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Multicentre, randomised study comparing autologous intravesical macrophage cell therapy (Bexidem®) to intravesical Bacillus Calmette-Guerin (BCG) therapy in patients with superficial papillary bladder cancer

Submission date	Recruitment status	[_] Prospectively registered
16/04/2009	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
27/05/2009	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
11/06/2010	Cancer	

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.idm-pharma.com

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
MAK-BLA-202

Study information

Scientific Title
Phase II/III, multicentre, open-label, randomised study comparing autologous intravesical macrophage cell therapy (Bexidem®) to intravesical Bacillus Calmette-Guerin (BCG) therapy in patients with superficial papillary bladder cancer who have undergone complete transurethral resection

Acronym
Bexidem®

Study objectives
1. Phase II step:
1.1. Primary objective: To demonstrate a superior safety profile of Bexidem® therapy with respect to 'frequent immunotherapy-linked adverse events' (FILAEs) compared to BCG therapy
1.2. Secondary objective: To evaluate overall efficacy and recurrence-free survival in patients treated with Bexidem® therapy

2. Phase III step:
2.1. Primary objective: To compare efficacy (recurrence-free survival) of Bexidem® therapy to BCG therapy
2.2. Secondary objective: To evaluate overall safety of Bexidem® therapy as compared to BCG therapy

Ethics approval required
Old ethics approval format

Ethics approval(s)
All participating centres received ethics approval prior to recruitment of the first participant:
1. Spain: Regional EC - CEIC Regional de la Comunidad de Madrid; Local EC - CEIC Autonomico de Ensayos Clinicos de Andalucia - Consejeria de Salud; Local EC - Comité Etico de Investigacion Clinica de Galicia SERGAS
2. Hungary: Central EC Central Ethics Committee - Egészségügyi és Tudományos Tanács; Institutional Research Ethic Committee - Fövàrosi Szent Istvàn Hospital; Institutional Research Ethic Committee - Budai Irgal Masrendi Intézményi Kutatàsetikai Bizottsàg; IKEB Hatarozat dön tésröl; Regionalis Kuratasetukai Bizottsaga (Györ - Moson - Sopron etc..) - Egészségügyi és Tudományos Tanács; Local Ethic Committee Bajcsy - Zsilinszky Hospital; Regional and Institutional Committee of Science and research Ethics - Semmelweis Hospital; Local Ethic Committee Jahn Ferenc South-Pest Hospital; Regionalis Kuratasetukai Bizottsaga (Györ - Moson - Sopron etc..) - Egészségügyi és Tudományos Tanács; Institutional Research Ethic Committee of lcal Government of Capital City; Local Ethic Committee Bàcs - Kiskun County Hospital
3. France: Central EC - CCPPRB du l'Hopital Paris
4. Germany: Ethik-Kommission Medizinische - Fakultät Universität Regensburg; Ethikkommission

Med. Fakultät der HHU Düsseldorf; Ethikkommission Charité - Universitätsmedizin; Ethikkommission - Medizinischen Fakultät der Technischen Universität; Ethikkommission der Landesärztekammer Rheinland-Pfalz
5. Belgium: Commission d'Ethique Biomédicale - Hospitalo-Facultaire; Comité Éthique - CHR de la Citadelle; Etisch Comité O.L. Vrouwziekenhuis; Etisch Comité AZ Groeninge
6. Luxembourg: Comité Éthique CNER 18

Study design
Phase II/III multicentre open-label randomised study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Superficial papillary bladder cancer

Interventions
Dosage and administration:
Three treatment cycles: first cycle consists of either 6 weekly Bexidem® instillations (0.5 - 2 x 10^8 cells in a total volume of 50 ml per instillation) or BCG instillations (1 - 19.2 x 10^8 CFU in a total volume of 50 ml). Maintenance consists of two cycles (at month 3 and month 6) of each three weekly Bexidem® instillations, or 3 weekly BCG instillations.

Study duration:
Phase II: Individual patient participation: 24 months including follow-up observation. Total study duration: 42 months
Phase III: Individual patient participation: 24 months including follow-up observation. Total study duration: dependent upon total number of patients

Intervention Type
Drug

Phase
Phase II/III

Drug/device/biological/vaccine name(s)
Bexidem®

Primary outcome measure

Phase II: To demonstrate a superior safety profile of Bexidem® with respect to FILAEs compared to BCG therapy.
Phase III: To compare efficacy (recurrence-free survival) of Bexidem® therapy to BCG therapy.

The comparison of toxicity will be performed after all patients in the Phase II step have completed all cycles of treatment and at least three months of follow up (month 9). The recurrence-free survival in each group will be estimated after all Phase II patients have completed at least six months of follow up after the last treatment (month 12 visit). These analyses will serve as the basis for a decision to proceed to the Phase III step as well as to estimate the expected recurrence-free survival in the two groups and recalculate the sample size required for the Phase III step.

Secondary outcome measures
Phase II: To evaluate overall efficacy and recurrence-free survival in patients treated with Bexidem® therapy.
Phase III: To evaluate overall safety of Bexidem® therapy as compared to BCG.

The comparison of toxicity will be performed after all patients in the Phase II step have completed all cycles of treatment and at least three months of follow up (month 9). The recurrence-free survival in each group will be estimated after all Phase II patients have completed at least six months of follow up after the last treatment (month 12 visit). These analyses will serve as the basis for a decision to proceed to the Phase III step as well as to estimate the expected recurrence-free survival in the two groups and recalculate the sample size required for the Phase III step.

Overall study start date
25/06/2004

Completion date
16/03/2007

Eligibility

Key inclusion criteria
1. Male and female patients
2. At least 18 years of age
3. Fully resected papillary transitional cell carcinoma
4. Stage TaGI, TaGII, TaGIII, T1GI or T1GII (N0, M0)
5. Either of the following:
5.1. Plurifocal tumours
5.2. Unifocal tumour provided greater than or equal to two tumour occurrences within the last 24 months
6. World Health Organization (WHO) performance status 0 - 2
7. Normal upper urinary tract as documented by intravenous (IV) urography or computed tomography (CT) scan
8. Blood creatinine less than 200 umol/L
9. Alanine aminotransferase (ALT) and aspartate aminotrasferase (AST) less than 2.5 x upper limit of normal (ULN)
10. Leukocytes greater than or equal to 3,500/mm^3
11. Able to understand and follow treatment scheme
12. Signed and dated Informed Consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Phase II: 138 patients (69 per arm); up to 512 additional patients for phase III

Key exclusion criteria
1. Greater than or equal to T1GIII bladder cancer
2. Carcinoma in situ (CIS)
3. Active tuberculosis
4. Other active infection (including urinary tract infection) and/or infections that may compromise the immune system such as human immunodeficiency virus (HIV), human T-lymphotropic virus (HTLV), hepatitis B or hepatitis C infection
5. History of other active malignancy within five years, except adequately treated basal cell and squamous cell carcinoma of the skin
6. Other serious illness or medical conditions (e.g. history of significant cardiac or respiratory dysfunction)
7. Patients with a contra-indication preventing apheresis
8. History of autoimmune-related disorder
9. Known hypersensitivity to any of the components of the study drugs (e.g. dimethylsulphoxide [DMSO])
10. Immunosuppression or congenital or acquired immune deficiencies, whether due to concurrent disease (e.g. acquired immune deficiency syndrome [AIDS], leukaemia, lymphoma), cancer therapy (cytotoxic drugs, radiotherapy) or immunosuppressive therapy (e.g. corticosteroids, cyclosporin)
11. Family history of Creutzfeldt-Jacob disease and/or risk of Creutzfeldt-Jacob disease defined as patient having received extracted growth hormone or neurosurgery before 1996
12. Prior systemic reaction to BCG therapy
13. Pregnant or nursing women

Date of first enrolment
25/06/2004

Date of final enrolment
16/03/2007

Locations

Countries of recruitment
Belgium

France

Germany

Hungary

Luxembourg

Spain

Study participating centre
Oberarzt
Regensburg
Germany
93053

Sponsor information

Organisation
IDM Pharma SA (France)

Sponsor details
172 rue de Charonne
Paris Cedex 11
France
75545

Sponsor type
Industry

Website
http://www.idm-pharma.com

ROR
https://ror.org/048p4wq89

Funder(s)

Funder type
Industry

Funder Name
IDM Pharma SA (France)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	08/06/2010		Yes	No