Cancer Research Consortium of West Michigan
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FAST FACTS

A022106: PHASE II/III SECOND-LINE NABPLAGEM VS. NAB-PACLITAXEL/GEMCITABINE IN BRCA1/2 OR PALB2 MUTANT METASTATIC PANCREATIC DUCTAL ADENOCARCINOMA (PLATINUM)

ELIGIBILITY CRITERIA

1. **Documentation of Disease**
   Metastatic pancreatic adenocarcinoma. Adenosquamous carcinoma, squamous carcinoma, acinar cell carcinoma, and carcinoma not otherwise specified are also acceptable.

2 **BRCA1/2 or PALB2 testing**
   BRCA1/2 or PALB2 mutation (somatic or germline) identified on any CLIA-certified gene panel. Mutations must be considered pathogenic or likely pathogenic by a reference database such as ClinVar or OncoKb.org. (Submission of mutation report will be required, see section 6.1.4)

3 **Measurable disease as defined in Section 11.0.**

4 **Potential trial participants should have recovered from clinically significant adverse events of their most recent herapy/intervention prior to enrollment.**

5 **Clinical or radiographic progression on first-line FOLFIRINOX (or NALIRIFOX) for metastatic disease.**
   - Patients whose front-line chemotherapy was required to be simplified due to toxicity associated with any of the constituent components of FOLFIRINOX/NALIRIFOX (e.g. simplified to FOLFOX, FOLFIRI, 5-FU (including capecitabine)) will be eligible.
   - Patients with progressive disease while on maintenance PARP inhibitor treatment after FOLFIRINOX (or NALIRIFOX), irrespective of how long ago they received FOLFIRINOX/NALIRIFOX, will also be eligible.
   - Patients who develop metastatic disease during or within 6 months after completing FOLFIRINOX/NALIRIFOX in either the locally advanced or adjuvant/neoadjuvant settings will be eligible.

6 **Patients may not have received prior cisplatin for their pancreatic cancer in any setting.** Note: Patients may have previously received gemcitabine +/- nab-paclitaxel for resectable (neoadjuvant/adjuvant) or locally advanced disease if (1) treatment was completed > 1 year ago and (2) in the opinion of the treating provider, re-treatment with gemcitabine/nab-paclitaxel is appropriate.

7 **Age ≥ 18 years**

8 **ECOG Performance Status 0-2 (Karnofsky Performance Status ≥60).**

9 **Required Initial Laboratory Values**

- Absolute Neutrophil Count ≥1,500/mm3
- Platelet Count ≥ 100,000/mm3
- Hemoglobin ≥ 8.0 g/dL
- Creatinine ≤ 1.8 x institutional upper limit of normal (ULN)

OR

Calc. CrCl > 40 mL/min

- Total Bilirubin ≤ 2.0 x institutional ULN*
- AST/ALT ≤ 3 x institutional ULN **

* Any elevated bilirubin should be asymptomatic at enrollment) except for participants with documented Gilbert's syndrome who may only be included if the total bilirubin ≤ 3 x ULN or direct bilirubin ≤ 1.5 x ULN).
** AST/ALT of ≤ 5 x ULN if liver metastases are present.

10 **Not pregnant and not nursing**, because this study involves an agent that has known genotoxic, mutagenic and teratogenic effects.
Therefore, for women of childbearing potential only, a negative pregnancy test done ≤ 14 days prior to registration is required.

11 Patients with > grade 2 peripheral sensory neuropathy are not eligible.

12 Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.

13 Brain metastases: Patients with treated brain metastases are eligible if followup brain imaging after CNS-directed therapy shows no evidence of progression for at least 8-weeks.

Patients with known, new or progressive brain metastases (active brain metastases) or leptomeningeal disease are ineligible.

14 HIV: HIV-infected patients on effective anti-retroviral therapy with undetectable viral load anytime within 6 months prior to registration are eligible for this trial.

15 **Hepatitis B**: For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated.

Hepatitis C: Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load.

16 Concomitant medications

Concomitant Chronic concomitant treatment with strong inhibitors of CYP3A4 is not allowed on this study. Patients on strong CYP3A4 inhibitors must discontinue the drug for 14 days prior to registration on the study. See section 8.1.9 for more information.

Chronic concomitant treatment with strong CYP3A4 inducers is not allowed. Patients must discontinue the drug 14 days prior to the start of study treatment. See section 8.1.10 for more information.

Schema

1 Cycle = 28 Days

Registration/ Randomization 1:1

Arm 1: Nab-paclitaxel 100 mg/m^2 + cisplatin 25 mg/m^2 + gemcitabine 800 mg/m^2 on days 1 and 15

Arm 2: Nab-paclitaxel 125 mg/m^2 + gemcitabine 1000 mg/m^2 on days 1 and 15

Treatment is to continue until disease progression or unacceptable adverse event. Patients will be followed for 2 years from the end of treatment or until death, whichever comes first.

Please refer to the full protocol text for a complete description of the eligibility criteria and treatment plan.

Chemotherapy will be conducted at the registering institution. Laboratory tests may be performed at a non-registering institution.

If the Group credited for enrollment is a non-Alliance Group, then other requirements from the credited Group may apply.