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SAFETY AND EFFICACY OF DEGARELIX IN THE TREATMENT OF PROSTATE CANCER IN A COHORT FROM A GERMAN OFFICE-BASED REGISTRY FOR URO-ONCOLOGICAL QUALITY ASSURANCE

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INTRODUCTION

Efficacy and safety of the GnRH blocker Degarelix was shown in a recent phase III pivotal trial (Klotz et al.). Degarelix was as effective as Leuprolide, maintaining testosterone at castrate levels in patients with all stages of prostate cancer (localised, locally advanced and metastatic). Tombal et al. showed that patients treated with Degarelix had a significantly better PSA progression-free survival compared to Leuprolide.

Results from clinical studies are not always reflected in daily practice, therefore efficacy and safety of the clinical usage of Degarelix should be confirmed in e.g. an uro-oncological quality assurance registry.

Recently the importance of regular testosterone measurements was discussed in several publications (Morote et al., Pickles et al.). Pickles et al. observed a testosterone breakthrough-rate of 3 - 27 % in a Canadian cohort of 2290 patients receiving continuous LHRH-analogue treatment. They concluded that regular testosterone measurements are required for patients being treated with LHRH-analogues.

Usually PSA-failure under LHRH-analogues leads to addition of antiandrogens, other secondary hormone manipulations or chemotherapy. The observed longer time to PSA PFS indicates, that Degarelix might offer a prolonged time to chemotherapy.

MATERIALS AND METHODS

The data collection was performed retrospectively. Moreover the data shown represent a "snapshot" at a defined time point of the registry as the data collection is ongoing.

Since the registry is of non-interventional nature the decision for the treatment with Degarelix was taken prior to inclusion of the patient. Common clinical and procedural parameters were recorded over a period of up to 19 months for patients with prostate cancer to be treated with Degarelix. In 219 patients data on previous treatment, concomitant medication and PCa-stage were collected at the beginning of treatment with Degarelix. Moreover, monthly follow-up findings and, if necessary, results after completion of therapy were recorded. Testosterone and PSA-values as well as side-effects were also documented.

RESULTS

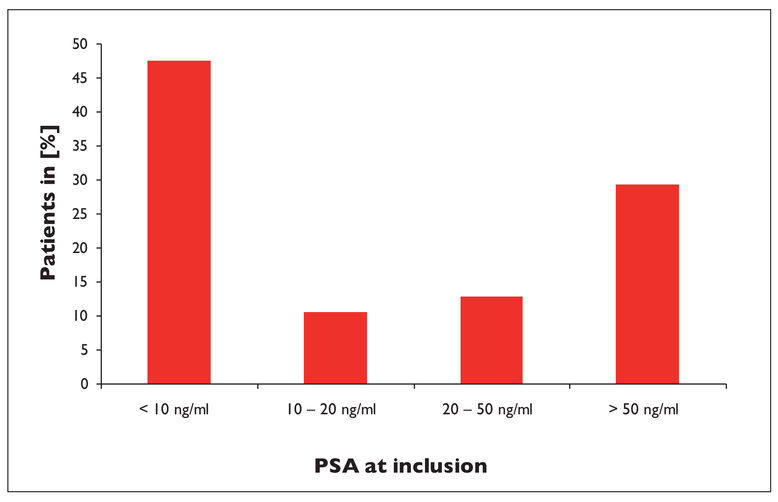
Baseline age and BMI are shown in Table 1. Tumour stages were diagnosed as T1, 27.4 %, T2, 19.6 %, T3, 26.9, T4, 13.7 %, Tx 5.9 % and in 5.9 % not documented. Lymph nodes were positive in 12.8 %, negative in 26.0 %, unknown in 45.7 % of patients and physician did not document the status in 15.5 %.

Tab. 1: Baseline characteristics BMI and age

	BMI	Age
Minimum	**18**	**45**
Maximum	**44**	**92**
Average	**26.39**	**69.82**
Standard deviation	**3.9**	**8.61**

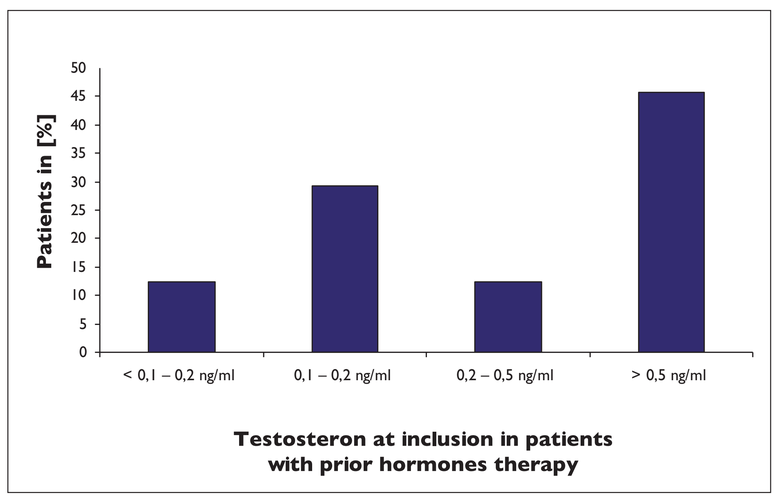
Distant metastases were seen in 21.0 %, no distant metastases in 33.3 %, unknown in 34.3 % and in 11.4 % the status was not documented. A Gleason-Score (GS) < 7 was found in 24.2 %, GS 7 in 30 % and GS > 7 in 42.1 % of the patients, in 3.7 % no documentation was available. GS distribution was quite similar to that found in the overall data of the IQUO-Registry covering a number of LHRH-analogues *(Schulze IQUO Congress, Berlin 2011)*. Median PSA was 12.8ng/mL (Fig. 1).

FIGURE 1



Testosterone was above castration level (> 0.5ng/mL) in 45.8 % of patients with previous hormone therapy and available testosterone value at inclusion (n = 48, Fig. 2). Total number of patients with previous hormone therapy was 74 of 219. The majority of the these were LHRH-Agonist (74.32 %), 17.57 % Antiandrogen and 8.11 % GnRH-Blocker.

FIGURE 2



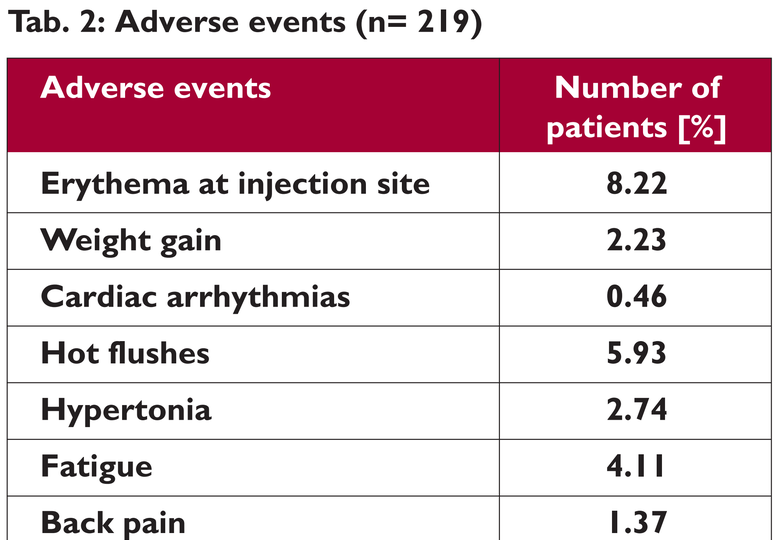
In total adverse events were documented with 70 patients i.e. 31.96 %. The most frequently observed adverse events were erythema at injection site (8.22 %) and hot flushes (5.93 %, Tab. 2). The frequency of injection site reactions documented in this registry is somewhat lower in comparison to the pivotal trial.

Tab. 2: Adverse events (n= 219)

Adverse events	Number of patients [%]
Erythema at injection site	**8.22**
Weight gain	**2.23**
Cardiac arrhythmias	**0.46**
Hot flushes	**5.93**
Hypertonia	**2.74**
Fatigue	**4.11**
Back pain	**1.37**
Pain	**3.2**
Other	**3.65**

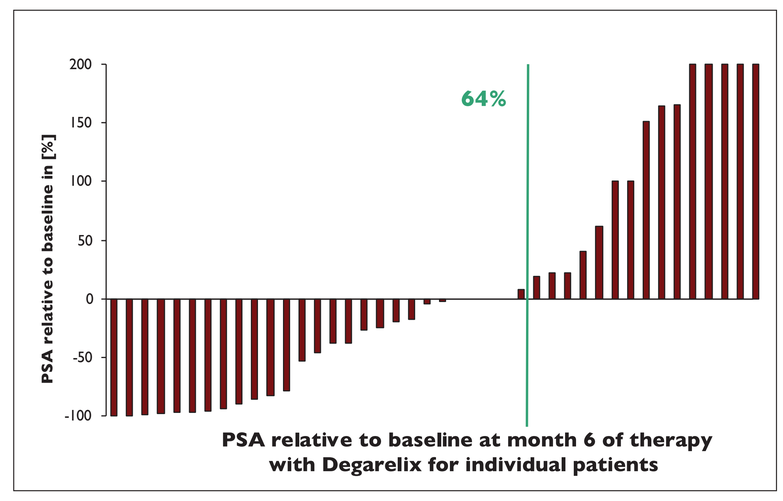
PSA-reduction to < 4ng/mL was achieved in 81.3 % of all patients, median PSA-reduction in patients without hormone pre-treatment was 93.0 % at month 12 compared to baseline (Fig. 3).

FIGURE 3



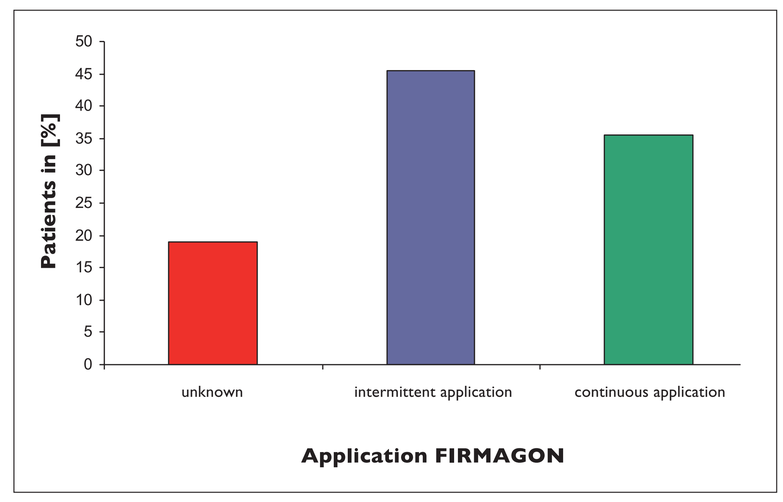
Average time to PSA-progression (2 consecutive rises above baseline) in patients with prior hormone therapy (n = 60) was 23.9 weeks with a maximum of 57 weeks. After 6 month of therapy with Degarelix following a previous hormone therapy 64 % of patients had a stable PSA, defined as PSA equal or lower than baseline, but not larger than 10 % versus baseline. After 12 months of Degarelix following prior hormone therapy, still 52 % of patients had a stable PSA.

FIGURE 4



In the group of hormone naïve patients (n = 163) intermittent androgen-deprivation therapy with Degarelix is quite common (45.4 %).

FIGURE 5



CONCLUSIONS

- The present study demonstrates the efficacy and safety of treatment with Degarelix in daily practice.
- Degarelix is primarily used as first-line androgen-deprivation therapy, like e.g. LHRH-analogues. This is also reflected by the frequent application in patients with a low risk profile.
- Patients treated second-line after LHRH-analogues did also benefit from Degarelix therapy, but not in the same magnitude as first-line treatment with Degarelix.
- Testosterone was above castration level (> 0.5ng/mL) in 45.8 % of patients with previous hormone therapy. The response to Degarelix therapy illustrates the fast, profound and lasting suppression of testosterone also in this population.

REFERENCES

Klotz et al., BJU Int. 2008; 102: 1531–1538

Tombal et al., Eur. Urol, 2010; Vol. 57 (1): 123–131

Morote, et al., J. Urol. 2007; Vol. 178: 1290–1295

Pickles et al., AUA 2011; Abstract 353

Schulze M., IQUO-Congress Berlin 2011; Presentation

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