réponse objective était de 50% (taux de contrôle 66,7%) dans la cohorte biopsie liquide et 45,1% (72,5%) dans la cohorte biopsie tissulaire. On notera que certains patients étaient traités en 1ère ligne avec une réponse objective de bonne qualité (58,8% et 44,4% respectivement). Enfin, le profil de tolérance était correct (19,5% de grades 3 et plus). De même, les données concernant le capmatinib ont été rapportées à l'ASCO 2019[18]. Au total, 69 patients pré-traités et 28 patients de 1ère ligne ont été étudiés. Le taux de réponse objective était respectivement de 40,6% et 67,9% et le taux de contrôle de 78,3% et 96,4%. Le profil de tolérance était correct avec 35,6% de grades 3 et plus.

OPTION : En cas de mutation dans l'exon 14 de MET, une inclusion dans un essai thérapeutique dédié doit être privilégié. Alternativement, une ATU nominative pour le capmatinib peut être demandée en seconde ligne.

11. Réarrangement de *RET*

On estime que 1 à 2% des CBNPC présentent une fusion dans *RET* (104,105). 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 (106).

Le pralsetinib (BLU-667) est un inhibiteur avec une haute affinité pour *RET* (107). A l'ASCO 2019, Gainor a rapporté les premiers 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 1ère ligne par sel de platine (N=40) ; ou progressant après une première ligne de platine (N=80)[19]. Le taux de réponse objective de l'ensemble de la population était de 58% (Taux de contrôle à 96%) sur les 58 patients évaluables (60% et 100% respectivement chez les 35 patients préalablement traités par sels de platine et évaluables).

Le selpercatinib (LOXO-292) est également un inhibiteur de RET. Il a montré son intérêt dans l'étude LIBRETTO rapportée au WCLC 2019[20], auprès de 105 patients avec un cancer bronchique, tous préalablement traités. Le taux de réponse objective était de 68% (Taux de contrôle à 94%) avec une médiane de survie sans progression de 18,4 mois.

OPTION : Les patients présentant un réarrangement de *RET* doivent être orientés vers des essais cliniques. Alternativement, une ATU nominative pour du Pralsetinib ou du Selpercatinib peut être demandée à partir de la seconde ligne.

12. Autres altérations oncogéniques cliniquement pertinentes

Les dossiers des patients présentant une altération oncogénique cliniquement pertinente (mutations *HER2*, autres altérations de *MET*, réarrangements *NRG1*, mutations G12C de *KRAS*) 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 traité par crizotinib dans la cohorte ACSé. Les résultats étaient décevant 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 (94).

On notera egalement l'émergence récente d'inhibiteurs spécifiques pour les mutations de *KRAS* G12C.

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