A Feasibility Study to Deplete Non-Essential Amino Acids in Patients with Prostate Cancer

Maggie Zhou[1], Deirdre Crommie[2], Ali R. Khaki[2], Sumit Shah[2], Sandy Srinivas[2], Shann Mika Ruiz[3], Kaidi Moore[3], Joanne Chien[3], Harcharan Gill[4], Geoffrey A. Sonn[4], Alice C. Fan [2#], Randall S. Stafford[1#]

[1]Department of Medicine, Stanford University School of Medicine, [2]Department of Medicine, Division of Oncology, Stanford University School of Medicine, [3]Cancer Center, Stanford HealthCare, [4]Department of Urology, Stanford University School of Medicine, # contributed equally

Objectives

1. Evaluate tolerability and adherence of an elemental synthetic meal replacement product (Tality™, Filtricine Inc) in patients with prostate cancer.
2. Observe changes in amino acids, PSA and weight.

Background

- Depletion of non-essential amino acids can inhibit tumor growth in xenograft models of prostate cancer and colon cancer, demonstrated by researchers at Filtricine Inc., based on a discovery by the Snyder lab.
- Tality™ is a lactose-free and gluten-free medical food program that supplies essential amino acids required by normal cells while eliminating non-essential amino acids that cancer cells may require for growth and replication.

Methods

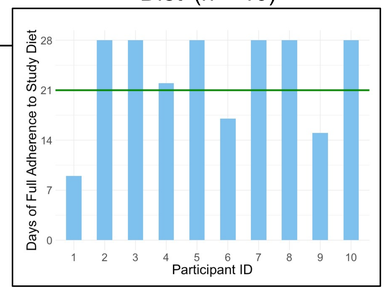
- **Study Design:** Investigator-initiated open label, single-arm pilot feasibility study
- **Inclusion/Exclusion Criteria:** Participants must have biopsy-proven prostate cancer with stable or rising PSA levels; may be on any stable form of anti-androgen therapy, but may not have chemotherapy within one month prior to enrollment.
- **Intervention:** Participants are instructed to use Tality™ as their sole nutritional intake for 28 days and asked to evaluate the product for palatability.
- **Outcomes:** Primary endpoint is proportion of participants that adhere to the diet for at least 21 out of 28-day study period. Secondary endpoints include changes in serum amino acids, PSA, weight, safety, and participant-reported palatability.

Results

Table 1. Demographic and Clinical Characteristics (n = 10)

Variable, n (%)	Value
Race/Ethnicity	
White/Non-Hispanic	9 (90)
Black/African American	1 (10)
Mean age in years (range)	67 (54-79)
Staging	
1	1 (10)
2	2 (20)
3	1 (10)
4	6 (60)
Intact prostate	5 (10)
On active surveillance	3 (30)
Never received systemic therapy	6 (60)
On ADT	2 (20)
On treatment for castrate sensitive disease	1 (10)
On treatment for castrate resistant disease	1 (10)
No. lines of prior therapy	
0	6 (60)
1	3 (30)
2	1 (10)
Prior therapy	
No prior therapy	6 (60)
Androgen deprivation therapy	4 (40)
Androgen receptor blockade	1 (10)
Chemotherapy (docetaxel)	2 (20)

Figure 1. Adherence to Tality™ Diet (n = 10)



Blue bars show number of days of full adherence. Green line indicates goal number of days of adherence (21 out of 28 days).

Figure 2. Body Mass Index (Baseline vs. End of Study) (n = 10)

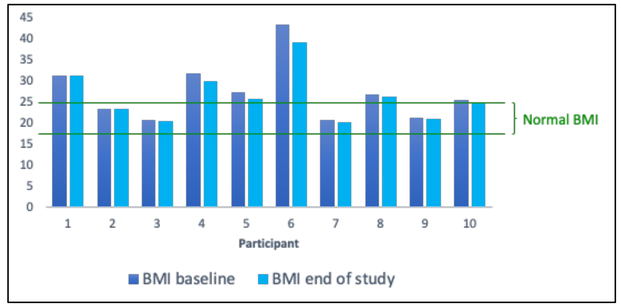
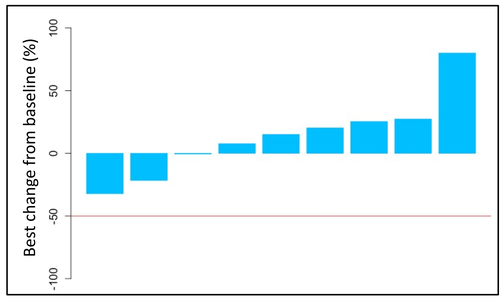


Figure 3. Best % change in PSA from baseline (n = 9)

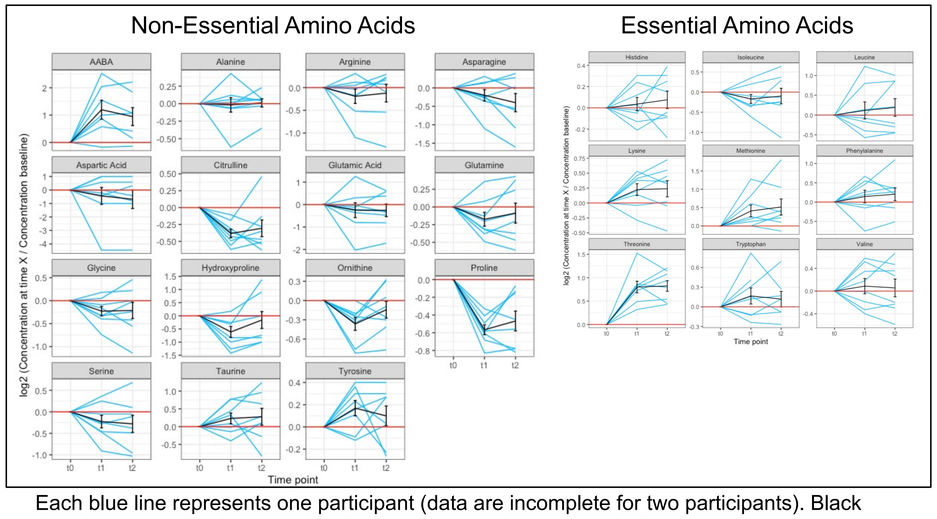


Red line indicates 50% decrease from baseline.

ID	Baseline	Best % Change
P5	107.9	-32.3
P10	7.4	-21.6
P9	16.9	-0.6
P7	3.9	7.7
P6	2.0	15.0
P4	9.4	20.2
P3	3.5	25.3
P8	1.1	27.3
P2	0.2	80.0

One participant (P1, baseline 1.1) is not included: P1 stopped the diet after 9 days due to a death in the family; subsequent study labs were deferred.

Figure 4. Amino Acid Profiles (n = 8)



Each blue line represents one participant (data are incomplete for two participants). Black lines indicate mean logarithmic value of concentration at time X relative to concentration at baseline for each amino acid. Whiskers represent standard error of the mean at t1 and t2. Abbreviations: AABA = α-aminobutyric acid.

Table 2. Adverse events attributed to study product (n = 10)

Adverse Events (All grade 1-2)	n (%)
Constipation*	5 (50)
Diarrhea	5 (50)
Flatulence	3 (30)
Fatigue	2 (20)
Abdominal pain*	2 (20)
Bloating	2 (20)
Headache*	2 (20)
Nausea	2 (20)
Memory impairment*	1 (10)
Dizziness	1 (10)
Dyspepsia	1 (10)
Hyperhidrosis	1 (10)
LUTS	1 (10)
Somnolence	1 (10)
Weight loss	1 (10)

*Indicates at least one participant experienced grade 2 adverse event.

Discussion

- To date, we have enrolled ten male participants (ages 54-79).
- Three participants had localized disease on active surveillance. Six participants had metastatic disease. Four patients had received androgen deprivation therapy, one patient had received concurrent androgen receptor blockade, and two patients had previously received chemotherapy.
- Seven participants demonstrated successful adherence (21 or more days out of 28-day total study period), and six participants completed 28 out of 28 days. Mean number of days of adherence was 23.1 days.
- Three participants experienced decrease in PSA; one participant experienced 32% decrease from baseline level of 107.9.
- Participants experienced the biggest declines in aspartic acid and proline and the largest increases in threonine and α-aminobutyric acid.
- All side effects were CTCAE grade 1 or 2. One patient was withdrawn by study team for grade 1 weight loss due to inadequate caloric intake. Range of weight change was zero to 14 kg loss (mean ± SD = -3 ± 4.2 kg).

Conclusions

- So far, we can conclude from the first ten participants that Tality™ is tolerable for the study period of 28 days, can preferentially reduce non-essential amino acids, and may reduce PSA for patients with high baseline PSA values.
- Changes in weight either maintained a normal BMI or helped overweight participants achieve a more normal BMI.

Funding:
This study is funded by Filtricine, Inc.