Cancer Research Consortium of West Michigan
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# FAST FACTS

**EAQ172** - Optimizing Immunosuppression for Steroid-Refractory Anti-PD-1/PD-L1 Pneumonitis

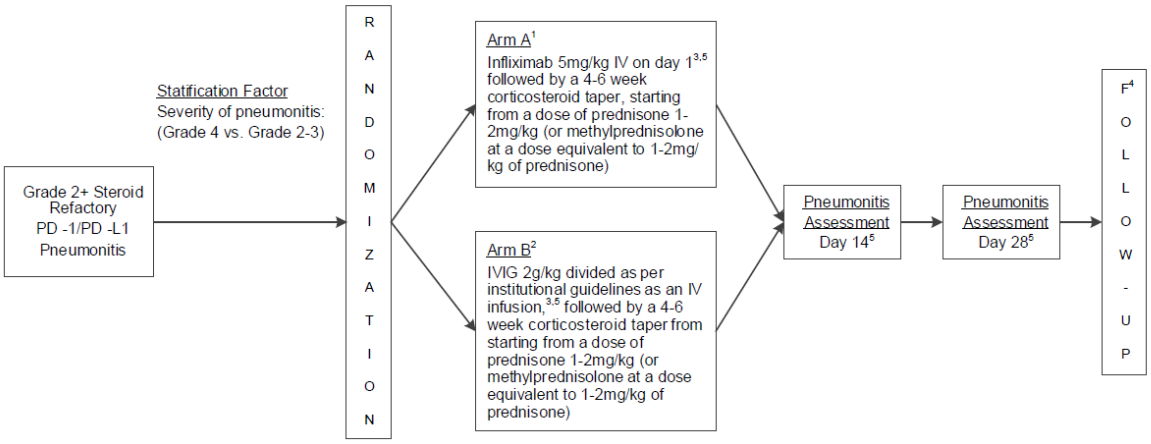
**Eligibility Criteria**

1. Patient must be ≥ 18 years of age.
2. Patient must be English-speaking and have the ability to understand and the willingness to sign a written informed consent document. Patients with impaired decision-making capacity (IDMC)who have a legally authorized representative (LAR) or caregiver and/or family member available will also be considered eligible.
    a. English speaking? (yes or no)
    b. Date of Written informed consent:_____
3. Patient must be willing and able to undergo arterial blood gas assessment as per the treating investigator. Patient must not have contraindication for arterial blood gas assessment.
4. Women must not be pregnant or breast-feeding due to the potential risk to the fetus with infliximab or IVIG.
   All females of childbearing potential must have a blood test or urine test within 14 days prior to randomization to rule out pregnancy.
   A female of childbearing potential is defined as any woman, regardless of sexual orientation or whether they have undergone tubal ligation, who meets the following criteria: 1) has achieved menarche at some point, 2) has not undergone a hysterectomy or bilateral oophorectomy; or 3) has not been naturally postmenopausal for at least 24 consecutive months (i.e., has had menses at any time in the preceding 24 consecutive months).
   Female of child bearing potential? _____ (Yes or No)
   Date of blood test or urine study: _____
5. Women of childbearing potential and sexually active males must not conceive or father children by using accepted and effective method(s) of contraception or to abstain from sexual intercourse for a minimum of 56 days (the duration of their participation in the study).
6. Patient must have an ECOG Performance Status of 0-3. Please see appendix III.
    a. PS: _____(0,1,2, or 3)
7. Patient with any solid tumor or hematologic malignancy is eligible.
   NOTE: Patient may have received any number of lines of prior systemic therapy.
8. Patient must have received treatment with an anti-PD-1/PD-L1 agent either alone or in combination with another anti-cancer agent, as their most recent therapy prior to development of pneumonitis.
   **NOTE:** Patient may have received anti-PD-1/PD-L1 therapy as standard-of-care or part of a clinical trial.
   Prior Anti-PD-1 or PD-L1: _____ (Yes or No)
   If yes, list agent and date of last dose: _____
9. Patient must not be receiving anti-PD-1/PD-L1 agent in combination with any of the following anti-cancer agents: docetaxel, cyclophosphamide, gefitinib, erlotinib, osimertinib, crizotinib, bleomycin, afatinib.
10. Patient must have steroid-refractory pneumonitis defined as:
    • Grade 2 pneumonitis that has not improved by a CTCAE grade in greater than 72 hours or maximum of 21 days or

• Grade 3 or higher pneumonitis that has not clinically improved by a CTCAE grade in greater than 48 hours or maximum of 21 days with high dose corticosteroids (methylprednisolone or prednisone 1-4mg/kg/equivalent) as their most recent treatment for pneumonitis, as determined by the treating investigator.

11. Patient must have had pathogen-negative infectious diagnostic evaluation within 21 days prior to randomization, and at a minimum these should include: blood culture, urine culture, sputum culture, and viral panel: rapid fluand RSH (respiratory syncytial virus). Empiric antibiotics for culture negative infections are not an exclusion for study entry.
    a. Date of pathogen-negative infectious diagnostic evaluation: _____
12. Patient must not have clinical evidence of cardiac dysfunction (as determined by the treating investigator) as an alternative diagnosis to steroid-refractory pneumonitis.
13. Patient must not be receiving concurrent radiation therapy to the chest.
    a. Concurrent radiation therapy: _____ (Yes or No)
    b. If yes, provide site(s): _____
14. Patient must not be deemed to have radiation pneumonitis. Patients with a history of stable radiation pneumonitis not requiring corticosteroid therapy within the last 3 months prior to randomization will be allowed on study.
    a. Date of last corticosteroid therapy: _____
15. Patient must not have pre-existing interstitial lung disease or pneumonitis requiring corticosteroid therapy from any other cause, as determined by the treating investigator.
16. Patient must not have an absolute contraindication to IVIG or infliximab, including: clinical history of severe hypersensitivity reaction, selective IgA deficiency, active hepatitis B, active tuberculosis, active human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) where a study subject has a CD4 count of ≤ 200 at screening, or drug interaction as detailed in Section 8.1.8 and 8.2.9.
17. Patient must have a negative tuberculosis assessment (TB spot test, quantiferon gold or tuberculin skin test) within 21 days prior to randomization and either negative or low clinical suspicion.
    a. Date of negative TB test: _____
18. Patient must have chest CT scan without contrast performed ≤14 days before randomization. Patient must not have a contraindication for CT.
    a. Date of CT chest: _____

**Schema**


Statification Factor
Severity of pneumonitis:
(Grade 4 vs. Grade 2-3)
Grade 2+ Steroid Refactory PD -1/PD -L1 Pneumonitis
RANDOMIZATION
Arm A[1]
Infliximab 5mg/kg IV on day 1[3,5] followed by a 4-6 week corticosteroid taper, starting from a dose of prednisone 1-2mg/kg (or methylprednisolone at a dose equivalent to 1-2mg/kg of prednisone)
Arm B[2]
IVIG 2g/kg divided as per institutional guidelines as an IV infusion,[3,5] followed by a 4-6 week corticosteroid taper from starting from a dose of prednisone 1-2mg/kg (or methylprednisolone at a dose equivalent to 1-2mg/kg of prednisone)
Pneumonitis Assessment Day 14[5]
Pneumonitis Assessment Day 28[5]
F[4] OLLOW-UP