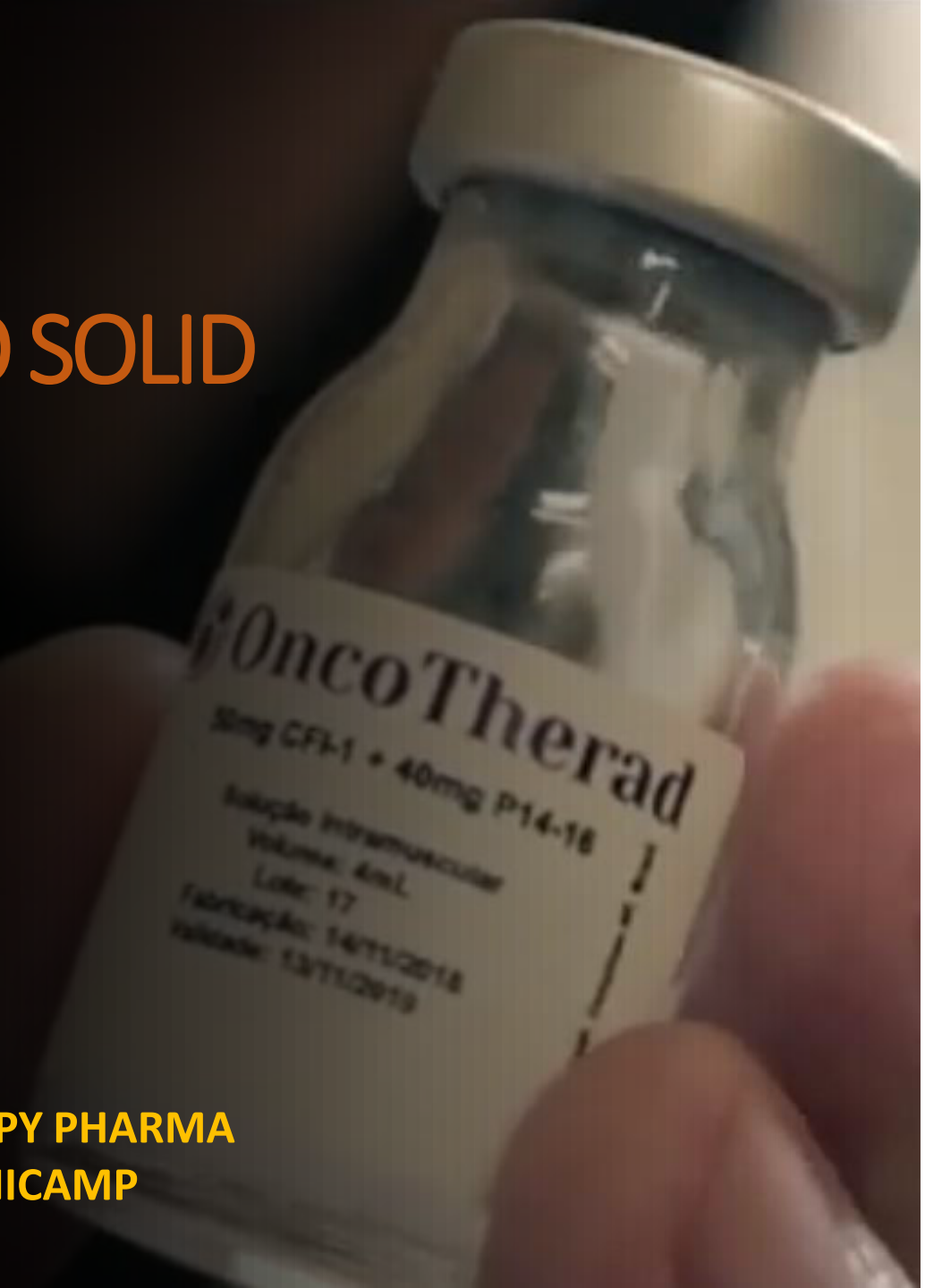
MRB-CFI-1: NEW IMMUNOTHERAPY TO SOLID TUMOR TREATMENT



OncoTherad
ONCOLOGY THERAPY ADJUVANT

UNICAMP

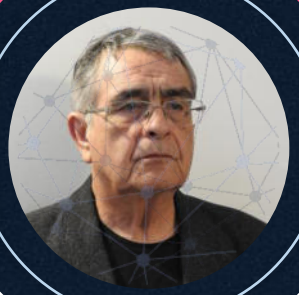
Prof. Dr. Wagner José Fávaro

Sócio-Fundador da NANOIMMUNOTHERAPY PHARMA
Professor Associado Depto. Anatomia/ UNICAMP
Membro Titular ASCO e ESMO

mm PHARMA

Há 15 anos, pesquisadores da UNICAMP vêm realizando pesquisas visando o desenvolvimento de medicamentos e novas plataformas terapêuticas para o tratamento de tumores sólidos.
O resultado dessas pesquisas foi o desenvolvimento do OncoTherad®, a primeira molécula de Imunoterapia totalmente criada e desenvolvida no Brasil

Prof. Dr. Wagner José Fávaro



Prof. Dr. Nelson Durán

Prof. Dr. João Carlos Cardoso Alonso

Prof. Dr. Andrigo Barboza De Nardi

Sr. Carlos Kleber de Andrade

mm PHARMA

OncoTherad

ONCOLOGY THERAPY ADJUVANT

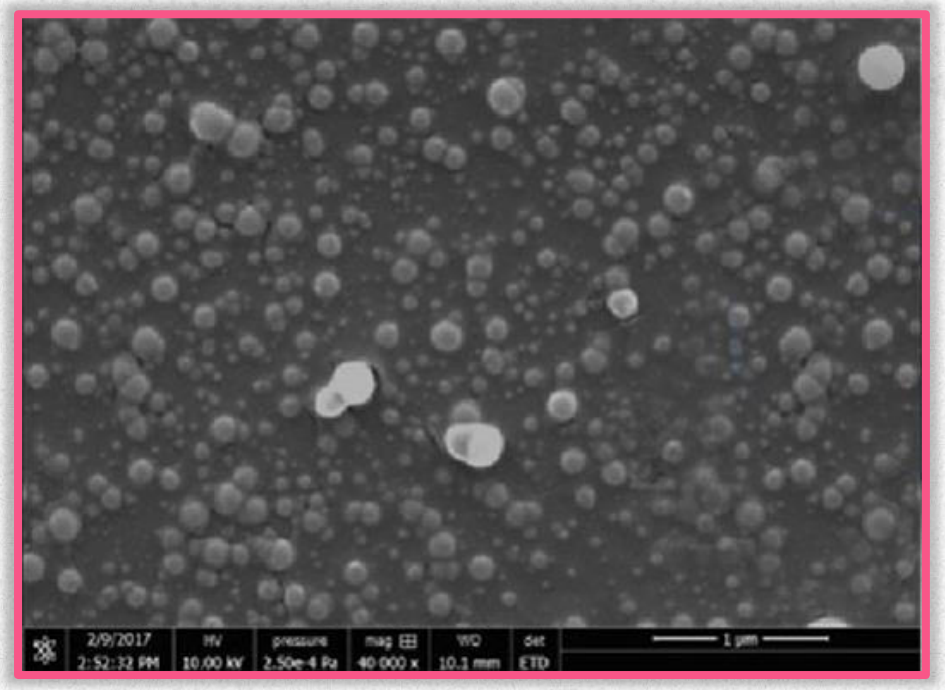
Protein
P14-16

Inorganic
Scaffold

Size by DLS: 31 0.3 +- 56.9 nm PI 0,567 and Zeta potential -21 ,8m

Size: 4 +- 2nm
Zeta Pot.:
+6,5 +- 0,7 mV.

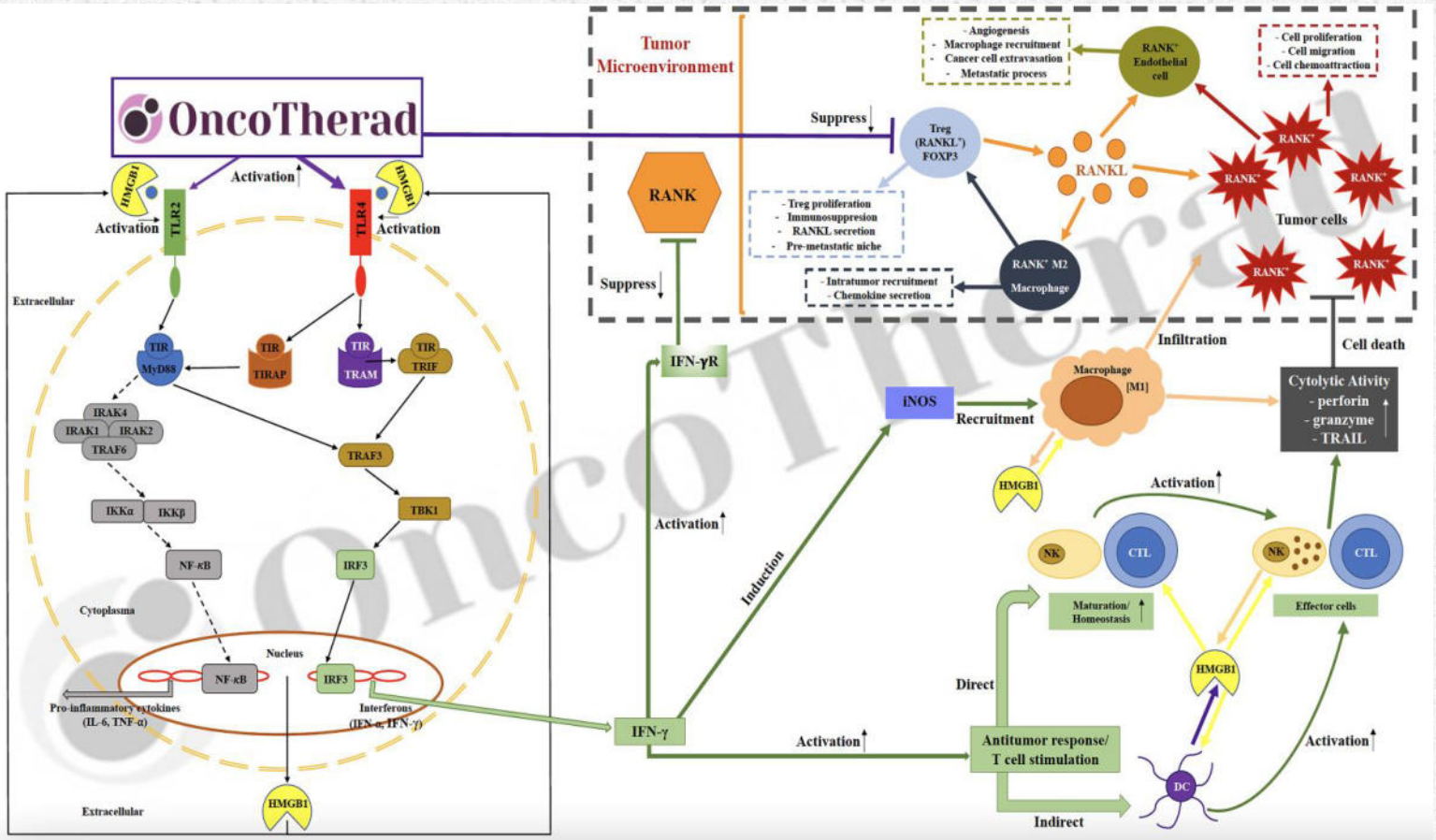
Size: 447 +- 1 27mm| PI 0.51
Zeta Pot. -28.6 mV



OncoTherad®

OncoTherad

ONCOLOGY THERAPY ADJUVANT



Tissue and Cell 80 (2023) 101988

Contents lists available at ScienceDirect

Tissue and Cell

journal homepage: www.elsevier.com/locate/tice

New synthetic nano-immunotherapy (OncoTherad®) for non-muscle invasive bladder cancer: Its synthesis, characterization and anticancer property

W.J. Fávaro [a,*], J.C.C. Alonso [a,b], B.R. de Souza [a], I.B. Reis [a], J.M. Gonçalves [a], A.C. Deckmann [a], G. Oliveira [a], Q.C. Dias [a], N. Durán [a,c,**]

[a] Laboratory of Urogenital Carcinogenesis and Immunotherapy (LCURGIN), University of Campinas (UNICAMP), Campinas, São Paulo, Brazil
[b] Paulínia Municipal Hospital, Paulínia, São Paulo, Brazil
[c] Nanomedicine Research Unit (Nanomed), Federal University of ABC (UFABC), Santo André, São Paulo, Brazil

ARTICLE INFO

Keywords:
Non-muscle invasive bladder cancer
OncoTherad®
Toll-like receptors
Nanotechnology
Immunotherapy
Nanomedicine

ABSTRACT

Bacillus Calmette-Guérin (BCG)-based intravesical immunotherapy has been applied as gold standard treatment for high-risk non-muscle invasive bladder cancer (NMIBC) for almost half a century. However, several patients with high-risk disease experience relapse, including those whose condition has worsened and who failed to respond to BCG. Non-significant therapeutic options have been developed for these at-risk patients, for many years. Immunotherapies have shown promising outcomes for bladder cancer treatment. Accordingly, our research group developed the OncoTherad® (MRB-CFI-1) immunotherapy, which has shown positive outcomes in NMIBC treatment. The aim of the current study is to describe, in details, the physicochemical features and potential action mechanisms of OncoTherad® nano-immunotherapy, based on toll-like receptor 4 (TLR4)-mediated interferon and on RANK/RANKL signaling pathways, in animal model with NMIBC. Based on the current findings, OncoTherad® nano-immunotherapy did not have genotoxic effect on the investigated model and did not show signs of limiting local and/or systemic toxicity at therapeutic doses. OncoTherad® nano-immunotherapy was more effective than the BCG treatment, since it reduced by 70% the malignancy rate. Furthermore, it was possible identifying an important action mechanism of OncoTherad®, which was based on the modulation of TLR4-mediated interferon and RANK/RANKL signaling pathways that, altogether, were essential to reduce malignancy rate. OncoTherad® mechanisms in these pathways helped preventing tumor recurrence.

International Immunopharmacology 123 (2023) 110723

Contents lists available at ScienceDirect

International Immunopharmacology

journal homepage: www.elsevier.com/locate/intimp

A novel therapeutic strategy for non-muscle invasive bladder cancer: OncoTherad® immunotherapy associated with platelet-rich plasma

Bianca Ribeiro de Souza [a,*], Ianny Brum Reis [b], Gabriela Cardoso de Arruda Camargo [a], Gabriela Oliveira [a], Queila Cristina Dias [a], Nelson Durán [a,c], Wagner José Fávaro [a]

[a] Department of Structural and Functional Biology, Institute of Biology – University of Campinas (UNICAMP), Campinas, São Paulo, Brazil
[b] Department of Diagnosis and Surgery, School of Dentistry - São Paulo State University (UNESP), Araraquara, São Paulo, Brazil
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ARTICLE INFO

Keywords:
Bladder cancer
Immunotherapy
OncoTherad
PRP
Toll-Like receptors

ABSTRACT

Patients with non-muscle invasive bladder cancer (NMIBC) that are unresponsive to Bacillus Calmette-Guérin (BCG) have historically had limited treatment options. A new perspective is represented by OncoTherad® (MRB-CFI-1) immunotherapy, a nanostructured inorganic phosphate complex associated with glycosidic protein, developed by the University of Campinas in Brazil. Previous studies have shown that Platelet-Rich Plasma (PRP) also acts on immune activation and exerts antitumor effects. This study characterized the effects of the OncoTherad® associated with PRP in the treatment of NMIBC chemically induced in mice. When treated intravesically with PRP only, mice showed 28.6% of tumor progression inhibition rate; with OncoTherad® 85.7%; and with OncoTherad®+PRP 71.4%. Intravesical treatments led to distinct activation of Toll-like Receptors (TLRs) 2 and 4-mediated innate immune system in the interleukins (canonical) and interferons (non-canonical) signaling pathways. OncoTherad® isolated or associated with PRP upregulated TLR4 and its downstream cascade mediators as well as increased interleukins 6 (IL-6) and 1β (IL-1β), and interferon-γ (IFN-γ). In this way, the NMIBC microenvironment was modulated to a cytotoxic profile correlated with the IL-1β increase by stimulating immune pathways for IFN-γ production and consequent cytotoxic T lymphocytes (as CD8+ T-cells) activation and regulatory T-cells (Tregs) reduction. In addition, PRP did not trigger carcinogenic effects through the biomarkers evaluated. Considering the possibility of personalizing the treatment with the PRP use as well as the antitumor properties of OncoTherad®, we highlight this association as a potential new therapeutic strategy for NMIBC,

Journal of Cancer Research and Clinical Oncology
https://doi.org/10.1007/s00432-022-04449-5

RESEARCH

OncoTherad® is an immunomodulator of biological response that downregulate RANK/RANKL signaling pathway and PD-1/PD-L1 immune checkpoint in non-muscle invasive bladder cancer

Ianny Brum Reis[1] · Luiz Henrique Soares Tibo[2] · Bianca Ribeiro de Souza[2] · Nelson Durán[2,3] · Wagner José Fávaro[2]

Received: 5 September 2022 / Accepted: 20 October 2022

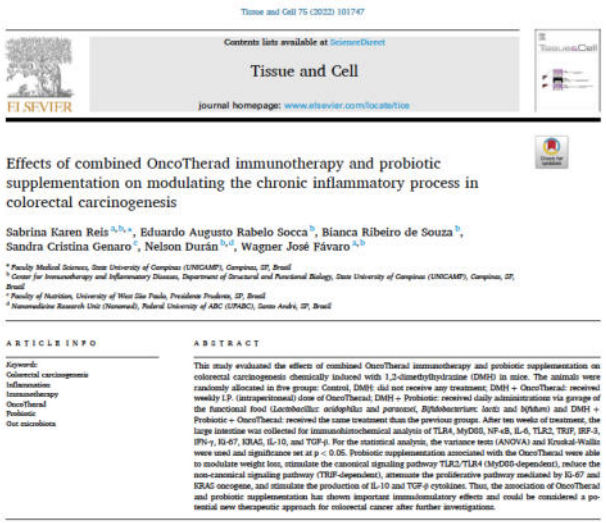
Abstract

Intoduction Bladder cancer is the second most common urinary tract cancer. Above 70% of the occurrence of bladder cancer is superficial (pTis, pTa, and pT1), non-muscle invasive tumor (NMIBC), and the incidence of invasive disease is occasional. Treatments for NMIBC consist of transurethral resection (TUR) and subsequently intravesical immunotherapy with *Bacillus Calmette-Guérin* (BCG), intending to prevent tumor progression and decrease recurrence. However, 20–30% of these tumors have progression, and 70% have a recurrence after exclusive TUR treatment. The immunomodulator of biological response, OncoTherad®, is an attractive potential to revolutionize cancer therapy. In our previous studies with mice, the results showed that treatment with OncoTherad® reduced 100% of tumor progression in NMIBC through the activation of Toll-Like Receptors' non-canonical pathway.

Materials and Methods In the present study, 36 female C57Bl/6J mice were divided into 6 groups ($n = 6$/group): Control, Cancer, Cancer + BCG, Cancer + OncoTherad® (MRB-CFI-1), Cancer + P14-16 and Cancer + CFI-1. NMIBC was chemically induced and the treatments were followed for 6 weeks. A week after the last dose of treatment, animals were euthanized, the bladder was collected and routinely processed for immunohistochemical analyses of RANK, RANKL, FOXP3, and PD-1/PD-L1, such as PD-1/PD-L1 western blotting.

Conclusion The immunohistochemical results showed that OncoTherad® reduced RANK and RANKL immunoreactivities compared to the cancer group, which indicates a good prognosis. Immunohistochemical and western blotting analyses confirmed that OncoTherad® modulated PD-1/PD-L1 immune checkpoint.

Keywords Immune checkpoint · Cancer treatment · Immune system · RANKL · FOXP3



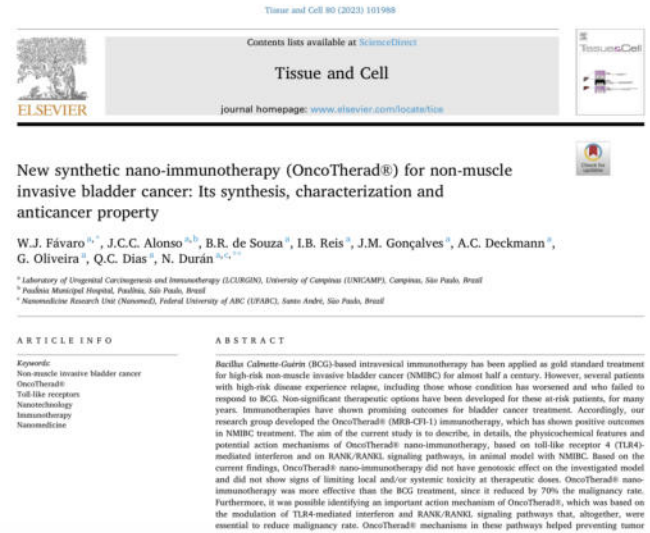
Tissue and Cell 75 (2022) 101747

Contents lists available at ScienceDirect

Tissue and Cell

journal homepage: www.elsevier.com/locate/tice

Effects of combined OncoTherad immunotherapy and probiotic supplementation on modulating the chronic inflammatory process in colorectal carcinogenesis



Tissue and Cell 80 (2023) 101988

Contents lists available at ScienceDirect

Tissue and Cell

journal homepage: www.elsevier.com/locate/tice

New synthetic nano-immunotherapy (OncoTherad®) for non-muscle invasive bladder cancer: Its synthesis, characterization and anticancer property

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Contents lists available at ScienceDirect

Tissue and Cell

journal homepage: www.elsevier.com/locate/tice

OncoTherad® (MRB-CFI-1) nano-immunotherapy reduced tumoral progression in non-muscle invasive bladder cancer through activation of *Toll-like* signaling pathway

REPÚBLICA FEDERATIVA DO BRASIL
MINISTÉRIO DA ECONOMIA
INSTITUTO NACIONAL DA PROPRIEDADE INDUSTRIAL

CARTA PATENTE Nº BR 102017012768-0

O INSTITUTO NACIONAL DA PROPRIEDADE INDUSTRIAL concede a presente PATENTE DE INVENÇÃO, que outorga ao seu titular a propriedade da invenção caracterizada neste título, em todo o território nacional, garantindo os direitos dela decorrentes, previstos na legislação em vigor.

(21) Número do Depósito: BR 102017012768-0

(22) Data do Depósito: 14/06/2017

(43) Data da Publicação Nacional: 15/01/2019

(51) Classificação Internacional: A61K 47/04; A61K 47/42; A61K 31/66; A61K 9/51; A61K 47/30; A61P 35/00.

(54) Título: PROCESSO DE OBTENÇÃO DE COMPLEXO NANOESTRUTURADO (CFI-1), COMPLEXO NANOESTRUTURADO ASSOCIADO A PROTEÍNA (MRB-CFI-1)

(73) Titular: UNIVERSIDADE ESTADUAL DE CAMPINAS - UNICAMP, Pessoa Jurídica. CGC/CPF: 46068425000133. Endereço: CIDADE UNIVERSITÁRIA ZEFERINO VAZ, CAMPINAS, SP, BRASIL(BR), 13084-971, Brasileira

(72) Inventor: WAGNER JOSÉ FÁVARO; NELSON EDUARDO DURAN CABALLERO.

Prazo de Validade: 20 (vinte) anos contados a partir de 14/06/2017, observadas as condições legais

Expedida em: 23/08/2022

US011136242B2

(12) **United States Patent**
Favaro et al.

(10) **Patent No.: US 11,136,242 B2**
(45) **Date of Patent: Oct. 5, 2021**

(54) **METHOD FOR PRODUCING A NANOSTRUCTURED COMPLEX (CFI-1), A PROTEIN-ASSOCIATED NANOSTRUCTURED COMPLEX (MRB-CFI-1) AND USE**

(71) Applicant: **UNIVERSIDADE ESTADUAL DE CAMPINAS—UNICAMP**, Campinas (BR)

(72) Inventors: **Wagner José Favaro**, Campinas (BR); **Nelson Eduardo Duran Caballero**, Paulinia (BR)

(73) Assignee: **UNIVERSIDADE ESTADUAL DE CAMPINAS—UNICAMP**

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **16/617,493**

(56) **References Cited**

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8,889,153	B2	11/2014	Nunes	A61K 45/06
9,295,682	B2	3/2016	Nunes	A61K 31/661
2012/0251441	A1	10/2012	Nunes	424/1.49
2014/0341940	A1	11/2014	Nunes	A61K 9/0014
2016/0166683	A1	6/2016	Nunes	A61K 39/39

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BR	PI0704797	3/2009	A61K 31/4045
WO	WO2009097670	8/2009	A61K 45/00
WO	WO2013067608	5/2013	A61P 31/12

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US011572284B2

(12) **United States Patent**
Favaro et al.

(10) **Patent No.: US 11,572,284 B2**
(45) **Date of Patent: *Feb. 7, 2023**

(54) **METHOD FOR PRODUCING A NANOSTRUCTURED COMPLEX (CFI-1), A PROTEIN-ASSOCIATED NANOSTRUCTURED COMPLEX (MRB-CFI-1) AND USE**

(71) Applicant: **UNIVERSIDADE ESTADUAL DE CAMPINAS—UNICAMP**, Campinas (BR)

(72) Inventors: **Wagner José Favaro**, Campinas (BR); **Nelson Eduardo Duran Caballero**, Paulinia (BR)

(73) Assignee: **UNIVERSIDADE ESTADUAL DE CAMPINAS—UNICAMP**

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 140 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **17/236,848**

9,295,682	B2	3/2016	Nunes	A61K 31/661
2012/0251441	A1	10/2012	Nunes	424/1.49
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2016/0166683	A1	6/2016	Nunes	A61K 39/39

FOREIGN PATENT DOCUMENTS

BR	PI0704797	3/2009	A61K 31/4045
WO	WO2009097670	8/2009	A61K 45/00
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US011623869B2

(12) **United States Patent**
Favaro et al.

(10) **Patent No.: US 11,623,869 B2**
(45) **Date of Patent: *Apr. 11, 2023**

(54) **METHOD FOR PRODUCING A NANOSTRUCTURED COMPLEX (CFI-1), A PROTEIN-ASSOCIATED NANOSTRUCTURED COMPLEX (MRB-CFI-1) AND USE**

(71) Applicant: **UNIVERSIDADE ESTADUAL DE CAMPINAS—UNICAMP**, Campinas (BR)

(72) Inventors: **Wagner José Favaro**, Campinas (BR); **Nelson Eduardo Duran Caballero**, Paulinia (BR)

(73) Assignee: **UNIVERSIDADE ESTADUAL DE CAMPINAS—UNICAMP**

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 152 days.

This patent is subject to a terminal disclaimer.

(56) **References Cited**

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6,476,082	B1	11/2002	Green	516/88
8,889,153	B2	11/2014	Nunes	A61K 45/06
9,295,682	B2	3/2016	Nunes	A61K 31/661
2012/0251441	A1	10/2012	Nunes	424/1.49
2014/0341940	A1	11/2014	Nunes	A61K 9/0014
2016/0166683	A1	6/2016	Nunes	A61K 39/39

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WO	WO2009097670	8/2009	A61K 45/00
WO	WO2013067608	5/2013	A61P 31/12

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U.S. Appl. No. 16/617,493, filed Nov. 26, 2019.
U.S. Appl. No. 17/236,848, filed Apr. 21, 2021, Favaro et al.
U.S. Appl. No. 17/236,861, filed Apr. 21, 2021, Favaro et al.
Afsharimoghaddam et al., Controversial roles played by toll like receptor 4 in urinary bladder cancer; A systematic review, Life

US011639294B2

(12) **United States Patent**
Favaro et al.

(10) **Patent No.: US 11,639,294 B2**
(45) **Date of Patent: May 2, 2023**

(54) **METHOD FOR PRODUCING A NANOSTRUCTURED COMPLEX (CFI-1), A PROTEIN-ASSOCIATED NANOSTRUCTURED COMPLEX (MRB-CFI-1) AND USE**

(71) Applicant: **UNIVERSIDADE ESTADUAL DE CAMPINAS—UNICAMP**, Campinas (BR)

(72) Inventors: **Wagner José Favaro**, Campinas (BR); **Nelson Eduardo Duran Caballero**, Paulinia (BR)

(73) Assignee: **UNIVERSIDADE ESTADUAL DE CAMPINAS—UNICAMP**

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 234 days.

(21) Appl. No.: **17/236,861**

(22) Filed: **Apr. 21, 2021**

8,889,153	B2	11/2014	Nunes	A61K 45/06
9,295,682	B2	3/2016	Nunes	A61K 31/661
2012/0251441	A1	10/2012	Nunes	424/1.49
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WO	WO2009097670	8/2009	A61K 45/00
WO	WO2013067608	5/2013	A61P 31/12

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U.S. Appl. No. 17/236,848, filed Apr. 21, 2021, Favaro et al.
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Allen et al., Multilocular Prostatic Cystadenoma with High-Grade Prostatic Intraepithelial Neoplasia, Case Report, Elsevier Science Inc. 2003 (3 pgs).
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Askeland et al., Bladder Cancer Immunotherapy: BCG and Beyond,

(19) Europäischen Patentamt
European Patent Office
Office européen des brevets

(11) **EP 3 626 746 B1**

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention of the grant of the patent:
12.07.2023 Bulletin 2023/28

(21) Application number: **18818605.0**

(22) Date of filing: **14.06.2018**

(51) International Patent Classification (IPC):
C01B 25/34 *(2006.01)* ***C07K 17/00*** *(2006.01)*
A61K 38/00 *(2006.01)* ***A61K 33/42*** *(2006.01)*
A61K 33/02 *(2006.01)* ***A61K 33/06*** *(2006.01)*
A61P 35/00 *(2006.01)*

(52) Cooperative Patent Classification (CPC):
C01B 25/34; A61K 33/02; A61K 33/06; A61K 33/42; A61K 38/00; A61P 35/00; C07K 17/00

(86) International application number:
PCT/BR2018/000031

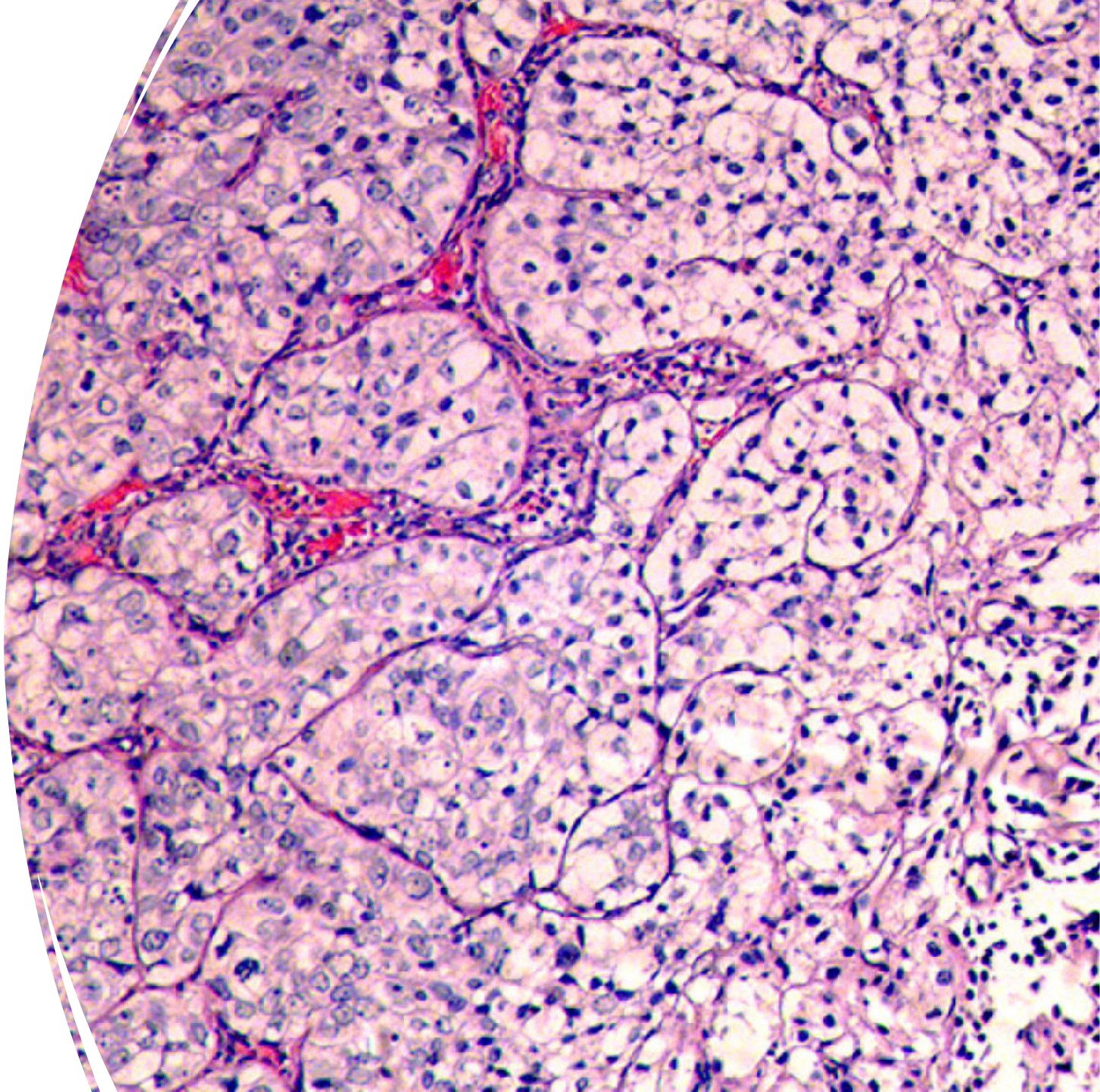
(87) International publication number:
WO 2018/227261 (20.12.2018 Gazette 2018/51)

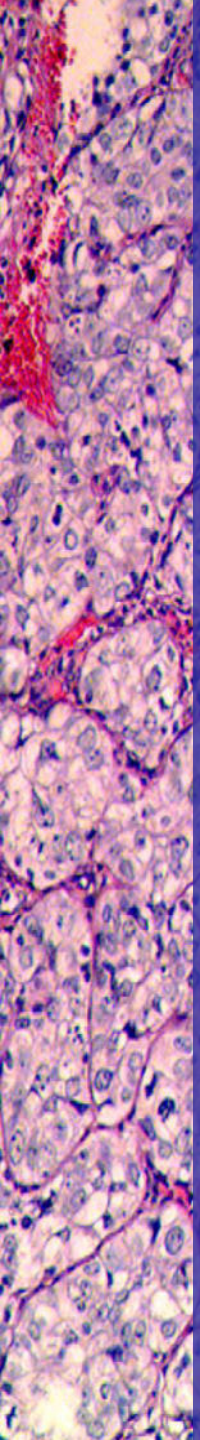
(54) **METHODS FOR PRODUCING A NANOSTRUCTURED COMPLEX (CFI-1) AND A PROTEIN-ASSOCIATED NANOSTRUCTURED COMPLEX (MRB-CFI-1) AND USE**

VERFAHREN ZUR HERSTELLUNG EINES NANOSTRUKTURIERTEN KOMPLEXES (CFI-1) UND EINES PROTEIN-ASSOZIIERTER NANOSTRUKTURIERTER KOMPLEX (MRB-CFI-1) UND VERWENDUNG

PROCÉDÉS DE PRÉPARATION D'UN COMPLEXE NANOSTRUCTURÉ (CFI-1) ET D'UN COMPLEXE NANOSTRUCTURÉ ASSOCIÉ À UNE PROTÉINE (MRB-CFI-1) ET UTILISATION

Protocols for Human Use: ONCOTHERAD NANO-IMMNOTHERAPY IN BCG-UNRESPONSIVE NON-MUSCLE INVASIVE BLADDER CANCER: AN OPEN-LABEL AND SINGLE-ARM PHASE 1/2 STUDY





~430,000
new cases each year globally[1,2]

BCG
SHORTAGE
is complicating patient care

AFTER BCG
a patient's only option is to undergo radical cystectomy or face cancer progression

Significant Unmet Medical Need in NMIBC

Bladder cancer is the 9th most prevalent cancer in the World, of which 75%-85% is NMIBC[1,2,3]

Bladder cancer is the single most expensive ($4 billion/year) cancer to treat in the US[4]

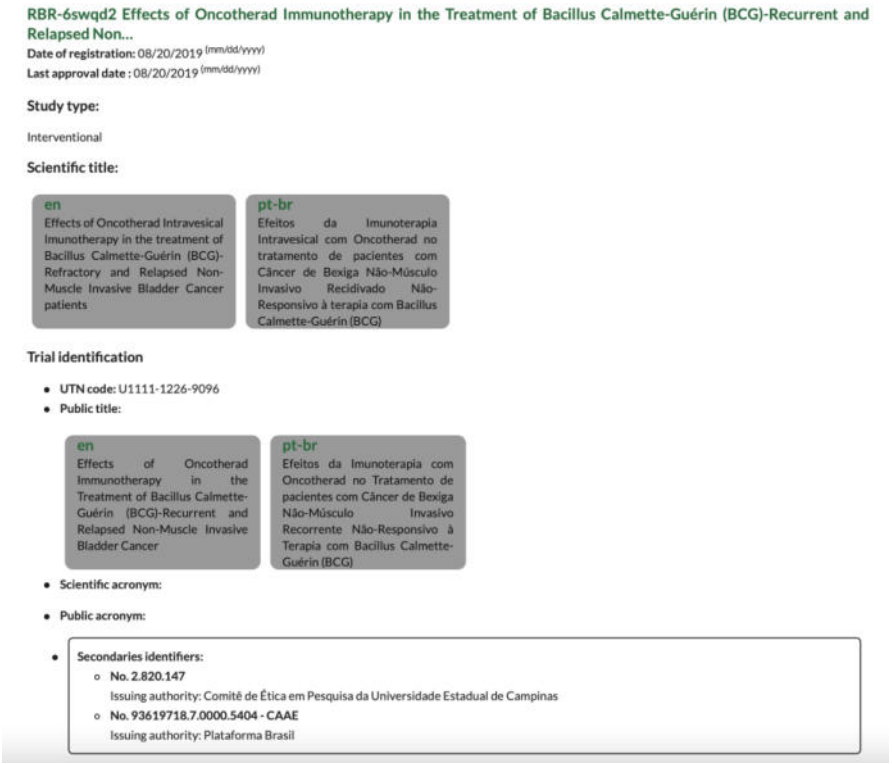
One of the worst patient experiences among common cancers

Survival rates for bladder cancer have decreased in recent years in the several countries, during which time there was also a BCG shortage[4]

[1] Siegel RL, et al. CA Cancer J Clin 2019; 69:7-34.
[2] American Cancer Society. https://www.cancer.org/cancer/bladder-cancer.html, 2020.
[3] Lamm D., et al. J Urol 2014; 191:20–27
[4] Bray F., et al. CA Cancer J Clin 2018; 68:394-424.

CLINICAL PROTOCOL: PHASE 1/2 BCG-UNRESPONSIVE NON-MUSCLE INVASIVE BLADDER CANCER

- Ethical Approvals



RBR-6swqd2 Effects of Oncotherad Immunotherapy in the Treatment of Bacillus Calmette-Guérin (BCG)-Recurrent and Relapsed Non...

Date of registration: 08/20/2019 (mm/dd/yyyy)
Last approval date : 08/20/2019 (mm/dd/yyyy)

Study type:

Interventional

Scientific title:

en	pt-br
Effects of Oncotherad Intravesical Imunotherapy in the treatment of Bacillus Calmette-Guérin (BCG)-Refractory and Relapsed Non-Muscle Invasive Bladder Cancer patients	Efeitos da Imunoterapia Intravesical com Oncotherad no tratamento de pacientes com Câncer de Bexiga Não-Músculo Invasivo Recidivado Não-Responsivo à terapia com Bacillus Calmette-Guérin (BCG)

Trial identification

- **UTN code:** U1111-1226-9096
- **Public title:**

en	pt-br
Effects of Oncotherad Immunotherapy in the Treatment of Bacillus Calmette-Guérin (BCG)-Recurrent and Relapsed Non-Muscle Invasive Bladder Cancer	Efeitos da Imunoterapia com Oncotherad no Tratamento de pacientes com Câncer de Bexiga Não-Músculo Invasivo Recorrente Não-Responsivo à Terapia com Bacillus Calmette-Guérin (BCG)

- **Scientific acronym:**
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UNICAMP - CAMPUS CAMPINAS

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: EFEITOS DA IMUNOTERAPIA INTRAVESICAL COM ONCOTHERAD NO TRATAMENTO DE PACIENTES COM CÂNCER DE BEXIGA NÃO-MÚSCULO INVASIVO RECIDIVADO NÃO RESPONSIVO À TERAPIA COM BACILLUS CALMETTE-GUÉRIN (BCG)

Pesquisador: Wagner José Fávaro

Área Temática:

Versão: 2

CAAE: 93619718.7.0000.5404

Instituição Proponente: Instituto de Biologia - Unicamp

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 2.820.147

CLINICAL PROTOCOL: PHASE 1/2 BCG-UNRESPONSIVE NON-MUSCLE INVASIVE BLADDER CANCER

- **Prospective, single-center (Municipal Hospital of Paulinia, São Paulo, Brazil), single-arm phase I/ II study in 44 (30 male, 14 female) consecutive patients with HGNMIBC-refractory or relapsed (≥ 1 previous course of BCG intravesical therapy);**

- **The schedule was initiated with weekly intravesical (120 mg/mL) and intramuscular (25 mg/mL) OncoTherad treatment for 6 weeks, followed by one every other week application for 3 months and, one monthly application until the end of the treatment (24 months);**

- **Follow-up was performed with systematic mapping biopsies of the bladder, cystoscopy and ultrasound;**

- **The primary endpoints were pathological complete response (pCR) and recurrence-free survival (RFS). The recurrence was defined as histology proven tumor recurrence (any grade) and monitored at 3-month intervals. Secondary endpoints were duration of response and safety.**

CLINICAL PROTOCOL: PHASE 1/2 BCG-UNRESPONSIVE NON-MUSCLE INVASIVE BLADDER CANCER

Primary and Secondary Endpoints: Results in our Phase 1/ 2 Clinical Trial

Endpoint	How Endpoint is Measured	Results
Pathological Complete Response Rate (pCRR) Primary Endpoint	Defined as the proportion of patients who show no evidence of high-risk disease, or disease progression	• 100% pCRR at 3 and 6 months • 97.7% pCRR at 9 months • 86.4% pCRR at 12 months • 77.3% pCRR at 18 months • 72.7% pCRR at 24 months
Recurrence-Free Survival (RFS) Primary Endpoint	Defined as the time from the date of first dose of study treatment to disease recurrence or death as a first event. The recurrence was defined as histology proven tumor recurrence (any grade).	• Median is 21.4 months (at 24-month follow-up)
Duration of Response (DoR) Secondary Endpoint	Defined as the time from complete response to treatment failure.	• Median Duration of Response is 429 days (95% CI) (14.3 months)
Safety Secondary Endpoint	Full review of all safety data from Phase 1/2 (Adverse Events 1-2 Grades and 3-4 Grades)	• 61.4% treatment-related Grade 1-2 Adverse Events • 11.4% treatment-related Grade 1-2 + Grade 3-4 Adverse Events • 27.2% no Adverse Events


assistência

PELA PRIMEIRA VEZ, UNIVERSIDADE PÚBLICA BRASILEIRA DESENVOLVE IMUNOTERÁPICO EFICAZ CONTRA CÂNCER DE BEXIGA

Para além da indústria farmacêutica

Um medicamento 100% desenvolvido por pesquisadores da Universidade Estadual de Campinas (Unicamp) tem mostrado bons resultados no tratamento do câncer de bexiga avançado em pacientes já submetidos, sem sucesso, a tratamentos convencionais e que tinham indicação para retirada do órgão (a chamada cistectomia).

O primeiro ensaio clínico, realizado no Hospital Municipal de Paulínia (SP), teve início em 2018, acompanhando 44 pacientes (30 homens e 14 mulheres). Após dois anos, o tratamento experimental havia eliminado o tumor em 72,7% dos casos. Nos demais, o câncer voltou, porém, com tamanho bem menor e menos agressivo. Nenhum paciente precisou retirar a bexiga nem morreu. Os resultados animadores foram apresentados no XXII Congresso Brasileiro de Oncologia Clínica, em novembro de 2021, e reconhecidos pela Sociedade Brasileira de Oncologia Clínica (Sboc) com o Prêmio Sboc de Ciência.

As pesquisas tiveram início há 15 anos. Um dos inventores do medicamento, o professor Wagner José Fávaro, do Instituto de Biologia da Unicamp, conta animado: "Iniciamos as pesquisas após a fusão de dois laboratórios: o meu, que já trabalhava com câncer, e o do professor Nelson Duran, do Instituto de Química, com experiência em nanotecnologia. Com a fusão, passamos

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GENITOURINARY (NONPROSTATE) CANCER

Single-arm phase I/II study of the safety and efficacy of OncoTherad immunomodulator in patients BCG-refractory or relapsed non-muscle invasive bladder cancer.

OPTIONS & TOOLS

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Meeting Abstract | 2019 ASCO Annual Meeting I

GENITOURINARY (NONPROSTATE) CANCER

Role of OncoTherad immunotherapy in the regulation of toll-like receptors-mediated immune system and RANK/RANKL signaling: New therapeutic perspective for non-muscle invasive bladder cancer.

OPTIONS & TOOLS

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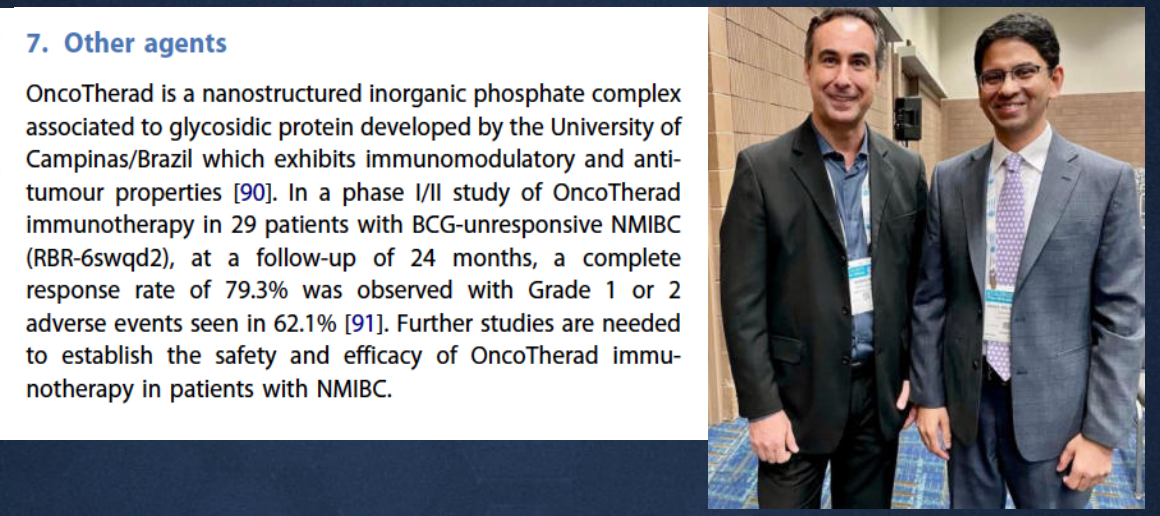
ARTICLE CITATION


Expert Review of Anticancer Therapy

Evolution of immunotherapy in the treatment of non-muscle-invasive bladder cancer

Niyati Lobo, Alberto Martini & Ashish M. Kamat


7. Other agents

OncoTherad is a nanostructured inorganic phosphate complex associated to glycosidic protein developed by the University of Campinas/Brazil which exhibits immunomodulatory and anti-tumour properties [90]. In a phase I/II study of OncoTherad immunotherapy in 29 patients with BCG-unresponsive NMIBC (RBR-6swqd2), at a follow-up of 24 months, a complete response rate of 79.3% was observed with Grade 1 or 2 adverse events seen in 62.1% [91]. Further studies are needed to establish the safety and efficacy of OncoTherad immunotherapy in patients with NMIBC.

OncoTherad®

é amplamente reconhecido pela **comunidade científica**

Reconhecido em **premiações Internacionais**

Papers publicados em **grandes revistas científicas**

Entrevistas em diversos **veículos de imprensa**

OncoTherad

ONCOLOGY THERAPY ADJUVANT

FDA U.S. FOOD & DRUG ADMINISTRATION

Orphan Drug Designation: Disease Considerations

When reviewing a request for orphan drug designation, FDA considers the mechanism of action of the drug to determine what distinct disease or condition the drug is intended to treat, diagnose or prevent.Whether a given medical condition constitutes a distinct disease or condition for the purpose of orphan-drug designation depends on a number of factors, assessed cumulatively, including: Pathogenesis of the disease or condition; course of the disease or condition; prognosis of the disease or condition; and resistance to treatment. These factors are analyzed in the context of the specific drug for which designation is requested. [1]

Dificuldades na Inovação Farmacêutica no Brasil

O Brasil é um ambiente altamente desafiador para empresas que queiram desenvolver e introduzir no mercado local inovações tecnológicas de um modo geral, e na indústria farmacêutica em particular:

• O Brasil carece de mecanismos de crédito para o desenvolvimento de novas drogas. Uma vez passada a fases de invenção/inovação, as fases posteriores como fabricação de lotes piloto e ensaios clínicos por exemplo, carecem de mecanismos oficiais de financiamento;

• O país ressente-se também de um ecossistema com infraestrutura mínima para serviços terceirizados, seja no desenvolvimento de novas drogas (CDMOs) seja no fornecimento de IFA ou condução de ensaios clínicos. Nosso setor farmoquímico é praticamente embrionário;

• A falta de tradição em pesquisa com novas moléculas também limita o desenvolvimento do mercado de financiamento privado à inovação nesta área (quer sejam investidores anjo quer sejam *private equity*);

• Muitas vezes os poucos Family Offices ou Fundos de *Private Equity* locais que investem na área, possuem política de só investir em novas startups, que tenham sede/operações nos EUA;

Assim, as novas empresas têm se esforçar muito e lutar para quebrar paradigmas em todas etapas do desenvolvimento de novos medicamentos: da fase da pesquisa científica, aos serviços terceirizados de projeto e produção, à procura de financiamento e a obtenção de aprovações regulatórias.

“Acreditamos que o que fizemos até aqui **pode mudar vidas**. E o que faremos no futuro, **mudar a saúde.** Você pode fazer parte dessa mudança com...”

OncoTherad®

Unidos pela vida, juntos pela saúde.