FAST FACTS

S2012: Randomized Phase II/III Trial of First Line Platinum/Etoposide with or without Atezolizumab (NSC#783608) in Patients with Advanced or Metastatic Poorly Differentiated Extrapulmonary Neuroendocrine Carcinomas (NEC)

1. Eligibility Criteria

Disease Related Criteria

a. Participants must have histologically confirmed (local site pathological confirmation sufficient) extrapulmonary poorly differentiated, neuroendocrine carcinoma (NEC) as defined in Section 4.0, Pathology Criteria.

b. Participants must have disease that is unresectable or metastatic and not eligible for definitive therapy as deemed per the treating investigator.

c. Participants must have radiologically evaluable disease, measurable or nonmeasurable, per RECIST 1.1 criteria. All measurable and non-measurable lesions must be assessed by CT scan with IV contrast of the chest/abdomen/and pelvis (or CT chest without contrast and MRI abdomen/pelvis with gadolinium contrast, if contraindication to CT iodinated contrast) within 28 days prior to registration. While may be used for routine clinical evaluation, PET scans and bone scans alone are not acceptable for disease assessment while participating in this study. All known sites of disease must be assessed and documented on the Baseline Tumor Assessment Form.

d. Participants must have brain MRI (or CT head with contrast if there is contraindication to MRI brain) if clinically indicated within 28 days prior to registration. Note: Brain imaging is not required in participants without known and/or clinical concern for brain

metastases. Participants with asymptomatic central nervous system (CNS) metastases are eligible if one or more of the following apply:

- Participants who have received treatment for brain metastases must have:

  - No evidence of radiological progression (by MRI brain or CT head with contrast if there is contraindication to MRI brain) within 28 days prior to registration

  -Discontinued all corticosteroids at least 14 days prior to registration

- Participants with treatment-naïve brain lesions must have:

  -No lesion measuring >2.0 cm in size in any axis o MRI brain or CT head with contrast (if there is contraindication to MRI brain) demonstrating no evidence for mass effect, edema, or other impending neurological compromise within 28 days prior to registration.

  -No evidence of radiological progression (by MRI brain or CT head with contrast if there is contraindication to MRI brain) within 28 days prior to registration

  -No need for >2 mg of dexamethasone (or equivalent of >10 mg prednisone) per day at time of registration

e. Participants must not have symptomatic central nervous system (CNS) metastases.

f. Participants must not have known or suspected leptomeningeal disease.

2. Prior/ Concurrent Therapy Criteria

   a. Participants with prior history of non-metastatic (localized/locally advanced disease) extrapulmonary poorly differentiated NEC may have had prior platinum-based therapy ± radiation ± surgery provided that all therapy was completed ≥ 6 months prior to registration.

   b. Participants must discontinue denosumab prior to study registration and plan to replace with a bisphosphonate while on the study.

   c. Participants must not have had prior treatment for advanced (except as outlined in 5.2a) or metastatic NEC EXCEPT one cycle of platinum (carboplatin/cisplatin) + etoposide is allowed prior to registration. Other chemotherapy regimens are not allowed. For participants with prostate or urothelial NEC, prior chemotherapy for the non-NEC component (e.g. adenocarcinoma or urothelial) is allowed as long as such therapy was completed ≥24 weeks prior to registration and participants have recovered from all prior toxicities to ≤grade 1.

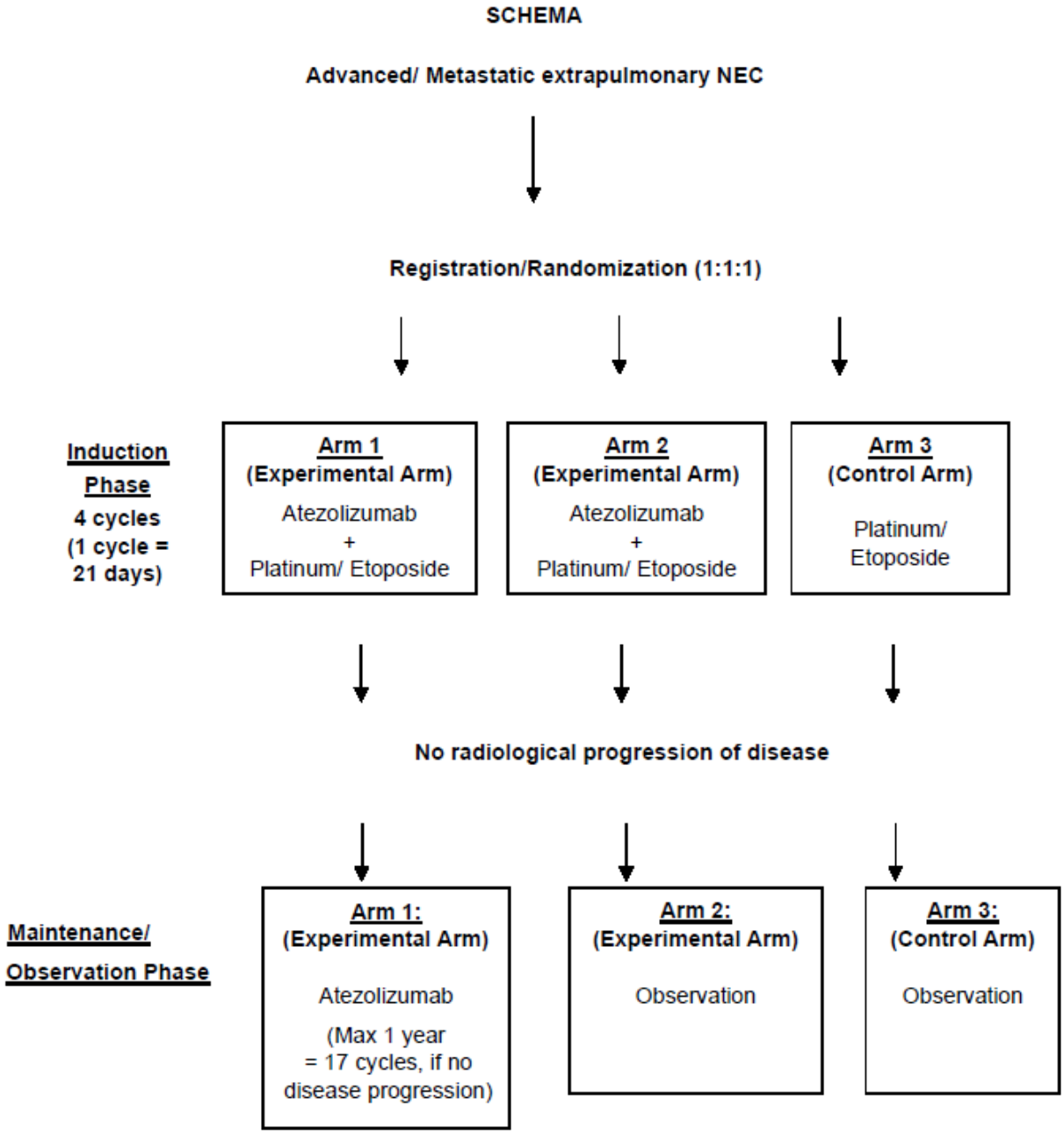
   d. Participants must not have had prior treatment with an anti-PD-1, anti-PD-L1, antiPD-L2, CD137 agonists, anti-CTLA-4 agent, or any other immune checkpoint inhibitors for any neuroendocrine neoplasm. Immune checkpoint inhibitors given for other cancer indications are allowed provided last therapy was given at least 12 months prior to study registration.

   e. Participants must not have received treatment with systemic immunostimulatory agents including, but not limited to, interferon and interleukin2 [IL-2] within 4 weeks or 5 half-lives of the drug (whichever is longer) prior to registration.

f. Participants must not have had history of known severe allergy, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies, including to Chinese hamster ovary cell products or to any component of the atezolizumab formulation, cisplatin, carboplatin, or etoposide.

g. Participants must not be on active systemic therapy for another cancer with the exception of hormonal therapy including androgen deprivation therapy (e.g., gonadotropin-releasing hormone (GnRH) agonists or antagonists), which can be continued while participants are receiving protocol therapy. Use of enzalutamide or apalutamide is permitted after completion of chemotherapy and must be held during chemotherapy for participants receiving prior to enrollment. Use of darolutamide is permitted during chemotherapy. Glucocorticoid-containing regimens, including abiraterone, are not permitted.

SCHEMA



Randomization Stratification Factors:

- Zubrod Performance Status: 0-1 vs. 2
- Disease origin: Prostate vs. Gastrointestinal vs. Other