PROTOCOL FOR CHEMOTHERAPY OF SUBCUTANEOUSLY IMPLANTED DU145 HUMAN PROSTATE TUMOR XENOGRAFT

MODEL: (3JV72) Subcutaneously Implanted DU145 Prostate Tumor Xenograft

Origin of Tumor Line: (No details).

Summary of Test Procedures: A tumor fragment is implanted sc in the axillary region of athymic random bred (NCr-nu) mice. IP test agent treatment starts when the tumor reaches ca 250 mg and is repeated every 4th day for a total of three treatments. The parameter is median tumor weight. Results are expressed as a percentage of the control tumor weight.

ANIMALS: (Refer to Protocol 8).

Propagation: Athymic random bred (NCr-nu) mice.

Testing: Athymic random bred (NCr-nu) mice.

Weight: Mice should be within a 5-g weight range, with a minimum weight of 18 g for males and 17 g for females.

Sex: One sex is used for all test and control animals in one experiment.

Source: One source, if feasible, for all animals in one experiment. Exceptions to be noted in comments.

EXPERIMENT SIZE: (Refer to Protocol 9).

General Testing: Six animals per test group.

Control Group: A minimum of 20 control animals must be used; otherwise, the number of control animals varies according to the number of test groups.

TUMOR TRANSFER: (Refer to Protocols 2, 5, and 6).

PROPAGATION

Fragment: Prepare a 30-mg (acceptable range 20-40 mg) fragment from 200-500 mg sc donor tumor without surface ulceration.

Time: When donor tumor reaches 200-500 mg (approximately Day 20-28 after implant).

Site: Implant 30-mg fragment sc into axillary region with puncture in inguinal region.

TESTING:

Injection: Inject by body weight (0.1 cc/10 g) unless otherwise specified.

Fragment: Prepare a 30-mg (acceptable range 20-40 mg) fragment from 200-500 mg sc donor tumor without surface ulceration.

Time: When donor tumor reaches 200-500 mg (approximately Day 20-28 after implant).

Site: Implant 30-mg fragment sc into axillary region with puncture in inguinal region. Implant 50-75% additional tumors so that a range in tumor size can be selected on staging day (SD).

TESTING SCHEDULE: (Refer to Protocols 3 and 4).

Day 0: Implant tumor. Run bacterial cultures (refer to Protocol 7).

Day 1: Check cultures. Discard experiment if contaminated.

Day 2: Recheck cultures. Discontinue experiment if contaminated and report accordingly.

SD*: Select mice bearing tumors with calculated weights in the range of 250-500 mg. Record tumor measurements (mm) and weights (mg) for mice selected for each group. Record total animal weights. Prepare materials. Record deaths daily. Administer test agent ip based on the individual body weight.

SD+4 and SD+8: Administer test agent ip based on the individual body weight on day of treatment.

SD+20: End and evaluate experiment. Record total animal weights (including tumor weights) (Weigh Day 2). Record survivors for toxicity day. Determine individual tumor weights by caliper measurements (refer to Protocol 11.301 and EVALUATION below). Individual tumor weights should be reported.

QUALITY CONTROL: (Refer to Protocol 7).

Not established.

---

*SD = Staging day.

EVALUATION: (Refer to Protocol 11).

The parameter measured is median tumor weight based on length and width measurements in millimeters. Report animal body weights for SD and SD+20; T/C will be computer determined for all test groups with >65% survivors on SD+20.

CRITERIA FOR ACTIVITY:

An initial T/C ≤42% is considered necessary to demonstrate moderate activity.

A reproducible T/C ≤10% is considered significant activity.

REPORTING OF DATA:

On the final day of testing, prepare final control and test reports.

Assign a Test Status Code (TSC) of 33 to any test group the screener considers to be invalid for any reason.

A comment must be provided stating the reason for a TSC of 33, when a nonstandard dose is administered (whether due to a solubility problem or special request), and for poor suspensions.