16. Inhibiteurs des Tyrosines Kinases utilisés dans les CBNPC

Le tableau 8 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 « réél » l'évolution des différents types d'autorisation d'accès des médicaments innovants[35].

[35] 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	Digestif - général (asthénie, perte appétit) - hépatique – hémato - cardiaque	ECG (QT)
Afatinib GIOTRIF (Boehringer Ingelheim)	40mg x1/j		20mg 30mg 40mg 50mg	/ 10 à 20mg	**EGFR**	AMM		BH, iono (K), créat	Digestif - Cutané - Pulmonaire - Oculaire ORL (épistaxis, rhinorrhée) - Général, Déshydratation	FEVG / 3 mois
Alectinib ALECENSA (Chugai / Roche)	600mg x2/j		150mg	/ 150mg	**ALK**	AMM		NFS, BH, CPK	Digestif – Cutané - Myalgie – Bradycardie - Pulmonaire – Oculaire – Œdèmes - Anémie	
Brigatinib ALUNBRIG (Takeda)	90mg x1/j 7j puis 180mg x1/j		30mg 90mg 180mg	Voir notice	**ALK**	AMM		NFS, BH, CPK Lipase, Amylase, Gly, iono, créat	Digestif, pancréatique - Général – Hyperglycémie - Pulmonaire – Oculaire - Cardiaque (HTA, Bradycardie) - Œdème - Céphalées, neuropathies périphériques - Cutané - Musculaire	ECG (QT), suivi tensionnel
Capmatinib TABRECTA (Novartis)	400mg x2/j		150mg 200mg	/ 100mg	**MET (ex14)**	Accès précoce (L2)		BH, Lipase, Amylase, Albumine, iono, créat, NFS	Digestif - Général - Cutané - Œdèmes	ECG (QT)
Ceritinib ZYKADIA (Novartis)	450mg x1/j		150mg	/ 150mg	**ALK**	AMM		NFS, BH, Amylase, Lipase, Iono (K), créat, Glycémie	Anémie - Hyperglycémie, hypophosphatémie Pulmonaire – Oculaire - Cardiaque (bradycardie, péricardite, QT) - Digestif, pancréatite - Cutané - Général	ECG (QT)
Crizotinib XALKORI (Pfizer)	250mg x2/j		200mg 250mg	A 200mgx2 ou à 250mgx1	**ALK, ROS1**	AMM		BH, NFS, iono (K), créat	Digestif - Cardiaque (bradycardie, QT) Cutané – hématologique - Pulmonaire - Oculaire	ECG (QT)
Dabrafenib[2] TAFINLAR (Novartis)	150mg x2/j		50mg 75mg	/ 50mg	**BRAF**	AMM (L2)		BH, créat	Hypophosphatémie, hyperglycémie - Céphalées - Pulmonaire – Oculaire - Digestif – Cutané - Musculaire - Général	Examen dermato /mois, jusque 6mois après arrêt (Cancers cutanés)
Entrectinib ROZLYTREK (Roche)	600mg x1/j		100mg 200mg	/ 200mg	**ROS1 NTRK**	AMM européenne (L1) (non remboursé)		BH, Uricémie, NFS, créat, Lipase, Amylase, Albumine, iono, Gly	Neurologique – Musculo-squelettique – Oculaire – Général – Digestif – Pulmonaire – Déshydratation – Cutané – Hypotension	FEVG, ECG (QT)
Erlotinib TARCEVA (Roche & génériques)	150mg x1/j		25mg 100mg 150mg	/ 50mg	**EGFR**	AMM		BH, iono, créat	Cutané – Digestif – Pulmonaire – Oculaire - Général	

Gefitinib IRESSA (Astra Zeneca & génériques)	250mg x1/j	⊕	250mg	Aucune	**EGFR**	AMM		BH, iono (K), créat	Digestif – Cutané – Pulmonaire – Oculaire - Epistaxis	
Larotrectinib VITRAKVI (Bayer)	100mg x2/j	💊	25mg 100mg Sol. Buv. 20mg/ml	/ 25mg	**NTRK**	AMM (L1) (non remboursé)		NFS, BH	Neurologique (vertige, trouble de la marche, paresthésies) – Digestif - Musculo-squelettique - Général	
Lorlatinib LORVIQUA (Pfizer)	100mg x1/j	⊕	25mg 100mg	/ 25mg	**ALK, ROS1**	ALK : AMM (L2 ; en attente du prix L1) ROS1 : Pas d'AMM		NFS, Lipase, Amylase, Cholesterol, Triglycérides, iono	Général – Psychiatrique – Neurologique – Cutané – Oculaire - Musculo-squelettique - Digestif, pancréatique – Oedèmes	ECG (PR)
Mobocertinib EXKIVITY (Takeda)	160mg/j	💊	40mg	NC	**EGFR ins 20**	Accès Compassionel	*(pauvre en matière grasse) Avec 240mL d'eau.*	NFS, créat, BH, amylase, lipase, ionogramme complet (avant, J1C1, J15C1, puis au J1 de chaque cycle)	Digestif, xérose & éruption cutanées, général (fatigue, perte de poids), hématologique (anémie), mucite (buccale), dyspnée & toux, RGO, infection cutannées et onichopathies, désydratation, augmentation de la créatinine de l'amylase et de la lipase, diminution de la natrémie, kaliémie, magnésémie, céphalée, élévation tension artérielle, douleur dorsale - Pulmonaire	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		NFS, BH, iono , créat	Digestif – Cutané – Pulmonaire - Hématologique	ECG (QT)
Poziotinib (Spectrum Pharm.)	16mg/j	⊕	2mg 8mg	/ 2mg	**EGFR ins 20**	Accès Compassionel		NFS, iono	Digestif – cutané -général	NC
Pralsetinib GAVRETO (Roche)	400mg x1/j	💊	100mg	/100mg	**RET**	AMM europpénne (L2) Accès précoce en France (L2)		BH, NFS, iono	Digestif – Pulmonaire - Cardiaque (**HTA**) - Hémato	ECG, TA
Selitrectinib *LOXO-195* (Loxo, Bayer)	NC	💊	25mg 50mg Sol. Buv. 20mg/ml	NC	**NTRK**	Arrêt de développement		NC	NC	NC
Selpercatinib RETEVMO (Lilly)	160mg x2/j	💊	40mg 80mg	/40mg	**RET**	AMM (L2, attente prix)	*si IPP ➔ au cours repas*	BH, créat	Digestif - Cardiaque (HTA) – Général – Œdèmes - Céphalées	ECG
Sotorasib LUMAKRAS	960mg x 1/j (N'est pas un TKI)	⊕	120mg	/240mg	**KRAS G12C**	ATU de cohorte		Iono, créat, NFP, au J1 de chaque cure	Digestif, Hématologique (cytopénies), rénale, hépatique	ECG avant, J1C1,

(Amgen)								Coag, TSH, cholesterol, TG au J1C1		
Tepotinib TEPMETKO (Merck)	2 x 225mg x 1/j	⊕	225mg	/ 225mg	**MET (Ex 14)**	Non disponible (attente AMM)		NFP, iono, créat, BH	Pumonaire – hépatique – oedemes – digestifs – douleurs musculaires – généraux – hématologique - créatinine	
Trametinib[2] MEKINIST (Novartis)	2mg x1/j	⊕	0,5mg 2mg	/ 0,5mg	**MEK**[2]	AMM (L2)		NFS, BH, CPK	Digestif – Oculaire – Musculaire – Cutané – Général – Œdème - Cardiaque (HTA, Altération FEVG) – Pulmonaire - Hématologique	Tension artérielle FEVG /3 mois
Vemurafenib ZELBORAF (Roche)	960mg x2/j	⊕	240mg	/ 240mg	**BRAF**	Hors AMM[1]	*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 (photosensibilité) ECG (QT)

Tableau 8 - Principales modalités d'utilisation des ITK 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. Le vemurafenib ne dispose pas d'AMM dans le cancer du poumon. 2. Utilisé en association au Dabrafénib pour cibler les BRAF V600E.

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

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