



Effectiveness of Zometa® treatment for the prevention of bone metastases in high risk prostate cancer patients. A randomized, open-label, multicenter study of the European Association of Urology (EAU) in Cooperation with the Scandinavian Prostate Cancer Group (SPCG) and the Arbeitsgemeinschaft Urologische Onkologie (AUO).

Protocol Number. CZOL446G DE08 Eudract Number 2004-001786-18

## Timeline

- Start date recruitment: June 2004
- End date of recruitment: August 2007
- End date of study: December 2011
- Status: Two-year extended follow up completed, published

## In Brief

Zoledronic acid (Zometa®) is a third-generation nitrogen-containing bisphosphonate which has been approved in Europe and the US for the treatment of bone metastases (4mg Zoledronic acid iv/month) in a broad range of tumors and for the treatment of malignancy-related hypercalcaemia. In animal models, bisphosphonates have been shown to reduce and even to prevent the development of bone metastases.

It is expected that in the present study Zometa® in addition to the prevention of bone metastases will show its potential in preventing hormone therapy induced bone loss.

Patients were randomised between standard treatment plus Zometa® 4 mg infusions every 3 months for a total of 48 months, or standard treatment only.

## Primary Outcome

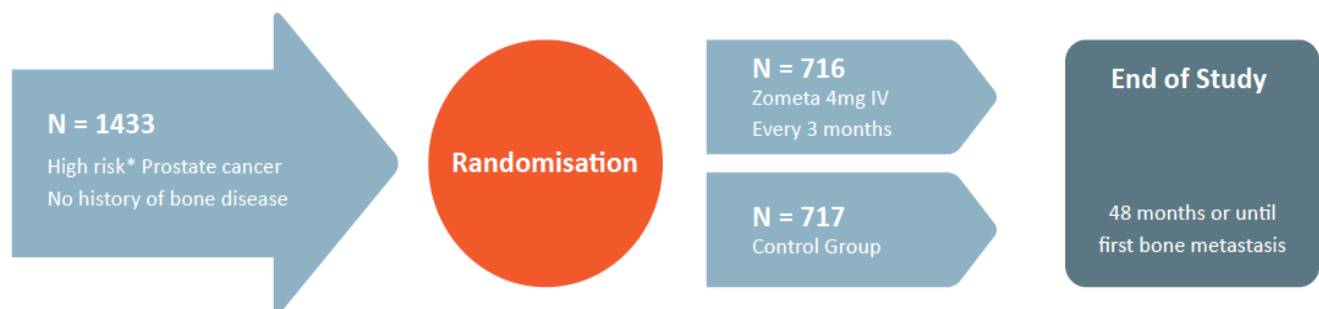
The proportion of patients who develop bone metastases during the study.

## Secondary Outcomes

1. Time to first bone metastasis;
2. Overall survival;
3. Time to PSA doubling;
4. Safety;
5. Bone mineral density (sub study in selected centres) and
6. Biochemical markers of bone turnover (sub study in selected centers only).

Please find the full description of the trial on the [NetherlandsTrial Register](#)

## Study Design



\* High risk prostate cancer



PSA at diagnosis  $\geq 20$  ng/ml  
or Gleason score 8-10  
or pN+

All patients are on daily supplements of  
500 mg Calcium and 400-500 IU of Vitamin D



## Patient Recruitment

Country	Centers	Recruited patients
Belgium	1	9
Denmark	5	66
Finland	5	86
France	8	79
Germany	62	741
Greece	3	24
Italy	16	123
Netherlands	13	121
Norway	5	45
Spain	6	70
Sweden	5	27
Switzerland	1	15
Turkey	3	27
<b>Total</b>	<b>133</b>	<b>1433</b>

## Publications on patient recruitment

Witjes W et al. Journal of Clinical Oncology, 2006 ASCO Annual Meeting Proceedings Part I. Vol 24, No. 18S (June 20 Supplement), 14644, 2006.  
 Wirth M et al. Proceedings ASCO Prostate Cancer Symposium, 2007.  
 Wirth M et al. Eur Urol Suppl 6(2) 201, A715, 2007.  
 Wirth M et al. Proceedings EMUC, Barcelona, 2007.  
 Wirth M et al. Proceedings ASCO Genitourinary Cancers Symposium, 2008.  
 Wirth M et al. Eur Urol Suppl 7(3) 232, A647, 2008.

## Study Publication

Wirth et al. Prevention of bone metastases in patients with high-risk non metastatic prostate cancer treated with Zoledronic Acid: Efficacy and safety results of the Zometa European Study (ZEUS). Eur. Urol. 67 (2015) 482–491. <http://dx.doi.org/10.1016/j.eururo.2014.02.014>

## National Coordinators

Belgium:	Prof. Thierry Roumeguere
Denmark:	Dr. Jesper-Rye Anderson
Finland:	Prof. Teuvo Tammela
France:	Prof. Clement-Claude Abbou
Germany:	Mr. Michael Lein
Greece:	Prof. Nikolaos Sofikitis
Italy:	Prof. Andrea Tubaro
Norway:	Dr. Anders Angelsen
Spain:	Dr. F. A. Gomez Veiga
Spain:	Dr. Juan Morote Robles
Switzerland:	Dr. Georg N. Thalmann
The Netherlands:	Dr. Theo M. de Reijke
Turkey:	Dr. Cag Cal

## Steering Committee

Prof. Manfred Wirth, Germany - Principal Investigator  
 Prof. Kurt Miller, Germany – AUO  
 Mr. Anup Patel, UK  
 Prof. Teuvo Tammela, Finland - SPCG  
 Prof. Andrea Tubaro, Italy  
 Dr. Wim Witjes, The Netherlands – EAU Central Research Office  
 Prof. Frans Debruyne, The Netherlands

## Independent Data Monitoring Committee

Prof. Fritz Schröder, The Netherlands  
 Prof. Cora Sternberg, Italy  
 Prof. Markus Löffler, Germany

## Project Manager

Christien Caris, MSc. EAU Central Research Office

## Contact

EAU Central Research Office

PO Box 30016, 6803 AA Arnhem, The Netherlands

Email: [researchfoundation@uroweb.org](mailto:researchfoundation@uroweb.org), Phone: +31 (0) 26 38 90 677