KURZPROTOKOLL
Keynote MK 355

Öffentlicher Titel	Phase-III-Studie zu first-line Pembrolizumab beim dreifach negativen Brustkrebs
Wissenschaftl. Titel	Randomisierte, doppelblinde Phase-III-Studie zu Pembrolizumab (MK-3475) plus Chemotherapie im Vergleich mit Placebo plus Chemotherapie beim nicht vorbehandelten lokal rezidivierten inoperablen oder metastasierten dreifach negativen Mammakarzinom
Kurztitel	Keynote MK 355
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, Pharma-Studie, doppelblind, zweiarmig, kontrolliert
Studienphase	Phase III
Erkrankung	Geschlechtsorgane: Brustkrebs: Erstlinie
Einschlusskriterien	- Have locally recurrent inoperable breast cancer not previously treated with chemotherapy and which cannot be treated with curative intent. OR Have metastatic breast cancer not previously treated with chemotherapy. Note: Subjects with a history of locally recurrent breast cancer, which was previously treated with curative intent, may be eligible. - Have centrally confirmed TNBC, as defined by the most recent ASCO/CAP guidelines. Note: Subjects initially diagnosed with hormone receptor–positive and/or HER2 positive breast cancer must have central confirmation of TNBC in a tumor biopsy obtained from a local recurrence or distant metastasis site. - Have completed treatment for Stage I-III breast cancer, if indicated, and >=6 months elapsed between the completion of treatment with curative intent (e.g., date of primary breast tumor surgery or date of last adjuvant chemotherapy administration, whichever occurred last) and first documented local or distant disease recurrence. Note: Adjuvant radiation therapy is not considered treatment with curative intent for the purpose of calculating the >=6 month interval requirement described above. Note: Subjects who received taxane, gemcitabine, or platinum agents in the (neo)adjuvant setting can be treated with same class of chemotherapy (taxane or gemcitabine/carboplatin), if 12 months have elapsed between the completion of treatment with curative intent (e.g., date of primary breast tumor surgery or date of last adjuvant chemotherapy administration, whichever occurred last) and first documented local or distant disease recurrence. - Have been treated with (neo)adjuvant anthracycline, if they received systemic treatment in the (neo)adjuvant setting, unless anthracycline was contraindicated or not considered the best treatment option for the subject in the opinion of the treating physician. Note: Subjects presenting with de novo metastatic TNBC are eligible for the study, if anthracycline is contraindicated or not considered the best treatment option for the subject in the opinion of the treating physician. - Have measurable disease based on RECIST 1.1 as determined by local radiology review. Note: Target lesions situated in a previously irradiated area are considered measurable, only if they have shown unequivocal progression based on RECIST 1.1 after radiation therapy. Note: Chest wall recurrence can be used as a target lesion, only if measurable by diagnostic quality imaging modality (digital photography alone is not adequate). - Have provided recently or newly obtained core or excisional biopsy from a locally recurrent inoperable or metastatic tumor lesion for central determination of TNBC status and PD-L1 expression, unless contraindicated due to site inaccessibility and/or subject safety concerns. Note: Adequacy of biopsy specimen for the above analyses must be confirmed by the central laboratory. Submission of another tumor specimen may be required, if adequate tumor tissue was not provided the first time. Note: An archival tumor specimen obtained before the diagnosis of locally recurrent inoperable or metastatic breast cancer may be submitted after consultation with the Sponsor, if neither a recently nor a newly obtained biopsy from a locally recurrent inoperable or a metastatic site is available.

- Have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, as assessed within 10 days prior to the start of study treatment.
- Have life expectancy >=12 weeks from randomization.
- Demonstrate adequate organ function, within 10 days prior to the start of study treatment, as defined in the following table.
- Refer to protocol for complete list.

Ausschlusskriterien

- Is currently participating in a clinical study and receiving an investigational agent and/or using an investigational device, or has participated in a clinical study and received an investigational agent and/or used an investigational device within 4 weeks prior to randomization. Note: Subjects who have entered the follow-up phase of a clinical study may participate as long as 4 weeks have elapsed since the last dose of the investigational Agent and/or removal of the device. Note: Subjects who were treated with radiation therapy may participate as long as at least 2 weeks have elapsed since the last dose of radiation therapy was administered.
- Has not recovered (e.g., to <=Grade 1 or to baseline) from AEs due to a previously administered therapy. Note: Alopecia of any grade is an exception to this criterion. Note: Prior to randomization, the subject must have recovered adequately from any toxicity and/or complications associated with any recent procedure.
- Has neuropathy >=Grade 2.
- Has an active autoimmune disease that has required systemic treatment in the past 2 years (e.g., with use of disease modifying agents, corticosteroids, or immunosuppressive drugs). Replacement therapy (e.g., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is not considered a form of systemic treatment.
- Has a diagnosis of immunodeficiency or is receiving systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to randomization.
- Has a known additional malignancy that progressed or required active treatment within the last 5 years. Exceptions include basal cell carcinoma of the skin, squamous cell carcinoma of the skin that has undergone potentially curative therapy, and in situ cervical cancer.
- Has known active CNS metastases and/or carcinomatous meningitis. Subjects with previously treated brain metastases may participate provided they have stable brain metastases and did not receive chemotherapy for metastatic breast cancer. Note: Known brain metastases are considered active, if any of the following criteria are applicable: a) Brain imaging during screening demonstrates progression of existing metastases and/or appearance of new lesions compared to brain imaging performed at least 4 weeks earlier. Radiographic stability of previously treated brain metastases is based on local radiology/investigator review, but dated reports of 2 imaging studies (the most recent performed during screening) documenting stability of brain metastasis(es) over >=4 weeks must be submitted to the Sponsor. Such brain imaging studies should be available at the site for submission to CIV, if later needed; b) Neurological symptoms attributed to brain metastases have not returned to baseline; c) Steroids were used for management of symptoms related to brain metastases within 28 days of randomization
- Has history of (non-infectious) pneumonitis that required steroids or current pneumonitis.
- Has received prior therapy with an anti–PD-1, anti–PD-L1, or anti–PD-L2 agent or with an agent directed to another co-inhibitory T cell receptor (such as CTLA-4, OX 40, CD137) or has previously participated in Merck pembrolizumab (MK-3475) clinical studies.
- Refer to protocol for compete list.

Alter

18 Jahre und älter

Molekularer Marker	Triple neg (HER2/ER/PR neg)
Sponsor	MSD Sharp & Dohme
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT02819518 (primäres Register) EudraCT 2016-001432-35