A Phase II Trial Using Grape Seed Extract for Prostate Cancer Patients with Non-Metastatic PSA Progression after Local Therapy

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Introduction and Objectives: Prostate cancer (PCa) patients with non-metastatic prostate specific antigen (PSA) progression after local therapy and a long PSA doubling time (PSA-DT) usually have a period of PSA observation prior to starting on androgen deprivation therapy (ADT). This presents an opportunity to treat patients with compounds that have a favorable side effect profile with the hope of delaying progression of disease.

• GSE is one such non-toxic natural compound, that has been shown to inhibit the growth of hormone-refractory PCAs in both cell culture and PCa xenografts 1,2. The unstructured covaraince structure was used to account for correlation between different visits for the same subject. A random slope and intercept model was fit with a knot at Day 1. The natural log of PSA was taken to satisfy the linearity assumption of this method. An unstructured covaraince structure was used to account for correlation between different visits for the same subject. A random slope and intercept model was fit with a knot at Day 1 on treatment (baseline). The figure shows the predicted values from this model. Individual DT was also calculated for pre- and post- GSE usage using an online tool3. These results are color coded to indicate an increase or decrease in DT on treatment.

Aim 2: To determine the association between changes in PSA level and the duration of prostate cancer patients treated with grape seed extract.

Methods:

• Open-label, single-arm study of GSE Product in 40 asymptomatic PCa patients with rising PSA treated with prior local therapy (radical prostatectomy and/or radiation therapy). This is an interim analysis of the first 20 patients. Patients had at least 3 PSA levels within the 6 months prior to enrollment.

• Treated with 150 mg of GSE (Leucoselect Phytosome® preparation, Indena S.p.A, Milan, Italy) product by mouth twice daily for one year.

• PSA levels were obtained every 6 weeks for 3 months, then every 3 months for the duration of the study.

• Patients were treated on study until clinical disease progression, PSA-DT <3 months based on at least 3 PSA values during treatment, or for one year (whichever comes first).

• Dietary surveys and biologic specimens (blood, urine, stool) for tissue banking were obtained.

• The association of time and PSA level was assessed using a mixed effect modeling approach with the intention of calculating the doubling time. The natural log of PSA was taken to satisfy the linearity assumption of this method.

Results

• Between January and August 2018 – 27 patients were screened and 20 patients enrolled in the GSE trial. A planned pause in enrollment was carried out awaiting assessment of a futility analysis from initial results.

• Median (range) age and baseline PSA were 71 (60-83) and 2.65 (0.44-17.44).

• PSA-DT increased from 5.4 months to 6.4 months after treatment with GSE. (P<0.0001).

• 9 patients had a PSA-DT increase of 30% or greater.

• 8 patients were withdrawn early due to PSA-DT progression <3 months.

• 11 adverse events were reported as possibly related to GSE. Hypertension (2) and dehydration (2) were reported most frequently.

Conclusions

• 300mg oral GSE (daily) may increase PSA-DT in non-metastatic PCa patients with a rising PSA. This may potentially delay progression in these patients.

• The majority of patients had an increase in PSA doubling time.

• Some patients on GSE also have a decrease in PSA levels.

• GSE was well tolerated in this small cohort.

• This is a trial in progress and results are pending for the second cohort of patients. Further study is needed.

References


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