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NCI National Clinical Trials Network

EA8231

ECOG-ACRIN cancer research group

For Patients with Advanced Urothelial Cancer

Please Enroll Your Eligible Patients!

EA8231 Available Through ECOG-ACRIN Cancer Research Group

A Phase III Randomized Trial of Pembrolizumab in Combination with Sacituzumab Govitecan vs Standard of Care in Anti-PD(L)1-Resistant Advanced Urothelial Cancer

Patient Population

See protocol Section 3 for complete eligibility criteria

- Age ≥ 18 years, ECOG PS 0-2, adequate lab values
- Must have histologically-proven conventional urothelial carcinoma (UC) of any urinary tract origin
  - ◊ Must be locally advanced (unresectable or not amenable to curative intent therapy) or metastatic
  - ◊ Any histologic subtype except neuroendocrine (small or large cell) is permitted, as long as tumors include ≥ 1% urothelial histology; pure non-urothelial histology is excluded
- Must have measurable disease (RECIST 1.1) on imaging ≤ 35 days prior to randomization
- Must have had the following prior treatment; must have had progression on/after the immediate prior therapy:
  - ◊ ≥ 1 dose of anti-PD(L)1 therapy (monotherapy or combination regimen) in any disease/therapy setting for UC (must not have had progression within 12 weeks of anti-PD(L)1 therapy)
  - ◊ ≥ 1 line of systemic therapy in advanced/metastatic disease setting (for tumors with FGFR3+ susceptible alteration [for FGFR inhibitor], must have received prior FGFR inhibitor unless contraindicated)
  - ◊ Must have received prior enfortumab vedotin in any disease/therapy setting (unless contraindicated)
- No prior exposure to sacituzumab govitecan/other TROP-2 directed therapies or antibody-drug conjugate that contains topo-isomerase I inhibitor
- Must have Bellmunt Score 0-2 (see Appendix V)
- No history of ≥ Grade 3 irAEs on prior anti-PD1/L1 therapies (exceptions per criterion 3.1.9)
- Must not have known genetic UGT1A1 deficiency (Gilbert's Syndrome) (see criterion 3.1.15 for details)
- Patients with treated brain metastases may be eligible (see criterion 3.1.19 for complete details)
- Must not be on systemic immunosuppressive medication, including steroids > 10 mg prednisone/equivalent QD

Treatment Plan

See protocol Section 5 for complete treatment details

1 cycle = 21 days (+/- 3 days)

Arm A: SOC Therapy of Physician's Choice

- Option 1(a or b): Platinum doublet (maximum of 6 cycles, if tolerated)
  - ◊ a) Carboplatin AUC 4-5 IV Day 1 + Gemcitabine 1000 mg/m² IV Days 1 and 8
  - ◊ b) Cisplatin* 70 mg/m² IV Day 1 + Gemcitabine 1000 mg/m² IV Days 1 and (*Cisplatin may be changed to split dosing or substituted with carboplatin if not tolerated)
- Option 2: Docetaxel 75 mg/m² IV Day 1, until disease progression or unacceptable toxicity
- Option 3: Paclitaxel 80 mg/m² IV Days 1 and 8, until disease progression or unacceptable toxicity
- Will be dosed using institutional standards for weight, BSA, and dose recalculation thresholds. Premedications, antiemetics, hydration, administration and infusion times will follow institutional guidelines
- Use of G-CSF is at investigator discretion, and is encouraged especially for carboplatin-containing regimen (FDA-approved biosimilars also acceptable)

Arm B: Pembrolizumab + Sacituzumab govitecan

- Pembrolizumab 200 mg IV on Day 1
- Sacituzumab govitecan 10 mg/kg on Days 1 and 8
- Continue until disease progression or unacceptable toxicity; pembrolizumab may be given for a maximum of 35 cycles or 2 years
- See Section 5.1.2 for required premedications
- Use of G-CSF is strongly recommended (see Sections 5.1 and 5.5 for recommendations and details)

Protocol treatment may continue beyond disease progression per certain conditions (see Sections 5.1.1-2).

Study Chair:
Monika Joshi, MD

Study Co-Chair:
Petros Grivas, MD, PhD

NCTN Study Champions:
•***Alliance:*** Melissa Reimers, MD

Patient Enrollment (Oncology Patient Enrollment Network [OPEN])

https://open.ctsu.org/open 1-888-823-5923

Protocol Information (ECOG-ACRIN Operations – Boston)

http://ecog-acrin.org (Member Login) 1-857-504-2900

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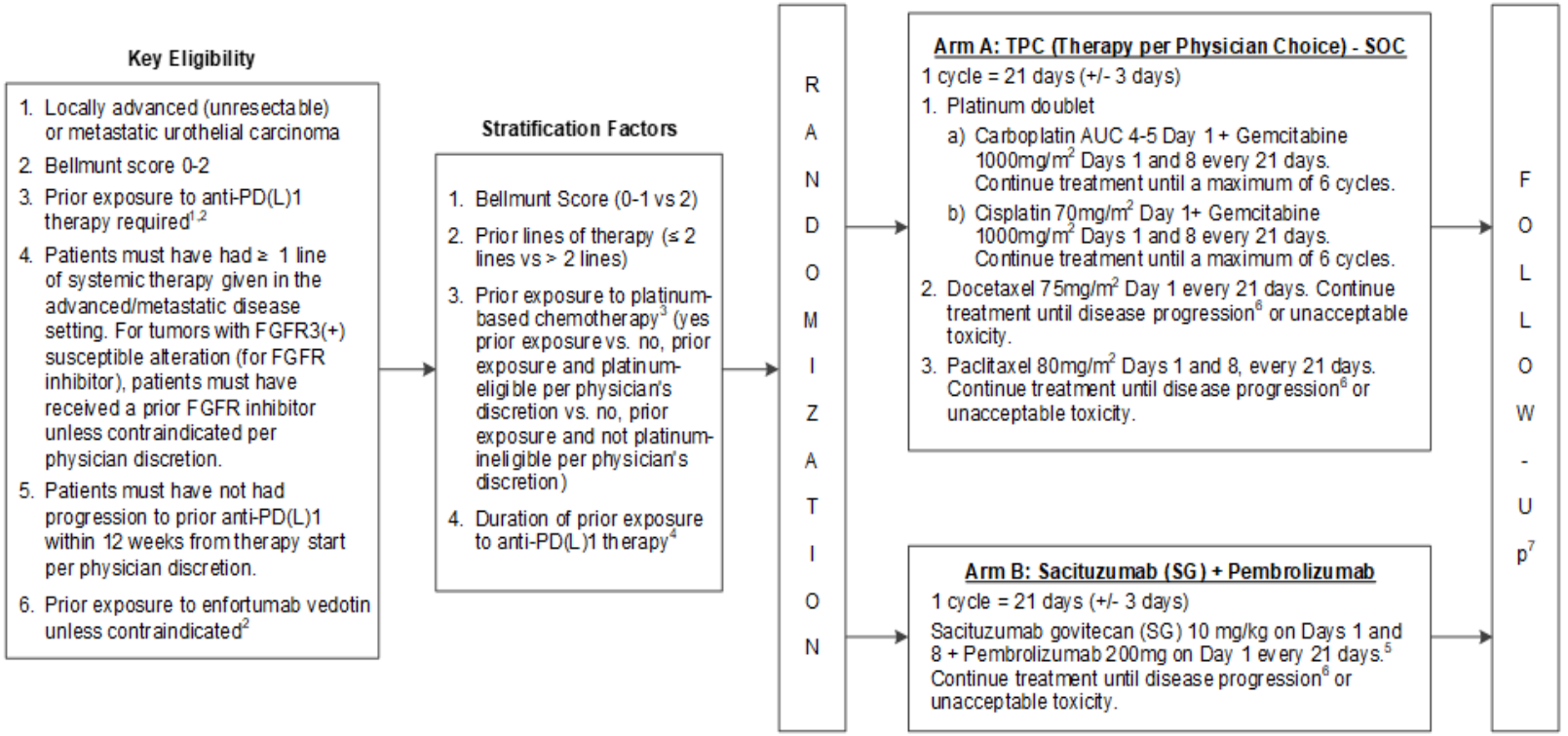
Schema



N = 320
1:1 Randomization

1. Prior use of anti-PD-(L)1 can be given in any disease/therapy setting.
2. Prior enfortumab vedotin (EV) is mandated (in any disease/therapy setting) unless contraindicated.
3. Platinum based chemotherapy= either cisplatin or carboplatin-based chemotherapy.
4. Duration of prior exposure to anti-PD(L)1 therapy: ≤6 months vs. >6 months.
5. Pembrolizumab may be given for up to 35 cycles. Please see Section 5.1 for more information.
6. Patients may be allowed to continue protocol treatment beyond disease progression if certain conditions are met including clinically stable disease, no deterioration in ECOG Performance Status, no adverse events requiring stopping therapy, and no requirement for immediate alternative treatment. The treating physician will discuss this option with the patient and document their agreement to continue protocol treatment beyond radiologic disease progression.
7. Patients will be followed for response assessment until progression, and for survival for 5 years from the date of randomization. Please see Section 5.7 and 5.8.