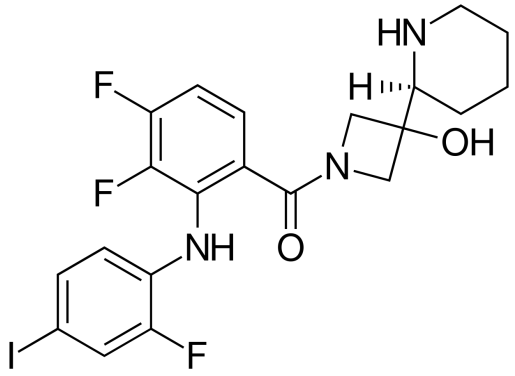
Brand Name: Cotellic
Generic: cobimetinib
Type: small molecule
Year Accepted/Phase: 2015

Mechanism:

Cobimetinib works by inhibiting the activity of MEK1 and MEK2, proteins that are part of the MAPK/ERK pathway. This pathway is often overactive in cancers with BRAF mutations, leading to uncontrolled cell growth. By inhibiting MEK, cobimetinib helps to slow down or stop the growth of these cancer cells.

Chemical Structure:



Indication:

Cotellic is indicated for use in combination with vemurafenib for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation. It may also be used in combination with vemurafenib and atezolizumab for certain patients with the same mutations.

Clinical trials:

BRIM-7 Trial (Phase Ib)
Purpose: Evaluate the safety and preliminary efficacy of cobimetinib in combination with vemurafenib in patients with BRAF V600E or V600K mutation-positive metastatic melanoma.
Dates: Results published in 2014.
Results: The combination showed promising antitumor activity with manageable safety profiles. These encouraging results led to further investigation in a larger Phase III trial.

coBRIM Trial (Phase III)
Purpose: Compare the efficacy and safety of cobimetinib in combination with vemurafenib versus vemurafenib alone in patients with BRAF V600 mutation-positive metastatic melanoma.
Dates: Results published in 2014; FDA approval in November 2015.
Results: The trial demonstrated that the combination of cobimetinib and vemurafenib significantly improved progression-free survival (PFS) and overall survival (OS) compared to vemurafenib alone. Patients receiving the combination therapy had a median PFS of 12.3 months compared to 7.2 months for those on vemurafenib alone. The overall response rate (ORR) was also higher with the combination therapy.

CoBRIM Extension Study (Phase III)
Purpose: Assess the long-term efficacy and safety of cobimetinib in combination with vemurafenib in patients with BRAF V600 mutation-positive metastatic melanoma.
Dates: Results published in subsequent years following the initial approval.
Results: Long-term follow-up data continued to support the benefits of the combination therapy, showing sustained improvements in PFS and OS, with manageable safety profiles.

IMspire150 Trial (Phase III)
Purpose: Evaluate the efficacy and safety of cobimetinib in combination with vemurafenib and atezolizumab (an anti-PD-L1 antibody) compared to cobimetinib and vemurafenib alone in patients with previously untreated BRAF V600 mutation-positive metastatic or unresectable melanoma.
Dates: Results published in 2020.
Results: The addition of atezolizumab to the combination of cobimetinib and vemurafenib showed a significant improvement in PFS, providing a new therapeutic option for these patients.