Cancer Research Consortium of West Michigan
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FAST FACTS

TAPUR: The Targeted Agent and Profiling Utilization Registry Study

***Schema on last page**

All Study drugs provided

Patients with metastatic or advanced solid tumors, multiple myeloma or B cell non-Hodgkin lymphoma who have exhausted standard treatment options or for whom no standard treatment is available are eligible to participate in this study. A potentially actionable genomic variant (see Section 5.0 for definition of actionable variant) must be present, as revealed by a tumor genomic test or immunohistochemistry test for protein overexpression, that has been previously performed on a specimen of the tumor or on cell-free DNA obtained from plasma ("liquid biopsy") in a CLIA-certified, CAP-accredited, New York State accredited (for labs offering services to residents of NY) laboratory that is either integrated with the Syapse Precision Medicine/TAPUR platform or registered with the NIH Genetic Test Registry. Patients whose tumor harbors a genomic variant known to confer resistance to a specific anti-cancer agent are not eligible to receive that agent. Additional inclusion and exclusion criteria may apply to specific drugs or drug-tumor type-variant matches and are listed in the appendices for the drugs included in this study. When drug-specific inclusion/exclusion criteria differ from those listed in section 3.0, the drug-specific criteria will take precedence.

To be eligible to participate in this study, a participant must meet all of the following criteria:

1. Adult (age≥ 18 years) patient with a histologically-proven locally advanced or metastatic solid tumor, multiple myeloma or B cell non-Hodgkin lymphoma who is no longer benefitting from standard anti-cancer treatment or for whom, in the opinion of the treating physician, no such treatment is available or indicated.
2. ECOG performance status 0-2
3. Patients must have acceptable organ function as defined below. However, as noted above, drug-specific inclusion/exclusion criteria specified in the appendix for each agent will take precedence for this and all inclusion criteria:
   - Absolute neutrophil count ≥ 1.5 x 106/µl
   - Hemoglobin > 9.0 g/dl
   - Platelets > 75,000/µl
   - Total bilirubin < 2.0 mg/ dl
   - AST (SGOT) and ALT(SGPT) < 2.5 x institutional upper limit of normal (ULN) (or < 5 x ULN in patients with known hepatic metastases)
   - Serum creatinine ≤ 1.5 × ULN or calculated or measured creatinine clearance ≥ 50mL/min/1.73 m2
4. Patients must have measurable or evaluable disease (per RECIST v1.1 for solid tumor, Lugano criteria for non Hodgkin lymphoma or International Myeloma Working Group criteria for multiple myeloma), defined, per RECIST 1.1, as at least one lesion that can be accurately measured in at least one dimension (longest diameter to be recorded for non-nodal lesions and short axis for nodal lesions) as ≥20 mm with conventional techniques or as ≥10 mm with spiral CT scan, MRI, or a subcutaneous or superficial lesion that can be measured with calipers by clinical exam. For lymph nodes, the short

axis must be ≥15 mm. Patients who have assessable disease by physical or radiographic examination but do not meet these definitions of measurable disease are eligible and will be considered to have evaluable disease. Patient's whose disease cannot be objectively measured by physical or radiographic examination (e.g., elevated serum tumor marker only) are NOT eligible.

5. Results must be available from a genomic test or immunohistochemistry (IHC) test for protein expression performed in a CLIA-certified, CAP-accredited, New York State accredited (for labs offering services to residents of NY) laboratory that has registered the test with the NIH Genetic Test Registry or has established an integration with the Syapse Precision Medicine/TAPUR platform. The genomic or IHC test used to qualify a patient for participation in TAPUR may have been performed on any specimen of the patient's tumor obtained at any point during the patient's care at the discretion of the patient's treating physician. Genomic assays performed on cell-free DNA in plasma ("liquid biopsies") will also be acceptable if the genomic analysis is performed in a laboratory that meets the criteria described above. Note: Eligible genomic tests may include any of the following technologies: fluorescence in situ hybridization (FISH), polymerase chain reaction (PCR), comparative genomic hybridization (CGH), next generation sequencing (NGS), whole exome sequencing (WES). The test may have been performed on a fresh or paraffin-embedded specimen of the primary tumor or a metastatic deposit or on cell free DNA derived from plasma, as determined by the treating physician, and must reveal a potentially actionable genomic variant as defined in Section 5.0, or protein overexpression by IHC.
6. Ability to understand and the willingness to sign a written informed consent document
7. Have a tumor genomic profile for which single agent treatment with one of the FDA approved targeted anti-cancer drugs included in this study has potential clinical benefit based on the criteria described in section 7.0.
8. For orally administered drugs, the patient must be able to swallow and tolerate oral medication and must have no known malabsorption syndrome.
9. Because of the risks of drug treatment to the developing fetus, women of child-bearing potential and men must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) for the duration of study participation, and for four months following completion of study therapy. Should a woman become pregnant or suspect she is pregnant while participating in this study or if she is the partner of a male participant in this study and becomes pregnant while he is participating in this study, she should inform her or her partner's treating physician immediately as well as her obstetrician. Female study patients who become pregnant must immediately discontinue treatment with any study therapy. Male patients should avoid impregnating a female partner. Male study patients, even if surgically sterilized, (i.e. post-vasectomy) must agree to one of the following: practice effective barrier contraception during the entire study treatment period and through 4 months after the last dose of study drug, or completely abstain from sexual intercourse.

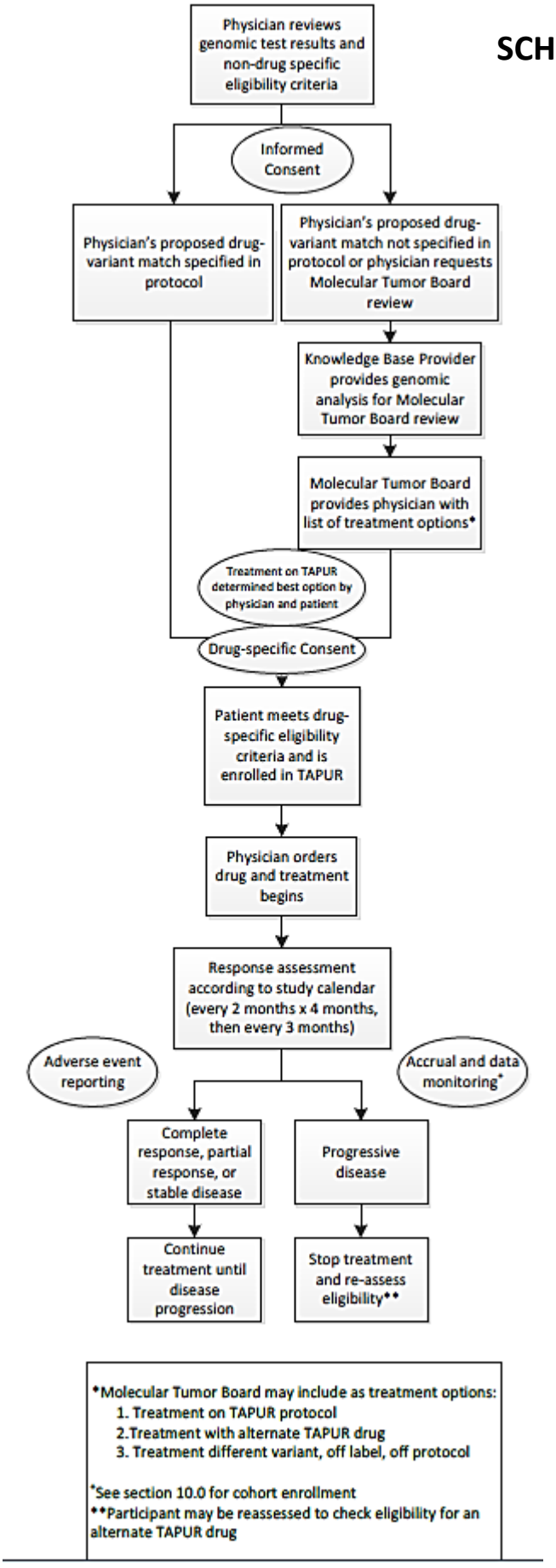
A potential participant who meets any of the following criteria will be excluded from participation in this study (other exclusion criteria might apply for specific drugs listed in Appendices 17.1-17.15):

1. Ongoing toxicity > CTCAE grade 2, other than peripheral neuropathy, related to antitumor treatment that was completed within 4 weeks prior to registration. Patients with ongoing peripheral neuropathy of > CTCAE grade 3 will be excluded.
2. Previous treatment with the selected study drug for the same malignancy.

3. If the patient's tumor has a genomic variant known to confer resistance to an anticancer agent available in this study, the patient will not be eligible to receive that agent but will be eligible to receive other drugs available in this study if all inclusion and exclusion criteria are met for that drug.
4. Patient is receiving any other anti-cancer therapy (cytotoxic, biologic, radiation, or hormonal other than for replacement) except for medications that are prescribed for supportive care but may potentially have an anti-cancer effect (e.g., megestrol acetate, bisphosphonates) or ongoing castration-intent therapy for prostate cancer. These medications must have been started ≥ 1 month prior to enrollment on this study. Patients may be on warfarin, low molecular weight heparin or direct factor Xa inhibitors, unless such therapies are prohibited by drug-specific exclusion criteria.
5. Female patients who are pregnant or nursing. Male patients who refuse to practice barrier contraception methods.
6. Patients with known active progressive brain metastases are not eligible. Patients with previously treated brain metastases are eligible, provided that the patient has not experienced a seizure or had a clinically significant change in neurological status within the 3 months prior to registration. All patients with previously treated brain metastases must be clinically stable for at least 1 month after completion of treatment and off steroid treatment prior to study enrollment.
7. Patients with preexisting cardiac conditions, including uncontrolled or symptomatic angina, uncontrolled atrial or ventricular arrhythmias, or symptomatic congestive heart failure are not eligible.
8. Patients with left ventricular ejection fraction (LVEF) known to be < 40% are not eligible.
9. Patients with stroke (including TIA) or acute myocardial infarction within 4 months before the first dose of study treatment are not eligible
10. Patients with acute gastrointestinal bleeding within 1 month of start of treatment are not eligible.
11. Patients with any other clinically significant medical condition which, in the opinion of the treating physician, makes it undesirable for the patient to participate in the study or which could jeopardize compliance with study requirements including, but not limited to: ongoing or active infection, significant uncontrolled hypertension, or severe psychiatric illness situations.
12. Patients who do not meet drug-specific eligibility requirements for the drug selected by the treating physician, are not eligible to receive that drug.
13. Patients whose disease is not measurable or assessable by radiographic imaging or physical examination (e.g., elevated serum tumor marker only) are not eligible.

Note: For each drug included in this protocol, specific inclusion and exclusion criteria (based on the Package Insert, Investigator's Brochure or manufacturer's recommendations) may also apply. These can be found in the supplemental information about each agent included in the appendices (see 17.1-17.15). Drug-specific inclusion and exclusion criteria will take precedence over the inclusion/exclusion criteria listed in Section 3.1 and 3.2.

SCHEMA



Pre-Study Parameters:

- History & Physical
- CBC/diff/plts
- CMP, Magnesium, LDH, Phosphorus, Pregnancy test,
- Urinalysis,
- Imaging for measurable disease (section 9.2.6), EKG, MUGA or ECHO (as clinically indicated)