CGFL CENTRE GEORGES FRANÇOIS LECLERC Ensemble, dépassons le cancer	**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 : *Magali poste 3210…..*

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 D : Cancer des voies biliaires

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	
1. Has histologically or cytologically confirmed, advanced (locally recurrent unresectable or metastatic) solid tumor as follows: **Cohort D**: unresectable biliary adenocarcinoma (gallbladder or biliary tree [intrahepatic or extrahepatic] cholangiocarcinoma) that has progressed after 1 prior systemic therapy but must not have been treated with prior anti-PD-1/ PD-L1 therapy. Note: participants with mixed HCC/cholangiocarcinoma may be included. Note: participants with Ampulla of Vater cancers are not eligible. Note: small cell cancer, neuroendocrine tumors, lymphoma, sarcoma, mixed tumor histology and/or mucinous cystic neoplasms are not eligible. Note: Participants may have received prior neoadjuvant or adjuvant therapy in consideration of following : • Assessment of disease progression should be confirmed by CT scan. In certain situations, clinical evidence of disease progression such as any new or worsening malignant effusion (documented by ultrasound) and confirmation by pathologic criteria (histology and/or cytology) may be acceptable for assessment after Sponsor consultation. • Treatment with curative intent, including neoadjuvant/adjuvant treatment, given as chemotherapy or chemoradiotherapy, using standard of care agents or definitive chemoradiation, will count as a line of therapy if disease progression occurs during treatment or within 6 months of cessation of treatment.	☐ oui ☐ non
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.	☐ oui ☐ non

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. Note: For planned exploratory biomarker analyses, FFPE tumor blocks are preferred to slides (refer to Section 8.1.12).	☐ oui ☐ non
Demographics	
4. Is male or female, who is at least 18 years of age at the time of signing the informed consent.	☐ oui ☐ non
5. Has an ECOG performance status of either 0 or 1, as assessed within 7 days before starting study intervention.	☐ oui ☐ non
6. Has a predicted life expectancy of at least 3 months.	☐ oui ☐ non
Female Participants for cohorte D (MK-7684A monotherapy)	
7. A female participant is eligible to participate if she is not pregnant or breastfeeding, and at least one of the following conditions applies: • Is not a WOCBP OR • Is a WOCBP and using a contraceptive method that is highly effective (with a failure rate of <1% per year), 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 study intervention. The investigator should evaluate the potential for contraceptive method failure (ie, noncompliance, recently initiated) in relationship to the first dose of study intervention. ➢ 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. ➢ Additional requirements for pregnancy testing during and after study intervention are in Section 8.3.7.1.	☐ oui ☐ non

➢ 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.	
Informed Consent	
8. The participant (or legally acceptable representative) has provided documented informed consent/assent for the study.	☐ oui ☐ non
Additional Categories	
9. HIV-infected participants must have well controlled HIV on ART, defined as: • 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 tenoforvir • 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	☐ oui ☐ non
10. 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. Note: 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	☐ oui ☐ non

11. Participants with history of HCV infection are eligible if HCV viral load is undetectable at Screening. Note: Participants must have completed curative antiviral therapy at least 4 weeks before randomization/allocation. 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.	☐ oui ☐ non
12. 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 Table 5 Adequate Organ Function Laboratory Values	☐ oui ☐ non

System	Laboratory Value
Hematological	
Absolute neutrophil count (ANC)	>1500/µL
Platelets	>100,000/µL
Hemoglobin	≥9 g/dL or ≥5.6 mmol/L[a]
Renal	
Creatinine AND[b]/OR Measured or calculated [c] creatinine clearance (GFR can also be used in place of creatinine or CrCl)	≤1.5 × ULN AND[b]/OR ≥30 mL/min for participants with creatinine levels >1.5 × institutional ULN ≥60 mL/min for participants with creatinine levels >1.5 × institutional ULN (**Cohort E only**)[d]
Hepatic	
Total bilirubin	≤1.5 ×ULN OR direct bilirubin ≤ULN for participants with total bilirubin levels >1.5 × ULN
AST (SGOT) and ALT (SGPT)	≤2.5 × ULN (≤5 × ULN for participants with liver metastases)
Coagulation	
INR or PT aPTT/PTT	≤1.5 × ULN unless participant is receiving anticoagulant therapy as long as PT or PTT is within therapeutic range of intended use of anticoagulants

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.

a. Criteria must be met without erythropoietin dependency and without packed red blood cell transfusion within last 2 weeks.
b. Applicable only when local guidelines require both assessments.
c. CrCl should be calculated per institutional standard.
d. The cisplatin product label should be followed for acceptable creatinine clearance rates.
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..

Critères de non inclusion

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

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Medical Conditions	
1. Has a history of a second malignancy, unless potentially curative treatment has been completed with no evidence of malignancy for 3 years. Note: 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.	□ oui □ non
2. HIV-infected participants with a history of Kaposi's sarcoma and/or Multicentric Castleman's Disease	□ oui □ non
Prior/Concomitant Therapy	
3. Has received prior therapy with an anti-PD-1, anti-PD-L1, anti-PD-L2, or anti-TIGIT agent.	□ oui □ non
4. Has received prior systemic anticancer therapy including investigational agents within 4 weeks before randomization/allocation. Note: Participants must have recovered from all AEs due to previous therapies to ≤Grade 1 or baseline. Participants with ≤Grade 2 neuropathy may be eligible. Participants with endocrine-related AEs Grade ≤2 requiring treatment or hormone replacement may be eligible. Participants with Grade ≤2 alopecia are eligible. Note: 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.	□ oui □ non
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 (≤2 weeks of radiotherapy) to non-CNS disease.	□ oui □ non
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.	□ oui □ non

Prior/Concurrent Clinical Study Experience	
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. Note: 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.	□ oui □ non
Diagnostic Assessments	
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.	□ oui □ non
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 (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. Note: 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.	□ oui □ non
10. Known severe hypersensitivity (≥Grade 3) to MK-7684A, and/or any of their excipients.	□ oui □ non
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.	□ oui □ non
12. Has a history of (noninfectious) pneumonitis/interstitial lung disease that required steroids or has current pneumonitis/interstitial lung disease.	□ oui □ non
13. Has an active infection requiring systemic therapy.	□ oui □ non

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.	□ oui □ non
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.	□ oui □ non
16. Has present or progressive accumulation of pleural, ascitic, or pericardial fluid requiring drainage or diuretic drugs within 2 weeks before randomization/allocation	□ oui □ non
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. Note: Hepatitis B and C screening tests are required for study entry and need to be performed to evaluate eligibility	□ oui □ non
Other Exclusions	
18. Participant, in the judgment of the investigator, is unlikely to comply with the study procedures, restrictions, and requirements of the study.	□ oui □ non
19. Has had an allogenic tissue/solid organ transplant.	□ oui □ non

Date : _____

Signature de l'investigateur : _____