13. Mutations G12C de *KRAS* et autres

Récemment, plusieurs inhibiteurs spécifiques pour les mutations de *KRAS* G12C ont émergé, en particulier le sotorasib (AMG-510) qui est disponible en ATU de cohorte à la date de rédaction du document (en monothérapie dans le traitement CBNPC KRAS p.G12C muté métastatique, prétraités). Dans une étude de phase I de 59 CBNPC lourdement prétraités, le taux de réponse était de 32,2 %, le taux de contrôle de 88,1 % et la médiane de survie sans progression de 6,3 mois (123).

L'adagrasib (MRTX-849) semble également intéressant dans les études de phase 1/2[34].

OPTION : Les patients présentant une mutation de *KRAS* doivent être orientés vers des essais cliniques, particulièrement ceux présentant une mutation G12C.
En seconde ligne, les patients présentant une mutation KRAS G12C doivent être orientés vers un accès précoce pour le sotorasib s'ils sont inéligibles aux essais cliniques.

14. Mutation HER2 (mutation ou insertion dans l'exon 20)

Plusieurs molécules ont démontrées leur intérêt dans cette indication.

L'anticorps conjugué trastuzumab-deruxtecan a montré un taux de contrôle à 84% et une médiane de durée de réponse à 9,3 mois dans l'essais DESTINY-Lung01 (124).

Le poziotinib a montré des résultats préliminaires intéressants (étude ZENITH 20) (125).

En revanche, l'association Traztuzumab + Pertuzumab + docetaxel (essai IFCT R2D2) est décevante(126).

OPTION : Les patients présentant une mutation ou une insertion dans l'exon 20 de *HER2* doivent être orientés vers des essais cliniques.

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 (103).

[34] Jänne P A et al. KRYSTAL-1: Updated Safety and Efficacy Data With Adagrasib (MRTX849) in NSCLC With KRASG12C Mutation From a Phase 1/2 Study. ENA 2020

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