Version 05/23/24

NCI National Clinical Trials Network

EA7222

ECOG-ACRIN cancer research group

For Patients with Sarcoma

EA7222 Available Through ECOG-ACRIN Cancer Research Group

A Randomized Phase III Trial of Doxorubicin + Pembrolizumab versus Doxorubicin Alone for the Treatment of Undifferentiated Pleomorphic Sarcoma (UPS) and Related Poorly Differentiated Sarcomas

Patient Population

See Protocol Section 3 for Complete Eligibility Details

- ≥ 18 years of age, adequate lab values, ECOG PS 0-1
- Confirmed histopathologic diagnosis of UPS/related poorly differentiated sarcoma (see protocol for details)
- Must have metastatic or unresectable sarcoma
- Must have LVEF > 50% by MUGA scan/echocardiogram obtained within 28 days prior to randomization
- Patients with treated brain metastases are eligible if follow-up brain imaging after CNS-directed therapy shows no evidence of progression; patients with new/active brain metastases or leptomeningeal disease are eligible if the treating physician determines that immediate CNS specific treatment is not required and is unlikely to be required during the first cycle of therapy
- Patients with a prior/concurrent malignancy whose natural history/treatment does not have the potential to interfere with the safety/efficacy assessment of the investigational regimen are elgible
- No history of/active interstitial lung disease
- Must have measurable disease, defined per protocol
- No prior treatment with an anthracycline
- No diagnosis of clinically significant immunodeficiency or an autoimmune disorder requiring the patient to use systemic steroid chronically, or systemic steroids within 7 days prior to randomization; no daily corticosteroid use > 10 mg of prednisone (or equivalent)
- No known history of active TB
- No known hypersensitivity to doxorubicin/pembrolizumab or any of their excipients
- Patients who received prior chemotherapy, targeted small molecule therapy, or radiation therapy must have recovered from the therapy prior to randomization; must have recovered from any prior major surgery
- No prior pericardial/mediastinal radiation
- Must not have received prior therapy with an anti-PD-1/L1/L2 or anti-CTLA4 agent

Treatment Plan

See Protocol Section 5 for Complete Treatment Details

- Each cycle = 21 days (+/- 3 days)
- **Arm A (doxorubicin + pembrolizumab)**
  - ◊ Doxorubicin 75 mg/m² IV push over 3-10 minutes or infused over up to 3 hours (according to institution preference) on day 1, followed by
  - ◊ Pembrolizumab 200 mg IV over 30 mins day 1
  - ◊ Repeat combination treatment for 6 cycles
  - ◊ After 6 cycles, continue pembrolizumab alone until progression, unacceptable toxicity, or up to 2 years total
- **Arm B (doxorubicin)**
  - ◊ Doxorubicin 75 mg/m² IV push over 3-10 minutes or infused over up to 3 hours (according to institution preference) on day 1
  - ◊ Repeat for 6 cycles
  - ◊ At the time of progression, patients randomized to receive doxorubicin alone may switch to receive pembrolizumab (200 mg IV over 30 minutes on day 1 every 21 days) until progression, unacceptable toxicity or up to 2 years from the start of pembrolizumab. If a patient completes all 6 cycles of doxorubicin, they will be followed until progression; at the time of progression, if the patient is within 5 years of randomization, they can receive pembrolizumab as stated above

Notes:

- *Patients should be treated with appropriate anti-emetic, cardioprotective agents, supportive care, and emergency medications per institutional standard*
- *Strong/moderate inhibitors or CYP2D6/CYP3A4 and P-gp should be avoided during doxorubicin cycles. Doxorubicin dose is calculated using BSA with actual body weight (capping at 2.2 m² for obese patients is permitted)*

Study Chair:
Seth Pollack, MD

Patient Enrollment

All Sites: Oncology Patient Enrollment Network (OPEN) https://open.ctsu.org/open

Protocol Information

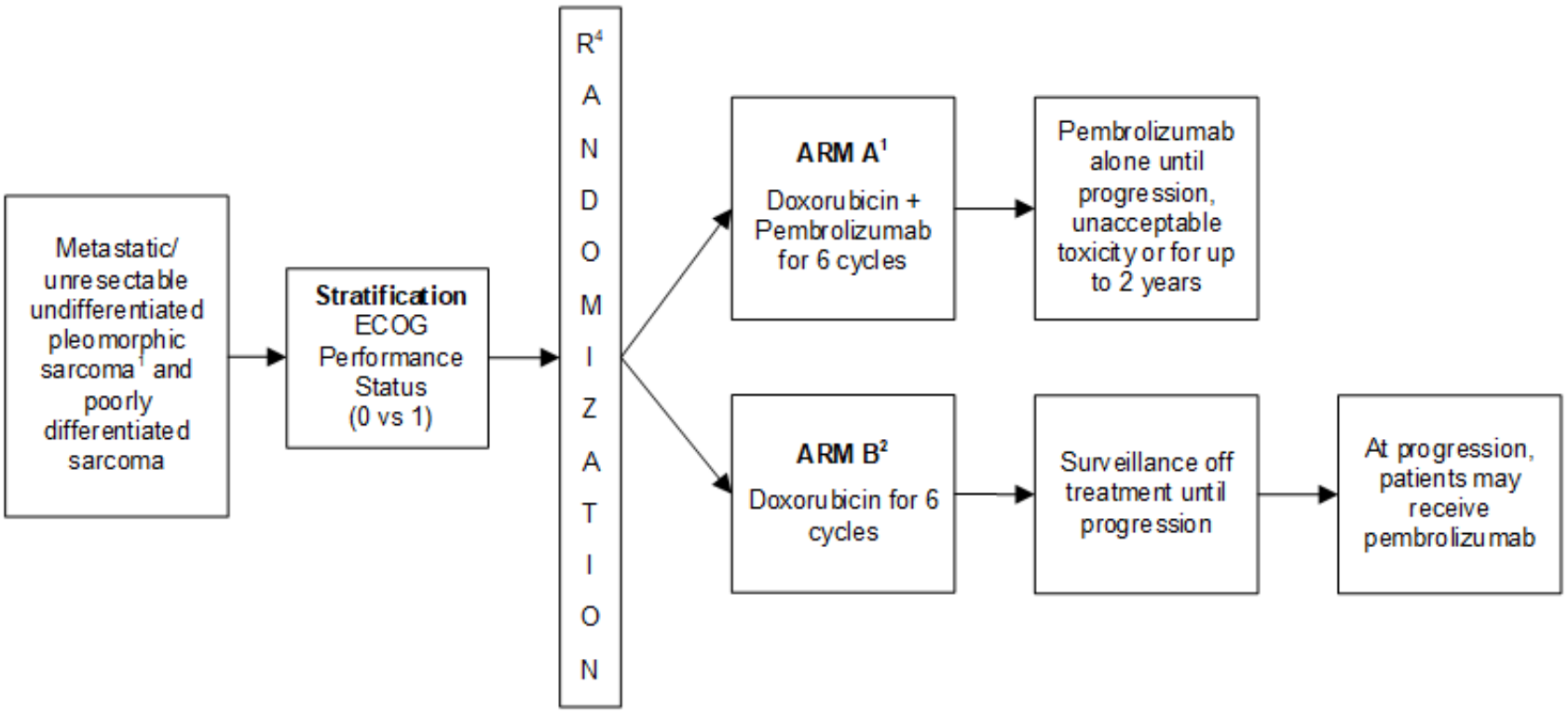
ECOG-ACRIN Operations-Boston: 857-504-2900, http://ecog-acrin.org (Member Login)

Please Enroll Your Eligible Patients!

Version 05/23/24

EA7222

Schema



N=180

1. Refer to Section 5.1.1 for treatment details.
2. Refer to Section 5.1.2 for treatment details.
3. At the time of progression, whether the patient is receiving doxorubicin or the patient is in the 5 year follow-up period, patients randomized to Arm B (doxorubicin alone) may receive pembrolizumab as indicated in Section 5.1.2.