KURZPROTOKOLL
Keylink

Öffentlicher Titel	Phase II/III Studie zu Olaparib plus Pembrolizumab nach der Induktion bei dreifach negativem Brustkrebs
Wissenschaftl. Titel	An Open-label, Randomized, Phase 2/3 Study of Olaparib Plus Pembrolizumab Versus Chemotherapy Plus Pembrolizumab After Induction of Clinical Benefit With First-line Chemotherapy Plus Pembrolizumab in Participants With Locally Recurrent Inoperable or Metastatic Triple Negative Breast Cancer (TNBC)
Kurztitel	Keylink
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, offen/unverblindet, zweiarmig
Studienphase	Phase II/III
Erkrankung	Geschlechtsorgane: Brustkrebs: Erstlinie
Einschlusskriterien	- Induction Period - Has locally recurrent inoperable TNBC that has not previously been treated with chemotherapy and that cannot be treated with curative intent OR has metastatic TNBC that has not been previously treated with chemotherapy - Has been treated with anthracycline and/or a taxane in the neoadjuvant/adjuvant setting, if they received systemic treatment in the neoadjuvant/adjuvant setting, unless anthracycline and/or taxane was contraindicated or not considered the best treatment option for the participant in the opinion of the treating physician - Has measurable disease based on RECIST 1.1 - Has provided a recently obtained or archival (no more than 3 years old) core or excisional biopsy of a tumor lesion not previously irradiated - Has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 as assessed within 7 days prior to the start of induction study treatment - Has a life expectancy >= 27 weeks from the day of first study treatment - A male participant must agree to be abstinent or use contraception and refrain from donating sperm during the intervention period and for at least 180 days after the last dose of study treatment - A female participant must not be pregnant or breastfeeding and must agree to the following if is a woman of childbearing potential (WOCBP): have a negative pregnancy test within 24 hours before the start of study treatment and agree to be abstinent or use contraception and refrain from donating eggs (ova, oocytes) during the intervention period and for at least 180 days after the last dose of study treatment - Post-induction Period - Has received up to 6 cycles but not less than 4 cycles of induction therapy without permanently discontinuing from pembrolizumab or both carboplatin and gemcitabine - Has achieved complete response (CR), partial response (PR), or stable disease (SD) based on RECIST 1.1 by Blinded Independent Central Review (BICR) at the Week 18 evaluation - Is able to complete during post-induction at least the Cycle 1, Day 1 doses of olaparib and pembrolizumab or the Cycle 1, Day 1 doses of at least one of the chemotherapy agents being administered at the end of induction (carboplatin and/or gemcitabine) in addition to pembrolizumab - Has ECOG performance status of 0 or 1, as assessed within 7 days prior to the start of post-induction study treatment - Has no higher than Grade 1 toxicities related to induction therapy (excluding alopecia) prior to randomization
Ausschlusskriterien	- Induction Period

- Has a known additional malignancy that is progressing or has required active treatment within the past 5 years with the exception of basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or carcinoma in situ (eg, cervical cancer in situ) that have undergone potentially curative therapy
- Has a diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy (in dosing exceeding 10 mg daily of prednisone equivalent) or any other form of immunosuppressive therapy within 7 days prior the first dose of study treatment
- Has an active autoimmune disease that has required systemic treatment in the past 2 years
- Has known active central nervous system (CNS) metastases and/or carcinomatous meningitis
- Has myelodysplastic syndrome (MDS)/acute myeloid leukemia (AML) or has features suggestive of MDS/AML
- Has a history of (non-infectious) pneumonitis that required steroids or current pneumonitis
- Has active, or a history of, interstitial lung disease
- Has a known history of active tuberculosis
- Has an active infection requiring systemic therapy
- Has a known history of human immunodeficiency virus (HIV) infection
- Has a known history of Hepatitis B (defined as Hepatitis B surface antigen [HBsAg] reactive) or known active Hepatitis C virus (defined as HCV RNA [qualitative] is detected) infection
- Has a history of class II-IV congestive heart failure or myocardial infarction within 6 months of first study treatment
- Has neuropathy >= Grade 2
- Has not recovered (eg, to <= Grade 1 or to baseline) from AEs due to a previously administered therapy
- Has a known history of hypersensitivity or allergy to pembrolizumab, olaparib and any of its components, and/or to any of the study chemotherapies (eg, carboplatin or gemcitabine) and any of their components
- Has severe hypersensitivity (>=Grade 3) to the study treatments and/or any of their excipients
- Has a known psychiatric or substance abuse disorder that would interfere with the participant's ability to cooperate with the requirements of the study
- Is pregnant or breastfeeding, or expecting to conceive or father children within the projected duration of the study, starting with the Screening Visit through 180 days after the last dose of study treatment
- Is a WOCBP who has a positive urine pregnancy test within 24 hours prior to randomization or treatment allocation
- Has received prior therapy with either olaparib or any other poly adenosine diphosphate ribose polymerase (PARP) inhibitor
- Has received prior radiotherapy within 2 weeks of start of study treatment
- Has received colony-stimulating factors (eg, granulocyte colony stimulating factor [G-CSF], granulocyte macrophage colony stimulating factor [GM-CSF] or recombinant erythropoietin) within 2 weeks prior to the first dose of study treatment
- Has had an allogenic tissue/solid organ transplant
- Has received previous allogenic bone marrow transplant or double umbilical cord transplantation (dUCBT)

	- Has had major surgery within 2 weeks of starting study treatment or has not recovered from any effects of any major surgery - Has received a live vaccine within 30 days prior to first study treatment - Is receiving any medication prohibited in combination with study chemotherapies unless medication was stopped within 7 days prior to first study treatment - 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 cytotoxic T-lymphocyte-associated protein 4 [CTLA-4], OX-40, CD137) or has previously participated in a study evaluating pembrolizumab regardless of treatment received - Is currently participating in or has participated in a study of an investigational agent or has used an investigational device within 4 weeks prior to the first dose of study treatment - Has a resting electrocardiogram (ECG) indicating uncontrolled, potentially reversible cardiac conditions, as judged by the investigator - Has a history or current evidence of any condition (eg, cytopenia, transfusion-dependent anemia, or thrombocytopenia), therapy, or laboratory abnormality that might confound the results of the study, interfere with the participant's involvement for the full duration of the study, or is not in the best interest of the participant to be involved, in the opinion of the treating investigator - Is either unable to swallow orally administered medication or has a gastrointestinal disorder affecting absorption (eg, gastrectomy, partial bowel obstruction, malabsorption) - Is unlikely to comply with the study procedures, restrictions, and requirements of the study; as judged by the investigator - Post-induction Period - Has severe hypersensitivity (>=Grade 3) to the study treatments and/or any of their excipients - Has permanently discontinued from both carboplatin and gemcitabine during induction due to toxicity - Has permanently discontinued from pembrolizumab during induction due to toxicity - Has received less than 4 cycles of chemotherapy plus pembrolizumab during induction - Is currently receiving either strong or moderate inhibitors of cytochrome P450 (CYP)3A4 that cannot be discontinued for the duration of the study - Is currently receiving either strong or moderate inducers of CYP3A4 that cannot be discontinued for the duration of the study
Alter	18 Jahre und älter
Molekularer Marker	HER2/neu neg. Triple neg (HER2/ER/PR neg) ER/PR neg.
Sponsor	MSD Sharp & Dohme (Hauptsponsor)
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT04191135 (primäres Register) EudraCT 2019-001892-35