Correlation of ctDNA and Response in Patients with PDGFRα D842 GIST Treated with Avapritinib

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INTRODUCTION

- Avapritinib, a potent and selective inhibitor of Kit/CD117 and PDGFRα, has demonstrated clinical activity in patients with PDGFRα-mutant GIST (NCT02508532). Results from the NAVIGATOR study demonstrated a 12-month progression-free survival (PFS) rate of 65% for patients with PDGFRα-mutant GIST treated with avapritinib.
- The objective of this exploratory analysis from the NAVIGATOR study was to determine the utility of ctDNA levels at baseline and on therapy as a correlate of clinical outcomes and potential predictive indicator of response to avapritinib.

METHODS

- Study design: NAVIGATOR is a phase 1, International, open-label, multicenter study evaluating the safety, tolerability, pharmacokinetics, and antitumor activity of avapritinib in patients with advanced solid tumors having activating or therapeutic-salvage Kit/CD117 or PDGFRα mutations.

RESULTS

- Patients and treatments: In the NAVIGATOR study, we evaluated baseline ctDNA levels and findings from ctDNA analyses in patients with PDGFRα-mutant GIST treated with avapritinib in the NAVIGATOR study. Nearly all D842V-mutant GIST treated with avapritinib in the NAVIGATOR study.
- Analysis of ctDNA: This analysis compared the correlation of change in ctDNA levels in patients with PDGFRα-mutant GIST at baseline and on therapy with clinical outcomes. A significant positive correlation was observed between baseline ctDNA levels and response to avapritinib treatment. Patients with lower baseline ctDNA levels had a higher likelihood of achieving an objective response to avapritinib treatment. On therapy, a similar trend was observed, with patients who experienced a reduction in ctDNA levels having a higher likelihood of responding to therapy.

Conclusions

- Avapritinib demonstrated robust clinical activity in patients with PDGFRα-mutant GIST, with a 12-month PFS rate of 65%.
- Large declines in on-treatment ctDNA levels were associated with high probability of response to avapritinib treatment.
- Overall, these data indicate that baseline ctDNA levels may be an additional predictive indicator of response to avapritinib treatment.

References


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