RANDOMIZED PHASE II STUDY OF NIVOLUMAB WITH OR WITHOUT IPILIMUMAB IN PATIENTS WITH METASTATIC OR UNRESECTABLE SARCOMA

Pre-Registration Eligibility Criteria (see Section 3.2)

Central pathology review submission (see § 3.2.1)

Registration Eligibility Criteria (See Section 3.3)

Histologically confirmed bone or soft tissue sarcoma by central pathology review

Measureable disease as defined in Section 11.0

Locally advanced/unresectable or metastatic disease

≥ 1 prior systemic therapy for sarcoma

No prior therapy with ipilimumab or nivolumab or other agent targeting PD-1, PD-L1 or CTLA-4.

No treatment with biologic therapy, immunotherapy, chemotherapy, investigational agent for malignancy, or radiation ≤ 28 days before study registration. No treatment with nitrosourea or mitomycin ≤ 42 days before study registration. *For GIST, tyrosine kinase inhibitor can be continued for up to 3 days prior to initiation of study treatment.

Required Initial Laboratory Values

Absolute neutrophil count (ANC)	≥ 1500/mm^3
Platelet Count	≥ 100,000/mm^3
Creatinine	< 1.5 x ULN
Calc. Creatinine Clearance (see Alliance website)	OR ≥ 45 mL/min*
Total Bilirubin	≤ 1.5 x ULN*
AST / ALT	≤ 3 x ULN
TSH	WNL*

*See section 3.3.9

Resolution of any toxic effects of prior therapy (except alopecia) to NCI CTCAE, Version 4.0, grade 1 or less.

No history of the following:

- Active known or suspected autoimmune disease
- Symptomatic, untreated, or uncontrolled brain metastases
- Active autoimmune colitis
- Autoimmune panhypopituitarism
- Autoimmune adrenal insufficiency
- Known active hepatitis B or C (see section 3.3.4 for definition)

No systemic treatment with corticosteroids or other immunosuppressive medications ≤ 14 days of registration.

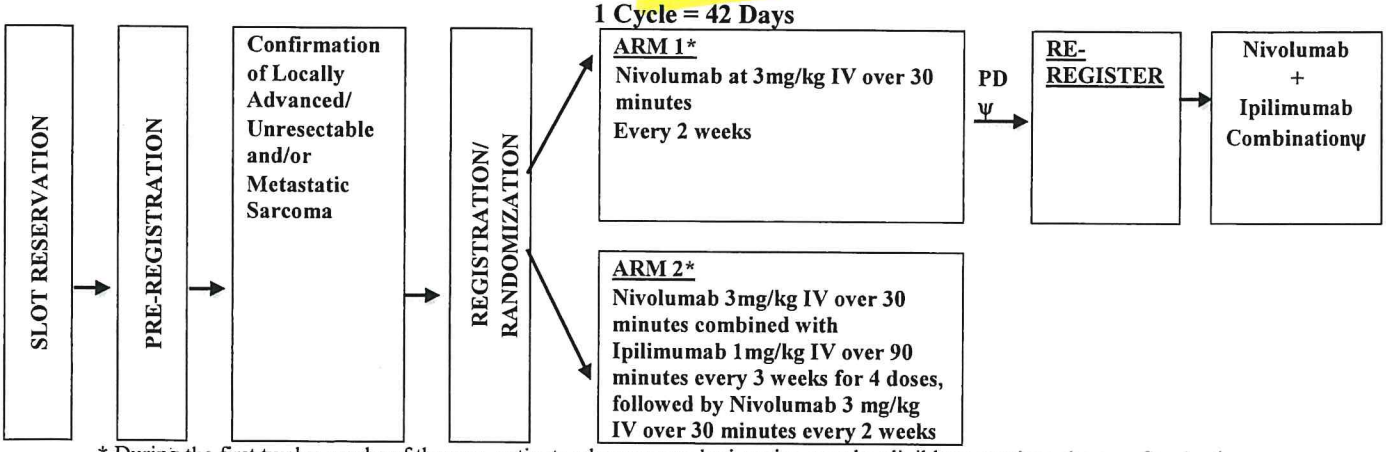
Not pregnant and not nursing (see Section 3.3.6)

Age ≥ 18 years

ECOG performance status 0 or 1

Schema

1 Cycle = 42 Days



* During the first twelve weeks of therapy, patients who progress by imaging may be eligible to continue therapy. See Section 7.1 for more information.

ψ Nivolumab 3mg/kg IV over 30 minutes combined with Ipilimumab 1mg/kg IV over 90 minutes every 3 weeks for 4 doses total followed by Nivolumab 3 mg/kg IV over 30 minutes every 2 weeks (See Section 3.4, Section 4.6 and Section 7.2 for further instructions).

Treatment is to continue for 108 weeks or until disease progression or unacceptable adverse events. Patients are followed for a maximum of three years post-randomization or until death, whichever comes first.

Please note that vaccinations should be administered prior to therapy (See Section 8.1).

Please refer to the full protocol text for a complete description of the eligibility criteria and treatment plan.