

## **Executive summary**

### **Colostrum affords mucosal protection in oncology - CAMPIO.**

We have studied the gastrointestinal side effects during cytotoxic therapy and radiotherapy (1-7), caused by an injury to the rapidly proliferating intestinal cells. The patients experience distressful symptoms such as abdominal pain, nausea/vomiting/diarrhoea and anorexia. These symptoms will increase resource utilization such as hospital care, i.v. nutrition, analgesics and antibiotics.

Further, the epithelial injury impairs the normal intestinal barrier function and bacteria and fungi may permeate the intestinal wall. After chemotherapy, a coexistent depressed immune system may lead to serious or even life-threatening systemic infections. After radiation therapy to the pelvis (indicated in uterine, rectal and anal cancer) there are no concomitant effects to the immune system and thus, the risk of systemic infections is not increased. However, the same injury will develop in the epithelium and cause acute (diarrhoea, painful and frequent defecation) as well as long term side effects (such as fibrosis of the anal channel leading to faecal incontinency).

Taken together, these side effects decrease quality of life, increase resource utilization, may be potentially life threatening and, if the cancer therapy has to be withheld, may endanger the therapeutic result. Today, there is no effective prophylaxis against these side effects. One drug (palifermin) has been approved for the prophylaxis against painful ulcerations in the oral cavity after bone marrow transplantation. We have recently found that palifermin exert some protective effects upon the intestinal tract (8). However, bone marrow transplantation is only indicated in haematology (leukaemia and aggressive lymphoma). In addition, palifermin stimulates the regeneration of mucosal cells and there are concerns that the malignant counterpart, constituting the large group of gastrointestinal tumours, would be stimulated by palifermin too. Therefore, palifermin will only be used during the treatment of haematological cancers (5 % of all malignancies). The other approved drug – amifostin – is a scavenger which detoxifies free radicals generated by radiation therapy. It has its one and only indication in radiation therapy for head/neck cancer, is expensive and has significant side effects. Therefore, it has not been introduced into clinical practice in Sweden.

**To summarize** – there is a great need in cancer therapy for effective prophylaxis against the gastrointestinal injury.

Colostrum is vital for the newborn ruminant. It contains antibodies and other mucosal protectants (e.g. transforming growth factor B - TGF B and lactoferrin) and protects the new born against intestinally derived infections.

Our hypothesis is that the same protection could be beneficial in the context of cancer therapy. We have the organization and the protocols ready to study this hypothesis in clinical studies.

As partners to ColoPlus AB, MALMO, Sweden, we are now conducting two phase II studies (one in abdominal radiation therapy and one in chemotherapy) on their patented colostrumbased therapeutic food product named ColoPlus *ONCARE*.

### **Scientific background for the choice of colostrum**

We were able to show that immunoglobulin A, an important component of colostrum, protected the intestinal mucosa during intensive chemotherapy (9). Other investigators have demonstrated a protection by colostrum after intake of anti-inflammatory drugs and during HIV associated diarrhoea (10-11). In laboratory studies bacterial translocation was reduced after the intake of colostrum (12). Thus, these observations provide a basis for clinical studies with colostrum. Our research plan is, in the first part of the developmental program, to study the efficacy, safety and feasibility in two clinical situations:

1. Treatment of colorectal cancer – causing extensive symptoms from the gastrointestinal tract
2. Radiation therapy to the abdomen (after surgery for cancer of the body of uterus, before surgery for rectal cancer and finally, as a curative treatment for anal cancer)

ColoPlus is today available as a therapeutic food product, *IMCARE* and *ONCARE* versions and could without side effects be recommended to the patients.

ColoPlus *ONCARE* was specifically designed for this collaboration and based on its concept of effective exposure to and regulated transport of bioactives in the intestine area. If the clinical studies demonstrate clinical benefit this would translate into important symptom reduction for the patients and an increase in quality of life during and after cancer treatment. Finally, it could be speculated that these beneficial effects may, by maintaining the therapeutic schedule, translate into improvements in the results of the therapy.

### **Commercial potential**

Will depend upon the demonstration of clinical efficacy: If important end points, such as the need for hospitalization and/or artificial nutrition or the numbers of serious infections are significantly reduced, ColoPlus *ONCARE* will quickly be recommended in cancer centres (the problem is well recognized among clinicians). Only in the western region of Sweden (population 1.6 million inhabitants) 20000 cytotoxic treatments are given annually. An estimate is that ¼ of these are associated with side effects to a degree that it could be expected that the patients would experience a benefit from prophylaxis with ColoPlus *ONCARE*.

### **Summary**

Our aim is to prove a beneficial effect by ColoPlus *ONCARE* upon the gastrointestinal side effects during cancer therapy (chemotherapy and abdominal irradiation). If our aim could be reached, the commercial potential would be of a substantial magnitude.

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