	CRITERES DE SELECTION ETUDE MK- 7684A-005	Identité patient (coller étiquette patient)
Version 2.0 du 27/04/2021	Investigateur en charge du patient : PI : Pr GHIRINGHELLI	Arc : <i>Magali poste 3210.</i>

ETUDE MK-7684A-005

« A Multicenter, Open-label, Phase 2 Basket Study of MK-7684A, a Coformation of Vibostolimab (MK-7684) with Pembrolizumab (MK-3475), With or Without Other Anticancer Therapies in Participants with Selected Solid Tumors »


Cohorte F : Cancer du Sein triple négatif

VALIDATION DES CRITERES DE SELECTION

Critères d'inclusion

A participant will be eligible for inclusion in the study if the participant :

Type of Participant and Disease Characteristics	
<p>1. Has histologically or cytologically confirmed, advanced (locally recurrent unresectable or metastatic) solid tumor as follows:</p> <p>Cohort F: locally confirmed TNBC, as defined by the most recent ASCO/CAP guidelines, that is either locally recurrent unresectable not previously treated with chemotherapy and that cannot be treated with curative intent or metastatic that has not been previously treated with chemotherapy.</p> <p><u>Note:</u> Participants initially diagnosed with hormone receptor positive and/or HER2/neupositive breast cancer must have local confirmation of TNBC in a tumor biopsy obtained from a local recurrence or distant metastasis site.</p> <p><u>Note:</u> Participants with a history of locally recurrent TNBC, which was previously treated with curative intent, may be eligible.</p> <p><u>Note:</u> Participants with de novo metastatic TNBC are eligible if anthracycline is contraindicated or not considered the best treatment option for the participant in the opinion of the treating physician.</p> <p><u>Note:</u> For participants initially diagnosed with Stage I-III breast cancer, ≥ 6 months must have elapsed between the completion of treatment with curative intent (eg, date of primary breast tumor surgery or date of last adjuvant chemotherapy administration, whichever occurred last) and first documented local or distant disease recurrence. Adjuvant radiation therapy is not considered treatment with curative intent for the purpose of calculating the ≥ 6-month interval requirement.</p> <p><u>Note:</u> First documentation of local or distant disease recurrence must be in the form of a dated biopsy, pathology, or imaging study report. A laboratory report indicating tumor marker elevation cannot be used as documentation of local or distant disease recurrence, unless accompanied by dated biopsy, pathology, or imaging study report.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non

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<p><u>Note:</u> For participants who received a taxane in the (neo)adjuvant setting, ≥ 12 months must have elapsed between the completion of treatment with curative intent (eg, date of primary breast tumor surgery or date of last adjuvant chemotherapy administration, whichever occurred last) and first documented local or distant disease recurrence.</p>	
<p>2. Has measurable disease per RECIST 1.1 local site investigator/radiology. Lesions situated in a previously irradiated area are considered measurable if progression has been demonstrated in such lesions.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>3. Can provide a newly obtained core or excisional biopsy of a tumor lesion or either an archival FFPE tumor tissue block or slides for determination of biomarker status (eg, PD-L1, MMR, ER, PgR, BRCA, and HER2/neu). A newly obtained biopsy is preferred, but not required if archival tissue is available for analysis.</p> <p><u>Note:</u> For planned exploratory biomarker analyses, FFPE tumor blocks are preferred to slides (refer to Section 8.1.12).</p> <p><u>Note:</u> Participants who have undergone ER and PgR, HER2/neu testing as part of standard of care do not need to have the test repeated for the purpose of this study.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
Demographics	
<p>4. Is male or female, who is at least 18 years of age at the time of signing the informed consent.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>5. Has an ECOG performance status of either 0 or 1, as assessed within 7 days before starting study intervention.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>6. Has a predicted life expectancy of at least 3 months.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
Male Participants cohorte F (MK-7684A+ chemotherapy)	
<p>7. Male participants are eligible to participate if they agree to the following during the intervention period and for at least 95 days after the last dose of chemotherapy:</p>	<input type="checkbox"/> oui <input type="checkbox"/> non

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<ul style="list-style-type: none"> • Refrain from donating sperm PLUS either: <ul style="list-style-type: none"> • Be abstinent from heterosexual intercourse as their preferred and usual lifestyle (abstinent on a long-term and persistent basis) and agree to remain abstinent OR <ul style="list-style-type: none"> • Must agree to use contraception unless confirmed to be azoospermic (vasectomized or secondary to medical cause [Appendix 5]) as detailed below: <ul style="list-style-type: none"> - Agree to use a male condom plus partner use of an additional contraceptive method when having penile-vaginal intercourse with a WOCBP who is not currently pregnant. Note: Men with a pregnant or breastfeeding partner must agree to remain abstinent from penile-vaginal intercourse or use a male condom during each episode of penile-vaginal penetration. • Contraceptive use by men should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies. If the contraception requirements in the local label for any of the study interventions is more stringent than the requirements above, the local label requirements are to be followed. 	
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Female Participants for cohorte F (MK-7684A+ chemotherapy)

<p>8 . A female participant is eligible to participate if she is not pregnant or breastfeeding, and at least one of the following conditions applies:</p> <ul style="list-style-type: none"> • Is not a WOCBP OR <ul style="list-style-type: none"> • Is a WOCBP and using a contraceptive method that is highly effective (with a failure rate of <1% per year), with low user dependency, or be abstinent from heterosexual intercourse as their preferred and usual lifestyle (abstinent on a long-term and persistent basis), as described in Appendix 5 during the intervention period and for at least 120 days after the last dose of MK-7684A or 180 days after the last dose of chemotherapy, whichever occurs last and/or is greater, and agrees not to donate eggs (ova, oocytes) to others or freeze/store for her own use for the purpose of reproduction during this period. The investigator should evaluate the potential for contraceptive method failure (ie, noncompliance, recently initiated) in relationship to the first dose of study intervention. <ul style="list-style-type: none"> ➤ A WOCBP must have a negative highly sensitive pregnancy test (urine or serum as required by local regulations) within either 24 hours (urine) or 72 hours (serum) before the first dose of study intervention. ➤ If a urine test cannot be confirmed as negative (eg, an ambiguous result), a serum pregnancy test is required. In such cases, the participant must be excluded from participation if the serum pregnancy result is positive. 	<input type="checkbox"/> oui <input type="checkbox"/> non
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<ul style="list-style-type: none"> ➤ Additional requirements for pregnancy testing during and after study intervention are in Section 8.3.7.2. ➤ The investigator is responsible for review of medical history, menstrual history, and recent sexual activity to decrease the risk for inclusion of a woman with an early undetected pregnancy. ➤ Contraceptive use by women should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies. 	
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Informed Consent

9. The participant (or legally acceptable representative) has provided documented informed consent/assent for the study.	<input type="checkbox"/> oui <input type="checkbox"/> non
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Additional Categories

10. HIV-infected participants must have well controlled HIV on ART, defined as: <ul style="list-style-type: none"> • Participants on ART must have a CD4+ T-cell count >350 cells/mm³ at the time of Screening • Participants on ART must have achieved and maintained virologic suppression defined as confirmed HIV RNA level below 50 or the LLOQ (below the limit of detection) using the locally available assay at the time of Screening and for at least 12 weeks before Screening • Participants on ART must have been on a stable regimen, without changes in drugs or dose modification, for at least 4 weeks before study entry (randomization/allocation). • The combination ART regimen must not contain any antiretroviral medications other than: abacavir, dolutegravir, emtricitabine, lamivudine, raltegravir, rilpivirine, or tenofovir • HIV screening test is required for study entry and need to be performed to evaluate eligibility. This testing can be performed at any time during the Screening period. Refer to Appendix 7 for country-specific requirements 	<input type="checkbox"/> oui <input type="checkbox"/> non
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11. Participants who are HBsAg positive are eligible if they have received HBV antiviral therapy for at least 4 weeks and have undetectable HBV viral load before randomization/allocation. <u>Note:</u> Participants should remain on antiviral therapy throughout study intervention and follow local guidelines for HBV antiviral therapy post completion of study intervention. Hepatitis B screening test is required for study entry and need to be performed to evaluate eligibility. This testing can be performed at any time during the Screening period. Refer to Appendix 7 for country-specific requirements	<input type="checkbox"/> oui <input type="checkbox"/> non
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<p>12. Participants with history of HCV infection are eligible if HCV viral load is undetectable at Screening.</p> <p><u>Note:</u> Participants must have completed curative antiviral therapy at least 4 weeks before randomization/allocation.</p> <p>Hepatitis C screening test is required for study entry and need to be performed to evaluate eligibility. This testing can be performed at any time during the Screening period. Refer to Appendix 7 for country-specific requirements.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non																								
<p>13. Has adequate organ function as defined in [Table 5]. Specimens must be collected within 10 days before the start of study intervention. Refer to Appendix 7 for country specific requirements</p> <p>Table 5 Adequate Organ Function Laboratory Values</p> <table border="1" style="width: 100%; border-collapse: collapse; margin-top: 10px;"> <thead> <tr> <th style="width: 50%; text-align: center;">System</th> <th style="width: 50%; text-align: center;">Laboratory Value</th> </tr> </thead> <tbody> <tr> <td colspan="2">Hematological</td> </tr> <tr> <td>Absolute neutrophil count (ANC)</td> <td>>1500/μL</td> </tr> <tr> <td>Platelets</td> <td>>100,000/μL</td> </tr> <tr> <td>Hemoglobin</td> <td>\geq9 g/dL or \geq5.6 mmol/L^a</td> </tr> <tr> <td colspan="2">Renal</td> </tr> <tr> <td> Creatinine AND^b/OR Measured or calculated e creatinine clearance (GFR can also be used in place of creatinine or CrCl) </td> <td> \leq1.5 \times ULN AND^b/OR \geq30 mL/min for participants with creatinine levels $>$1.5 \times institutional ULN \geq60 mL/min for participants with creatinine levels $>$1.5 \times institutional ULN (Cohort E only)^a </td> </tr> <tr> <td colspan="2">Hepatic</td> </tr> <tr> <td>Total bilirubin</td> <td>\leq1.5 \timesULN OR direct bilirubin \leqULN for participants with total bilirubin levels $>$1.5 \times ULN</td> </tr> <tr> <td>AST (SGOT) and ALT (SGPT)</td> <td>\leq2.5 \times ULN (\leq5 \times ULN for participants with liver metastases)*</td> </tr> <tr> <td colspan="2">Coagulation</td> </tr> <tr> <td>INR or PT aPTT/PTT</td> <td>\leq1.5 \times ULN unless participant is receiving anticoagulant therapy as long as PT or PTT is within therapeutic range of intended use of anticoagulants</td> </tr> </tbody> </table>	System	Laboratory Value	Hematological		Absolute neutrophil count (ANC)	>1500/ μ L	Platelets	>100,000/ μ L	Hemoglobin	\geq 9 g/dL or \geq 5.6 mmol/L ^a	Renal		Creatinine AND ^b /OR Measured or calculated e creatinine clearance (GFR can also be used in place of creatinine or CrCl)	\leq 1.5 \times ULN AND ^b /OR \geq 30 mL/min for participants with creatinine levels $>$ 1.5 \times institutional ULN \geq 60 mL/min for participants with creatinine levels $>$ 1.5 \times institutional ULN (Cohort E only) ^a	Hepatic		Total bilirubin	\leq 1.5 \times ULN OR direct bilirubin \leq ULN for participants with total bilirubin levels $>$ 1.5 \times ULN	AST (SGOT) and ALT (SGPT)	\leq 2.5 \times ULN (\leq 5 \times ULN for participants with liver metastases)*	Coagulation		INR or PT aPTT/PTT	\leq 1.5 \times ULN unless participant is receiving anticoagulant therapy as long as PT or PTT is within therapeutic range of intended use of anticoagulants	<input type="checkbox"/> oui <input type="checkbox"/> non
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<p>Abbreviations: ALT (SGPT) = alanine aminotransferase (serum glutamic-pyruvic transaminase); aPTT = activated partial thromboplastin time; AST (SGOT) = aspartate aminotransferase (serum glutamic-oxaloacetic transaminase); GFR=glomerular filtration rate; INR = international normalized ratio; PT = prothrombin time; PTT = partial thromboplastin time; ULN=upper limit of normal.</p> <p>a. Criteria must be met without erythropoietin dependency and without packed red blood cell transfusion within last 2 weeks.</p> <p>b. Applicable only when local guidelines require both assessments.</p> <p>c. CrCl should be calculated per institutional standard.</p> <p>d. The cisplatin product label should be followed for acceptable creatinine clearance rates.</p> <p>Note: This table includes eligibility-defining laboratory value requirements for treatment; laboratory value requirements should be adapted according to local regulations and guidelines for the administration of specific chemotherapies..</p>	
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Critères de non inclusion

The participant must be excluded from the study if the participant :


Medical Conditions	
<p>1. Has a history of a second malignancy, unless potentially curative treatment has been completed with no evidence of malignancy for 3 years.</p> <p><u>Note:</u> The time requirement does not apply to participants who underwent successful definitive resection of basal cell carcinoma of the skin, squamous cell carcinoma of the skin, in-situ cervical cancer, or other in-situ cancers.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>2. HIV-infected participants with a history of Kaposi's sarcoma and/or Multicentric Castleman's Disease</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
Prior/Concomitant Therapy	
<p>3. Has received prior therapy with an anti-PD-1, anti-PD-L1, anti-PD-L2, or anti-TIGIT agent.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>4. Has received prior systemic anticancer therapy including investigational agents within 4 weeks before randomization/allocation.</p> <p><u>Note:</u> Participants must have recovered from all AEs due to previous therapies to \leqGrade 1 or baseline. Participants with \leqGrade 2 neuropathy may be eligible. Participants with endocrine-related AEs Grade \leq2 requiring treatment or hormone replacement may be eligible. Participants with Grade \leq2 alopecia are eligible.</p> <p><u>Note:</u> If the participant had a major operation, the participant must have recovered adequately from the procedure and/or any complications from the operation before starting study intervention.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>5. Has received prior radiotherapy within 2 weeks of start of study intervention. Participants must have recovered from all radiation-related toxicities, not require corticosteroids, and not have had radiation pneumonitis. A 1-week washout is permitted for palliative radiation (\leq2 weeks of radiotherapy) to non-CNS disease.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non

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<p>6. Has received a live or live-attenuated vaccine within 30 days before the first dose of study intervention. Administration of killed vaccines are allowed.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
Prior/Concurrent Clinical Study Experience	
<p>7. Is currently participating in or has participated in a study of an investigational agent or has used an investigational device within 4 weeks before the first dose of study intervention.</p> <p><u>Note:</u> Participants who have entered the follow-up phase of an investigational study may participate as long as it has been 4 weeks after the last dose of the previous investigational agent.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
Diagnostic Assessments	
<p>8. Has a diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy (dosing exceeding 10 mg daily of prednisone equivalent) or any other form of immunosuppressive therapy within 7 days before the first dose of study medication.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>9. Has known active CNS metastases and/or carcinomatous meningitis. Participants with previously treated brain metastases may participate provided they are radiologically stable, (ie, without evidence of progression) for at least 4 weeks by repeat imaging</p> <p>(Note: The repeat imaging should be performed during study Screening.), clinically stable, and without requirement of steroid treatment for at least 14 days before the first dose of study intervention.</p> <p><u>Note:</u> Participants with known untreated, asymptomatic brain metastases (ie, no neurological symptoms, no requirement for corticosteroids, no or minimal surrounding edema, and no lesion >1.5 cm) may participate but will require regular imaging of the brain as a site of disease.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>10. Known severe hypersensitivity (\geqGrade 3) to MK-7684A, paclitaxel and/or any of their excipients.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non

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<p>11. Has an active autoimmune disease that has required systemic treatment in past 2 years (ie, with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (eg, thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is not considered a form of systemic treatment and is allowed.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>12. Has a history of (noninfectious) pneumonitis/interstitial lung disease that required steroids or has current pneumonitis/interstitial lung disease.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>13. Has an active infection requiring systemic therapy.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>14. Has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the study, interfere with the participant's participation for the full duration of the study, or is not in the best interest of the participant to participate, in the opinion of the treating investigator.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>15. Has a known psychiatric or substance abuse disorder that would interfere with the participant's ability to cooperate with the requirements of the study.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>16. Has present or progressive accumulation of pleural, ascitic, or pericardial fluid requiring drainage or diuretic drugs within 2 weeks before randomization/allocation</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>17. Has concurrent active Hepatitis B (defined as HBsAg positive and /or detectable HBV DNA) and Hepatitis C virus (defined as anti-HCV Ab positive and detectable HCV RNA) infection.</p> <p><u>Note:</u> Hepatitis B and C screening tests are required for study entry and need to be performed to evaluate eligibility</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
Other Exclusions	
<p>18. Participant, in the judgment of the investigator, is unlikely to comply with the study procedures, restrictions, and requirements of the study.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>19. Has had an allogenic tissue/solid organ transplant.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non

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For participants who will receive paclitaxel in Cohort F:	
<p>20. Has a history of class II-IV congestive heart failure or myocardial infarction within 6 months of allocation.</p> <p>Refer to Appendix 7 for country-specific exclusion criteria.</p>	<input type="checkbox"/> oui <input type="checkbox"/> non

Date : _____

Signature de l'investigateur : _____