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Exploring Chimeric White Blood Cell Therapy for Advanced, Treatment-Resistant Solid Respiratory Organ Cancers

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ABSTRACT

We conducted a study using Glyco-polypeptides in human subjects to stimulate immune responses, including corpuscle production, interleukins, and Tumor Necrotizing Factors (TNF). These responses led to significant effects on late-stage cancers of the respiratory organs, prostate, and bladder, resulting in necrosis, dissolution, and anti-metastatic effects. Subsequent animal experiments were carried out in our laboratory. Neoplastic cell cultures were injected into the cavities of white rabbits, leading to tumor growth within three months. However, when polypeptides were injected into the cavities every two weeks for six months at a dose of 15 mg, followed by the animals' examination, no tumor growth was observed in the serous membrane.

We proceeded to conduct phase 2 clinical trials (IND 116911) in two groups of patients: a low-dose group receiving 5 mg/kg/day and a high-dose group receiving 50 mg/kg/day for over 6-8 months. A total of 35 patients with third and fourth stages of refractory solid tumors in the respiratory organs, prostate, and bladder were enrolled from a referral center. Twenty-four patients were deemed ineligible and were excluded, having previously failed on at least two chemotherapy regimens and/or immunotherapy. In the high-dose cohort, the results were remarkable, with a complete response rate of 74% and a partial response rate of 20%. Stable disease and progressive disease rates were 3% and 2.7%, respectively. The implications and outcomes of our findings are discussed. Notably, Glyco-polypeptides were found to be effective in treating various types of cancers, particularly at high doses. Importantly, no hepato-renal toxicities or adverse effects were observed during the study.

Keywords: Glyco-Polypeptides; Blood Cell; Refractory Solids; Immune production; Cancer cell; Toxicity.

INTRODUCTION

In our pursuit to find innovative treatments for patients who have not responded to traditional therapies, we explored the potential of Comosain in cancer treatment based on both our own experiences and existing literature evidence. Our trial involved 14 patients in the low-dose cohort and 21 patients in the high-dose cohort. We transitioned the low-dose group to the high-dose category due to ineffectiveness after six weeks, resulting in a total of 35 patients in the high-dose group, whose outcomes were meticulously analyzed.

Reports of orally administered Glyco-polypeptides (Comosain) in cancer treatment date back to 1968 by Wolf M and Ransberger K [1]. Studies, both in vitro and in animals, indicated anti-metastatic effects of Glycopolypeptides (Comosain). In 1988, Batkin and Taussig observed a reduction in pulmonary metastasis in mice with Lewis carcinoma cells after oral administration of Glyco-polypeptides (Comosain) [2,3]. Further research by Batkin and Taussig in 1988 suggested that Glyco-polypeptides (Comosain) exerted its effects through fibrinolytic mechanisms [4]. Additionally, Glyco-polypeptides (Comosain) were found to inhibit platelet aggregation [5] and hinder the growth of various tumor cells, including those from lung, gastric, and leukemia cancers [6]. Studies also indicated that Glyco-polypeptides (Comosain) activated key protein kinases, including MMAPK and TPK [7], and stimulated T-cell activation and production of cytokines like IL-2, IL-6, IL-8, and TNF-a [8-13]. Moreover, Glyco-polypeptides (Comosain) demonstrated the ability to reduce surface antigens in breast cancer cells [7].

Based on these experimental findings, it was concluded that Glyco-polypeptides (Comosain) activation in lymphocytes and T-cells exhibited anti-metastatic effects both in vitro and in vivo. In our present study, we compared the effects of low-dose and high-dose Comosain administration on patients with stage three and stage four refractory solid tumors, including various types of lung, prostate, and bladder cancers. All patients had previously failed on at least two chemotherapy regimens and/or immunotherapy. The treatment duration ranged from 24 to 28 weeks, during which regular evaluations of blood count, liver and kidney functions, hematopoietic components, and tumor markers were conducted every 2 to 4 weeks. X-ray scans were performed every 3 to 4 months to monitor tumor size. The tumor response was assessed according to the National Cancer Institute's Standard Response Criteria, considering Complete Response (CR), Partial Response (PR), Stable Disease (SD), and Progressive Disease (PD). Adverse effects were recorded following the NCI's Standard Toxicity Criteria. Encouragingly, the high-dose group showed promising Complete and Partial Responses when treated with Comosain.

MATERIALS AND METHODS

Glyco-polypeptides (Comosain) were procured from Natural Organics Laboratories, Amityville, N.Y. The capsules containing Glyco-polypeptides (Comosain) were obtained from Capusugel Co., Greenwood, North Carolina. Comosain purity and separation were analyzed using techniques such as SDS-Polyacrylamide Gel Electrophoresis (SDS-PAGE), Ion Exchange Chromatography (CEC), and Fast Protein Liquid Chromatography (FPLC). The study focused on the fractions F1, F2, F3, F4, F5, F6, and F9 in stem (Figures 1-3) for further investigation.

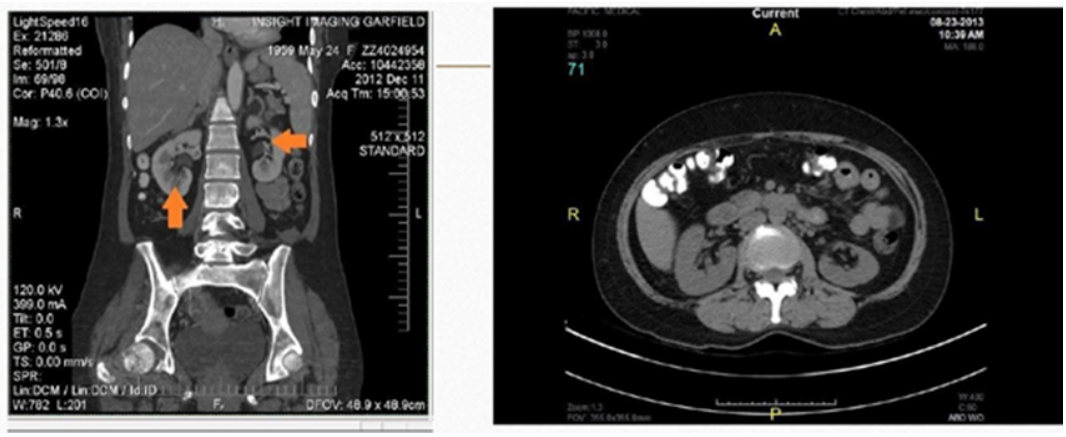
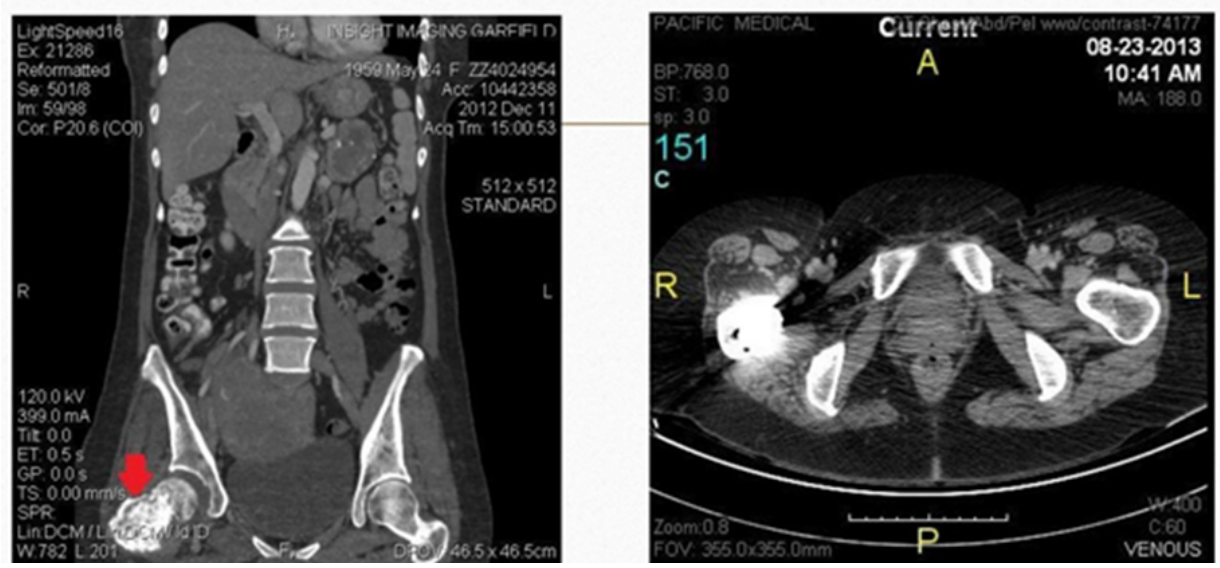
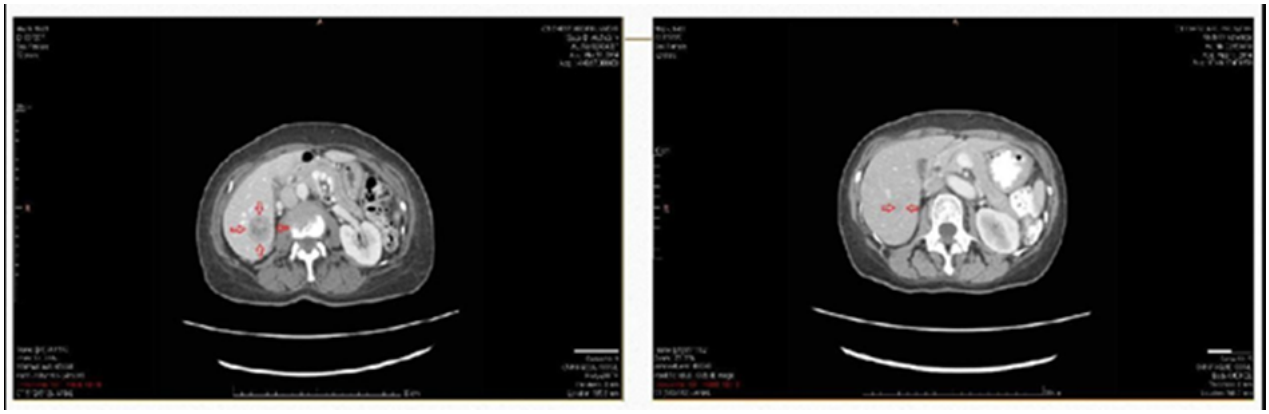


Figure 1: Breast cancer pre and post treatment (Kidney mets).



Case 2: Breast cancer pre and post treatment (Bone Mets).



Case 3: Breast cancer pre and post treatment (Liver Mets, 9.2 cm shrinkage to 2.6 cm).

Glyco-polypeptides (Comosain) were identified using Amperometry detection [9]. The monosaccharide components included L-fructose, D-galactosamine, D-glucosamine, D-xylose, D-mannose, D-glucose, D-galactose, D-fructose, and sugar.

CLINICAL APPLICATION AND STUDY PROTOCOL

Eligible patients for our study were those diagnosed with stage III and IV solid cancers of the lung, prostate, and bladder, confirmed through tissue biopsies, who had not responded to standard therapies or chemotherapy in at least two prior regimens. Patients between 18 and 95+ years, not on anticoagulants, with no recent history of abdominal complications or surgeries, and without uncontrolled hypertension, diabetes, or allergies to Glyco-polypeptides (Comosain) were enrolled. Pregnant or breastfeeding patients were excluded.

RESULTS

After six months, patients' responses were evaluated based on the NCI standard response criteria. Target lesion analysis included disappearance, a minimum 30% decrease, or at least a 20% increase in total

diameters. Stable disease was defined as neither significant shrinkage nor increase in lesions. Tumor markers such as CEA, CA-125, CA-199, PSA, and alpha-feto-protein were monitored and correlated with tumor status.

DISCUSSION

Tumor markers mirrored tumor masses; their normalization indicated tumor regression, while elevation signified progression. No serious adverse effects like hematopoietic or hepato-renal toxicity occurred. Minor side effects, including nausea, vomiting, and insomnia, were rare. Glyco-polypeptides (Comosain) at 2500 to 3000 mg/day in patients of average weight were effective and safe.

CONCLUSION

In summary, Glyco-polypeptides (Comosain) exhibited effectiveness in the high-dose cohort (50 mg/kg/day) but not in the low-dose group. Serious adverse effects were absent, and minor side effects occurred infrequently. The remarkable cancer-killing effects were attributed to increased production of Interleukin-II, VI, VIII, and tumor necrotizing factors from CD2 and CD-3 in monocytes and lymphocytes. Additionally, the inhibition of Major agent Activating Protein Kinases and Tyrosine Phosphorylation Kinases contributed to the fibrinolytic effects on tumor surface antigens (CD-44, CD-44V, CD-44S, CD-45, and CD-47), inducing dehydration, necrosis, and possible calcification within tumor cells. The study demonstrated exceptional complete response rates of 74%, partial response rates of 20%, stable disease rates of 30%, and progression rates of 6.7% in the high-dose cohort. Long-term administration (1 to 3 years) of Glyco-polypeptides (Comosain) at 1000 to 3000 mg/day exhibited no severe side effects or life-threatening events.

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