uncertain, given the current status of this field. However, the efforts by Ma and colleagues will certainly contribute to a growing body of literature that will eventually guide management of this disease.

References

Commentary: Every detail matters—Understanding the impact of KRAS mutations

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Despite surgical resection, 30% to 60% of patients with early-stage non–small cell lung cancer (NSCLC) develop recurrent disease. Adjuvant chemotherapy has shown survival benefit in stages Ib and II NSCLC, but several genetic mutations have been identified in the pathogenesis of lung cancer that affect both prognosis and response to treatment. Moreover, some of these genetic modifications serve as potential targets for therapy in certain patients. Thus, genetic mutation mapping has the potential to guide the staging and treatment of lung cancer. As such, some centers perform mapping on all adenocarcinomas and in up to three-quarters of patients with early-stage disease.

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CENTRAL MESSAGE
The presence of certain KRAS mutations in early-stage lung adenocarcinoma may portend a worse clinical prognosis.
30% of lung adenocarcinomas, have not been identified as a poor prognostic marker despite extensive analyses. This is likely due to heterogeneity among patient cohorts and tumor type. Consistent evidence does show that patients with KRAS mutation do not benefit from adjuvant chemotherapy, but some recent studies have reported variable responses depending on the mutation subtype.

In this issue of the Journal, Ma and colleagues looked to further elucidate the prognostic value of varying KRAS mutations among patients with resected lung adenocarcinoma. As shown in previous studies, the authors found that KRAS mutations were more common in males, smokers (current and former), and patients with solid tumors. Although KRAS mutation was not identified as a prognostic factor for recurrence-free survival or overall survival in the entire cohort, multivariate analyses showed that KRAS mutation was independently associated with shorter recurrence-free and overall survival in part-solid tumors and stage I disease. Survival analysis showed a higher cumulative recurrence rate and worse overall survival in patients with KRAS mutation. Furthermore, mutations in the G12 codon, the most common site of mutation, including those with hydrophobic subgroups G12C and G12V, were associated with worse overall survival compared with non-G12 mutations. This supports the notion that clinical outcomes in patients with KRAS mutation differ depending on codon subtype. While analysis of the cohort as a whole was consistent with previous research, this study shows that the clinical outcomes in patients with KRAS mutation differ depending on codon subtype, among other factors.

Although the application of targeted therapies for KRAS mutations has been largely unsuccessful so far, this type of careful subset analysis of genetic mutation analysis provides valuable information about prognosis for individual patients and may yet lead to alterations in treatment pathways.

References