The morbidity of cutaneous melanoma has continued to increase in recent years [1]. Patients with stage III disease are at higher risk for recurrence after locoregional resection and many will ultimately die from metastatic melanoma. BRAF inhibitors vemurafenib and dabrafenib have significantly improved progression-free survival (PFS) and overall survival (OS) as single agents compared with cytotoxic chemotherapy. Acquired resistance to BRAF inhibitors inevitably develops, resulting in a median progression-free survival of 6 to 8 months [6].

Mechanisms of acquired resistance include secondary NRAS or MEK mutations [7]. In preclinical models, combined BRAF and MEK inhibition achieves more via abrogation of MAPK signaling, thereby forestalling the development of acquired resistance and suppressing paradoxical activation of the MAPK pathway [8-14]. Several clinical trials with combination treatment of dabrafenib(150 mg twice daily) plus trametinib(2 mg once daily) in stage III/IV BRAF-mutated melanoma have been reported. These clinical trials identify combination treatment of dabrafenib plus trametinib as front-line therapy in stage III/IV BRAF-mutated melanoma.

Keywords: Dabrafenib; Trametinib; Braf; Mek; Mutant; Melanoma

<table>
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<tr>
<th>Clinical Trial Information</th>
<th>Phase</th>
<th>Stage</th>
<th>Patients Status</th>
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<th>Prior BRAFi</th>
<th>ORR(%)</th>
<th>Efficacy</th>
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<td>Phase I/II trial</td>
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NCT02296996 [12] phase 2 trial IIIc,IV PD 0, 1, or 2 yes 32 Yes (Re-challenge)
NCT01597908 [13] phase 3 trial IIIc,IV untreated patients 0 or 1 no 64 yes
NCT01682083 [14] phase 3 trial III Complete resected 0 or 1 no 3-year OS rate 86 yes

Result

Table 1 the fundamental parameters and efficacy of clinical trials.

Conclusion

These clinical trials identify combination treatment of dabrafenib (150 mg twice daily) plus trametinib (2 mg once daily) as front-line therapy in stage III/IV BRAF-mutated melanoma.

References


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