5.0 ELIGIBILITY CRITERIA

Each of the criteria in the following section must be met in order for a patient to be considered eligible for registration. Use the spaces provided to confirm a patient's eligibility. For each criterion requiring test results and dates, please record this information on the Onstudy Form and submit via Medidata Rave® (see Section 14.0). Any potential eligibility issues should be addressed to the Data Operations Center in Seattle at 206/652-2267 or earlytxquestion@crab.org prior to registration. NCI policy does not allow for waiver of any eligibility criterion (http://ctep.cancer.gov/protocolDevelopment/policies_deviations.htm).

In calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test is done on a Monday, the Monday 4 weeks later would be considered Day 28. This allows for efficient patient scheduling without exceeding the guidelines. **If Day 14, 28, or 56 falls on a weekend or holiday, the limit may be extended to the next working day.**

SWOG Patient No. _____

Patient's Initials (L, F, M) _____

5.1 Disease Related Criteria

Except where otherwise indicated below, all baseline assessments must have been completed within 28 days prior to registration.

_____ a. Patients must have histologically confirmed rare cancer and/or cancer of unknown primary, identified in Section 18.1 that did not have a match to a molecularly-guided therapy on EAY131 "NCI-MATCH" protocol or who progressed on molecularly-matched therapy and have no further molecularly-matched treatment recommendations per EAY131, "NCI-MATCH". **Please See Section 18.1 for a list of eligible Rare Cancer Histologies.**

Except where otherwise indicated below, all baseline assessments must have been completed within 28 days prior to registration.

_____ b. Patients who meet criteria 5.1a and do not qualify for one of the histologic cohorts in Section 18.1 (and are not on the ineligible histology list in Section 18.2) may be considered for registration in the "Not Otherwise Categorized" Rare Tumors cohort with confirmation of the study chairs via email to S1609SC@swog.org. See Section 18.3 Study Chair Approval Process for the Not Otherwise Categorized (NOC) Cohort.

_____ c. Patients who meet criteria 5.1a and are determined to have a rare cancer with unknown primary site are eligible provided that there is histologic documentation of metastatic malignancy with no discernible primary site identified from histopathologic review, physical exam and associated cross-sectional imaging of the chest, abdomen, and pelvis.

_____ d. Patients must have a diagnostic quality CT scan or MRI, performed within 28 days prior to registration, which demonstrates measurable disease, as defined in Section 10.1 (RECIST v. 1.1). All disease must be assessed and documented on the **S1609** Baseline Tumor Assessment Form.

SWOG Patient No. _____

Patient's Initials (L, F, M) _____

5.1 Disease Related Criteria (contd.)

_____ e. No other prior malignancy is allowed except for the following:

- Adequately managed Stage I or II cancer from which the patient is currently in complete remission
- Any other cancer from which the patient has been disease free for one year.
- Adequately managed Stage I or II follicular thyroid or prostate cancer is also eligible, wherein patient is not required to be in complete remission.

5.2 Prior/Concurrent Therapy Criteria

_____ a. Patients may have received either prior anti-CTLA4 or other prior anti-PD-1/anti-PD-L1 therapy, not both, provided that it is completed ≥ 4 weeks prior to registration for monoclonal therapy, ≥ 8 weeks prior to registration if therapy involved immune-stimulatory mAbs, and ≥ 28 days for all other immunotherapy.

_____ b. Patients who had prior immune-related adverse event (Grade 3 or higher immune-related pneumonitis, hepatitis, colitis, endocrinopathy) with prior immunotherapy (e.g. cancer vaccine, cytokine, etc.) are not eligible.

_____ c. Patients with clinically controlled thyroiditis or pituitary disorders on stable replacement therapy are eligible.

_____ d. Patients are not eligible if they have had or are planned for solid organ transplant. Patients who have received allogeneic hematopoietic stem cell transplant are eligible if the transplant occurred at least 90 days prior to registration, patient has no prior acute graft versus host disease (GVHD), and within 48 hours of registration, patient demonstrates at least 90% engraftment, defined as: ANC ≥ 500 mcl, measured over 3 consecutive days or 1 day with an ANC ≥ 1,000 mcl, or platelets ≥ 50,000 mcl measured, wherein the patient did not receive any platelet transfusions within 7 days prior to laboratory assessment, Patients with autoimmune disease who are otherwise eligible under criterion 5.3k must not have received steroid and immunosuppressive therapy within 28 days prior to registration.

_____ e. Patients with brain metastases or primary brain tumors must have completed treatment, surgery or radiation therapy ≥ 28 days prior to registration and have stable disease at time of registration. Metastatic brain parenchymal disease must have been treated and patient must be off steroids for 7 days prior to registration.

_____ f. Patients must not currently be receiving any other investigational agents or any other systemic anti-cancer therapy (including radiation). In event patient recently received any other systemic anti-cancer therapy, patient must be off therapy at least 7 days prior to registration and any therapy-induced toxicity must have recovered to ≤ Grade 1.

SWOG Patient No. _____

Patient's Initials (L, F, M) _____

5.3 Clinical/Laboratory Criteria

_____ a. Patients must be ≥ 18 years of age.

_____ b. Patients must have a Zubrod Performance Status of 0-2. (See Section 10.8)

_____ c. Patients must have adequate hematologic function as evidenced by all of the following within 28 days prior to registration: ANC ≥ 1,000/mcL; platelets ≥ 75,000/mcL; hemoglobin ≥ 8 g/dL.

_____ d. Patients must have adequate hepatic function as evidenced by all of the following within 28 days prior to registration: total bilirubin ≤ 2.0 x Institutional Upper Limit of Normal (IULN) or for documented/suspected Gilbert's disease, total bilirubin ≤ 3.0 x IULN; AST and ALT both ≤ 3 x IULN.

_____ e. Patients must have evidence of adequate renal function, as defined by ONE of the following within 28 days prior to registration:

- Serum creatinine ≤ 2.0 IULN
- Creatinine clearance (CrCl) ≥ 50 mL/min., as estimated by the Cockcroft and Gault formula. The serum creatinine value used in the calculation must have been obtained within 28 days prior to registration. Estimated creatinine clearance is based on actual body weight.
- Estimated creatinine clearance = $\frac{(140 - \text{age}) \times \text{wt (kg)} \times 0.85 \text{ (if female)}}{72 \quad \text{creatinine (mg/dl)}}$

_____ f. Patients must have adequate thyroid function, as evidenced by TSH, free T4 serum tests demonstrating values within the normal range, within 28 days prior to registration. Note: TSH, with reflex T4 is allowable if per institutional standard. Otherwise, both TSH and free-T4 must be obtained.

_____ g. Patients must have adequate adrenal axis function, as evidenced by Adrenocorticotropic Hormone (ACTH) values within the normal ranges, within 28 days prior to registration.

_____ h. Females of childbearing potential must have negative serum pregnancy test within 48 hours prior to registration and agree to use birth control throughout study and for 23 weeks after completion of protocol therapy. Patients must not be pregnant or nursing due to risk of fetal or nursing infant harm. Women of reproductive potential must have agreed to use an effective contraceptive method. A woman is considered to be of "reproductive potential" if she has had menses at any time in the preceding 12 consecutive months. In addition to routine contraceptive methods, "effective contraception" also includes heterosexual celibacy and surgery intended to prevent pregnancy (or with a side-effect of pregnancy prevention) defined as a hysterectomy, bilateral oophorectomy or bilateral tubal ligation. However, if at any point a previously celibate patient chooses to become heterosexually active during the time period for use of contraceptive measures outlined in the protocol, she is responsible for beginning contraceptive measures.

SWOG Patient No. _____

Patient's Initials (L, F, M) _____

5.3 Clinical/Laboratory Criteria (contd.)

_____ i. Men of reproductive potential must have agreed to use birth control throughout the study and for 31 weeks after completion of protocol therapy. In addition to routine contraceptive methods, "effective contraception" also includes heterosexual celibacy and surgery intended to prevent pregnancy (vasectomy). However, if at any point a previously celibate patient chooses to become heterosexually active during the time period for use of contraceptive measures outlined in the protocol, he is responsible for beginning contraceptive measures.

_____ j. Patients must not have known active Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV) infection at time of registration. Patients with previously treated HBV or HCV that have an undetectable viral load and no residual hepatic impairment are eligible.

_____ k. Patients who are known to be HIV-positive at registration are eligible at the time of registration:

1. CD4+ cell count greater or equal to 250 cells/mm3.
2. If patient is on antiretroviral therapy, there must be minimal interactions or overlapping toxicity of the antiretroviral therapy with the experimental cancer treatment. Once daily combinations that use pharmacologic boosters may not be used.
3. No history of non-malignancy AIDS-defining conditions other than historical low CD4+ cell counts.

_____ l. Patients must not have active autoimmune disease that has required systemic treatment in past 2 years (i.e., with use of disease modifying agents, immunosuppressive drugs, or corticosteroids with doses higher than prednisone 10mg or equivalent). 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. Autoimmune diseases include but are not limited to autoimmune hepatitis, inflammatory bowel disease (including ulcerative colitis and Crohn's disease), as well as symptomatic disease (e.g.: rheumatoid arthritis, systemic progressive sclerosis [scleroderma], systemic lupus erythematosus, autoimmune vasculitis [e.g., Wegener's Granulomatosis]); CNS or motor neuropathy considered of autoimmune origin (e.g., Guillain-Barre Syndrome and Myasthenia Gravis, multiple sclerosis or glomerulonephritis). Vitiligo, alopecia, hypothyroidism on stable doses of thyroid replacement therapy, psoriasis not requiring systemic therapy within the past 3 years is permitted. Short-term steroid premedication for contrast allergy is permitted.

_____ m. Patients must not have any uncontrolled intercurrent illness including (not limited to): Symptomatic CHF (NYHA III/IV), unstable angina pectoris or coronary angioplasty, or stenting within 24 weeks prior to registration, Unstable cardiac arrhythmia (ongoing cardiac dysrhythmias of NCI CTCAE v4 Grade ≥ 2), known psychiatric illness that would limit study compliance, intra-cardiac defibrillators, known cardiac metastases, or abnormal cardiac valve morphology (≥ Grade 3).

Note: ECHO and EKG are clinically indicated at baseline for any patient with a history of CHF or a risk due to underlying cardiovascular disease or prior exposure to cardiotoxic drugs. If patient has any evidence of CHF, MI, cardiomyopathy, or myositis cardiac evaluation (NYHA I/II) patient, cardiology consultation is also clinically indicated at baseline (in addition to ECHO and EKG), with CPK and troponin testing.

5.4 Specimen Submission Criteria

_____ a. Patients must be offered participation in specimen banking for future research. With patient's consent, specimens must be submitted as outlined in Section 15.1.

5.5 Regulatory Criteria

_____ a. Patients must be informed of the investigational nature of this study and must sign and give written informed consent in accordance with institutional and federal guidelines.

_____ b. As a part of the OPEN registration process (see Section 13.2 for OPEN access instructions) the treating institution's identity is provided in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the system.