NCI National Clinical Trials Network

E4412

ECOG-ACRIN cancer research group
Reshaping the future of patient care

For Patients with Hodgkin Lymphoma

E4412 Available Through ECOG-ACRIN Cancer Research Group

A Phase I Study with an Expansion Cohort/Randomized Phase II Study of the Combinations of Ipilimumab, Nivolumab and Brentuximab Vedotin in Patients with Relapsed/Refractory Hodgkin Lymphoma

Patient Population

See Section 3.0 for Complete Eligibility Details

Phase I (Arms A, B, C, D, E, F, G, H, I X, Y, Z):

- Age ≥ 18 years, ECOG PS 0-2, and adequate lab values
- Must have pathologically confirmed relapsed/refractory classical HL, and measurable disease per protocol
- Must have relapsed after first line chemotherapy; may have relapsed after autologous/allogeneic stem cell transplant, or have primary refractory disease
- May have received prior brentuximab vedotin, ipilimumab, and other prior activating immunotherapies **per protocol**; no prior nivolumab or PD1/PDL1 axis agents
- No evidence of dyspnea at rest and a pulse oximetry > 92% while breathing room air
- No current or prior history of CNS involvement
- All prior therapy must have been completed at least 21 days prior to enrollment; no concomitant anti lymphoma therapy, including systemic corticosteroids for the purpose of treatment of lymphoma
- No history of Steven's Johnson's/TENs syndrome, or motor neuropathy
- Patients with poorly controlled HIV or other chronic active viral infections will be excluded
- Must not have autoimmune disorders or conditions of immunosuppression that require current ongoing treatment with systemic corticosteroids
- No history of symptomatic autoimmune disease, motor neuropathy considered of autoimmune origin, or other CNS autoimmune disease
- No ≥ grade 2 peripheral sensory neuropathy
- No NYHA Class III/IV heart failure, uncontrolled angina, severe uncontrolled ventricular arrhythmias, or electrocardiographic evidence of acute ischemia
- Arms D, E, F, G, H, I X, Y: cannot have smoked tobacco or other substances within the past 6 months

Phase II (Arms K, L): See protocol for criteria, including modifications for pediatric patients age ≥ 12 years

Treatment Plan

See Section 5.0 for Complete Treatment Details

Refer to protocol for details on the Phase I dose escalation treatment (CLOSED TO ACCRUAL):

- **Arms A, B, C, Z:** Brentuximab + Ipilimumab
- **Arms D, E, F, Y:** Brentuximab + Nivolumab
- **Arms G, H, I, X:** Brentuximab + Nivolumab + Ipilimumab)

Treatment design– Phase II:

- 1 cycle = 21 days
- **Arm K:** Brentuximab + Nivolumab
  - ◊ Nivolumab 360 mg IV (adult patients) or 3 mg/kg (pediatric patients) day 1 cycles 1-34
  - ◊ Brentuximab vedotin 1.8 mg/kg (max 180 mg) IV days 1 cycles 1-16
- **Arm L:** Brentuximab + Nivolumab + Ipilimumab
  - ◊ Ipilimumab 1 mg/kg IV day 1 beginning cycle 1, every 12 weeks for up to 9 doses
  - ◊ Nivolumab 360 mg (adult patients) or 3 mg/kg (pediatric patients) day 1 cycles 1-34
  - ◊ Brentuximab vedotin 1.8 mg/kg IV (max 180 mg) day 1 cycles 1-16
- A maximum of 16 cycles of brentuximab vedotin will be given, for a maximum of 16 cycles
- A maximum of up to 34 doses of nivolumab (2 years) will be given for patients who are deriving clinical benefit (SD, PR, CR, IR) without excessive toxicity
- Patients who do not have a transplant or other curative therapy option may remain on nivolumab for up to 1 year or 17 further doses after completing brentuximab

Note: 30 minute observation period surrounding therapies per protocol; prophylactic premedication per protocol

Study Chair:
Catherine Diefenbach, MD

Co-Chair:
Stephen Ansell, MD, PhD

Patient Enrollment

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

Protocol Information

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

Please Enroll Your Eligible Patients!

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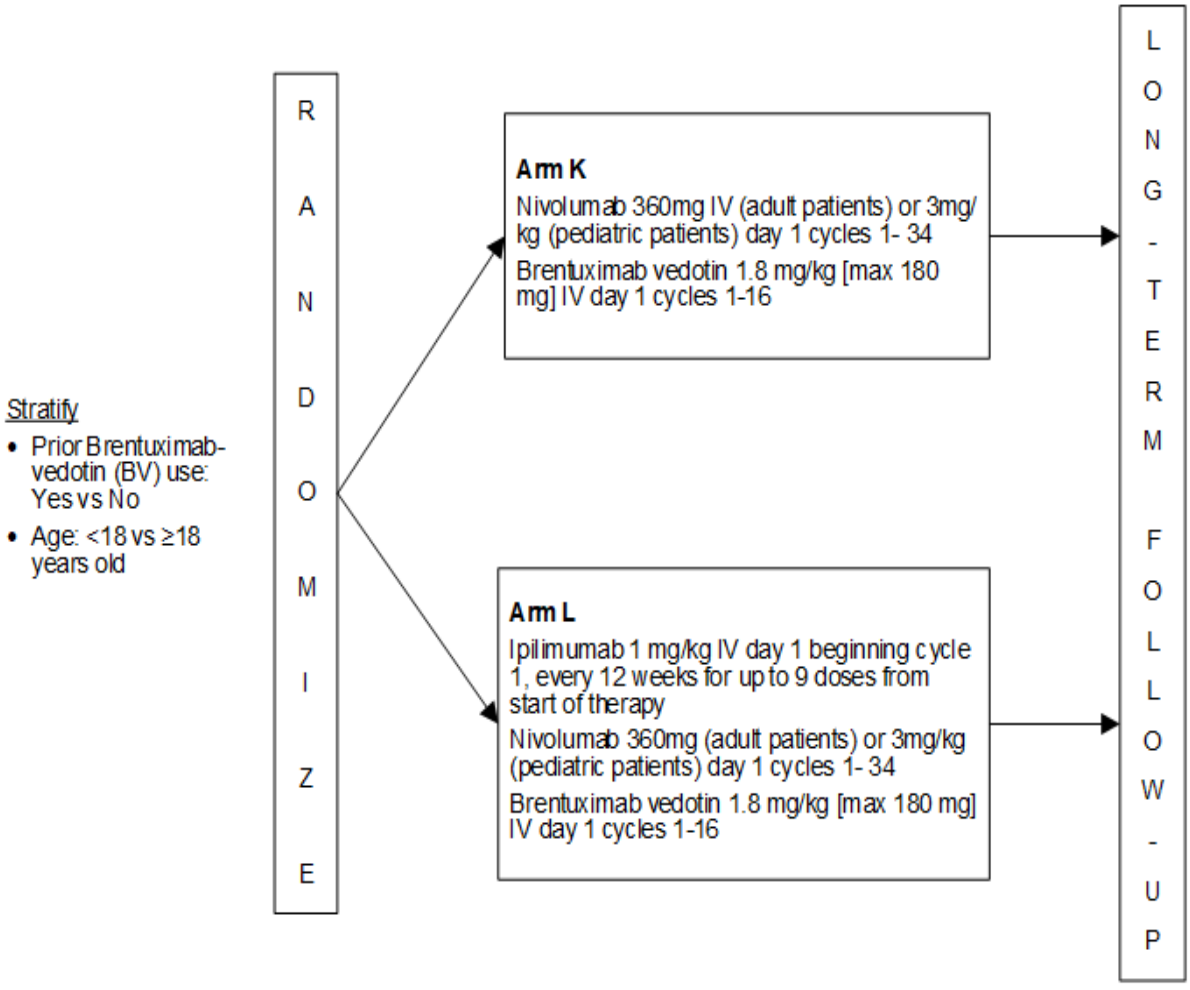
Refer to the protocol for the Phase I dose escalation schemas for Brentuximab Vedotin + Ipilimumab/Nivolumab/Nivolumab + Ipilimumab
ALL CLOSED TO ACCRUAL

Schema – Phase II



Phase II Accrual Goal=146 patients
Cycle=21 days