



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

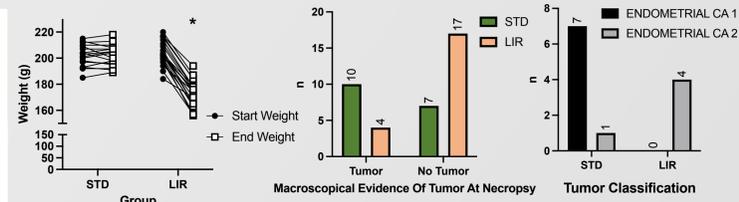
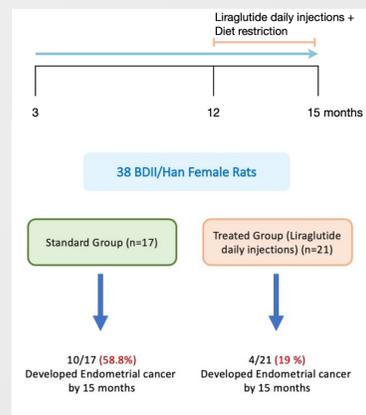
Twelve-month-old BDII/Han rats (n=38) were randomised to either *ad libitum* access to a standard rodent chow diet (STD n=17) or Liraglutide (1mg/kg/d) therapy plus 50% calorie (LIR-diet n=21). After 3 months, animals were euthanised and uterine horns retrieved to record tumour incidence and assess both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

Results

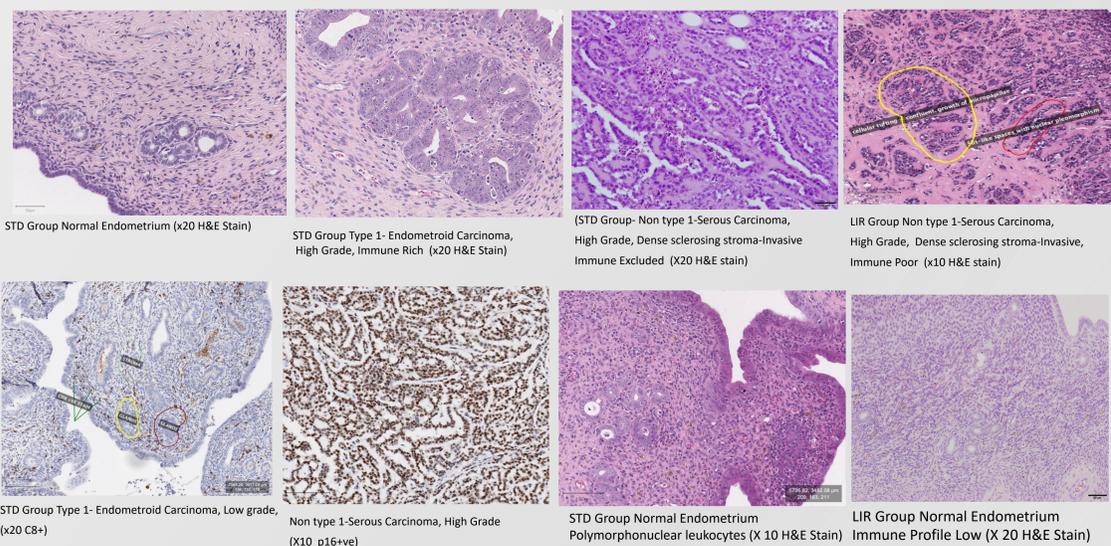
The LIR-diet regimen resulted in 15% weight loss. Tumour incidence was 58% (10 of 17) in STD and 19% (4 of 21) in the LIR group ($p = 0.0184$). In the STD group, 7 of the 8 tumours assessed histologically were EC1 type, with one animal developing a serous type tumour (EC2). All tumours in the LIR-diet 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.
- Calorie restriction complimented with Liraglutide may have suppressed the HPG axis, leading to the downregulation of GnRH, estrogen and ovarian function, resulting in endometrial atrophy giving rise to EC2.



Endometrium Histology



Ovarian Histology

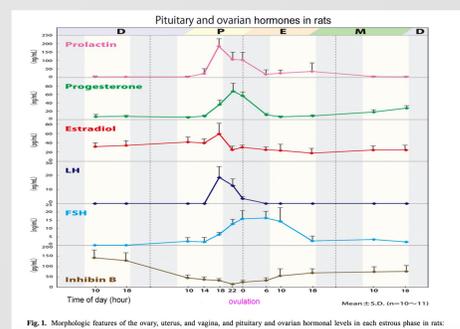
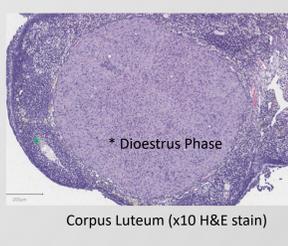
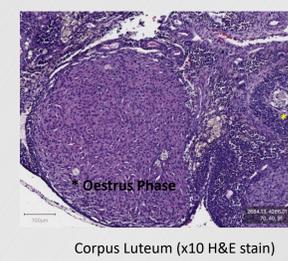
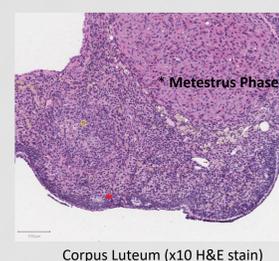
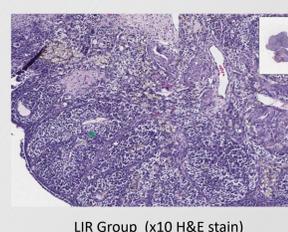
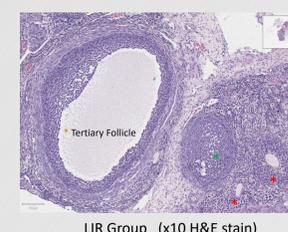
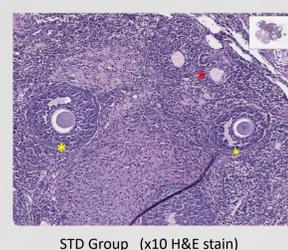
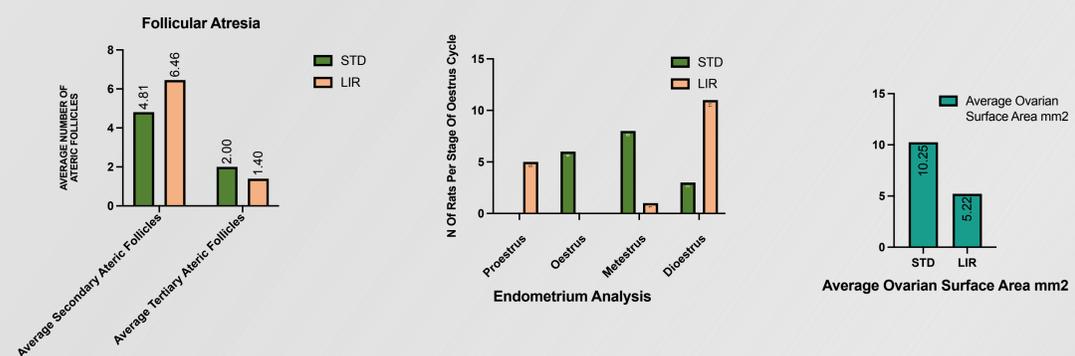


Fig. 1. Morphologic features of the ovary, uterus, and vagina, and pituitary and ovarian hormonal levels in each oestrous phase in rats: D=diestrus, P=proestrus, E=estrus, M=metestrus.

Ovarian Histology Key

- Primary Follicle
- Secondary Follicle
- Tertiary Follicle
- Atretic Follicle
- Corpus Luteum



Corpus Luteum (x10 H&E stain)

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