *Rev Mal Respir.* 1997;14(Suppl.3):3S3-39.
- Brunelli A, Charloux A, Bolliger CT, Rocco G, Sculier JP, Varela G, et al. ERS/ESTS clinical guidelines on fitness for radical therapy in lung cancer patients (surgery and chemo-radiotherapy). *Eur Respir J.* juill 2009;34(1):17-41.
- Brunelli A, Kim AW, Berger KI, Addrizzo-Harris DJ. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest.* mai 2013;143(5 Suppl):e166S-90S.
- Brunelli A, Varela G, Salati M, Jimenez MF, Pompili C, Novoa N, et al. Recalibration of the revised cardiac risk index in lung resection candidates. *Ann Thorac Surg.* juill 2010;90(1):199-203.
- Lin Y, Yang H, Cai Q, Wang D, Rao H, Lin S, et al. Characteristics and Prognostic Analysis of 69 Patients With Pulmonary Sarcomatoid Carcinoma. *Am J Clin Oncol.* juin 2016;39(3):215-22.
- Travis WD, World Health Organization, International Agency for Research on Cancer, International Association for the Study of Lung Cancer, International Academy of Pathology, éditeurs. *Pathology and genetics of tumours of the lung, pleura, thymus and heart.* Lyon : Oxford: IARC Press, Oxford University Press (distributeur); 2004. 344 p. (World Health Organization classification of tumours).
- Nakajima M, Kasai T, Hashimoto H, Iwata Y, Manabe H. Sarcomatoid carcinoma of the lung: a clinicopathologic study of 37 cases. *Cancer.* 15 août 1999;86(4):608-16.
- Ro JY, Chen JL, Lee JS, Sahin AA, Ordóñez NG, Ayala AG. Sarcomatoid carcinoma of the lung. Immunohistochemical and ultrastructural studies of 14 cases. *Cancer.* 15 janv 1992;69(2):376-86.
- Chang YL, Lee YC, Shih JY, Wu CT. Pulmonary pleomorphic (spindle) cell carcinoma: peculiar clinicopathologic manifestations different from ordinary non-small cell carcinoma. *Lung Cancer.* oct 2001;34(1):91-7.
- Cabarcos A, Gomez Dorransoro M, Lobo Beristain JL. Pulmonary carcinosarcoma: a case study and review of the literature. *Br J Dis Chest.* janv 1985;79(1):83-94.
- Razzuk MA, Urschel HC, Albers JE, Martin JA, Paulson DL. Pulmonary giant cell carcinoma. *Ann Thorac Surg.* juin 1976;21(6):540-5.
- Shin MS, Jackson LK, Shelton RW, Greene RE. Giant cell carcinoma of the lung. Clinical and roentgenographic manifestations. *Chest.* mars 1986;89(3):366-9.
- Nappi O, Glasner SD, Swanson PE, Wick MR. Biphasic and monophasic sarcomatoid carcinomas of the lung. A reappraisal of « carcinosarcomas » and « spindle-cell carcinomas ». *Am J Clin Pathol.* sept 1994;102(3):331-40.
- Fishback NF, Travis WD, Moran CA, Guinee DG, McCarthy WF, Koss MN. Pleomorphic (spindle/giant cell) carcinoma of the lung. A clinicopathologic correlation of 78 cases. *Cancer.* 15 juin 1994;73(12):2936-45.
- Raveglia F, Mezzetti M, Panigalli T, Furia S, Giuliani L, Conforti S, et al. Personal experience in surgical management of pulmonary pleomorphic carcinoma. *Ann Thorac Surg.* nov 2004;78(5):1742-7.
- Rossi G, Cavazza A, Sturm N, Migaldi M, Facciolo N, Longo L, et al. Pulmonary carcinomas with pleomorphic, sarcomatoid, or sarcomatous elements: a clinicopathologic and immunohistochemical study of 75 cases. *Am J Surg Pathol.* mars 2003;27(3):311-24.
- Moon KC, Lee GK, Yoo SH, Jeon YK, Chung JH, Han J, et al. Expression of caveolin-1 in pleomorphic carcinoma of the lung is correlated with a poor prognosis. *Anticancer Res.* déc 2005;25(6C):4631-7.
- Holst VA, Finkelstein S, Colby TV, Myers JL, Yousem SA. p53 and K-ras mutational genotyping in pulmonary carcinosarcoma, spindle cell carcinoma, and pulmonary blastoma: implications for histogenesis. *Am J Surg Pathol.* juill 1997;21(7):801-11.
- Blaukovitsch M, Halbwedl I, Kothmaier H, Gogg-Kammerer M, Popper HH. Sarcomatoid carcinomas of the lung--are these histogenetically heterogeneous tumors? *Virchows Arch.* oct 2006;449(4):455-61.
- Yendamuri S, Caty L, Pine M, Adem S, Bogner P, Miller A, et al. Outcomes of sarcomatoid carcinoma of the lung: a Surveillance, Epidemiology, and End Results Database analysis. *Surgery.* sept 2012;152(3):397-402.
- Mochizuki T, Ishii G, Nagai K, Yoshida J, Nishimura M, Mizuno T, et al. Pleomorphic carcinoma of the lung: clinicopathologic characteristics of 70 cases. *Am J Surg Pathol.* nov 2008;32(11):1727-35.
- Liu X, Wang F, Xu C, Chen X, Hou X, Li Q, et al. Genomic origin and intratumor heterogeneity revealed by sequencing on carcinomatous and sarcomatous components of pulmonary sarcomatoid carcinoma. *Oncogene.* janv 2021;40(4):821-32.

30. D'Antonio F, De Sanctis R, Bolengo I, Destro A, Rahal D, De Vincenzo F, et al. Pulmonary sarcomatoid carcinoma presenting both ALK rearrangement and PD-L1 high positivity: A case report on the therapeutic regimen. *Medicine (Baltimore)*. août 2019;98(32):e16754.
31. Qin J, Chen B, Li C, Yan J, Lu H. Genetic heterogeneity and predictive biomarker for pulmonary sarcomatoid carcinomas. *Cancer Genet*. janv 2021;250-251:12-9.
32. Fallet V, Saffroy R, Girard N, Mazieres J, Lantuejoul S, Vieira T, et al. High-throughput somatic mutation profiling in pulmonary sarcomatoid carcinomas using the LungCarta™ Panel: exploring therapeutic targets. *Annals of Oncology*. août 2015;26(8):1748-53.
33. Kwon D, Koh J, Kim S, Go H, Kim YA, Keam B, et al. MET exon 14 skipping mutation in triple-negative pulmonary adenocarcinomas and pleomorphic carcinomas: An analysis of intratumoral MET status heterogeneity and clinicopathological characteristics. *Lung Cancer*. avr 2017;106:131-7.
34. Maneenil K, Xue Z, Liu M, Boland J, Wu F, Stoddard SM, et al. Sarcomatoid Carcinoma of the Lung: The Mayo Clinic Experience in 127 Patients. *Clinical Lung Cancer*. mai 2018;19(3):e323-33.
35. Vieira T, Antoine M, Ruppert AM, Fallet V, Duruisseaux M, Giroux Leprieur E, et al. Blood vessel invasion is a major feature and a factor of poor prognosis in sarcomatoid carcinoma of the lung. *Lung Cancer*. août 2014;85(2):276-81.
36. Hou J, Xing L, Yuan Y. A clinical analysis of 114 cases of sarcomatoid carcinoma of the lung. *Clin Exp Med*. nov 2018;18(4):555-62.
37. Le Caer H, Teissier E, Barriere JR, Venissac N. Classic biphasic pulmonary blastoma: A case report and review of the literature. *Crit Rev Oncol Hematol*. mai 2018;125:48-50.
38. Zombori-Tóth N, Kiss S, Oštarijaš E, Alizadeh H, Zombori T. Adjuvant chemotherapy could improve the survival of pulmonary sarcomatoid carcinoma: A systematic review and meta-analysis. *Surg Oncol*. sept 2022;44:101824.
39. Girard N, al. *Lymphoma, Lymphoproliferative Diseases, and Other Primary Malignant Tumors*. Fifth edition. Philadelphia, PA: Elsevier Saunders; 2009. (Mason RJ, Broaddus VC, Murray JF, Nadel JA. Murray and Nadel's textbook of respiratory medicine.).
40. Ung M, Rouquette I, Filleron T, Taillandy K, Brouchet L, Bennouna J, et al. Characteristics and Clinical Outcomes of Sarcomatoid Carcinoma of the Lung. *Clin Lung Cancer*. sept 2016;17(5):391-7.
41. Karim NA, Schuster J, Eldessouki I, Gaber O, Namad T, Wang J, et al. Pulmonary sarcomatoid carcinoma: University of Cincinnati experience. *Oncotarget*. 9 janv 2018;9(3):4102-8.
42. Babacan NA, Pina IB, Signorelli D, Prelaj A, Garassino MC, Tanvetyanon T. Relationship Between Programmed Death Receptor-Ligand 1 Expression and Response to Checkpoint Inhibitor Immunotherapy in Pulmonary Sarcomatoid Carcinoma: A Pooled Analysis. *Clin Lung Cancer*. sept 2020;21(5):e456-63.
43. Lu S, Fang J, Li X, Cao L, Zhou J, Guo Q, et al. Once-daily savolitinib in Chinese patients with pulmonary sarcomatoid carcinomas and other non-small-cell lung cancers harbouring MET exon 14 skipping alterations: a multicentre, single-arm, open-label, phase 2 study. *Lancet Respir Med*. oct 2021;9(10):1154-64.
44. Herpel E, Rieker RJ, Dienemann H, Muley T, Meister M, Hartmann A, et al. SMARCA4 and SMARCA2 deficiency in non-small cell lung cancer: immunohistochemical survey of 316 consecutive specimens. *Ann Diagn Pathol*. févr 2017;26:47-51.
45. Rekhman N, Montecalvo J, Chang JC, Alex D, Ptashkin RN, Ai N, et al. SMARCA4-Deficient Thoracic Sarcomatoid Tumors Represent Primarily Smoking-Related Undifferentiated Carcinomas Rather Than Primary Thoracic Sarcomas. *Journal of Thoracic Oncology*. févr 2020;15(2):231-47.
46. Le Loarer F, Watson S, Pierron G, de Montpreville VT, Ballet S, Firmin N, et al. SMARCA4 inactivation defines a group of undifferentiated thoracic malignancies transcriptionally related to BAF-deficient sarcomas. *Nat Genet*. oct 2015;47(10):1200-5.
47. Decroix E, Leroy K, Wislez M, Fournel L, Alifano M, Damotte D, et al. Les tumeurs thoraciques SMARCA4 déficientes : une nouvelle entité. *Bulletin du Cancer*. janv 2020;107(1):41-7.
48. Naito T, Umemura S, Nakamura H, Zenke Y, Udagawa H, Kirita K, et al. Successful treatment with nivolumab for SMARCA4-deficient non-small cell lung carcinoma with a high tumor mutation burden: A case report. *Thorac Cancer*. mai 2019;10(5):1285-8.
49. Fekkar A, Emprou C, Lefebvre C, Ferretti G, Stephanov O, Pissaloux D, et al. Thoracic NUT carcinoma: Common pathological features despite diversity of clinical presentations. *Lung Cancer*. août 2021;158:55-9.
50. Chau NG, Ma C, Danga K, Al-Sayegh H, Nardi V, Barrette R, et al. An Anatomical Site and Genetic-Based Prognostic Model for Patients With Nuclear Protein in Testis (NUT) Midline Carcinoma: Analysis of 124 Patients. *JNCI Cancer Spectrum*. 1 avr 2020;4(2):pkz094.
51. Salati M, Baldessari C, Bonetti LR, Messina C, Merz V, Cerbelli B, et al. NUT midline carcinoma: Current concepts and future perspectives of a novel tumour entity. *Critical Reviews in Oncology/Hematology*. déc 2019;144:102826.
52. Piha-Paul SA, Hann CL, French CA, Cousin S, Braña I, Cassier PA, et al. Phase 1 Study of Molibresib (GSK525762), a Bromodomain and Extra-Terminal Domain Protein Inhibitor, in NUT Carcinoma and Other Solid Tumors. *JNCI Cancer Spectrum*. 1 avr 2020;4(2):pkz093.
53. Lewin J, Soria JC, Stathis A, Delord JP, Peters S, Awada A, et al. Phase Ib Trial With Birabresib, a Small-Molecule Inhibitor of Bromodomain and Extraterminal Proteins, in Patients With Selected Advanced Solid Tumors. *JCO*. 20 oct 2018;36(30):3007-14.
54. Shapiro GI, LoRusso P, Dowlati A, T. Do K, Jacobson CA, Vaishampayan U, et al. A Phase 1 study of RO6870810, a novel bromodomain and extra-terminal protein inhibitor, in patients with NUT carcinoma, other solid tumours, or diffuse large B-cell lymphoma. *Br J Cancer*. 16 févr 2021;124(4):744-53.
55. French C. NUT midline carcinoma. *Nat Rev Cancer*. mars 2014;14(3):149-50.
56. Ramnath N, Dilling TJ, Harris LJ, Kim AW, Michaud GC, Balekian AA, et al. Treatment of stage III non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. mai 2013;143(5 Suppl):e314S-40S.
57. Saji H, Okada M, Tsuboi M, Nakajima R, Suzuki K, Aokage K, et al. Segmentectomy versus lobectomy in small-sized peripheral non-small-cell lung cancer (JCOG0802/WJOG4607L): a multicentre, open-label, phase 3, randomised, controlled, non-inferiority trial. *Lancet*. 23 avr 2022;399(10335):1607-17.
58. Nitadori JI, Bograd AJ, Morales EA, Rizk NP, Dunphy MPS, Sima CS, et al. Preoperative consolidation-to-tumor ratio and SUVmax stratify the risk of recurrence in patients undergoing limited resection for lung adenocarcinoma ≤2 cm. *Ann Surg Oncol*. déc 2013;20(13):4282-8.

59. Jeon JH, Kang CH, Kim HS, Seong YW, Park IK, Kim YT, et al. Video-assisted thoracoscopic lobectomy in non-small-cell lung cancer patients with chronic obstructive pulmonary disease is associated with lower pulmonary complications than open lobectomy: a propensity score-matched analysis. *Eur J Cardiothorac Surg.* avr 2014;45(4):640-5.
60. Lim E, Batchelor TJP, Dunning J, Shackcloth M, Anikin V, Naidu B, et al. Video-Assisted Thoracoscopic or Open Lobectomy in Early-Stage Lung Cancer. *NEJM Evidence* [Internet]. 22 févr 2022 [cité 20 mars 2023];1(3). Disponible sur: <https://evidence.nejm.org/doi/10.1056/EVIDoa2100016>
61. Silvestri GA, Handy J, Lackland D, Corley E, Reed CE. Specialists achieve better outcomes than generalists for lung cancer surgery. *Chest.* sept 1998;114(3):675-80.
62. Thomas P, Dahan M, Riquet M, Massart G, Falcoz PE, Bouchet L, et al. [Practical issues in the surgical treatment of non-small cell lung cancer. Recommendations from the French Society of Thoracic and Cardiovascular Surgery]. *Rev Mal Respir.* oct 2008;25(8):1031-6.
63. Edwards JG, Chansky K, Van Schil P, Nicholson AG, Boubia S, Brambilla E, et al. The IASLC Lung Cancer Staging Project: Analysis of Resection Margin Status and Proposals for Residual Tumor Descriptors for Non-Small Cell Lung Cancer. *Journal of Thoracic Oncology.* mars 2020;15(3):344-59.
64. Rami-Porta R, Wittekind C, Goldstraw P. Complete Resection in Lung Cancer Surgery: From Definition to Validation and Beyond. *J Thorac Oncol.* déc 2020;15(12):1815-8.
65. Strauss GM, Herndon JE, Maddaus MA, Johnstone DW, Johnson EA, Harpole DH, et al. Adjuvant paclitaxel plus carboplatin compared with observation in stage IB non-small-cell lung cancer: CALGB 9633 with the Cancer and Leukemia Group B, Radiation Therapy Oncology Group, and North Central Cancer Treatment Group Study Groups. *J Clin Oncol.* 1 nov 2008;26(31):5043-51.
66. Pignon JP, Tribodet H, Scagliotti GV, Douillard JY, Shepherd FA, Stephens RJ, et al. Lung adjuvant cisplatin evaluation: a pooled analysis by the LACE Collaborative Group. *J Clin Oncol.* 20 juill 2008;26(21):3552-9.
67. Kenmotsu H, Yamamoto N, Yamanaka T, Yoshiya K, Takahashi T, Ueno T, et al. Randomized Phase III Study of Pemetrexed Plus Cisplatin Versus Vinorelbine Plus Cisplatin for Completely Resected Stage II to IIIA Nonsquamous Non-Small-Cell Lung Cancer. *J Clin Oncol.* 1 juill 2020;38(19):2187-96.
68. Postoperative radiotherapy in non-small-cell lung cancer: systematic review and meta-analysis of individual patient data from nine randomised controlled trials. PORT Meta-analysis Trialists Group. *Lancet.* 25 juill 1998;352(9124):257-63.
69. Le Pechoux C, Pourel N, Barlesi F, Lerouge D, Antoni D, Lamezec B, et al. Postoperative radiotherapy versus no postoperative radiotherapy in patients with completely resected non-small-cell lung cancer and proven mediastinal N2 involvement (Lung ART): an open-label, randomised, phase 3 trial. *The Lancet Oncology.* janv 2022;23(1):104-14.
70. Zarinshenas R, Ladbury C, McGee H, Raz D, Erhunmwunsee L, Pathak R, et al. Machine learning to refine prognostic and predictive nodal burden thresholds for post-operative radiotherapy in completely resected stage III-N2 non-small cell lung cancer. *Radiother Oncol.* août 2022;173:10-8.
71. Westeel V, Quoix E, Puyraveau M, Lavolé A, Braun D, Laporte S, et al. A randomised trial comparing preoperative to perioperative chemotherapy in early-stage non-small-cell lung cancer (IFCT 0002 trial). *Eur J Cancer.* août 2013;49(12):2654-64.
72. Felip E, Altorki N, Zhou C, Csősz T, Vynnychenko I, Goloborodko O, et al. Adjuvant atezolizumab after adjuvant chemotherapy in resected stage IB-IIIA non-small-cell lung cancer (IMPpower010): a randomised, multicentre, open-label, phase 3 trial. *Lancet.* 9 oct 2021;398(10308):1344-57.
73. O'Brien M, Paz-Ares L, Marreaud S, Dafni U, Oselin K, Havel L, et al. Pembrolizumab versus placebo as adjuvant therapy for completely resected stage IB-IIIA non-small-cell lung cancer (PEARLS/KEYNOTE-091): an interim analysis of a randomised, triple-blind, phase 3 trial. *Lancet Oncol.* oct 2022;23(10):1274-86.
74. Forde PM, Spicer J, Lu S, Provencio M, Mitsudomi T, Awad MM, et al. Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer. *N Engl J Med.* 26 mai 2022;386(21):1973-85.
75. Heymach JV, Mitsudomi T, Harpole D, Aperghis M, Jones S, Mann H, et al. Design and Rationale for a Phase III, Double-Blind, Placebo-Controlled Study of Neoadjuvant Durvalumab + Chemotherapy Followed by Adjuvant Durvalumab for the Treatment of Patients With Resectable Stages II and III non-small-cell Lung Cancer: The AEGEAN Trial. *Clin Lung Cancer.* mai 2022;23(3):e247-51.
76. Ricardi U, Badellino S, Filippi AR. Stereotactic body radiotherapy for early stage lung cancer: History and updated role. *Lung Cancer.* déc 2015;90(3):388-96.
77. Onishi H, Araki T, Shirato H, Nagata Y, Hiraoka M, Gomi K, et al. Stereotactic hypofractionated high-dose irradiation for stage I nonsmall cell lung carcinoma: Clinical outcomes in 245 subjects in a Japanese multiinstitutional study. *Cancer.* 1 oct 2004;101(7):1623-31.
78. Wu YL, Tsuboi M, He J, John T, Grohe C, Majem M, et al. Osimertinib in Resected EGFR-Mutated Non-Small-Cell Lung Cancer. *N Engl J Med.* 29 oct 2020;383(18):1711-23.
79. Giraud P, Lacornerie T, Mornex F. [Radiotherapy for primary lung carcinoma]. *Cancer Radiother.* sept 2016;20 Suppl:S147-156.
80. Le Pechoux C, Faivre-Finn C, Ramella S, McDonald F, Manapov F, Putora PM, et al. ESTRO ACROP guidelines for target volume definition in the thoracic radiation treatment of small cell lung cancer. *Radiotherapy and Oncology.* nov 2020;152:89-95.
81. Noël G, Antoni D. Organs at risk radiation dose constraints. *Cancer/Radiothérapie.* févr 2022;26(1-2):59-75.
82. Aupérin A, Le Pechoux C, Rolland E, Curran WJ, Furuse K, Fournel PJ, et al. Meta-analysis of concomitant versus sequential radiochemotherapy in locally advanced non-small-cell lung cancer. *J Clin Oncol.* 1 mai 2010;28(13):2181-90.
83. Antonia SJ, Villegas A, Daniel D, Vicente D, Murakami S, Hui R, et al. Durvalumab after Chemoradiotherapy in Stage III Non-Small-Cell Lung Cancer. *N Engl J Med.* 16 2017;377(20):1919-29.
84. Antonia SJ, Villegas A, Daniel D, Vicente D, Murakami S, Hui R, et al. Overall Survival with Durvalumab after Chemoradiotherapy in Stage III NSCLC. *N Engl J Med.* 13 2018;379(24):2342-50.
85. Bruni A, Scotti V, Borghetti P, Vagge S, Cozzi S, D'Angelo E, et al. A Real-World, Multicenter, Observational Retrospective Study of Durvalumab After Concomitant or Sequential Chemoradiation for Unresectable Stage III Non-Small Cell Lung Cancer. *Front Oncol.* 2021;11:744956.
86. Zhou Q, Chen M, Jiang O, Pan Y, Hu D, Lin Q, et al. Sugemalimab versus placebo after concurrent or sequential chemoradiotherapy in patients with locally advanced, unresectable, stage III non-small-cell lung cancer in China (GEMSTONE-301): interim results of a randomised, double-blind, multicentre, phase 3 trial. *Lancet Oncol.* févr 2022;23(2):209-19.

87. Senan S, Brade A, Wang LH, Vansteenkiste J, Dakhil S, Biesma B, et al. PROCLAIM: Randomized Phase III Trial of Pemetrexed-Cisplatin or Etoposide-Cisplatin Plus Thoracic Radiation Therapy Followed by Consolidation Chemotherapy in Locally Advanced Nonsquamous Non-Small-Cell Lung Cancer. *J Clin Oncol.* 20 mars 2016;34(9):953-62.
88. Rusch VW, Giroux DJ, Kraut MJ, Crowley J, Hazuka M, Winton T, et al. Induction chemoradiation and surgical resection for superior sulcus non-small-cell lung carcinomas: long-term results of Southwest Oncology Group Trial 9416 (Intergroup Trial 0160). *J Clin Oncol.* 20 janv 2007;25(3):313-8.
89. Reck M, Rodríguez-Abreu D, Robinson AG, Hui R, Csösz T, Fülöp A, et al. Pembrolizumab versus Chemotherapy for PD-L1-Positive Non-Small-Cell Lung Cancer. *New England Journal of Medicine.* 10 nov 2016;375(19):1823-33.
90. Mok TSK, Wu YL, Kudaba I, Kowalski DM, Cho BC, Turna HZ, et al. Pembrolizumab versus chemotherapy for previously untreated, PD-L1-expressing, locally advanced or metastatic non-small-cell lung cancer (KEYNOTE-042): a randomised, open-label, controlled, phase 3 trial. *Lancet.* 04 2019;393(10183):1819-30.
91. Garassino MC, Cho BC, Kim JH, Mazières J, Vansteenkiste J, Lena H, et al. Durvalumab as third-line or later treatment for advanced non-small-cell lung cancer (ATLANTIC): an open-label, single-arm, phase 2 study. *Lancet Oncol.* avr 2018;19(4):521-36.
92. Mazières J, Drilon A, Lusque A, Mhanna L, Cortot AB, Mezquita L, et al. Immune checkpoint inhibitors for patients with advanced lung cancer and oncogenic driver alterations: results from the IMMUNOTARGET registry. *Ann Oncol.* 24 mai 2019;
93. Herbst RS, Giaccone G, de Marinis F, Reinmuth N, Vergnenegre A, Barrios CH, et al. Atezolizumab for First-Line Treatment of PD-L1-Selected Patients with NSCLC. *N Engl J Med.* 1 oct 2020;383(14):1328-39.
94. Sezer A, Kilickap S, Gümüş M, Bondarenko I, Özgüroğlu M, Gogishvili M, et al. Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial. *The Lancet.* févr 2021;397(10274):592-604.
95. Zukin M, Barrios CH, Pereira JR, Ribeiro RDA, Beato CA de M, do Nascimento YN, et al. 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. *J Clin Oncol.* 10 août 2013;31(23):2849-53.
96. Ferrara R, Mezquita L, Texier M, Lahmar J, Audigier-Valette C, Tessonnier L, et al. Hyperprogressive Disease in Patients With Advanced Non-Small Cell Lung Cancer Treated With PD-1/PD-L1 Inhibitors or With Single-Agent Chemotherapy. *JAMA Oncol.* 01 2018;4(11):1543-52.
97. Gandhi L, Rodríguez-Abreu D, Gadgeel S, Esteban E, Felip E, De Angelis F, et al. Pembrolizumab plus Chemotherapy in Metastatic Non-Small-Cell Lung Cancer. *N Engl J Med.* 31 mai 2018;378(22):2078-92.
98. Socinski MA, Jotte RM, Cappuzzo F, Orlandi F, Stroyakovskiy D, Nogami N, et al. Atezolizumab for First-Line Treatment of Metastatic Nonsquamous NSCLC. *N Engl J Med.* 14 juin 2018;378(24):2288-301.
99. Paz-Ares L, Luft A, Vicente D, Tafreshi A, Gümüş M, Mazières J, et al. Pembrolizumab plus Chemotherapy for Squamous Non-Small-Cell Lung Cancer. *New England Journal of Medicine.* 22 nov 2018;379(21):2040-51.
100. Reck M, Ciuleanu TE, Cobo M, Schenker M, Zurawski B, Menezes J, et al. First-line nivolumab plus ipilimumab with two cycles of chemotherapy versus chemotherapy alone (four cycles) in advanced non-small-cell lung cancer: CheckMate 9LA 2-year update. *ESMO Open.* oct 2021;6(5):100273.
101. Schiller JH, Harrington D, Belani CP, Langer C, Sandler A, Krook J, et al. Comparison of four chemotherapy regimens for advanced non-small-cell lung cancer. *N Engl J Med.* 10 janv 2002;346(2):92-8.
102. Scagliotti GV, Parikh P, von Pawel J, Biesma B, Vansteenkiste J, Manegold C, et al. Phase III study comparing cisplatin plus gemcitabine with cisplatin plus pemetrexed in chemotherapy-naïve patients with advanced-stage non-small-cell lung cancer. *J Clin Oncol.* 20 juill 2008;26(21):3543-51.
103. Novello S, Barlesi F, Califano R, Cufer T, Ekman S, Levra MG, et al. Metastatic non-small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* sept 2016;27(suppl 5):v1-27.
104. Sandler A, Gray R, Perry MC, Brahmer J, Schiller JH, Dowlati A, et al. Paclitaxel-carboplatin alone or with bevacizumab for non-small-cell lung cancer. *N Engl J Med.* 14 déc 2006;355(24):2542-50.
105. Soria JC, Maugué A, Reck M, Sandler AB, Saijo N, Johnson DH, et al. Systematic review and meta-analysis of randomised, phase II/III trials adding bevacizumab to platinum-based chemotherapy as first-line treatment in patients with advanced non-small-cell lung cancer. *Annals of Oncology.* 1 janv 2013;24(1):20-30.
106. Reck M, von Pawel J, Zatloukal P, Ramlau R, Gorbounova V, Hirsh V, et al. Phase III trial of cisplatin plus gemcitabine with either placebo or bevacizumab as first-line therapy for nonsquamous non-small-cell lung cancer: AVAIL. *J Clin Oncol.* 10 mars 2009;27(8):1227-34.
107. Johnson ML, Cho BC, Luft A, Alatorre-Alexander J, Geater SL, Laktionov K, et al. Durvalumab With or Without Tremelimumab in Combination With Chemotherapy as First-Line Therapy for Metastatic Non-Small-Cell Lung Cancer: The Phase III POSEIDON Study. *J Clin Oncol.* 20 févr 2023;41(6):1213-27.
108. Calvert AH, Newell DR, Gumbrell LA, O'Reilly S, Burnell M, Boxall FE, et al. Carboplatin dosage: prospective evaluation of a simple formula based on renal function. *J Clin Oncol.* nov 1989;7(11):1748-56.
109. Quoix E, Zalcman G, Oster JP, Westeel V, Pichon E, Lavolé A, et al. Carboplatin and weekly paclitaxel doublet chemotherapy compared with monotherapy in elderly patients with advanced non-small-cell lung cancer: IFCT-0501 randomised, phase 3 trial. *Lancet.* 17 sept 2011;378(9796):1079-88.
110. Reck M, Rodríguez-Abreu D, Robinson AG, Hui R, Csösz T, Fülöp A, et al. Pembrolizumab versus Chemotherapy for PD-L1-Positive Non-Small-Cell Lung Cancer. *N Engl J Med.* 10 2016;375(19):1823-33.
111. Paz-Ares LG, de Marinis F, Dediu M, Thomas M, Pujol JL, Bidoli P, et al. PARAMOUNT: Final Overall Survival Results of the Phase III Study of Maintenance Pemetrexed Versus Placebo Immediately After Induction Treatment With Pemetrexed Plus Cisplatin for Advanced Nonsquamous Non-Small-Cell Lung Cancer. *Journal of Clinical Oncology.* 10 août 2013;31(23):2895-902.
112. Barlesi F, Scherpereel A, Rittmeyer A, Pazzola A, Ferrer Tur N, Kim JH, et al. Randomized phase III trial of maintenance bevacizumab with or without pemetrexed after first-line induction with bevacizumab, cisplatin, and pemetrexed in advanced nonsquamous non-small-cell lung cancer: AVAPERL (MO22089). *J Clin Oncol.* 20 août 2013;31(24):3004-11.



113. Barlesi F, Scherpereel A, Gorbunova V, Gervais R, Vikström A, Chouaid C, et al. Maintenance bevacizumab-pemetrexed after first-line cisplatin-pemetrexed-bevacizumab for advanced nonsquamous non-small-cell lung cancer: updated survival analysis of the AVAPERL (MO22089) randomized phase III trial. *Ann Oncol.* mai 2014;25(5):1044-52.
114. Pérol M, Chouaid C, Pérol D, Barlési F, Gervais R, Westeel V, et al. Randomized, phase III study of gemcitabine or erlotinib maintenance therapy versus observation, with predefined second-line treatment, after cisplatin-gemcitabine induction chemotherapy in advanced non-small-cell lung cancer. *J Clin Oncol.* 1 oct 2012;30(28):3516-24.
115. Barlesi F, Scherpereel A, Rittmeyer A, Pazzola A, Ferrer Tur N, Kim JH, et al. Randomized phase III trial of maintenance bevacizumab with or without pemetrexed after first-line induction with bevacizumab, cisplatin, and pemetrexed in advanced nonsquamous non-small-cell lung cancer: AVAPERL (MO22089). *J Clin Oncol.* 20 août 2013;31(24):3004-11.
116. Ramalingam SS, Dahlberg SE, Belani CP, Saltzman JN, Pennell NA, Nambudiri GS, et al. Pemetrexed, Bevacizumab, or the Combination As Maintenance Therapy for Advanced Nonsquamous Non-Small-Cell Lung Cancer: ECOG-ACRIN 5508. *J Clin Oncol.* 10 sept 2019;37(26):2360-7.
117. Cortot AB. weekly paclitaxel plus bevacizumab versus Docetaxel as second or third line in advanced non squamous NSCLC: results from the phase III study IFCT-1103 ULTIMATE. ASCO 2016. (abstract 9005).
118. Zhao N, Zhang XC, Yan HH, Yang JJ, Wu YL. Efficacy of epidermal growth factor receptor inhibitors versus chemotherapy as second-line treatment in advanced non-small-cell lung cancer with wild-type EGFR: a meta-analysis of randomized controlled clinical trials. *Lung Cancer.* juill 2014;85(1):66-73.
119. Brahmer J, Reckamp KL, Baas P, Crinò L, Eberhardt WEE, Poddubska E, et al. Nivolumab versus Docetaxel in Advanced Squamous-Cell Non-Small-Cell Lung Cancer. *N Engl J Med.* 9 juill 2015;373(2):123-35.
120. Herbst RS, Baas P, Kim DW, Felip E, Pérez-Gracia JL, Han JY, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial. *Lancet.* 9 avr 2016;387(10027):1540-50.
121. Rittmeyer A, Barlesi F, Waterkamp D, Park K, Ciardiello F, von Pawel J, et al. Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial. *Lancet.* 21 2017;389(10066):255-65.
122. Champiat S, Ferrara R, Massard C, Besse B, Marabelle A, Soria JC, et al. Hyperprogressive disease: recognizing a novel pattern to improve patient management. *Nat Rev Clin Oncol.* déc 2018;15(12):748-62.
123. Nishino M, Tirumani SH, Ramaiya NH, Hodi FS. Cancer immunotherapy and immune-related response assessment: The role of radiologists in the new arena of cancer treatment. *European Journal of Radiology.* juill 2015;84(7):1259-68.
124. Dingemans AMC, Hendriks LEL, Berghmans T, Levy A, Hasan B, Faivre-Finn C, et al. Definition of Synchronous Oligometastatic Non-Small Cell Lung Cancer—A Consensus Report. *Journal of Thoracic Oncology.* déc 2019;14(12):2109-19.
125. Soria JC, Ohe Y, Vansteenkiste J, Reungwetwattana T, Chewaskulyong B, Lee KH, et al. Osimertinib in Untreated EGFR-Mutated Advanced Non-Small-Cell Lung Cancer. *N Engl J Med.* 18 nov 2017;
126. Ramalingam SS, Vansteenkiste J, Planchard D, Cho BC, Gray JE, Ohe Y, et al. Overall Survival with Osimertinib in Untreated, EGFR-Mutated Advanced NSCLC. *N Engl J Med.* 02 2020;382(1):41-50.
127. Reungwetwattana T, Nakagawa K, Cho BC, Cobo M, Cho EK, Bertolini A, et al. CNS Response to Osimertinib Versus Standard Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitors in Patients With Untreated EGFR-Mutated Advanced Non-Small-Cell Lung Cancer. *J Clin Oncol.* 28 août 2018;JCO2018783118.
128. Forde PM, Ettinger DS. Managing acquired resistance in EGFR-mutated non-small cell lung cancer. *Clin Adv Hematol Oncol.* août 2015;13(8):528-32.
129. Yang JCH, Sequist LV, Geater SL, Tsai CM, Mok TSK, Schuler M, et al. Clinical activity of afatinib in patients with advanced non-small-cell lung cancer harbouring uncommon EGFR mutations: a combined post-hoc analysis of LUX-Lung 2, LUX-Lung 3, and LUX-Lung 6. *Lancet Oncol.* juill 2015;16(7):830-8.
130. Bar J, Peled N, Schokrpur S, Wolner M, Rotem O, Girard N, et al. UNcommon EGFR Mutations: International Case Series on Efficacy of Osimertinib in Real-Life Practice in First-Line Setting (UNICORN). *Journal of Thoracic Oncology.* févr 2023;18(2):169-80.
131. Eide IJZ, Stensgaard S, Helland Å, Ekman S, Mellemegaard A, Hansen KH, et al. Osimertinib in non-small cell lung cancer with uncommon EGFR-mutations: a post-hoc subgroup analysis with pooled data from two phase II clinical trials. *Transl Lung Cancer Res.* juin 2022;11(6):953-63.
132. Cho JH, Lim SH, An HJ, Kim KH, Park KU, Kang EJ, et al. Osimertinib for Patients With Non-Small-Cell Lung Cancer Harboring Uncommon EGFR Mutations: A Multicenter, Open-Label, Phase II Trial (KCSG-LU15-09). *JCO.* 10 févr 2020;38(5):488-95.
133. Saito H, Fukuhara T, Furuya N, Watanabe K, Sugawara S, Iwasawa S, et al. Erlotinib plus bevacizumab versus erlotinib alone in patients with EGFR-positive advanced non-squamous non-small-cell lung cancer (NEJ026): interim analysis of an open-label, randomised, multicentre, phase 3 trial. *Lancet Oncol.* mai 2019;20(5):625-35.
134. Hosomi Y, Seto T, Nishio M, Goto K, Yamamoto N, Okamoto I, et al. Erlotinib with or without bevacizumab as a first-line therapy for patients with advanced nonsquamous epidermal growth factor receptor-positive non-small cell lung cancer: Exploratory subgroup analyses from the phase II JO25567 study. *Thorac Cancer.* août 2022;13(15):2192-200.
135. Nakagawa K, Garon EB, Seto T, Nishio M, Ponce Aix S, Paz-Ares L, et al. Ramucirumab plus erlotinib in patients with untreated, EGFR-mutated, advanced non-small-cell lung cancer (RELAY): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol.* 4 oct 2019;
136. Hosomi Y, Morita S, Sugawara S, Kato T, Fukuhara T, Gemma A, et al. Gefitinib Alone Versus Gefitinib Plus Chemotherapy for Non-Small-Cell Lung Cancer With Mutated Epidermal Growth Factor Receptor: NEJ009 Study. *J Clin Oncol.* 4 nov 2019;JCO1901488.
137. Noronha V, Patil VM, Joshi A, Menon N, Chougule A, Mahajan A, et al. Gefitinib Versus Gefitinib Plus Pemetrexed and Carboplatin Chemotherapy in EGFR-Mutated Lung Cancer. *J Clin Oncol.* 14 août 2019;JCO1901154.
138. Cheng Y, Murakami H, Yang PC, He J, Nakagawa K, Kang JH, et al. Randomized Phase II Trial of Gefitinib With and Without Pemetrexed as First-Line Therapy in Patients With Advanced Nonsquamous Non-Small-Cell Lung Cancer With Activating Epidermal Growth Factor Receptor Mutations. *J Clin Oncol.* 20 2016;34(27):3258-66.
139. Mok TS, Wu YL, Ahn MJ, Garassino MC, Kim HR, Ramalingam SS, et al. Osimertinib or Platinum-Pemetrexed in EGFR T790M-Positive Lung Cancer. *N Engl J Med.* 16 2017;376(7):629-40.

140. Lemoine A, Couraud S, Fina F, Lantuejoul S, Lamy PJ, Denis M, et al. Recommandations du GFCO pour l'utilisation diagnostique des analyses génétiques somatiques sur l'ADN tumoral circulant. *Innov Ther Oncol.* 2016;2(5):225-32.
141. Goss G, Tsai CM, Shepherd FA, Bazhenova L, Lee JS, Chang GC, et al. Osimertinib for pretreated EGFR Thr790Met-positive advanced non-small-cell lung cancer (AURA2): a multicentre, open-label, single-arm, phase 2 study. *Lancet Oncol.* 14 oct 2016;
142. Chmielecki J, Gray JE, Cheng Y, Ohe Y, Imamura F, Cho BC, et al. Candidate mechanisms of acquired resistance to first-line osimertinib in EGFR-mutated advanced non-small cell lung cancer. *Nat Commun.* 27 févr 2023;14(1):1070.
143. Schoenfeld AJ, Chan JM, Kubota D, Sato H, Rizvi H, Daneshbod Y, et al. Tumor Analyses Reveal Squamous Transformation and Off-Target Alterations As Early Resistance Mechanisms to First-line Osimertinib in *EGFR*-Mutant Lung Cancer. *Clinical Cancer Research.* 1 juin 2020;26(11):2654-63.
144. Jänne PA, Baik C, Su WC, Johnson ML, Hayashi H, Nishio M, et al. Efficacy and Safety of Patritumab Deruxtecan (HER3-DXd) in EGFR Inhibitor-Resistant, *EGFR*-Mutated Non-Small Cell Lung Cancer. *Cancer Discov.* janv 2022;12(1):74-89.
145. Reck M, Mok TSK, Nishio M, Jotte RM, Cappuzzo F, Orlandi F, et al. Atezolizumab plus bevacizumab and chemotherapy in non-small-cell lung cancer (IMpower150): key subgroup analyses of patients with EGFR mutations or baseline liver metastases in a randomised, open-label phase 3 trial. *Lancet Respir Med.* mai 2019;7(5):387-401.
146. Park K, Haura EB, Leigh NB, Mitchell P, Shu CA, Girard N, et al. Amivantamab in EGFR Exon 20 Insertion-Mutated Non-Small-Cell Lung Cancer Progressing on Platinum Chemotherapy: Initial Results From the CHRYSALIS Phase I Study. *JCO.* 20 oct 2021;39(30):3391-402.
147. Peters S, Camidge DR, Shaw AT, Gadgeel S, Ahn JS, Kim DW, et al. Alectinib versus Crizotinib in Untreated ALK-Positive Non-Small-Cell Lung Cancer. *N Engl J Med.* 31 2017;377(9):829-38.
148. Mok T, Camidge DR, Gadgeel SM, Rosell R, Dziadziuszko R, Kim DW, et al. Updated overall survival and final progression-free survival data for patients with treatment-naïve advanced ALK-positive non-small-cell lung cancer in the ALEX study. *Ann Oncol.* août 2020;31(8):1056-64.
149. Gandhi L, Ou SHI, Shaw AT, Barlesi F, Dingemans AMC, Kim DW, et al. Efficacy of alectinib in central nervous system metastases in crizotinib-resistant ALK-positive non-small-cell lung cancer: Comparison of RECIST 1.1 and RANO-HGG criteria. *Eur J Cancer.* sept 2017;82:27-33.
150. Gadgeel SM, Shaw AT, Govindan R, Gandhi L, Socinski MA, Camidge DR, et al. Pooled Analysis of CNS Response to Alectinib in Two Studies of Pretreated Patients With ALK-Positive Non-Small-Cell Lung Cancer. *J Clin Oncol.* déc 2016;34(34):4079-85.
151. Gadgeel S, Peters S, Mok T, Shaw AT, Kim DW, Ou SI, et al. Alectinib versus crizotinib in treatment-naïve anaplastic lymphoma kinase-positive (ALK+) non-small-cell lung cancer: CNS efficacy results from the ALEX study. *Ann Oncol.* 1 nov 2018;29(11):2214-22.
152. Camidge DR, Dziadziuszko R, Peters S, Mok T, Noe J, Nowicka M, et al. Updated Efficacy and Safety Data and Impact of the EML4-ALK Fusion Variant on the Efficacy of Alectinib in Untreated ALK-Positive Advanced Non-Small Cell Lung Cancer in the Global Phase III ALEX Study. *J Thorac Oncol.* juill 2019;14(7):1233-43.
153. Zhou C, Kim SW, Reungwetwattana T, Zhou J, Zhang Y, He J, et al. Alectinib versus crizotinib in untreated Asian patients with anaplastic lymphoma kinase-positive non-small-cell lung cancer (ALESIA): a randomised phase 3 study. *The Lancet Respiratory Medicine.* mai 2019;7(5):437-46.
154. Camidge DR, Kim HR, Ahn MJ, Yang JCH, Han JY, Lee JS, et al. Brigatinib versus Crizotinib in ALK-Positive Non-Small-Cell Lung Cancer. *N Engl J Med.* 22 nov 2018;379(21):2027-39.
155. Shaw AT, Bauer TM, de Marinis F, Felip E, Goto Y, Liu G, et al. First-Line Lorlatinib or Crizotinib in Advanced ALK-Positive Lung Cancer. *N Engl J Med.* 19 nov 2020;383(21):2018-29.
156. Solomon BJ, Bauer TM, Mok TSK, Liu G, Mazieres J, de Marinis F, et al. Efficacy and safety of first-line lorlatinib versus crizotinib in patients with advanced, ALK-positive non-small-cell lung cancer: updated analysis of data from the phase 3, randomised, open-label CROWN study. *Lancet Respir Med.* 16 déc 2022;S2213-2600(22)00437-4.
157. Solomon BJ, Mok T, Kim DW, Wu YL, Nakagawa K, Mekhail T, et al. First-line crizotinib versus chemotherapy in ALK-positive lung cancer. *N Engl J Med.* 4 déc 2014;371(23):2167-77.
158. Soria JC, Tan DSW, Chiari R, Wu YL, Paz-Ares L, Wolf J, et al. First-line ceritinib versus platinum-based chemotherapy in advanced ALK-rearranged non-small-cell lung cancer (ASCEND-4): a randomised, open-label, phase 3 study. *Lancet.* 4 mars 2017;389(10072):917-29.
159. Gainor JF, Dardaei L, Yoda S, Friboulet L, Leshchiner I, Katayama R, et al. Molecular Mechanisms of Resistance to First- and Second-Generation ALK Inhibitors in ALK-Rearranged Lung Cancer. *Cancer Discov.* 2016;6(10):1118-33.
160. Shaw AT, Gandhi L, Gadgeel S, Riely GJ, Cetnar J, West H, et al. Alectinib in ALK-positive, crizotinib-resistant, non-small-cell lung cancer: a single-group, multicentre, phase 2 trial. *Lancet Oncol.* févr 2016;17(2):234-42.
161. Kim ES, Barlesi F, Mok T, Ahn MJ, Shen J, Zhang P, et al. ALTA-2: Phase II study of brigatinib in patients with ALK-positive, advanced non-small-cell lung cancer who progressed on alectinib or ceritinib. *Future Oncology.* mai 2021;17(14):1709-19.
162. Ou SHI, Nishio M, Ahn MJ, Mok T, Barlesi F, Zhou C, et al. Efficacy of Brigatinib in Patients With Advanced ALK-Positive NSCLC Who Progressed on Alectinib or Ceritinib: ALK in Lung Cancer Trial of brigatinib-2 (ALTA-2). *Journal of Thoracic Oncology.* déc 2022;17(12):1404-14.
163. Shaw AT, Engelman JA. Ceritinib in ALK-rearranged non-small-cell lung cancer. *N Engl J Med.* 26 juin 2014;370(26):2537-9.
164. Cho BC, Kim DW, Bearz A, Laurie SA, McKeage M, Borra G, et al. ASCEND-8: A Randomized Phase 1 Study of Ceritinib, 450 mg or 600 mg, Taken with a Low-Fat Meal versus 750 mg in Fasted State in Patients with Anaplastic Lymphoma Kinase (ALK)-Rearranged Metastatic Non-Small Cell Lung Cancer (NSCLC). *J Thorac Oncol.* sept 2017;12(9):1357-67.
165. Kim DW, Tiseo M, Ahn MJ, Reckamp KL, Hansen KH, Kim SW, et al. Brigatinib in Patients With Crizotinib-Refractory Anaplastic Lymphoma Kinase-Positive Non-Small-Cell Lung Cancer: A Randomized, Multicenter Phase II Trial. *J Clin Oncol.* 1 août 2017;35(22):2490-8.
166. Shaw AT, Felip E, Bauer TM, Besse B, Navarro A, Postel-Vinay S, et al. Lorlatinib in non-small-cell lung cancer with ALK or ROS1 rearrangement: an international, multicentre, open-label, single-arm first-in-man phase 1 trial. *Lancet Oncol.* déc 2017;18(12):1590-9.
167. Lee HY, Ahn HK, Jeong JY, Kwon MJ, Han JH, Sun JM, et al. Favorable clinical outcomes of pemetrexed treatment in anaplastic lymphoma kinase positive non-small-cell lung cancer. *Lung Cancer.* janv 2013;79(1):40-5.



168. Mazières J, Zalcman G, Crinò L, Biondani P, Barlesi F, Filleron T, et al. Crizotinib therapy for advanced lung adenocarcinoma and a ROS1 rearrangement: results from the EUROS1 cohort. *J Clin Oncol.* 20 mars 2015;33(9):992-9.
169. Moro-Sibilot D, Cozic N, Pérol M, Mazières J, Otto J, Souquet PJ, et al. Crizotinib in c-MET- or ROS1-positive NSCLC: results of the AcSé phase II trial. *Ann Oncol.* 4 oct 2019;
170. Drilon A, Siena S, Ou SHI, Patel M, Ahn MJ, Lee J, et al. Safety and Antitumor Activity of the Multitargeted Pan-TRK, ROS1, and ALK Inhibitor Entrectinib: Combined Results from Two Phase I Trials (ALKA-372-001 and STARTRK-1). *Cancer Discov.* 2017;7(4):400-9.
171. Lim SM, Kim HR, Lee JS, Lee KH, Lee YG, Min YJ, et al. Open-Label, Multicenter, Phase II Study of Ceritinib in Patients With Non-Small-Cell Lung Cancer Harboring ROS1 Rearrangement. *J Clin Oncol.* 10 août 2017;35(23):2613-8.
172. Shaw AT, Solomon BJ, Chiari R, Riely GJ, Besse B, Soo RA, et al. Lorlatinib in advanced ROS1-positive non-small-cell lung cancer: a multicentre, open-label, single-arm, phase 1-2 trial. *Lancet Oncol.* 25 oct 2019;
173. Baldacci S, Besse B, Avrillon V, Mennecier B, Mazieres J, Dubray-Longeras P, et al. Lorlatinib for advanced anaplastic lymphoma kinase-positive non-small cell lung cancer: Results of the IFCT-1803 LORLATU cohort. *Eur J Cancer.* mai 2022;166:51-9.
174. the Israel Lung Cancer Group, Dudnik E, Agbarya A, Grinberg R, Cyjon A, Bar J, et al. Clinical activity of brigatinib in ROS1-rearranged non-small cell lung cancer. *Clin Transl Oncol.* déc 2020;22(12):2303-11.
175. Yun MR, Kim DH, Kim SY, Joo HS, Lee YW, Choi HM, et al. Repotrectinib Exhibits Potent Antitumor Activity in Treatment-Naïve and Solvent-Front-Mutant ROS1-Rearranged Non-Small Cell Lung Cancer. *Clin Cancer Res.* 1 juill 2020;26(13):3287-95.
176. Planchard D, Besse B, Groen HJM, Souquet PJ, Quoix E, Baik CS, et al. Dabrafenib plus trametinib in patients with previously treated BRAF(V600E)-mutant metastatic non-small cell lung cancer: an open-label, multicentre phase 2 trial. *Lancet Oncol.* juill 2016;17(7):984-93.
177. Planchard D, Kim TM, Mazieres J, Quoix E, Riely G, Barlesi F, et al. Dabrafenib in patients with BRAF(V600E)-positive advanced non-small-cell lung cancer: a single-arm, multicentre, open-label, phase 2 trial. *Lancet Oncol.* mai 2016;17(5):642-50.
178. Planchard D, Smit EF, Groen HJM, Mazieres J, Besse B, Helland Å, et al. Dabrafenib plus trametinib in patients with previously untreated BRAF V600E -mutant metastatic non-small-cell lung cancer: an open-label, phase 2 trial. *The Lancet Oncology.* oct 2017;18(10):1307-16.
179. Couraud S, Barlesi F, Fontaine-Deraluelle C, Debieuvre D, Merlio JP, Moreau L, et al. Clinical outcomes of non-small-cell lung cancer patients with BRAF mutations: results from the French Cooperative Thoracic Intergroup biomarkers France study. *Eur J Cancer.* juill 2019;116:86-97.
180. Ascierto PA, Ferrucci PF, Fisher R, Del Vecchio M, Atkinson V, Schmidt H, et al. Dabrafenib, trametinib and pembrolizumab or placebo in BRAF-mutant melanoma. *Nat Med.* juin 2019;25(6):941-6.
181. Drilon A, Laetsch TW, Kummar S, DuBois SG, Lassen UN, Demetri GD, et al. Efficacy of Larotrectinib in TRK Fusion-Positive Cancers in Adults and Children. *N Engl J Med.* 22 2018;378(8):731-9.
182. Drilon A, Tan DSW, Lassen UN, Leyvraz S, Liu Y, Patel JD, et al. Efficacy and Safety of Larotrectinib in Patients With Tropomyosin Receptor Kinase Fusion-Positive Lung Cancers. *JCO Precision Oncology.* mai 2022;(6):e2100418.
183. Paik PK, Felip E, Veillon R, Sakai H, Cortot AB, Garassino MC, et al. Tepotinib in Non-Small-Cell Lung Cancer with MET Exon 14 Skipping Mutations. *N Engl J Med.* 3 sept 2020;383(10):931-43.
184. Wolf J, Seto T, Han JY, Reguart N, Garon EB, Groen HJM, et al. Capmatinib in MET Exon 14-Mutated or MET-Amplified Non-Small-Cell Lung Cancer. *N Engl J Med.* 3 sept 2020;383(10):944-57.
185. Lipson D, Capelletti M, Yelensky R, Otto G, Parker A, Jarosz M, et al. Identification of new ALK and RET gene fusions from colorectal and lung cancer biopsies. *Nat Med.* 12 févr 2012;18(3):382-4.
186. Takeuchi K, Soda M, Togashi Y, Suzuki R, Sakata S, Hatano S, et al. RET, ROS1 and ALK fusions in lung cancer. *Nat Med.* 12 févr 2012;18(3):378-81.
187. Cong XF, Yang L, Chen C, Liu Z. KIF5B-RET fusion gene and its correlation with clinicopathological and prognostic features in lung cancer: a meta-analysis. *Onco Targets Ther.* 2019;12:4533-42.
188. Subbiah V, Gainor JF, Rahal R, Brubaker JD, Kim JL, Maynard M, et al. Precision Targeted Therapy with BLU-667 for RET-Driven Cancers. *Cancer Discov.* 2018;8(7):836-49.
189. Gainor JF, Curigliano G, Kim DW, Lee DH, Besse B, Baik CS, et al. Pralsetinib for RET fusion-positive non-small-cell lung cancer (ARROW): a multi-cohort, open-label, phase 1/2 study. *Lancet Oncol.* juill 2021;22(7):959-69.
190. Drilon A, Oxnard GR, Tan DSW, Loong HHF, Johnson M, Gainor J, et al. Efficacy of Selpercatinib in RET Fusion-Positive Non-Small-Cell Lung Cancer. *N Engl J Med.* 27 août 2020;383(9):813-24.
191. Kalchiem-Dekel O, Falcon CJ, Bestvina CM, Liu D, Kaplanis LA, Wilhelm C, et al. Brief Report: Chylothorax and Chylous Ascites During RET Tyrosine Kinase Inhibitor Therapy. *J Thorac Oncol.* sept 2022;17(9):1130-6.
192. Hong DS, Fakih MG, Strickler JH, Desai J, Durm GA, Shapiro GI, et al. KRASG12C Inhibition with Sotorasib in Advanced Solid Tumors. *N Engl J Med.* 24 sept 2020;383(13):1207-17.
193. de Langen AJ, Johnson ML, Mazieres J, Dingemans AMC, Mountzios G, Pless M, et al. Sotorasib versus docetaxel for previously treated non-small-cell lung cancer with KRASG12C mutation: a randomised, open-label, phase 3 trial. *Lancet.* 4 mars 2023;401(10378):733-46.
194. Jänne PA, Riely GJ, Gadgil SM, Heist RS, Ou SHI, Pacheco JM, et al. Adagrasib in Non-Small-Cell Lung Cancer Harboring a *KRAS*^{G12C} Mutation. *N Engl J Med.* 14 juill 2022;387(2):120-31.
195. Li BT, Smit EF, Goto Y, Nakagawa K, Udagawa H, Mazières J, et al. Trastuzumab Deruxtecan in HER2-Mutant Non-Small-Cell Lung Cancer. *N Engl J Med.* 20 janv 2022;386(3):241-51.
196. Le X, Cornelissen R, Garassino M, Clarke JM, Tchekmedyian N, Goldman JW, et al. Pozotinib in Non-Small-Cell Lung Cancer Harboring HER2 Exon 20 Insertion Mutations After Prior Therapies: ZENITH20-2 Trial. *J Clin Oncol.* 29 nov 2021;JCO2101323.
197. Mazieres J, Lafitte C, Ricordel C, Greillier L, Negre E, Zalcman G, et al. Combination of Trastuzumab, Pertuzumab, and Docetaxel in Patients With Advanced Non-Small-Cell Lung Cancer Harboring *HER2* Mutations: Results From the IFCT-1703 R2D2 Trial. *JCO.* 24 janv 2022;JCO.21.01455.
198. Westeel V, Foucher P, Scherpereel A, Domas J, Girard P, Trédaniel J, et al. Chest CT scan plus x-ray versus chest x-ray for the follow-up of completely resected non-small-cell lung cancer (IFCT-0302): a multicentre, open-label, randomised, phase 3 trial. *The Lancet Oncology.* sept 2022;23(9):1180-8.



199. Couraud S, Cortot AB, Greillier L, Gounant V, Mennecier B, Girard N, et al. From randomized trials to the clinic: is it time to implement individual lung-cancer screening in clinical practice? A multidisciplinary statement from French experts on behalf of the french intergroup (IFCT) and the groupe d'Oncologie de langue française (GOLF). *Ann Oncol.* mars 2013;24(3):586-97.
200. Nguyen TK, Senan S, Bradley JD, Franks K, Giuliani M, Guckenberger M, et al. Optimal imaging surveillance after stereotactic ablative radiation therapy for early-stage non-small cell lung cancer: Findings of an International Delphi Consensus Study. *Pract Radiat Oncol.* avr 2018;8(2):e71-8.
201. Denis F, Lethrosne C, Pourel N, Molinier O, Pointreau Y, Domont J, et al. Randomized Trial Comparing a Web-Mediated Follow-up With Routine Surveillance in Lung Cancer Patients. *J Natl Cancer Inst.* 01 2017;109(9).
202. Travis WD, Brambilla E, Burke AP, Marx A, Nicholson AG. Introduction to The 2015 World Health Organization Classification of Tumors of the Lung, Pleura, Thymus, and Heart. *J Thorac Oncol.* sept 2015;10(9):1240-2.
203. Travis WD, Brambilla E, Nicholson AG, Yatabe Y, Austin JHM, Beasley MB, et al. The 2015 World Health Organization Classification of Lung Tumors: Impact of Genetic, Clinical and Radiologic Advances Since the 2004 Classification. *J Thorac Oncol.* sept 2015;10(9):1243-60.