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OHR Pharmaceutical Inc.

A Phase II Study of OHR/AVR118 in Anorexia-Cachexia

Martin Chasen, MBChB, FCP (SA), MPhil (Pall Med)[1,2], Ravi Bhargava, MD[2], Shalom Z. Hirschman, MD[3], and Irach B. Taraporewala, Ph.D.[3]*
[1]University of Ottawa Cancer Centre,[2] Elizabeth Bruyere Hospital, Ottawa, ON Canada; [3]OHR Pharmaceutical, Inc., New York, NY, USA

Background

OHR/AVR118 is a novel peptide–nucleic acid immune modulator that modulates the effects of chemokines and cytokines, including tumor necrosis factor-alpha (TNF-alpha). The drug has a singular chemical structure with a favorable safety profile both in animal toxicity studies and in human clinical trials. It is composed of two small peptides, Peptide A, that is 31 amino acids long, and Peptide B, that is 21 amino acids long. Peptide B is unique in that the dinucleotide, diadenosine, is covalently attached to a serine residue in the peptide

In two previous clinical trials, OHR/AVR 118 showed significant activity in the treatment of cachexia in AIDS patients. Treatment with the product restored appetite, effected weight gain and improved quality of life in the cachectic AIDS patients.

Aim

The purpose of the phase II study was to evaluate OHR/AVR118 in patients with advanced cancer to determine if daily administration could mitigate symptoms of cachexia and provide improvement in functional status and quality of life.

Study Scheme

Patients enrolling in the study took OHR/AVR118 4.0mL per day via subcutaneous injection for a 28 day period. At day 28, the patient was able to continue receiving OHR/AVR118 in the extension period, if the patient agreed that it was in their best interest to continue. The study was conducted at the McGill University Cancer Centre and the University of Ottawa Cancer Centre hospitals. The McGill University Institutional Review Board (IRB) and the Ethics Committee reviewed all appropriate study documentation to safeguard the rights, safety, and well-being of the patients. After the study was fully explained, written informed consent was obtained from the patients.

Primary and Secondary Outcomes

•Alleviation of multiple cachexia symptoms at day 28
•Functional Status/Quality of Life as assessed by Simmonds Functional Assessment (SFA); Appetite and early satiety as assessed by patient-generated subjective global assessment (PG-SGA), Edmonton Symptom assessment Scale (ESAS) and dyspepsia symptom severity index (DSSI); weight gain; increase in lean body mass.
•Impact on inflammatory markers and hormonal milieu at day 28.

Inclusion Criteria:

- Histologically confirmed solid tumor cancer, leukemia, lymphoma, or multiple myeloma.
- Concurrent anti-cancer treatment, such as chemotherapy or radiation therapy is permitted except for neo-adjuvant or adjuvant programs.
- Between the ages of 18-85.
- Symptoms of recurrent or metastatic cancer in which anorexia is a predominant symptom, not necessarily associated with cachexia, and are not attributed to anemia, concomitant illnesses, obstruction or loss of organ function.
- Karnofsky performance status of at least 40%
- Palliative Prognostic Score (PaP) of less than 6.
- Pretreatment laboratory data within 7 days of enrollment were: hemoglobin $\geq$8.5 g/dL, absolute neutrophil count (ANC)$\geq$ 1500/mm^3, platelets > 50,000/mm^3, total bilirubin $\leq$2.0, ALT/AST < 2.5 times the upper limit of normal, or, if the patient had liver metastases $\leq$5 times the upper limit of normal, creatinine $\leq$1.5 mg/dL and normal TSH.

Exclusion Criteria:

- Uncontrolled brain metastases or central nervous system disease.
- Mechanical, non-reversible reason for not being able to eat, or have a potential for developing malignant bowel obstruction during the course of the induction phase of treatment, or patients requiring a PEG for obstruction.
- Patient has had any major surgery within four weeks of enrollment.
- Patient has an uncontrolled concomitant illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, or cardiac arrhythmia.

Demographics

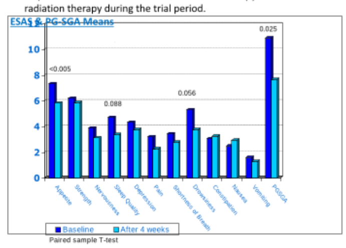
- Sex: Of 29 patients enrolled, 18 - 15 males and 3 females completed the 28 day protocol.
- Age: 7 were <65 years old, 11 were >65 years old.

Tumor type	Patients Enrolled	Patients Completing 28 day Protocol	Patients Continuing Treatment in Extension
Pancreas	7	5	3
Lung	6	5	1
Prostate	2	2	1
Colon	3	1	1
Stomach	4	1	1
Esophageal	1	1	1
Liver	1	1	1
Multiple myeloma	1	1	1
Carcinoid	1	0	0
Head and neck	3	1	1

Results

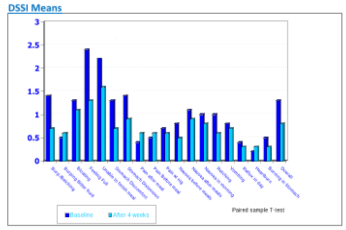
- Of 29 enrolled; 18 patients completed the 28 day protocol (Phase A).
- 11 patients continued in the extension phase (Phase B) up to 153 days.
- 7 patients received concomitant chemotherapy and 1 radiation therapy during the trial period.

ESAS & PG-SGA Means



Paired sample T-test

DSSI Means



Paired sample T-test

Simmonds Functional Assessment

	Baseline (mean)	After 28 days (mean)	p value
Hand grip (kilogram force)	31.7	30.7	0.32
Time sit to stand (seconds)	[illegible]	[illegible]	0.02
50 feet back and forth timed walk (sec)	25.6	[illegible]	0.18
Reach forward (centimeters)	[illegible]	23	[illegible]
Coin Pick up Task Time (seconds)	[illegible]	[illegible]	[illegible]

Body Composition

	Baseline (mean)	After 28 days (mean)	p value
Total BodyWeight (Kg)	68.7	67.1	0.83
Fat (%)	29.8	29.4	0.60
Water (%)	56	58	0.11
BMI (kg/m2)	23	23.4	0.12
Triceps skin fold (mm)	11.6	11.3	0.85

Hematology and Biomarkers

Marker (unit)	Baseline (mean)	After 28 days (mean)	p value
CRP (mg/L)	39.8	40.5	0.84
Albumin (g/L)	31.6	30.2	[illegible]
WBC (mcL)	6.7	5.9	0.15
TSH (mIU/L)	2.5	2.7	0.15
Total Testosterone (ng/dL)	6.5	5.8	[illegible]
Hemoglobin (g/L)	112	107	0.15

Conclusion

- Stabilization of body weight, BMI, body fat and Karnofsky score (no statistical difference from baseline) over the trial period with no rapid decline over time.
- Stable blood marker levels
- Statistically significant Improvement in:
- Edmonton Symptom Assessment score (ESAS)
    - Appetite
- Patient Generated Global Assessment (PG-SGA) score
- Well tolerated therapy with minimal side effects

R/AVR118 Phase II Cancer Cachexia Trial Results