
Overview

The NIMBUS trial assessed whether a reduced number of Bacillus Calmette-Guerin (BCG) instillations is not inferior to standard number and dose intravesical BCG treatment in patients with high grade non-muscle invasive bladder cancer (NMIBC).

Study Objectives

- **Primary Endpoint:**
  Time to first recurrence [Reduced Number of BCG Instillations not inferior to Standard Number Intravesical BCG treatment].

- **Secondary Endpoints:**
  - Number and Grade of Recurrent Tumors
  - Rate of Disease Progression to a higher stage (T2 or higher)
  - Incidence and Severity of Side Effects.

In Brief

Intravesical instillation of BCG is a widely accepted strategy to prevent recurrence of non-muscle invasive bladder cancer. The most accepted treatment schedule is induction of BCG: weeks 1 through 6 plus maintenance (weeks 1, 2, 3) at months 3, 6 and 12, but it is unknown how many administrations are really necessary. Scientific evidence supports the hypothesis that after an initial sensitization to BCG antigens has occurred, the number of instillations can be reduced for a proper anamnestic immune response resulting in similar clinical efficacy and potentially less side-effects and costs.

The NIMBUS was a multicenter prospective, randomized, parallel group, not blinded trial to compare the efficacy and safety of two different Adjuvant treatment schedules randomized into two groups:

**Group 1: Standard Frequency**
Induction cycle BCG-full dose; weeks 1 through 6 plus maintenance cycles at months 3, 6 and 12 (weeks 1, 2, 3); total 15 full dose BCG instillations

**Group 2: Reduced Frequency**
Induction cycle BCG-full dose; weeks 1, 2, and 6 plus maintenance cycles at months 3, 6 and 12 (weeks 1, 3); total 9 full dose BCG instillations.

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

Study Design

**Standard Frequency**
- Arm 1 – N= 412
- Induction/maintenance Cycle - Full Dose
- Total 15 BCG Instillations

**Reduced Frequency**
- Arm 2 – N= 412
- Induction/maintenance Cycle - Full Dose
- Total 9 BCG Instillations

Study Duration:
- 6-year recruitment
- 3-year observation

N = 824
High Grade Non-Muscle Invasive Bladder Cancer

RANDOMIZATION
Study status (1 Nov 2019)

Safety analyses by the Independent Data Monitoring Committee (IDMC) showed reduced frequency schedule of BCG to be inferior to standard frequency schedule for the primary endpoint (time to recurrence) according to the previously defined stop criterion. Recruitment was immediately stopped and all participating sites were instructed to inform patients and offer patients in the reduced frequency treatment arm the possibility to switch to the standard frequency. The follow-up period, which was initially 3 years, will be shortened until all patients have at least 6 months of follow-up. At the time of stopping recruitment, a total of 359 patients were randomised (see recruitment graph below).

Recruitment graph all patients randomized:

Protocol Committee
- Prof. Dr. Marko Babjuk, Prague
- Prof. Dr. Luis Martinez-Piñeiro, Madrid
- Prof. Dr. Joan Palou Redorta, Barcelona
- Mr. Anup Patel, London
- Prof. Dr. Levent Türkeri, Istanbul
- Prof. Dr. Marc-Oliver Grimm, Jena
- Dr. Wim Witjes, Arnhem

Study Principal Coordinators
- Prof. Dr. Levent Türkeri
  Marmara University Medical School – Istanbul, Turkey
- Prof. Dr. Marko Babjuk
  Charles University 2nd Faculty of Medicine – Prague, Czech Republic

EAU Research Foundation
- Dr. Wim Witjes, Scientific and Clinical Research Director
- Dr. Raymond Schipper, Clinical Project Manager
- Drs. Christien Caris, Clinical Project Manager
- Mrs. Ilse Christ, Clinical Research Associate
- Mrs. Joke van Egmond, Clinical Data Manager
- Mrs. Xandra Helmonds, Financial Manager
- Mr. Hans Noordzij, Marvin Management Assistant

National Coordinators
- Germany: Prof. Dr. Marc-Oliver Grimm
- The Netherlands: Dr. Toine van der Heijden
- France: Prof. Dr. Marc Colombel
- Belgium: Dr. Tim Mulwijk
- Spain: Prof. Dr. Luis Martinez-Piñeiro
- Portugal: Dr. Pedro Costa
- Turkey: Prof. Dr. Levent Türkeri
- Italy: Dr. Andrea Gallina
- Czech Republic: Prof. Dr. Marko Babjuk

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