

Efficacy and Safety of Testosterone in Metastatic Renal Cell Carcinoma Patients with Fatigue: Multicenter Randomized Phase 2 Study (FARETES)



2018

28-30 JUNE
VIENNA, AUSTRIA

SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE

Ilya Tsimafeyeu, Ruslan Zukov, Pavel Borisov, Anastasia Bondarenko,
Kristina Zakurdaeva, Yulia Tishova

Kidney Cancer Research Bureau, Moscow

V.F. Voino-Yasenetsky Krasnoyarsk State Medical University,
Krasnoyarsk

City Clinical Oncology Center, St. Petersburg

I.M. Sechenov First Moscow State Medical University, Moscow

RakFond, Moscow

RUDN University, Moscow



2018
28-30 JUNE
VIENNA

MASCC/ISOO
ANNUAL MEETING
SUPPORTIVE CARE IN CANCER



MAKES EXCELLENT
CANCER CARE POSSIBLE

Faculty Disclosure

Consulting and advisory role: Bristol-Myers Squibb, Eisai, Novartis, Pfizer

Travel grant: Biocad



BACKGROUND

- Fatigue is a frequent symptom of metastatic renal cell carcinoma (mRCC), and most common adverse event of treatment with tyrosine kinase inhibitors and checkpoint inhibitors

Compound / Study	All grades	3-4 grades
Lenvatinib + Everolimus Motzer et al. Lancet Oncol. 2015	59%	14%
Cabozantinib Choueiri et al. NEJM 2015	56%	9%
Sunitinib Motzer et al. JCO 2009	54%	11%
Axitinib Motzer et al. Lancet Oncol. 2013	37%	10%
Nivolumab + Ipilimumab Motzer et al. NEJM 2018	37%	4%
Nivolumab Motzer et al. NEJM 2015	33%	2%
Everolimus Motzer et al. Cancer 2010	31%	5%
Pazopanib Sternberg et al. EJC 2013	20%	2%



2018

28-30 JUNE
VIENNA, AUSTRIA

**SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE**



FARETES STUDY

- The **aim** of this multicenter randomized phase 2 study was to determine efficacy and safety of testosterone undecanoate in mRCC patients with fatigue developed during targeted therapy



2018

28-30 JUNE
VIENNA, AUSTRIA

**SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE**

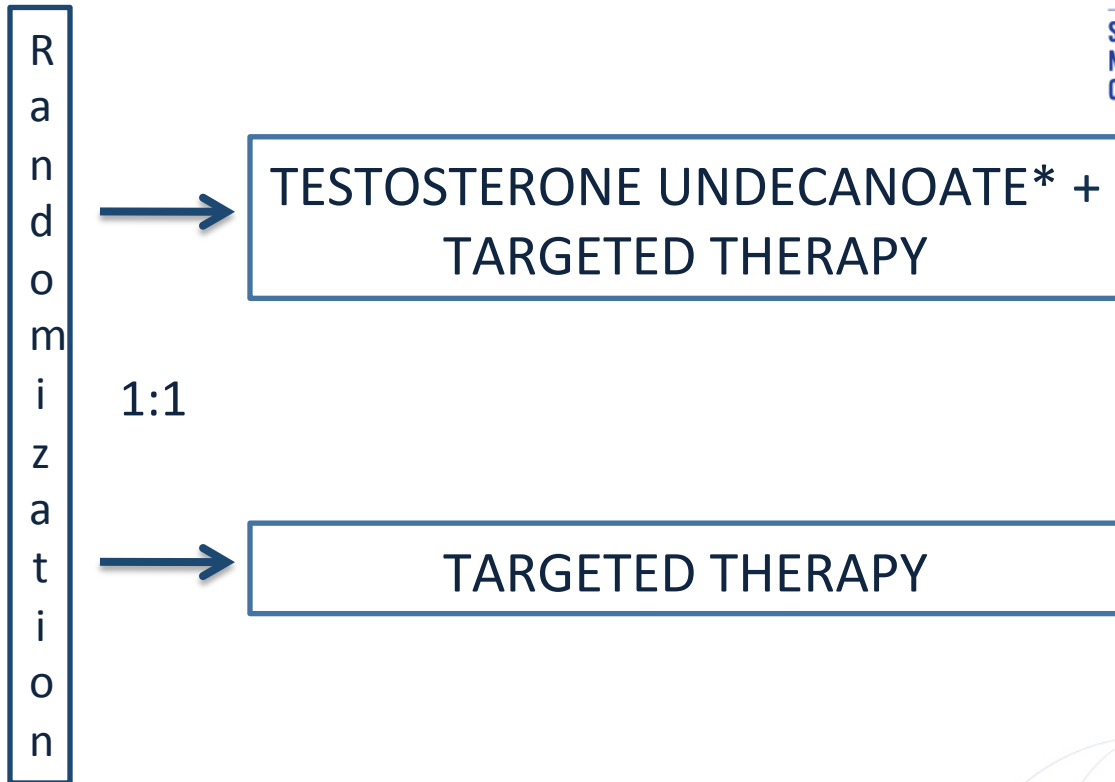


STUDY DESIGN

- multicenter randomized phase 2 study FARETES, N=60

Male patient with:

- clear cell mRCC
- normal PSA level
- low testosterone level (<12.1 nmol/L)
- no evidence of hypothyroidism
- fatigue as side effect of first-line sunitinib or pazopanib



*Nebido®, 1,000 mg, was injected intramuscular deeply on Day 1 of a new treatment cycle



2018
28-30 JUNE
VIENNA, AUSTRIA

SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE



ENDPOINTS

Primary endpoint:

difference in mean change of fatigue according to Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue)

Secondary endpoints:

safety
FKSI-19 score,
testosterone serum concentrations,
red blood cells count
hemoglobin level

Exploratory endpoints:

Duration of TT, ORR, PFS, OS

Assessments:

The assessments were performed at baseline and Day 28 of a treatment cycle



2018

28-30 JUNE
VIENNA, AUSTRIA

SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE



RESULTS (1): PATIENT CHARACTERISTICS & TOXICITY



2018
28-30 JUNE
VIENNA, AUSTRIA

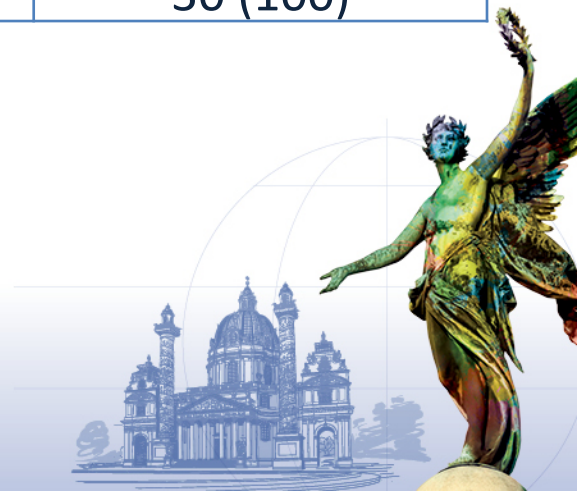
SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE

- Rate of hypogonadism was 75.6% (62 from 82 screened patients)

Patient characteristics

	T group, N=30	Control group, N=30
Age (years), mean (range)	52 (33-71)	55 (42-69)
Sunitinib, N (%)	28 (93)	28 (93)
Pazopanib, N (%)	2 (7)	2 (7)
IMDC poor risk factors, 0-2, N (%)	21 (70)	22 (73)
Previous nephrectomy, N (%)	30 (100)	30 (100)

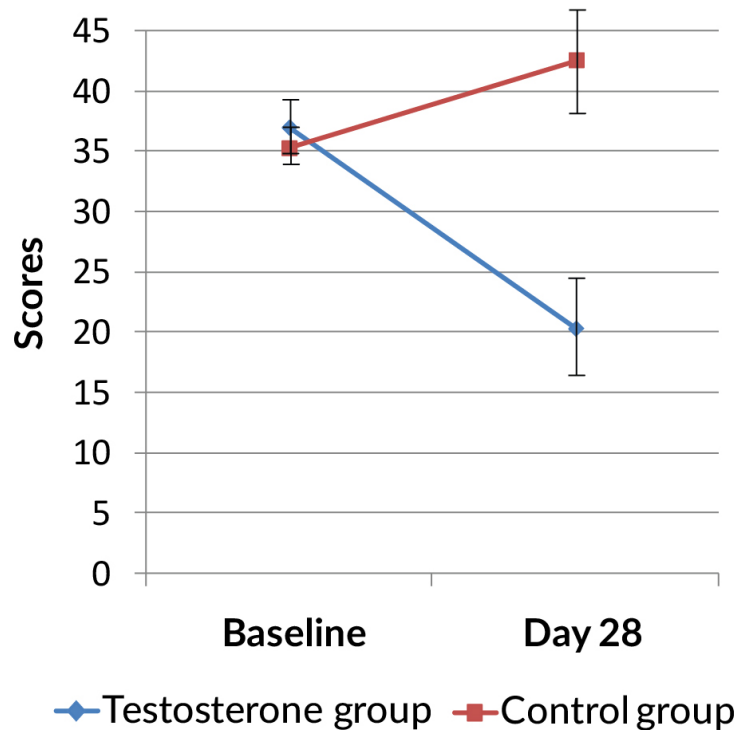
- Testosterone was well tolerated in mRCC patients
- No unexpected and grade 2-4 toxicity was observed



RESULTS (2): FACIT-F

- Change from baseline in the fatigue score on the Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-Fatigue) questionnaire

Scoring is based on a scale from 0 to 52, with lower scores indicating less fatigue



The current study did achieve its primary endpoint based on the significant differences favored Testosterone over targeted therapy alone regarding fatigue ($P=0.012$)



2018

28-30 JUNE
VIENNA, AUSTRIA

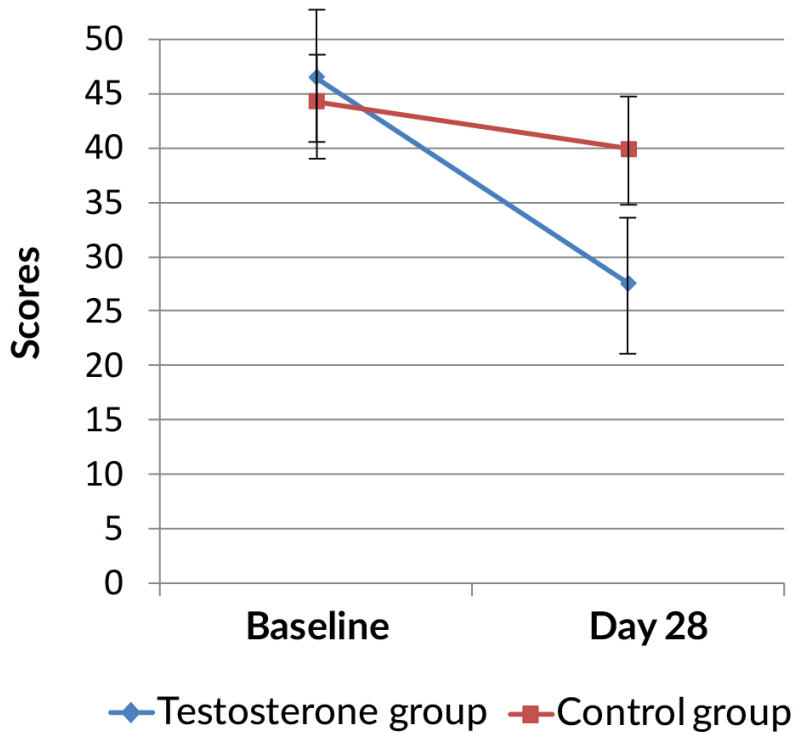
SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE



RESULTS (3): NCCN-FACT FKSI-19

- Change from baseline in the fatigue score on the NCCN/ Functional Assessment of Cancer Therapy (FACT)-Kidney Symptom Index 19 (NCCN-FACT FKSI-19) questionnaire (Ver. 2)

Scoring is based on a scale from 0 to 76, with lower scores indicating less fatigue



The health-related quality-of-life scores in the Testosterone group were better than those in the control group (P = 0.01)



2018

28-30 JUNE
VIENNA, AUSTRIA

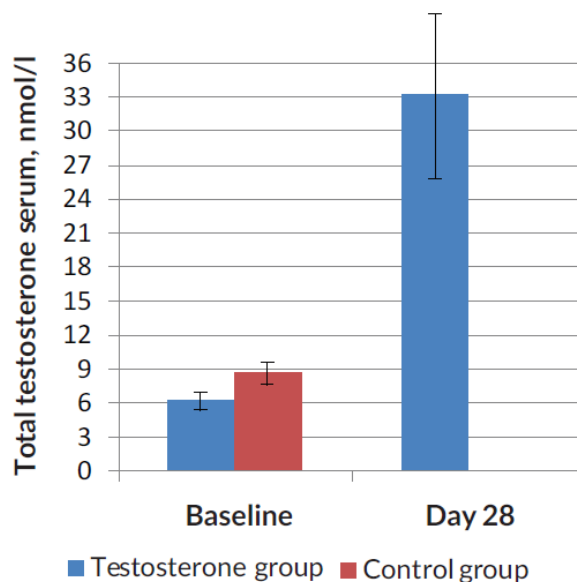
SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE



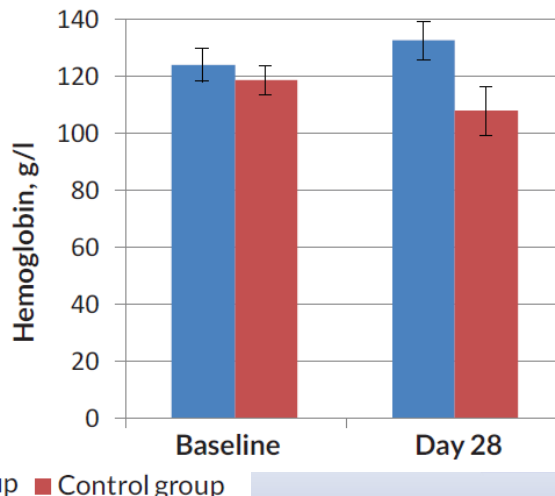
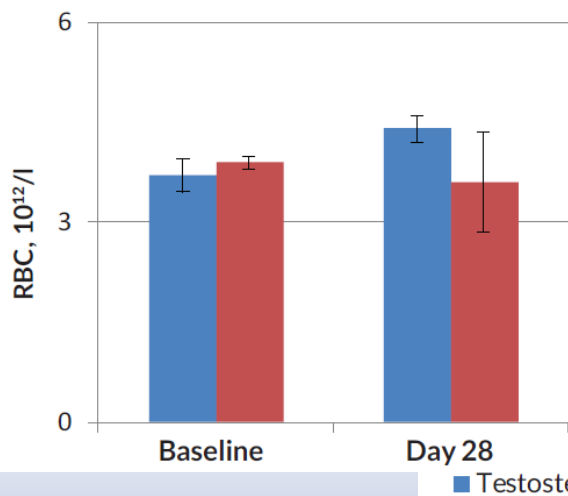
RESULTS (4): TESTOSTERONE, RBC, HB

- Testosterone serum concentration was significantly higher on the Day 28 ($P = 0.029$)
- There was non-significant positive trend in RBC count and hemoglobin level between 2 groups

Testosterone concentration



Red blood cell count & Hemoglobin level



2018

28-30 JUNE
VIENNA, AUSTRIA

SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE



RESULTS (5): EXPLORATORY ENDPOINTS

- At data cutoff (June 20, 2018), median (range) follow-up was 11.2 (7.8 -14.6) mo
- **Objective response rate:**
 - 46.7% (14/30) including 1 CR and 13 PRs in the Testosterone arm
 - 33.3% (10/30) including all PRs in the Control arm (P=0.3)
- **Median duration of targeted therapy (from the start of first-line):**
 - was not reached for Testosterone
 - was 8.3 (95% CI 7-9.6) mo for Targeted therapy alone
- **Discontinuation** due to SU/PAZ-related adverse events was occurred in 3% (1/30) of patients in the Testosterone group and in 17% (5/30) of patients in the Control group
- **Median PFS and OS** has not been reached in both arms



2018
28-30 JUNE
VIENNA, AUSTRIA
SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE



CONCLUSIONS

- Male patients with mRCC receiving targeted therapy had significantly less fatigue and better symptom control with Testosterone
- Testosterone therapy was safe
- Testosterone can prolong the duration of targeted therapy
- PFS and OS will be reported



2018

28-30 JUNE
VIENNA, AUSTRIA

SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE

