Cancer Research Consortium of West Michigan
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FAST FACTS

S1937 - A Phase III Randomized Trial of Eribulin (NSC #707389) with or without Gemcitabine Versus Standard of Care (Physician's Choice) for Treatment of Metastatic Urothelial Carcinoma Refractory to, or Ineligible for, Anti PD1/PDL1 Therapy.

ELIGIBILITY CRITERIA

1. Disease Related Criteria

    i. Participant must have predominant histologically and cytologically proven urothelial carcinoma in a metastatic site.

    ii. Participant must have evidence of metastatic urothelial carcinoma based on CT or MRI within 28 days prior to registration.

    iii. Participant must have had progression of disease following prior therapy at the discretion of the treating investigator.

    iv. Participants must not require immediate CNS-specific treatment, in the opinion of the treating investigator if they have active brain metastases (defined as new or progressive brain metastases) or leptomeningeal disease.

2. Prior/Concurrent Therapy Criteria

    i. Participant must meet ALL of the requirements listed below. There is no limit to the number or sequence of prior regimens participant may have received for urothelial carcinoma.

        1. Participant must have received platinum based chemotherapy either in frontline metastatic setting or in the perioperative setting within 12 monthsprior to diagnosis of metastatic disease. Participants who have received anon-platinum systemic therapy within 12 months prior to diagnosis of metastatic disease are not required to have received platinum based chemotherapy.

        2. Participant must have received PD1/PDL1 antibody systemic therapy either in frontline metastatic setting or in the perioperative setting within 12 monthsprior to diagnosis of metastatic disease. Participants who, in the opinion of the treating physician, are not candidates for PD1/PDL1 antibody systemic therapy are exempt.

        3. Participant must have received enfortumab vedotin in a prior line of systemictherapy for urothelial carcinoma.

    ii. Participant must have received any planned surgery prior to registration.

    iii. Participant must not have progressed within 3 months following last dose of gemcitabine, if patient has previously received gemcitabine.

iv. Participant must not have unresolved toxicities from prior surgeries or radiation therapy > Grade 1 at the time of registration.

Clinical/Laboratory Criteria

1. Participant must be ≥ 18 years of age.

2. Participant must have Zubrod Performance Status 0-2 (see Section 10.0).

3. Participant must have history and physical examination within 28 days prior to registration.

4. Participant must have complete blood count (CBC), complete metabolic panel including liver function tests, and LDH obtained within 28 days prior to registration.

5. Participant must have adequate kidney function as evidenced by measured or calculated creatinine clearance ≥ 30 mL/min within 28 days prior to registration.

$$\text{Calculated creatinine clearance} = \frac{(140 - \text{age}) \times \text{wt (kg)} \times 0.85 \text{ (if female)}}{\times \text{ creatinine (mg/dl)}}$$

6. Participant must have adequate hepatic function documented by either AST or ALT ≤ 3 x IULN within 28 days prior to registration. If both AST and ALT are performed,both must be ≤ 3 x IULN. For participants with liver metastases, AST or ALT mustbe ≤ 5 x IULN.
7. Participant must be on effective anti-retroviral therapy and have undetectable viralload at their most recent viral load test and within 6 months prior to registration if they are known to have human immunodeficiency virus (HIV)-infection.

8. Participants must have undetectable HBV viral load within 28 days prior toregistration if participant has known chronic hepatitis B virus (HBV) infection.

9. Participants with a known history of hepatitis C virus (HCV) infection must have anundetectable HCV viral load within 28 days prior to registration.

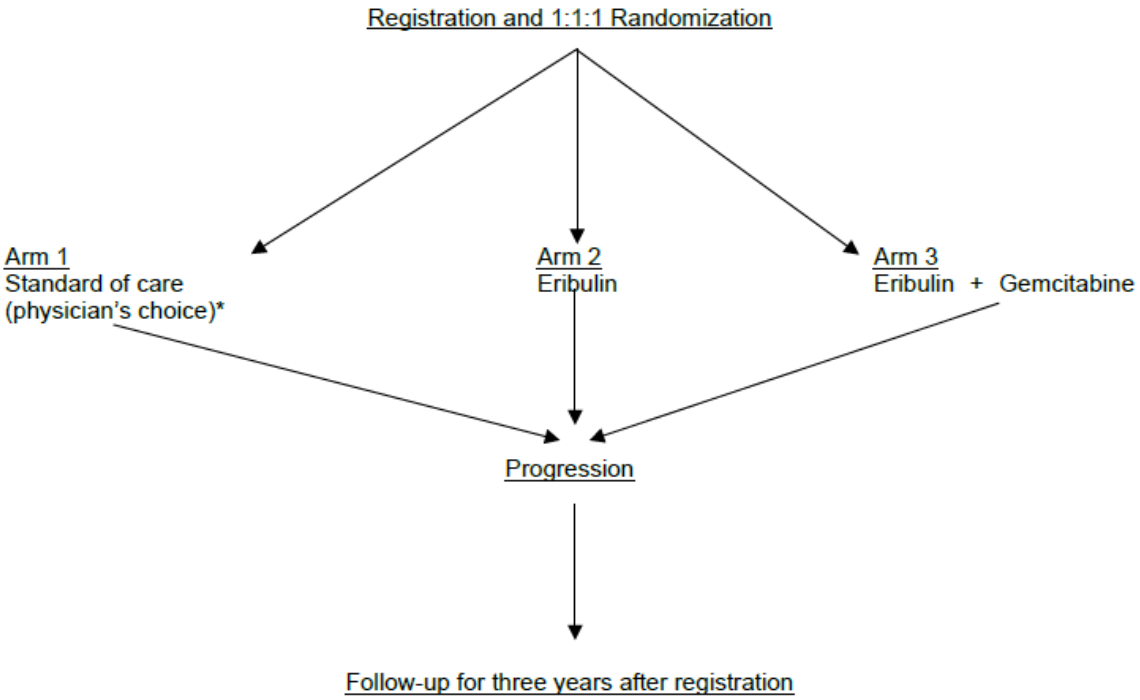
10. Participants may have a prior or concurrent malignancy provided the natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen per the opinion of the treating investigator.

11. Participants must not be planning to take strong or moderate CYP3A or CYP2C8 inhibitors or inducers if randomized to Arm 1 and SOC regimen chosen is Paclitaxel or Docetaxel. Participants receiving strong or moderate CYP3A or CYP2C8 inducers must discontinue use at least 2 weeks prior to randomization.

12. Participant must not have a known history of QTc prolongation.

13. Participants must not be pregnant or nursing due to the risk of harm to a fetus or nursing infant. Women and men of reproductive potential must have agreed to use an effective contraceptive method for the course of the study and 6 months (females) or 3.5 months (males) after the last dose. 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 anypoint a previously celibate participant chooses to become heterosexually active during the time period for use of contraceptive measures outlined in the protocol, he/she is responsible for beginning contraceptive measures.

SCHEMA


Registration and 1:1:1 Randomization
Arm 1
Standard of care
(physician's choice)*
Arm 2
Eribulin
Arm 3
Eribulin + Gemcitabine
Progression
Follow-up for three years after registration