

Treatment of High Grade Non-Muscle Invasive Urothelial Carcinoma of the Bladder by Standard Number and Dose of Intravesical BCG Instillations versus Reduced Number of Intravesical Instillations with Standard Dose of BCG. A European Association of Urology Research Foundation Randomized Phase III Clinical Trial. Protocol Number: EAU-RF 2008-01. Eudract Number: 2010-019181-91

Timelines

The study includes a 6-year recruitment phase, followed by a 3-year observation phase. Germany started recruitment in December 2013, The Netherlands were initiated in October 2014. France started recruitment in July 2017. Belgium and Spain are expected to start mid 2018. Possibilities to start up in other countries like Turkey, Portugal and Italy are currently being evaluated.

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 is 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

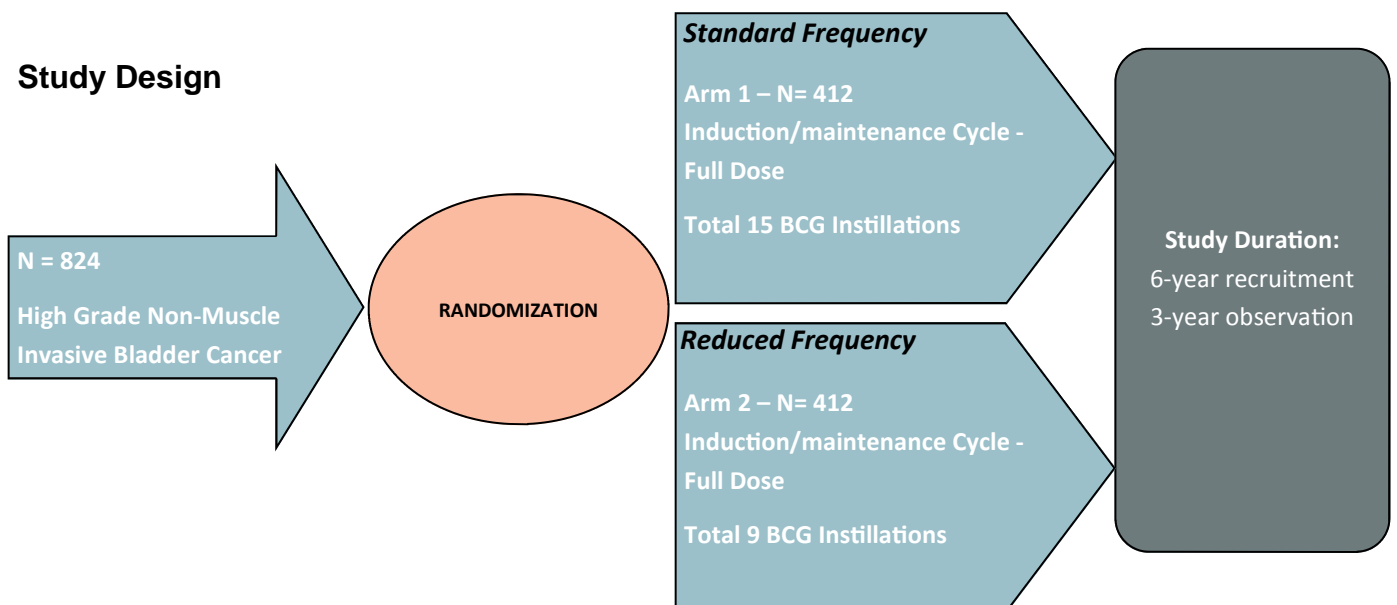
Induction cycle BCG-full dose; weeks 1 through 6 plus maintenance cycles at months 3, 6 and 12 (weeks 1, 2, 3); total 15 full dose BCG instillations

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



Study status (cut-off date 1 March 2018)

Twenty-eight centres are open for recruitment in Germany of which 26 sites randomized, in total, 123 patients. In the Netherlands, 13 centres are initiated of which 12 sites recruited, in total, 77 patients. France started recruitment in July 2017; 3 of 5 initiated centres randomized, in total, 23 patients.

Randomization status GERMANY (cut-off date 1 March 2018)

No.	Name of PI	Name Institution/hospital	City	No. of pts
1	Dr. Jörg Horstmann	Urologische Praxisklinik am Franziskushospital	Aachen	2
2	Dr. Stephan Machtens	MarienKrankenhaus Bergisch Gladbach	Bergisch Gladbach	6
3	Dr. Roger Zillmann	Urologische Gemeinschaftspraxis	Berlin-Pankow	3
4	Dr. Holger Schreier	Urologie im SchlossCarrée	Braunschweig	2
5	Prof. Dr. Manfred Wirth	Universitätsklinikum Dresden, Klinik für Urologie	Dresden	14
6	Dr. Eva Hellmis	Urologicum - Duisburg	Duisburg	0
7	Dr. Wolfgang Rulf	Überörtliche Gemeinschaftspraxis Praxis Erkrath-Hochdahl	Erkrath	2
8	Dr. Henrik Suttman	Urologikum Hamburg Standort Alstertal	Hamburg	2
9	Dr. Torsten Werner	Urologische Praxis	Herzberg am Harz	3
10	Prof. Dr. Marc-Oliver Grimm	Universitätsklinikum Jena Klinik für Urologie	Jena	14
11	Dr. Jan Marin	Urologische Gemeinschaftspraxis	Kempen	3
12	Dr. Jan Lehmann	Urologische Gemeinschaftspraxis Prüner Gang	Kiel	1
13	Dr. Robert Rudolph	GUT GbR Urologische Gemeinschaftspraxis	Kirchheim / Teck	4
14	Dr. Jörg Klier	Urologisches Tumorzentrum Köln (UTK)	Köln	9
15	Dr. Eberhard Mumperow	Praxis für Urologie	Langenfeld	9
16	Dr. Michael Stephan-Odenthal	Praxis Urologie RheinBerg	Leverkusen	1
17	Dr. Mario Kramer	Universitätsklinikum Schleswig-Holstein	Lübeck	5
18	Dr. Winfried Spiegelhalder	Urologische Praxis	Mettman	5
19	Dr. Michael Siebels	Gemeinschaftspraxis Urologie	München-Pasing	3
20	Prof. Dr. Bernd Schmitz-Dräger	Schön Klinik Nürnberg Fürth. Praxis für Urologie	Nürnberg	2
21	Prof. Oliver Hakenberg	Universitätsmedizin Rostock—Urologische Klinik und Poliklinik	Rostock	0
22	Dr. Andreas Schneider	Kooperative Gemeinschaftspraxis - Belegabteilung	Salzhausen	2
23	Prof. Dr. Dirk Zaak	Urologisches Praxiszentrum Traunstein	Traunstein	1
24	Dr. Georgios Gakis	Klinik für Urologie Tübingen	Tübingen	1
25	Dr. Andreas Al Ghazal	Klinik für Urologie und Kinderurologie	Ulm	2
26	Prof. Dr. Theodor Klotz	Kliniken Nordoberpfalz AG, Urologische Klinik	Weiden	5
27	Dr. Gerd Rodemer	Praxisgemeinschaft für Onkologie & Urologie	Wilhelmshaven	10
28	Dr. Thomas Pulte	Urologische Praxis am Wasserturm	Würselen	12
			Total	123

Randomization status THE NETHERLANDS (cut-off date 1 March 2018)

No.	Name of PI	Name Institution/hospital	City	Number of pts
1	Dr. Siebe Bos	Medisch Centrum Alkmaar	Alkmaar	4
2	Prof. Dr. Jeroen van Moorselaar	VU Medisch Centrum	Amsterdam	4
3	Prof. Dr. Theo de Reijke	Academisch Medisch Centrum	Amsterdam	3
4	Dr. Erika van Boven	Maasziekenhuis Pantein	Beugen	3
5	Dr. Annemarie Leliveld -Kors	UMC Groningen	Groningen	9
6	Dr. Harm van Melick	St. Antonius Ziekenhuis	Nieuwegein	1
7	Dr. Toine van der Heijden	Radboudumc	Nijmegen	10
8	Dr. Henk Vergunst	Canisius-Wilhelmina Ziekenhuis	Nijmegen	12
9	Dr. Marcel de Bruin	Laurentius Ziekenhuis	Roermond	4
10	Dr. Joost Boormans	Erasmus MC	Rotterdam	6
11	Dr. Bart Wijsman	ETZ	Tilburg	0
12	Dr. Richard Meijer	UMC Utrecht	Utrecht	1
13	Dr. Ed te Slaa	Isala Klinieken	Zwolle	20
		Total		77

Randomization status FRANCE (cut-off date 1 March 2018)

No.	Name of PI	Name Institution/hospital	City	Number of pts
1	Prof. Dr. Marc Colombel	Hôpital Edouard Herriot	Lyon	19
2	Prof. Dr. Alain Ruffon	Hôpital Lyon Sud	Pierre-Bénite	0
3	Dr. Christian Pfister	CHU de Rouen	Rouen	1
4	Prof. Dr. Morgan Roupret	CHU La Pitié-Salpêtrière, APHP	Paris	3
5	Prof. Dr. Jacques Irani	APHP Hôpital Bicêtre	Le Kremlin-Bicêtre	0
6	Prof. Dr. Nicolas Mottet	CHU St Etienne	St.-Priest-en-Jarez	-
7	Prof. Dr. Jean-Luc Descottes	CHU A. Michallon	Grenoble	-
		Total		23

- = not yet initiated

Study Principal Coordinators

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Marmara University Medical School – Istanbul, Turkey

Prof. Dr. Marko Babjuk
Charles University 2nd Faculty of Medicine – Prague, Czech Republic

National Coordinators

- ◆ Germany: Prof. Dr. Marc-Oliver Grimm
- ◆ The Netherlands: Dr. Toine van der Heijden
- ◆ France: Prof. Dr. Marc Colombel
- ◆ Belgium: TBD
- ◆ Spain: Prof. Dr. Luis Martinez-Piñeiro
- ◆ Portugal: Dr. Pedro Costa
- ◆ Turkey: Prof. Dr. Levent Türkeri
- ◆ Italy: Prof. Dr. Francesco Montorsi
- ◆ Czech Republic: Prof. Dr. Marko Babjuk

Protocol Committee

- ◆ Prof. Dr. Marko Babjuk, Prague
- ◆ Prof. Dr. Luis Martinez-Pineiro, 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

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