# Essai Clinique

Généré le 01 juin 2023 à partir de

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| Titre | A Phase II Randomized Controlled Trial of Neoadjuvant Pembrolizumab With Radiotherapy and Adjuvant Pembrolizumab in Patients With High-Risk, Localized Soft Tissue Sarcoma of the Extremity |
| Protocole ID | SU2C-SARC032 |
| ClinicalTrials.gov ID | NCT03092323 |
| Type(s) de cancer | Sarcome |
| Phase | Phase II |
| Stade | Sarcome des tissus mous |
| Type étude | Traitement |
| Médicament | Pembrolizumab avec radiothérapie |
| Institution | CENTRE UNIVERSITAIRE DE SANTE MCGILL |
| Ville | Montréal |
| Investigateur principal | Dre Carolyn Freeman |
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| Statut | Actif en recrutement |
| But étude | This is a multicenter, randomized phase II trial with an initial safety run-in to test the safety and efficacy of neoadjuvant pembrolizumab with image-guided radiotherapy and adjuvant pembrolizumab compared to radiation therapy alone in patients with clinically localized extremity soft tissue sarcoma at high risk for developing metastatic disease (tumor size > 5 cm, intermediate- to high-grade; approximately 50% risk for distant disease at 2 years). Histologies will be limited to undifferentiated pleomorphic sarcoma and dedifferentiated/pleomorphic liposarcoma based on preliminary data from SARC028. Other terms for undifferentiated pleomorphic sarcoma may include, but are not limited to. pleomorphic undifferentiated sarcoma, unclassified spindle cell sarcoma, spindle cell sarcoma not otherwise specified, pleomorphic spindle cell sarcoma, pleomorphic fibroblastic sarcoma, undifferentiated high-grade pleomorphic sarcoma, pleomorphicsarcoma with prominent inflammation, pleomorphic sarcoma with giant cells, malignant fibrous histiocytoma (including storiform-pleomorphic and inflammatory subtypes), fibrosarcoma, and myxofibrosarcoma (located deep to the fascia in muscle). Radiation therapy with three cycles of pembrolizumab will be administered as neoadjuvant therapy for patients randomized to the experimental arm. These patients will also receive up to fourteen cycles of adjuvant pembrolizumab after surgical resection. Patients in the standard of care arm will receive neoadjuvant radiotherapy (50 Gy in 25 fractions) followed by surgical resection as in RTOG 0630. |
| Critères d'éligibilité | • Age ≥ 12 years<br>• Histologically confirmed diagnosis of grade 2 or 3 out of 3 UPS or dedifferentiated/pleomorphic LPS of the extremity (including limb girdle, i.e. shoulder or hip) that measures greater than 5 cm in any direction as assessed by imaging; Alternative terms for UPS meeting inclusion criteria include but are not limited to the following<br>• Patients with non-melanomatous skin cancer, in situ carcinoma, or low-risk prostate cancer can be enrolled.<br>• ECOG Performance Status of 0 or 1<br>• Resectable primary tumor with no evidence of metastatic disease by imaging. Imaging must be performed within 45 days of Day 1 of study.<br>• Adequate organ function within 10 days of Day 1<br>• Written, voluntary informed consent<br>• Fertile men and women of childbearing potential must agree to use an effective method of birth control from Day 1 of study and for 120 days after last pembrolizumab administration in both |

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| | sexes. Women of childbearing potential include pre-menopausal women and women within the first 2 years of the onset of menopause. Women of childbearing potential must have a negative pregnancy test ≤ 72 hours prior to Day 1 of study. |
| Critères d'exclusion | • Prior chemotherapy, targeted small molecule therapy, or radiation therapy for current diagnosis of sarcoma<br>• Prior radiation therapy in excess of 20 Gy to the site of the current diagnosis of sarcoma. No overlap with prior radiation fields in excess of 20 Gy is allowed.<br>• Concurrent, clinically significant, active malignancies within two years of study enrollment.<br>• Patients with locally recurrent sarcoma after surgery alone are eligible for enrollment if other inclusion criteria are met.<br>• Patients with severe and/or uncontrolled concurrent medical disease that in the opinion of the investigator could cause unacceptable safety risks or compromise compliance with the protocol<br>• Major surgery within three months prior to Day 1 of study or who have not recovered adequately from prior surgery.<br>• Currently receiving a study therapy or if they had an investigational agent within 4 weeks at the time of enrollment.<br>• Women who are pregnant or nursing/breastfeeding, or expecting to conceive or men who are expecting to father children within the projected duration of the trial, starting with the pre-screening or screening visit through 120 days after the last dose of pembrolizumab.<br>• Inability to comply with protocol required procedures<br>• Diagnosis of immunodeficiency or is receiving systemic steroid therapy or any other form of immunosuppressive therapy by oral or IV routes within 7 days prior to the first dose of trial treatment<br>• Known history of active TB (Bacillus Tuberculosis)<br>• Hypersensitivity to pembrolizumab or any of its excipients<br>• Metastatic disease or regional lymph node involvement. Chest CT will be mandatory prior to enrollment to evaluate for the presence of metastatic disease. Pulmonary nodule(s) < 5 mm without a histological diagnosis may not be the basis for study exclusion given the lack of specificity of chest CT. If pulmonary nodule(s) > 5 mm are noted on chest CT but appear stable relative to prior chest imaging of at least 6 months duration, then this is permitted.<br>• Unresectable disease or medically inoperable<br>• Planned to receive neoadjuvant or adjuvant chemotherapy for current diagnosis of localized soft tissue sarcoma<br>• Active autoimmune disease that has required systemic treatment in the past two years (i.e. with use of disease modifying agents, systemic corticosteroids or immunosuppressive drugs). Replacement therapy (e.g., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment.<br>• Has a history of (non-infectious) pneumonitis that required systemic steroids or current pneumonitis.<br>• Active infection requiring systemic therapy<br>• Known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the trial<br>• Prior therapy with an anti-PD-1, anti-PD-L1, or anti-PD-L2 agent<br>• Known history of Human Immunodeficiency Virus (HIV) (HIV 1/2 antibodies)<br>• Known active Hepatitis B (e.g., HBsAg reactive, confirmed by detectable viral load) or Hepatitis C (e.g., HCV RNA [qualitative] detected)<br>• Received a live vaccine within 30 days of planned start of study therapy. Note: Seasonal influenza vaccines for injection are generally inactivated flu vaccines and are allowed; however intranasal influenza vaccines (e.g., Flu-Mist®) are live attenuated vaccines, and are not allowed.<br>• Diagnosis of scleroderma.<br>• Diagnosis of inflammatory bowel disease (Crohn's disease or Ulcerative Colitis). |