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TAF MEK melanoma - Mechanism of action - HCP

Prescribing information

Image

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Mechanisms of action of TAFINLAR® (dabrafenib) + MEKINIST® (trametinib)

TAFINLAR in combination with MEKINIST is indicated in adult patients with unresectable or metastatic melanoma with a *BRAF* V600 mutation.[1,2]

TAFINLAR in combination with MEKINIST is indicated for the adjuvant treatment of adult patients with Stage III melanoma with a *BRAF* V600 mutation, following complete resection.[1,2]

For the full safety profile, please refer to the Summary of Product Characteristics (SmPC) for TAFINLAR and MEKINIST.

Adverse event reporting: Details of how to report adverse events are available at the bottom of the page. Please refer to the respective SmPC for all licensed indications.

TAFINLAR + MEKINIST target two distinct points on the mitogen-activated protein kinase (MAPK) pathway to provide concomitant inhibition[1,2]

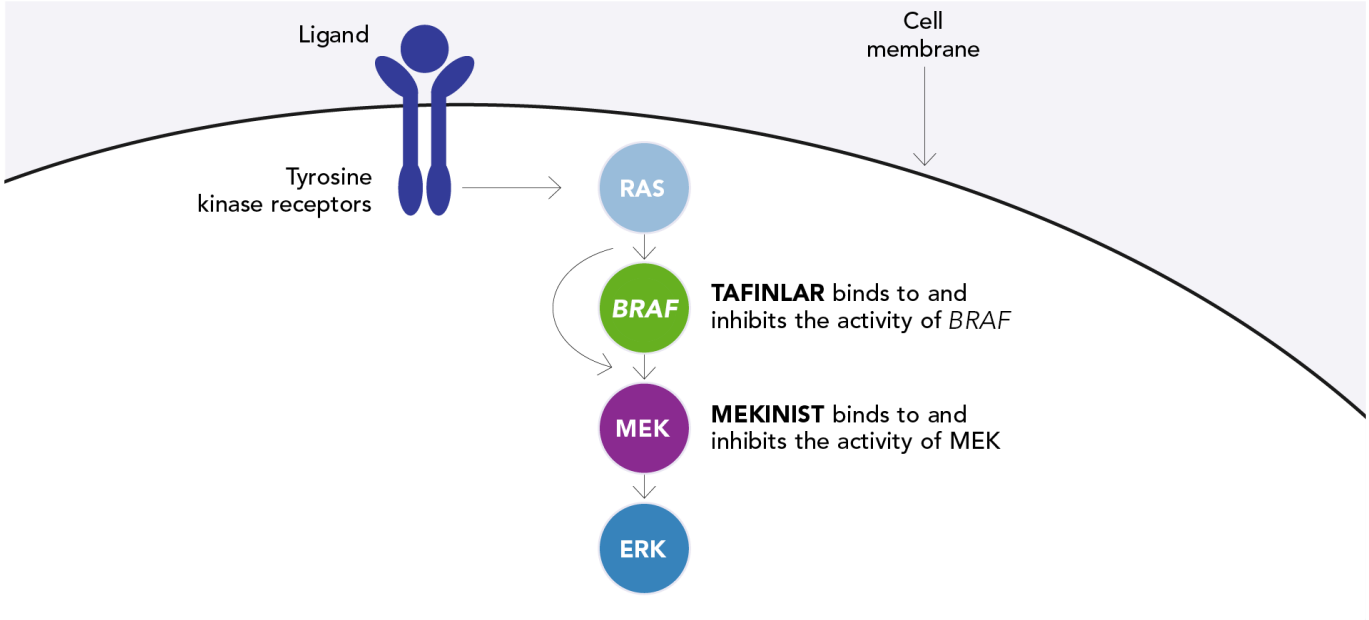
BRAF V600 mutations result in constitutive activation of the MAPK pathway, which plays a key role in regulating the growth, proliferation and survival of normal cells, including melanocytes, which are the cells from which melanoma originates.[3,4] As many as 50% of patients with melanoma harbour mutations of the *BRAF* V600 gene.[5]

In melanoma cells with a *BRAF* V600 mutation, the *BRAF* V600 and mitogen-activated extracellular signal-regulated kinase (MEK) proteins send signals that cause melanoma cells to grow and increase uncontrollably. TAFINLAR + MEKINIST work together to block these signals.[1,2]

TAFINLAR, in combination with MEKINIST, is designed to target the oncogenic driver of *BRAF* V600-positive melanoma. TAFINLAR is an inhibitor of the mutated *BRAF* V600 kinase[1] and MEKINIST is a reversible and highly selective inhibitor of MEK 1 and MEK 2, which sit downstream of *BRAF*.[2] Based on pre-clinical research, combined inhibition of *BRAF* and MEK reduces extracellular signal-related kinase (ERK)-driven gene expression that can cause tumour growth.

Schematic of the MAPK signalling pathway showing where TAFINLAR and MEKINIST act[1,2]

Image



Further information about *BRAF* V600 mutations, the *BRAF* pathway, and the importance of *BRAF* testing in melanoma can also be found here.

Benefits of blocking MEK, in addition to BRAF

Combining TAFINLAR + MEKINIST results in greater inhibition of tumour growth versus either drug alone in *BRAF* V600-positive melanoma[1,2]

Blocking MEK, in addition to *BRAF* in *BRAF* V600-positive melanoma:

- Prolonged inhibition of tumour growth with TAFINLAR + MEKINIST vs TAFINLAR alone (median progression-free survival was 11.0 vs 8.8 months, respectively [hazard ratio=0.67; 95% CI: 0.53–0.84, p= 0.0004])[6]

- Is thought to reduce the risk of treatment resistance vs *BRAF* inhibitor alone, based on pre-clinical research[1–3,7–10]

Cutaneous malignancies are a special warning associated with TAFINLAR + MEKINIST. Please refer to the SmPC for the full guidance.

BRAF V600, mutation of the *BRAF* gene in which valine (V) at amino acid 600; CI, confidence interval; ERK, extracellular signal-related kinase; MAPK, mitogen-activated protein kinase; MEK, mitogen-activated extracellular signal-regulated kinase; RAS, rat sarcoma; SmPC, summary of product characteristics.

References

1. TAFINLAR (dabrafenib) Summary of Product Characteristics.
2. MEKINIST (trametinib) Summary of Product Characteristics.
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