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A randomized, double blind, placebo controlled phase II trial to evaluate the safety and efficacy of recMAGE-A3 + AS15 ASCI in patieNts with MAGE-A3 pOsitive muscLe Invasive blAdder cancer after cystectomy. A European Association of Urology Research Foundation Randomized Phase II Clinical Trial. Number: EAU-RF 2010-01. Eudract Number: 2010-019181-91

Overview

This study's goal was to assess an investigational cancer immunotherapeutic treatment for patients with Muscle Invasive Bladder Cancer in whom the urinary bladder was surgically removed. The investigational treatment was aimed to increase the body's immune response to a specific antigen expressed by the cancer. The tumour tissue was first tested whether it expressed the MAGE-A3 antigen.

Entry Criteria

The MAGNOLIA study was open to male and female patients with pathologically confirmed muscle invasive transitional cell carcinoma of the urinary bladder with expression of the antigen MAGE-A3 with or without limited lymph node involvement who had no evidence of disease after radical cystectomy confirmed with imaging procedures (scans CT/ MRI).

Primary Outcome Measure

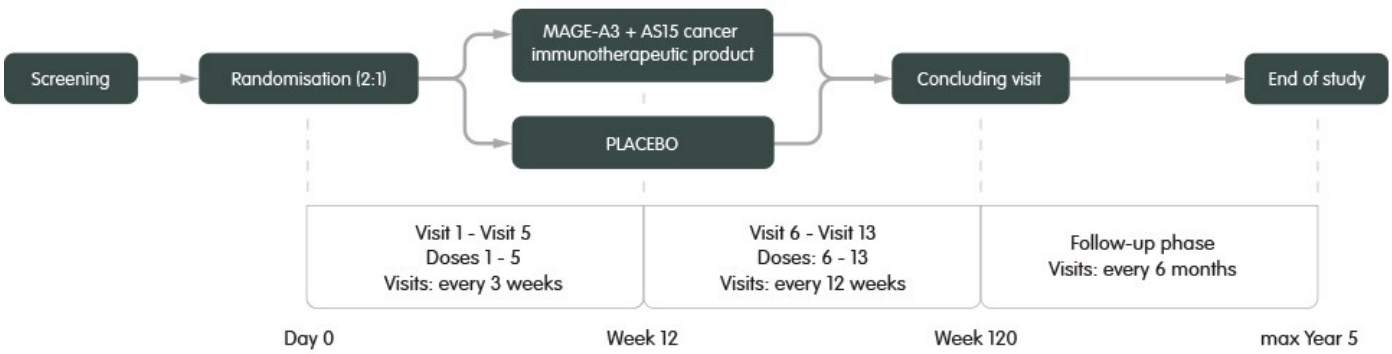
The primary outcome measure of this Phase II study was to evaluate the clinical efficacy in terms of Disease-free Survival of recMAGE-A3 + AS 15 cancer immunotherapeutic product versus placebo in the overall population patients with bladder cancer with MAGE-A3 expression after surgical removal of the urinary bladder.

Secondary Outcome Measures

- To evaluate overall survival in the overall study population;
- To evaluate Disease-free specific survival in the overall study population;
- To evaluate distant metastasis-free survival in the overall study population;
- To evaluate the safety of recMAGE-A3 + AS15 cancer immunotherapeutic prodcut in the overall study population;
- To evaluate the impact of predictive gene signature on efficacy of treatment in terms of disease-free survival and overall survival;
- To evaluate the immune response to recMAGE-A3 + AS15 cancer immunotherapeutic product in the overall study population;
- To evaluate the gene expression profile of the bladder tumour.

Please find the full description of the trial on the NederlandsTrial Register.

Study Design



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Study status

Upon release and analysis of the MAGRIT trial results, the rationale of the MAGNOLIA study was changed. As of 23 September 2014, the recruitment was put on hold.

GlaxoSmithKline Biologicals recently reported the negative outcome of the MAGE3-AS15-NSC-003 (ADJ) (109493 - EudraCT number: 2007-001283-73) MAGRIT study (A double-blind, randomized, placebo-controlled Phase III study to assess the efficacy of the recMAGE-A3 + AS15 Antigen-Specific Cancer Immunotherapeutic as adjuvant therapy in patients with resected MAGE-A3-positive Non-Small Cell Lung Cancer.

In addition, also for the MAGE3-AS15-MEL-005 (ADJ) (111482 - EudraCT number: 2008-002447-16) DERMA study, (A double-blind, randomized, placebo-controlled Phase III study to assess the efficacy of MAGE-A3 cancer immunotherapeutic adjuvant therapy in patients with resected MAGE-A3-positive Stage III melanoma) treatment of cutaneous melanoma patients with the MAGE-A3 immunotherapeutic did not increase DFS compared to placebo either in the overall population or in patients with a potential predictive GS.

A substantial protocol amendment of the MAGNOLIA study was required. The recruitment was stopped and the study population was unblinded. For patients randomized to the placebo group, no further protocol visits were to be performed except for the concluding visit and no further doses were administered. As it could not be excluded that one or more patients would benefit from investigational treatment on an individual basis, patients receiving active treatment (patients not on placebo, and patients that have not already completed or interrupted their MAGE-A3 ASCI treatment) were offered the option to continue the administration of the study treatment until the last dose was administered or until recurrence, whichever came first, or until the patient or the investigator decided to stop study treatment. As a result, the study continued only with patients from the active treatment group who decided to stay in the study. During the treatment period, safety monitoring was continued as initially foreseen during the treatment period.

Study locations

Ten European countries participated with a total of 50 centres. Sites contributed 0-28 screened patients in the recruitment period of 40 months. Enrolment in this study was competitive.

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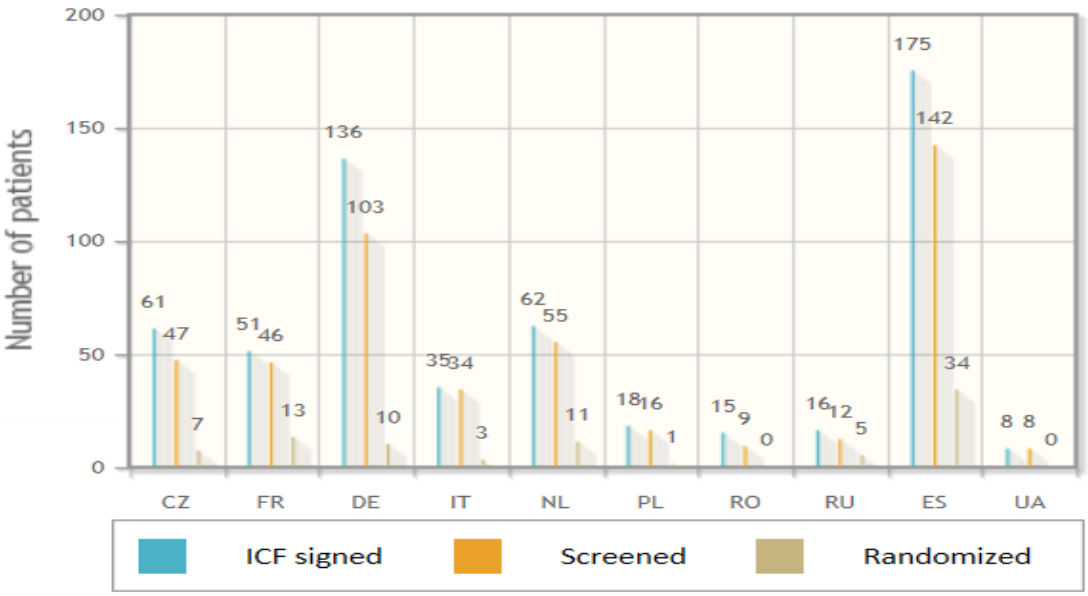
Final Patient Recruitment Status

529 ICFs were signed and 448 tumour tissue samples were screened. 83 out of 205 patients with MAGE A3 positive results were randomized.



Study Principal Coordinator:

- Prof. Dr. Peter Mulders
  Radboudumc, Nijmegen, The Netherlands

EAU Research Foundation

- Dr. Wim Witjes, Scientific and Clinical Research Director
- Dr. Raymond Schipper, Clinical Project manager
- Mrs. Joke van Egmond, Clinical Data manager
- Mrs. Xandra Helmonds, Financial manager

National Coordinators

- Germany: Prof. Dr. Axel Heidenreich
- France: Prof. Dr. Marc Colombel
- Spain: Prof. Dr. Luis Martínez-Piñeiro
- Italy: Prof. Dr. Renzo Colombo
- The Netherlands: Prof. Dr. Fred Witjes
- Poland: Prof. Dr. Piotr Radziszewski
- Czech Republic: Prof. Dr. Marko Babjuk
- Ukraine: Prof. Dr. Pavlo Yakovlev
- Romania: Ass. Prof. Dr. Christian Surcel
- Russia: Prof. Dr. Igor Korneyev

Publication

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Bioamples available for future research

Biosamples from randomized patients (tissue, blood, urine) are available for use in future translational research in the targeted therapy area.

Contact

EAU RF Central Research Office
PO Box 30016, 6803 AA Arnhem, The Netherlands
Email: researchfoundation@uroweb.org, Phone: +31 (0) 26 38 90 677