

## 12. Réarrangement de *RET*

On estime que 1 à 2% des CBNPC présentent une fusion dans *RET* (117,118). Dans une méta-analyse récente, il semble que les caractéristiques cliniques des patients présentant ce type d'anomalie soient le sexe féminin et le jeune âge (<60 ans), sans impact évident du statut tabagique (119).

Le pralsetinib (BLU-667) est un inhibiteur avec une haute affinité pour *RET* (120). Gainor a rapporté les résultats de l'étude ARROW évaluant le Pralsetinib (400mg x 1/j) chez des patients avec un cancer broncho-pulmonaire présentant un réarrangement *RET* avant 1<sup>ère</sup> ligne par sel de platine (N=29) ; ou progressant après une première ligne de platine (N=92)(121). Le taux de réponse objective de l'ensemble de la population était de 61% (IC95% 50-71) sur les 53 patients évaluable. Le pralsetinib dispose d'une AMM européenne « en monothérapie dans le traitement des patients adultes atteints d'un cancer bronchique non à petites cellules (CBNPC) avancé présentant une fusion positive de *RET* (*REarranged during Transfection*) non précédemment traités par un inhibiteur de *RET* »<sup>32</sup>. Il est disponible en France dans le cadre d'un accès précoce, mais uniquement après un traitement à base de sels de platine<sup>33</sup>.

Le selpercatinib (LOXO-292) est également un inhibiteur de *RET*. Il a montré son intérêt dans le CBNPC dans l'étude LIBRETTO. Le taux de réponse objective était de 70% (taux de contrôle à 95%) avec une médiane de survie sans progression de 18,4 mois chez 105 patients prétraités par une chimiothérapie à base de platine ; chez 39 patients naïfs de traitement : taux de réponse objective à 90%, taux de contrôle à 92% et une médiane de survie sans progression non atteinte (122).

### Recommandation – Cancers de stades avancés avec fusion *RET*

- Le Pralsetinib (4x100mg/j en une fois à jeun) est indiqué chez les patients présentant un réarrangement de *RET*, après progression sous chimiothérapie à base de sel de platine.
- L'inclusion en essai clinique est à privilégier.
- Le Selpercatinib a une AMM en seconde ligne après sel de platine (depuis février 2021) mais ne peut pas être prescrit à la date de rédaction de ce document (attente du prix).

**OPTION :** Les patients présentant un réarrangement de *RET* doivent être orientés vers des essais cliniques.

<sup>32</sup> [https://www.ema.europa.eu/en/documents/product-information/gavreto-epar-product-information\\_fr.pdf](https://www.ema.europa.eu/en/documents/product-information/gavreto-epar-product-information_fr.pdf)

<sup>33</sup> Avis conditionnel HAS juin 2021 : [https://www.has-sante.fr/upload/docs/evamed/CT-19095\\_RETSEVMO\\_PIC\\_INS\\_AvisDef\\_CT19095.pdf](https://www.has-sante.fr/upload/docs/evamed/CT-19095_RETSEVMO_PIC_INS_AvisDef_CT19095.pdf)



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