**Liraglutide Plus Calorie Restriction Prevents the Spontaneous Development of Type 1 Endometrial Cancer in BDII/Hans Rats**

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**Introduction:**

Glucagon-like 1 peptide (GLP-1) based therapies may hold potential for the prevention and arrest of early-stage Type 1 endometrial cancer (EC1) We investigated the impact of the GLP-1 analogue liraglutide in combination with caloric restriction on tumor dynamics in the BDII/Han rat model of spontaneous EC1.

**Methodology:**

Twelve-month-old BDII/Han rats (n=38) were randomised to either *ad libitum* access to a standard rodent chow diet (STD n=17) or Liraglutide (1mg/kg/d) therapy plus 50% calorie (LIR-diet n=21). After 3 months, animals were euthanised and uterine horns retrieved to record tumour incidence and assess both tumour type and grade. Oestrus cycle stage was established via assessment of ovarian and endometrial histology.

**Results:**

The LIR-diet regimen resulted in 15% weight loss. Tumour incidence was 58% (10 of 17) in STD and 19% (4 of 21) in the LIR group (*p* = 0.0184). In the STD group, 7 of the 8 tumours assessed histologically were EC1 type, with one animal developing a serous type tumour (EC2). All tumours in the LIR-diet group were EC2 type, as confirmed by p16 immunohistochemistry and were immune poor/excluded and CD8+ lymphocyte negative. LIR rats were predominantly arrested in diestrus (64%) and proestrus (29.4%), with follicular atresia frequently observed

**Conclusion:**

Liraglutide in combination with dietary restriction prevented the development of type 1 endometrial cancer-like disease in BDII/Han rats. Evidence suggests that the treatment also selected for the development of serous type, hormone-independent cancer in a smaller number of animals.

KEYWORDS: Endometrial cancer; Liraglutide; BDII/Han rats, GLP-1 analogue

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