Editorial Comment on: Degarelix: a Novel Gona
dotropin-Releasing Hormone (GnRH) Receptor
Blocker—Results from a 1-yr, Multicentre, Ran
domised, Phase 2 Dose-Finding Study in the
Treatment of Prostate Cancer
Patrick J. Bastian
Urologische Klinik und Poliklinik, Ludwig-Maximilians-
Universität München, Klinikum Großhadern,
Marchioninistr. 15, 81377 München
patrick.bastian@med.uni-muenchen.de

The Nobel prize-winning discovery of the impor-
tance of androgenic influences on the growth of
prostate cells by Charles B. Huggins and C.V.
Hodges in 1941 established androgen-deprivation
therapy (ADT) as a treatment for metastatic
prostate cancer. As known from the literature,
androgen-deprivation therapy reduces bone pain
in 80–90% of cases, leads to objective responses in
soft tissue and bone, and normalizes serum
prostate-specific antigen (PSA) in over 90% of
patients [1,4,5].

However, ADT results in erectile dysfunction,
loss of libido, fatigue, hot flashes, and loss of
muscle and bone mass, all of which adversely
impact quality of life.

Various forms of ADT exist today, including
bilateral orchiectomy, GnRH agonists, estrogen
therapy, ketokonazole to block adrenal androgens,
and combined androgen blockage, where a GnRH
agonist or orchiectomy is combined with an
antiandrogen.

The study of van Poppel et al describes a
multicentre, randomised phase 2 dose-finding trial
of the novel GnRH antagonist degarelix [2]. A faster
and more profound testosterone suppression can
be achieved using this novel agent compared to
other GnRH antagonists.

The authors defined the castration levels as
≤50 ng/dl. Due to novel, more sensitive assays —
such as the radioimmunoassay technique and the
chemiluminescent technique—levels as low as
20 ng/dl can be detected. There is limited clinical
basis for reducing castrate levels, and no studies
have shown that by lowering the level of testoster-
one to ≤20 ng/dl survival is statistically improved.
It would be interesting to see what the response
rate in this lower castration level group may be.

However, it must be recognized that 2–13% of
patients fail to achieve <50 ng/dl testosterone
following LHRH therapy and 13–37% fail to reach
<20 ng/dl [3].

Another interesting point that warrants discus-
sion is the rate of withdrawals. Fifteen percent of
the enrolled patients withdrew due to adverse
events or insufficient castration level. This level
seems very high and needs additional corrobora-
tion.

Nevertheless, this is an interesting and impor-
tant study to mark the emerging role of GnRH
antagonists in the treatment of prostate cancer.

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