European Association of Urology

Paris 2006

21st

Annual Congress, France, 5-8 April 2006

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Dr Finn Larsen

Edinburgh, United Kingdom

Title: “Efficacy and safety profile of Teverelix, a new gonadotropin releasing hormone antagonist in patients with advanced prostate cancer”

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Study Description

2 phase II multi-centre, open-label, pilot studies investigating 2 different initial "loading" dose regimens of Teverelix LA (TVX)

- **Study A013:** subcutaneous doses of Teverelix LA 90 mg Day 1 + 90 mg Day 2 + 90 mg Day 3 (n=14)
- **Study A014:** intramuscular doses of Teverelix LA 90 mg Day 1 + 90 mg Day 8 (n=14)

TVX admin. as 1.2 ml of a 75 mg/ml suspension using:

- 0.60 x 25 mm (blue 23G) needle (subcutaneous)
- 0.80 x 50 mm (green 21G) needle (intramuscular)

Study Aims

Primary objective:

- to assess the duration of action of initial "loading" dose regimens of Teverelix LA in terms of suppression of testosterone to below castrate level (0.5 ng/ml)

Secondary objectives:

- to assess the effects on LH and PSA
- to assess the safety of Teverelix LA in terms of local tolerability and systemic tolerability
- to delineate PK parameters

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Investigational Sites

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Dept. of Abdominal Surgery, Subdivision of Oncourology
LITHUANIA

(Studies approved by the Lithuanian Bioethics Committee)

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Study Population

Eligibility Criteria:

- histologically proven adenocarcinoma of the prostate
- androgen deprivation therapy suitable (advanced prostate cancer *i.e. with local invasion or/and metastasis)*

Demographics:

Parameter	A013	A014
Age (yrs [mean])	70.7	73.4
Weight (kg [mean])	80.93	76.14
Height (cm [mean])	170.4	173.9
Ethnicity	Caucasian	

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Prostate Cancer Staging

Staging	A013 (sc)	A014 (im)	TOTAL
T2	1	1	2
T3	3	7	10
T3A	9	4	13
T3B	1	2	3
Nx	3	7	10
N0	11	7	18
Mx	0	0	0
M0	14	12	26
M1	0	2	2

Gleason Score	A013 (sc)	A014 (im)	TOTAL
6	11	8	19
7	2	3	5
8	1	2	3
9	0	1	1
Grading	A013 (sc)	A014 (im)	TOTAL
GRADE I	0	0	0
GRADE II	13	10	23
GRADE III	1	4	5

Results - PK/PD

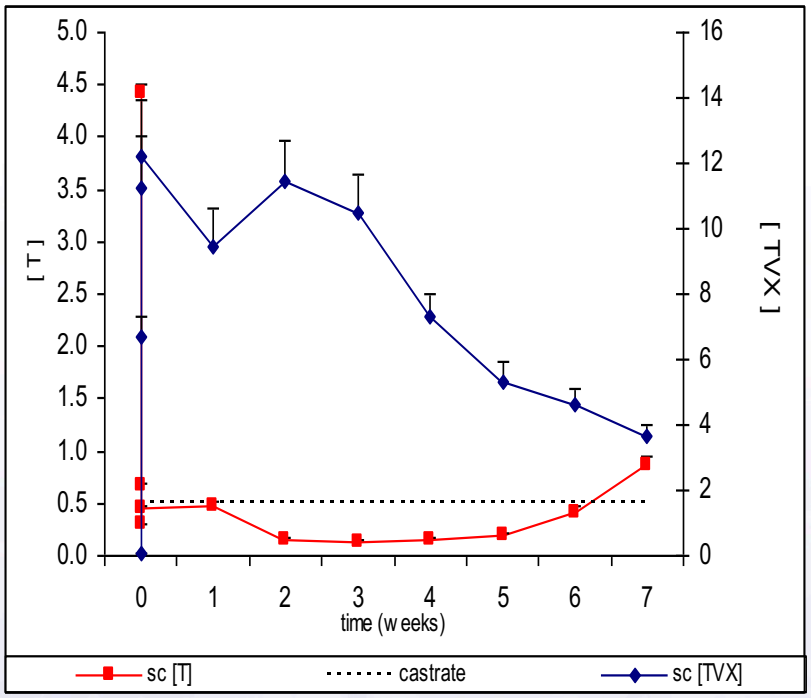

Fig 1 Mean [TVX] (ng/ml) and mean [T] (ng/ml) Following sc (90+90+90 mg D1;D2;D3) dosing of Teverelix

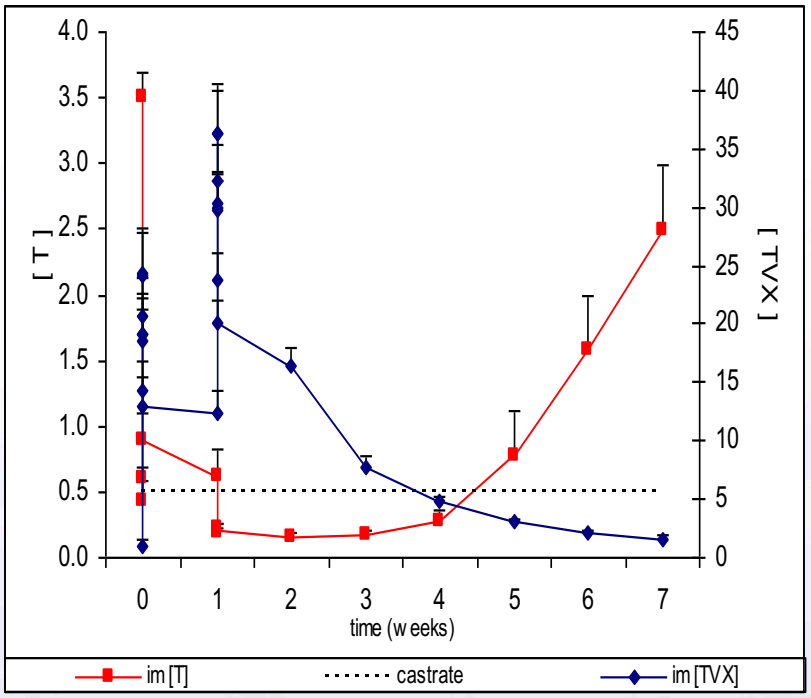

Fig 2 Mean [TVX] (ng/ml) and mean [T] (ng/ml) Following im (90+90 mg D1;D8) dosing of Teverelix

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Results – serum testosterone & PSA

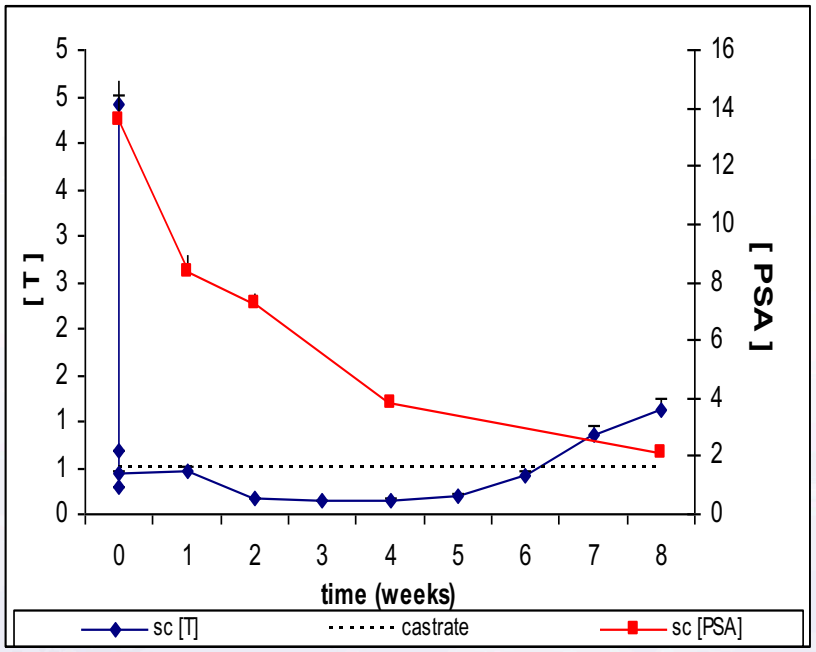

Fig 3 mean [T] and [PSA] (ng/ml) following sc dosing of TVX 90+90+90 mg (D1;D2;D3)

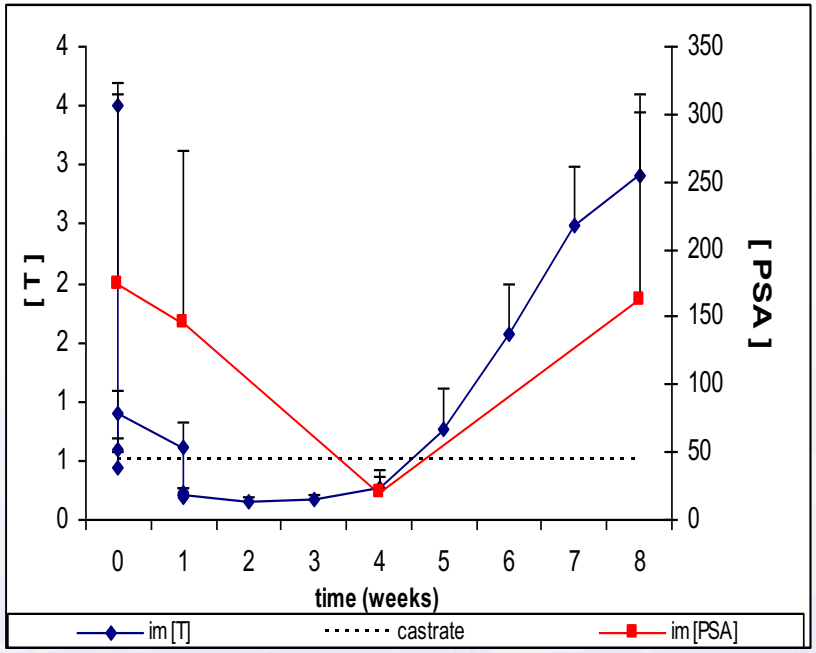

Fig 4 mean [T] and [PSA] (ng/ml) following im dosing of TVX 90+90 mg (D1;D8)

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Summary

Parameter	A013	A014
Onset of castration	1.77 days	2.40 days
Mean duration of castration	55.32 days (range 4 - 14 weeks)	34.77 days (range 3 – 8 weeks)
Mean escape from castration	70.14 days	46.17 days
T below baseline	≥ End Week 6	≥ End Week 4
LH	Decreased following first administration of teverelix on Day 1 and remained below baseline until at least the end of Week 6	Decreased appreciably following administration of Teverelix LA and remained below baseline values until at least the end of Week 5 (LH) and Week 4 (PSA)
PSA		
Tolerability	Very good/good for all patients	

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Conclusions

- Of the "loading" dose regimens investigated in these studies the sc regimen is superior to the im regimen
- The sc dosing regimen achieved:-
  - **100% castration within 1 week p.f.a.**
  - **Castration was maintained for ≥ 4 weeks in 100% of patients (mean ~8 weeks)**
- Teverelix LA was well tolerated with no signs of allergic reactions
- The sc regimen appears to be a suitable "loading" dose regimen for Teverelix LA in the treatment of hormone-sensitive prostate cancer