What Is Tabrecta™ (capmatinib) Tablets?

Indication

TABRECTA™ (capmatinib) tablets is a prescription medicine used to treat adults with a kind of lung cancer called non-small cell lung cancer (NSCLC) that has spread to other parts of the body or cannot be removed by surgery (metastatic), and whose tumors have an abnormal mesenchymal-epithelial transition (MET) gene.

The effectiveness of TABRECTA in these patients is based on a study that measured 2 types of response to treatment (response rate and duration of response). There is no clinical information available to show if patients treated with TABRECTA live longer or if their symptoms improve. There are ongoing studies to find out how TABRECTA works over a longer period of time.

It is not known if TABRECTA is safe and effective in children.[1]

About MET exon 14 skipping

MET exon 14 skipping which occurs in 3%-4% of newly diagnosed patients with metastatic NCSLC, is a recognized oncogenic driver that can result in overstimulation of the MET pathway.[2-4]

Patients with this aggressive form of lung cancer are generally older and often have a poor prognosis.[5]

About Tabrecta

Tabrecta is a kinase inhibitor that targets MET, including the mutant variant produced by exon 14 skipping. Tabrecta blocks the mutant MET signaling pathway.[1]

Pivotal Clinical Trial

GEOMETRY mono-1

GEOMETRY mono-1 is a Phase II multi-center, non-randomized, open-label, multi-cohort study in adult patients with metastatic NSCLC with a mutation that leads to MET exon 14 skipping, and EGFR wild-type, ALK-negative rearrangement. GEOMETRY mono-1 is the pivotal trial that supported the FDA approval of Tabrecta.[1]

The trial evaluated 97 adult patients with metastatic NSCLC harboring mutations that lead to MET exon 14 skipping (centrally confirmed) who were assigned to Cohorts 4 (previously treated patients) or 5B (treatment naive) and received capmatinib tablets 400 mg orally twice daily.[1]

Major efficacy outcome: Overall response rate (ORR) based on Blinded Independent Review Committee (BIRC) assessment set by the Response Evaluation Criteria in Solid Tumors (RECIST v1.1). RECIST measures whether tumors shrink, increase in size, or stay the same in response to treatment.[1]

Additional efficacy outcome: Median duration of response (DOR) by BIRC.[1]

Efficacy

In the population with MET exon 14 skipping (n=97), the confirmed ORR was:

- **68%** (95% CI, 48-84) among treatment-naive patients (n=28)[1]
- **41%** (95% CI, 29-53) among previously treated patients (n=69)[1]

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In patients taking Tabrecta, the study also demonstrated a median DOR of:

- **12.6 months** (95% CI, 5.5-25.3) in treatment-naive patients (19 responders)[1]
  - Patients with DOR ≥ 12 months: 47%[1]
- **9.7 months** (95% CI, 5.5-13) in previously treated patients (28 responders)[1]
  - Patients with DOR ≥ 12 months: 32%[1]

All results were based on independent assessment by the BIRC.[1]

Safety

The most common treatment-related adverse events (incidence ≥20%, all grades) were peripheral edema (52%), nausea (44%), fatigue (32%), vomiting (28%), dyspnea (24%), and decreased appetite (21%).[1]

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Important Safety Information

TABRECTA may cause serious side effects, such as lung or breathing problems. TABRECTA may cause inflammation of the lungs during treatment that may lead to death. Patients should be advised to contact their health care provider right away if they develop any new or worsening symptoms, including cough, fever, trouble breathing, or shortness of breath.

TABRECTA may cause abnormal blood test results, which may be a sign of liver problems. Patients should be advised that their health care provider will do blood tests to check their liver before starting and during treatment with TABRECTA. Patients should be advised to contact their health care provider right away if they develop any signs and symptoms of liver problems including the skin or the white part of their eyes turning yellow (jaundice), dark or “tea-colored” urine, light-colored stools (bowel movements), confusion, loss of appetite for several days or longer, nausea and vomiting, pain, aching, or tenderness on the right side of the stomach area (abdomen), or weakness or swelling in the stomach area.

The skin may be sensitive to the sun (photosensitivity) during treatment with TABRECTA. Patients should be advised to use sunscreen or wear clothes that cover their skin during treatment with TABRECTA to limit direct sunlight exposure.

For women of reproductive potential, TABRECTA can harm their unborn baby. They should use an effective method of birth control during treatment with TABRECTA and for 1 week after the last dose. Men who have partners who can become pregnant should use effective birth control during treatment with TABRECTA and for 1 week after the last dose.

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Before taking TABRECTA, patients should tell their health care provider about all their medical conditions, including if they have or have had lung or breathing problems other than lung cancer, have or have had liver problems, or if they are pregnant or plan to become pregnant, as TABRECTA can harm their unborn babies. Females who are able to become pregnant should have a pregnancy test before they start treatment with TABRECTA and should use effective birth control during treatment and for 1 week after the last dose of TABRECTA. Patients should be advised to talk to their health care provider about birth control choices that might be right for them during this time and to tell their health care provider right away if they become pregnant or think they may be pregnant during treatment with TABRECTA. Males who have female partners who can become pregnant should use effective birth control during treatment and for 1 week after their last dose of TABRECTA.

Patients should tell their health care provider about all the medicines they take or start taking, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

The most common side effects of TABRECTA include swollen hands, ankles, or feet (peripheral edema); nausea and/or vomiting; tiredness and/or weakness (fatigue, asthenia); shortness of breath (dyspnea); loss of appetite; changes in bowel movements (diarrhea or constipation); cough; pain in the chest; fever (pyrexia); back pain; and decreased weight.

Please see full Prescribing Information for Tabrecta available at https://www.novartis.us/sites/www.novartis.us/files/tabrecta.pdf

ALK, anaplastic lymphoma kinase; CT, computer tomography; EGFR, epidermal growth factor receptor; MET, mesenchymal epithelial transition; NSCLC, non-small cell lung cancer.

1. Tabrecta [prescribing Information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2020. **2.** Smyth EC, et al. Emerging molecular targets in oncology: clinical potential of MET/hepatocyte growth-factor inhibitors. *Onco Targets Ther.* 2014;7:1001-1014. **3.** Sadiq AA, Salgia R. MET as a possible target for non-small-cell lung cancer. *J Clin Oncol.* 2013;31:1089-1096. **4.** Salgia R. MET in lung cancer: biomarker selection based on scientific rationale. *Mol Cancer Ther.* 2017;16(4):555-565. **5.** Cappuzzo F, et al. Increased MET gene copy number negatively affects survival of surgically resected non-small-cell lung cancer patients. *J Clin Oncol.* 2009;27:1667-1674.

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