

Sotorasib for Lung Cancers with KRAS p.G12C Mutation

Skoulidis F et al. DOI: 10.1056/NEJMoa2103695

CLINICAL PROBLEM

The prognosis in patients receiving second or subsequent lines of therapy for advanced non–small-cell lung cancer, including patients with the molecularly diverse and clinically heterogeneous group of cancers with KRAS mutations, is unsatisfactory. A treatment that inhibits the KRAS protein may improve outcomes in patients with these mutations.

CLINICAL TRIAL

Design: A multicenter, single-group, open-label, phase 2 trial to evaluate the efficacy and safety of sotorasib, a selective irreversible inhibitor of the G12C-activated KRAS oncogene.

Intervention: 126 patients with KRAS p.G12C–mutated advanced non–small-cell lung cancer previously treated with standard therapies received an oral dose of 960 mg of sotorasib once daily. The primary end point was objective response as assessed by radiologic review.

RESULTS

Efficacy: Among 124 patients with measurable lesions at baseline, 3.2% had a complete response to sotorasib and 33.9% had a partial response. Median progression-free survival was nearly 7 months.

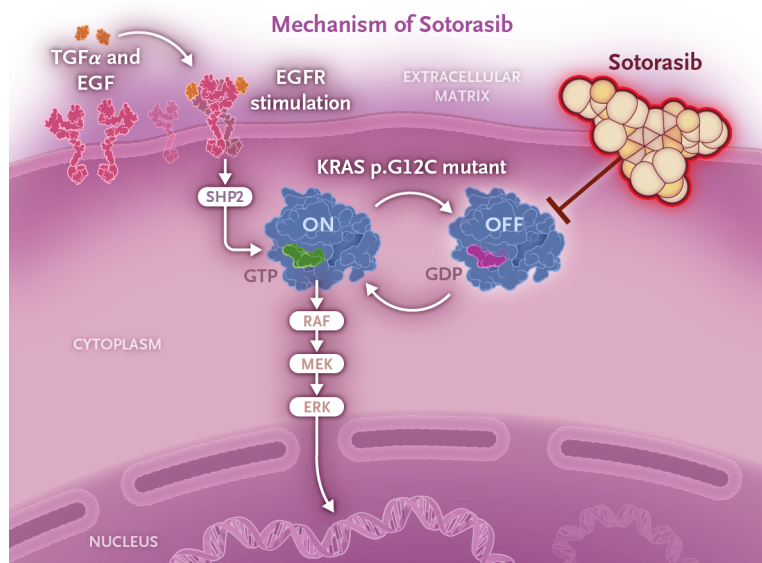
Safety: Grade 4 adverse events deemed to be related to treatment (pneumonitis and dyspnea) were noted in 1 patient, and 25 patients had treatment-related grade 3 events.

LIMITATIONS AND REMAINING QUESTIONS

Further study is required to understand the following:

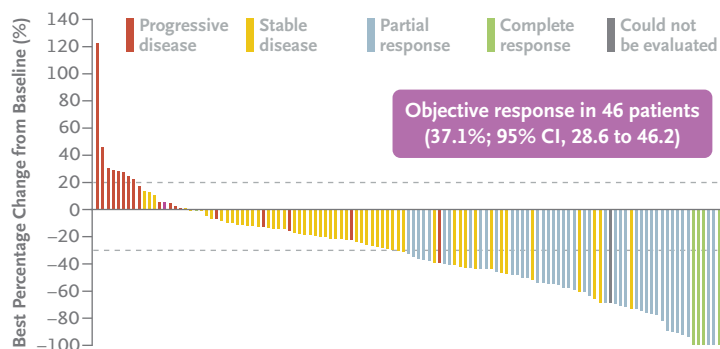
- How sotorasib would fare against a comparison treatment in a randomized clinical trial
- Whether sotorasib combination therapies would improve outcomes
- Whether a subgroup of patients would benefit from sotorasib regimens as first-line treatment

Links: [Full article](#) | [NEJM Quick Take](#)

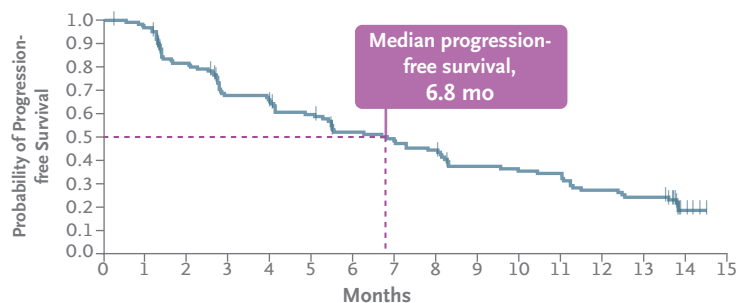


Efficacy of Sotorasib Therapy

Best Percentage Change in Tumor Burden



Progression-free Survival



CONCLUSIONS

In a phase 2 trial, sotorasib therapy led to a durable clinical benefit without new safety signals in patients with previously treated KRAS p.G12C–mutated non–small-cell lung cancer.