Clínica Universidad de Navarra

cima
CENTER FOR APPLIED MEDICAL RESEARCH
UNIVERSITY OF NAVARRA

Criterios de Excelencia para la Selección de Centros de Excelencia

Felipe Prosper. Clinica Universidad de Navarra

Clínica Universidad de Navarra

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CENTER FOR APPLIED MEDICAL RESEARCH
UNIVERSITY OF NAVARRA

Modelo de Investigación Traslacional del Servicio de Hematologia y Terapia Celular

Interacción Academia-Industria

Felipe Prosper. Clinica Universidad de Navarra

FUNDACIÓN INSTITUTO DE INVESTIGACIÓN SANITARIA DE NAVARRA_Recinto de Complejo Hospitalario de Navarra c/Irunlarrea 3 Pamplona 31008

Complejo Hospitalario de Navarra · Clínica Universidad de Navarra · NAVARRABIOMED Fundación Miguel Servet · cima Centro de Investigación Médica Aplicada Universidad de Navarra · ISPLN Instituto de Salud Pública y Laboral de Navarra · Universidad de Navarra · Servicio Navarro de Salud Osasunbidea

Un modelo de Investigación Traslacional

Clínica Universidad de Navarra

Problema de salud pública o enfermedad rara con necesidades no cubiertas

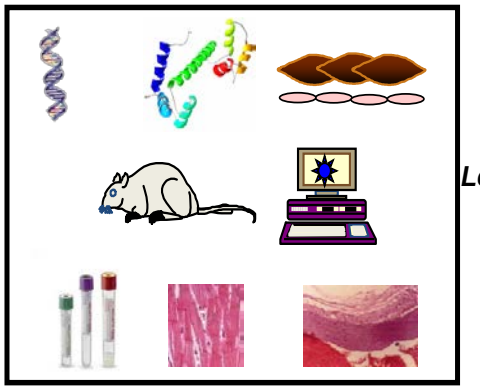
Morbilidad y mortalidad elevadas y baja calidad de vida

Población

pacientes de la CUN

La empresa farmaceútica y biotecnológica

Nuevas moléculas o dispositivos terapeúticos, y nuevos métodos diagnósticos

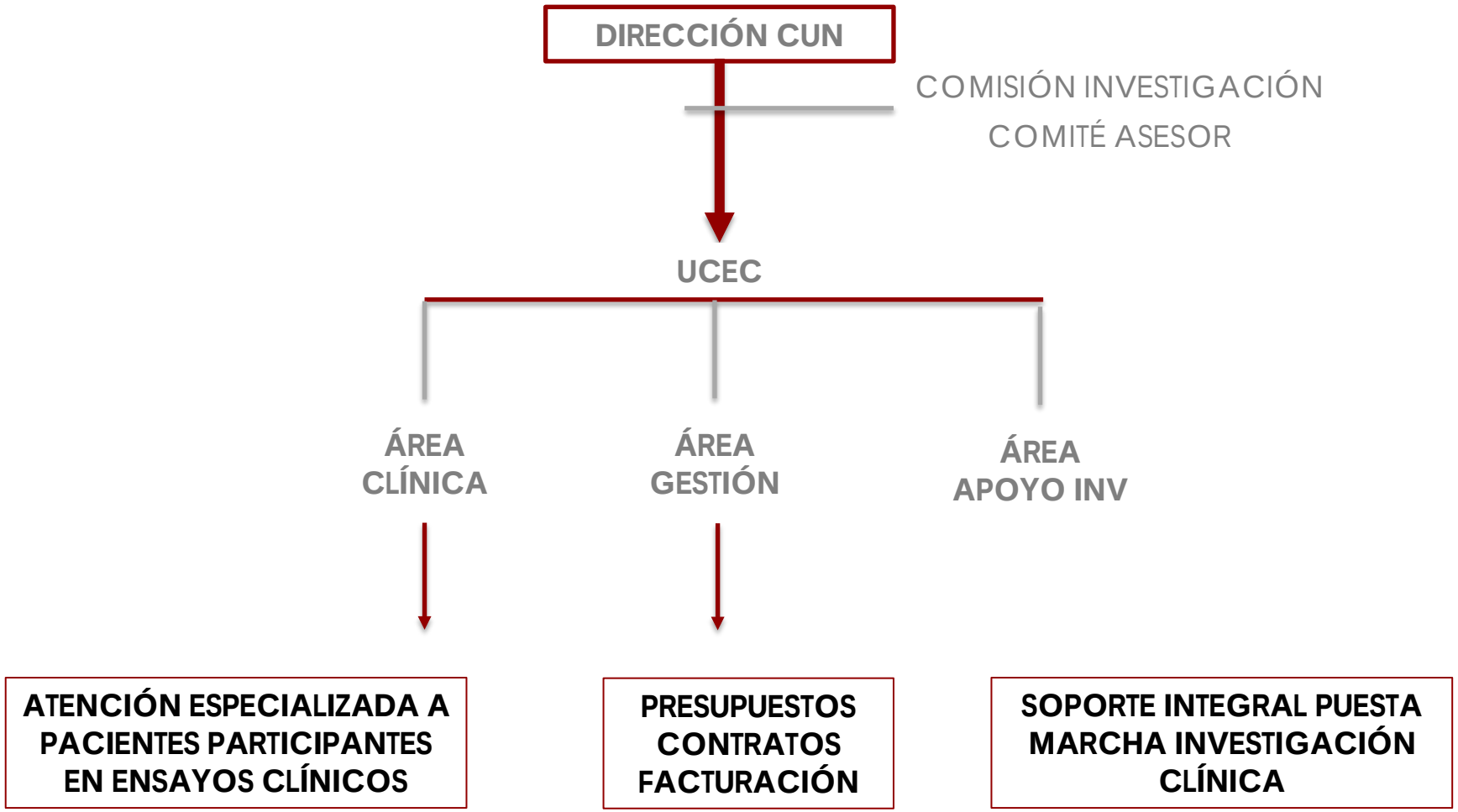


Nuevos mecanismos, vías y dianas de enfermedad

Los laboratorios del CIMA

Unidad de Ensayos Clinicos

Clínica Universidad de Navarra



Unidad de Ensayos Clinicos

Clínica Universidad de Navarra

SALA FASE I

ALMACÉN/ARCHIVO

CONSULTAS MÉDICAS

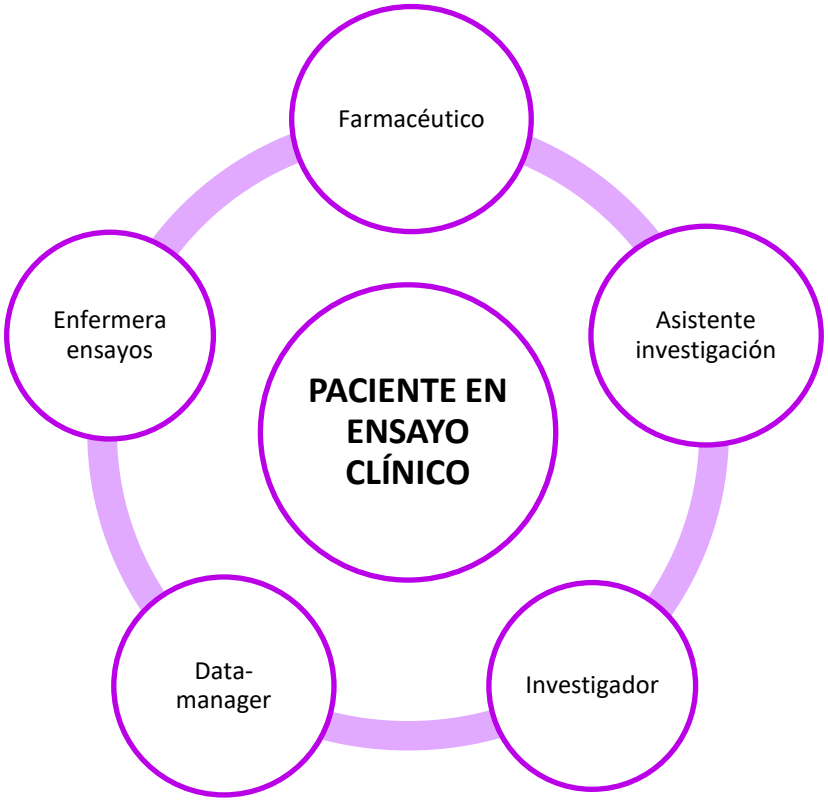
SALAS DE REUNIONES

DESPACHOS

LABORATORIO

Unidad de Ensayos Clinicos

Clínica Universidad de Navarra



INVESTIGADOR
- Médico especialista en la patología investigada
- Formación y experiencia en investigación
- Atención continuada al paciente durante el estudio

ENFERMERA ENSAYOS CLÍNICOS/COORDINADOR
- Atención integral al paciente
- Seguimiento presencial y telefónico
- Formación y experiencia en investigación
- Coordinación estudio con promotor

ASISTENTE INVESTIGACIÓN
- Gestión de muestras de investigación (biopsias, muestras biológicas)
- Gestión de imágenes radiológicas

DATA-MANAGER
- Gestión de datos clínicos obtenidos durante el estudio

FARMACEUTICO
- Control exclusivo de medicamentos en investigación
- Preparación medicamentos según protocolo

Mas de 400 EECC y mas de 1800 pacientes activos

CIMA Lab Diagnostics

Clínica Universidad de Navarra

CIMA LAB DIAGNOSTICS, LABORATORIO DE DIAGNÓSTICO GENÉTICO Y FENOTÍPICO INTEGRAL DE LA CLÍNICA UNIVERSIDAD DE NAVARRA

RELLENE EL FORMULARIO Y SOLICITE UNA PRUEBA

Área de enfermedad constitucional	Área de tumores sólidos	Área de enfermedades hematológicas	Citometría de flujo
C PANELES DE NGS ENFERMEDADES CONSTITUCIONALES	TS PANELES DE NGS TUMORES SÓLIDOS	H PANELES DE NGS ENFERMEDADES HEMATOLÓGICAS	

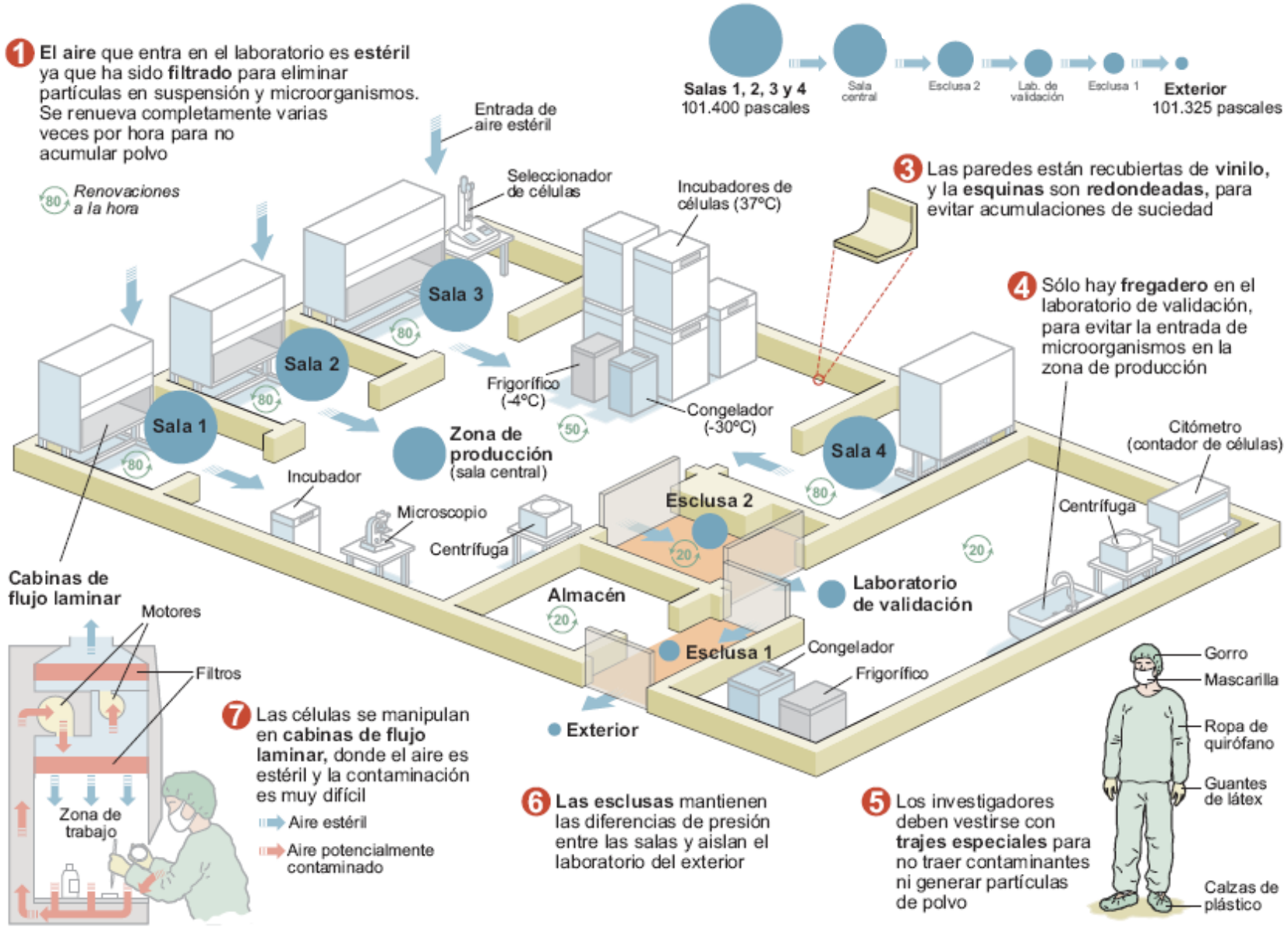
International Organization for Standardization ISO 9001:2015

International Organization for Standardization ISO 15189

EMQN

Unidades Singulares: Laboratorio GMP

Clínica Universidad de Navarra



Acreditaciones de Calidad: GMP, CAT, JACIE

Clínica Universidad de Navarra

2010

CERTIFICADO DE CUMPLIMIENTO DE NCF DE MEDICAMENTOS/
CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER

Parte 1/*Part 1*

Emitido tras una inspección de acuerdo con el artículo 15 de la Directiva 2001/20/CE
Issued following an inspection in accordance with article 15 of Directive 2001/20/EC

2013

Certificado Nº / Certificate No: ES/162/14

CERTIFICADO DE CUMPLIMIENTO DE NCF[1,2] /
CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER[1,2]

Parte 1 / *Part 1*

Emitido en virtud de una inspección segun artículo 15 de la Directiva 2001/20/CE. / *Issued following an inspection in accordance with article 15 of Directive 2001/20/EC.*

La autoridad competente de España certifica lo siguiente: — *The competent authority of Spain confirms the following:*

El fabricante **CLÍNICA UNIVERSIDAD DE NAVARRA. LABORATORIO DE TE** — *The manufacturer **CLÍNICA UNIVERSIDAD DE***

ubicada en Avda. Pío XII
España ha sido inspecc
13 de la Directiva 2
siguiente legislación nac
223/2004, de 6 de febre

En base a la informac
inspección a este fabric
el 09/06/2014, se consa
los principios y directric
Fabricación establecida

Este certificado refleja
fabricación en la fecha
antes citada, y no pued
cumplimiento si han tran
esa fecha de inspección
validez podrá verse re
empleo de la herramier
inclusión en el correspo
y Aclaraciones.

Este certificado es valid
todas las páginas y las

La autenticidad de este
en EudraGMP. Si no ap
la autoridad emisora.

2017

Certificado Nº / Certificate No: ES/127I/17

CERTIFICADO DE CUMPLIMIENTO DE NCF /
CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER

Parte 1 / *Part 1*

Emitido en virtud de una inspección segun artículo 15 de la Directiva 2001/20/CE. / *Issued following an inspection in accordance with article 15 of Directive 2001/20/EC.*

La autoridad competente de España certifica lo siguiente: — *The competent authority of Spain confirms the following:*

El fabricante **CLÍNICA UNIVERSIDAD DE NAVARRA. LABORATORIO DE TERAPIA CELULAR** en su planta ubicada en Avda. Pío XII, 36, Pamplona, 31008 Navarra España ha sido inspeccionado de acuerdo con: artículo 13 de la Directiva 2001/20/EC incorporada en la siguiente legislación nacional: Real Decreto 824/2010, de 25 de junio y artículo 63, Real Decreto Legislativo 1/2015, de 24 de julio y artículo 31, Real Decreto 223/2004, de 6 de febrero. — *The manufacturer **CLÍNICA UNIVERSIDAD DE NAVARRA. LABORATORIO DE TERAPIA CELULAR** site address Avda. Pío XII, 36, Pamplona, 31008 Navarra España has been inspected in accordance with: article 13 of Directive 2001/20/EC transposed in the following national legislation: Royal Decree 824/2010 of 25 June and article 63, Royal Legislative Decree 1/2015, of 24th of July and article 31, Royal Decree 223/2004, of 6th February.*

En base a la información obtenida en las visitas de inspección a este fabricante, la última de ellas realizada el 14/06/2017, se considera que el mismo cumple con los principios y directrices de las Normas de Correcta Fabricación establecidas en Directiva 2003/94/CE. — *From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on 14/06/2017, it is considered that it complies with the principles and guidelines of Good Manufacturing Practice laid down in Directive 2003/94/EC.*

Este certificado refleja la situación de la planta de fabricación en la fecha en que se efectúa la inspección antes citada, y no puede considerarse que acredite el cumplimiento si han transcurrido más de tres años desde esa fecha de inspección. Sin embargo, este período de validez podrá verse reducido o ampliado mediante el empleo de la herramienta de análisis de riesgos y su inclusión en el correspondiente campo de Restricciones y Aclaraciones. — *This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the date of that inspection. However, this period of validity may be reduced or extended using regulatory risk management principles by an entry in the Restrictions or Clarifying remarks field.*

Este certificado es válido sólo cuando se presente con todas las páginas y las Partes 1 y 2. — *This certificate is valid only when presented with all pages and both Parts 1 and 2.*

- Mioblastos diferenciados autologos de musculo esqueléticos expandidos
- Células Mesenquimales troncales autólogas de médula ósea expandidas
- Células Mesenquimales troncales alogénicas de médula ósea expandidas
- Células Mesenquimales troncales autólogas de tejido adiposo expandidas
- Células Mesenquimales troncales alogénicas de tejido adiposo expandidas
- Células dendríticas diferenciadas autólogas de sangre periférica no expandidas derivadas de monocitos y pulsadas con lisado tumoral.
- Melanocitos diferenciados adultos autólogos de piel expandidos
- Células limbares troncales adultas autólogas de limbo esclerocorneal expandidas
- Células limbares troncales adultas alogénicas de limbo esclerocorneal expandidas
- Linfocitos diferenciados adultos infiltrantes de tumor autologos expandidos.
- Células linfoides diferenciadas adultas autólogas de sangre periférica expandidas estimuladas por citoquinas.
- Células mononucleares adultas autólogas de medula ósea no expandidas.
- Colirio de extracto de membrana amniótica.
- Células dendríticas tolerogénicas adultas autólogas diferenciadas de monocitos de sangre periférica, no expandidas pulsadas con péptidos.

Productos de Terapia Génica 2011

Certificado Nº / Certificate No: ES/079I/11

CERTIFICADO DE CUMPLIMIENTO DE NCF /
CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER

Parte 1 / *Part 1*

Emitido en virtud de una inspección según artículo 15 de la Directiva 2001/20/CE.

Issued following an inspection in accordance with article 15 of Directive 2001/20/EC.

La autoridad competente de España certifica lo siguiente: — *The competent authority of Spain confirms the following:*

El fabricante **LABORATORIO DE TERAPIA CELULAR** en su planta ubicada en Avda. Pío XII, 36, Pamplona 31008 (Navarra) España ha sido inspeccionado de acuerdo con: artículo 13 de la Directiva 2001/20/EC incorporada en la siguiente legislación nacional: artículo 31, Real Decreto 223/2004, de 6 de febrero. — *The manufacturer **LABORATORIO DE TERAPIA CELULAR** site address Avda. Pío XII, 36, Pamplona 31008 (Navarra) España has been inspected in accordance with: article 13 of Directive 2001/20/EC transposed in the following national legislation: article 31, Royal Decree 223/2004, of 6th February.*

En base a la información obtenida en las visitas de inspección a este fabricante, la última de ellas realizada el 16/06/2011, se considera que el mismo cumple con los principios y directrices de las Normas de Correcta Fabricación establecidas en: Directiva 2003/94/CE. — *From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on 16/06/2011, it is considered that it complies with the principles and guidelines of Good Manufacturing Practice laid down in: Directive 2003/94/EC.*

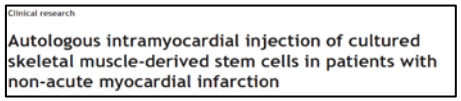
Este certificado refleja la situación de la planta de fabricación en la fecha en que se efectúa la inspección antes citada, y no puede considerarse que acredite el cumplimiento a partir del 16/06/2014. Pasada esta fecha, deberá consultarse con la autoridad emisora sobre la validez del certificado. — *This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status after 16/06/2014. Should this date be elapsed, the issuing authority must be consulted regarding the certificate validity.*

Este certificado es válido sólo cuando se presente con todas las páginas y las Partes 1 y 2. La autenticidad de este certificado puede ser verificada con la autoridad emisora. — *This certificate is valid only when presented with all pages and both Parts 1 and 2. The authenticity of this certificate may be verified with the issuing authority.*

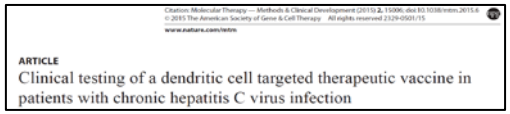
Ensayos Clínicos de Terapias Avanzadas

Clínica Universidad de Navarra

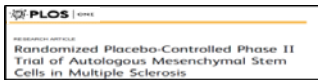
Código	EudraCT	PEI	Nº pacientes
CSM/EICH2005	2005-003674-14	06-076	18
Mio/Reg/perc	2006-000679-14	06-014	36
Mio/Reg/quirur	2006-000955-17	06-014	-
CD-2007-01	2006-005238-19	09-033	31
CD133/isquemiaDM	2008-000693-20	08-068	8
CD-2009-01	2008-007795-23	09-033	26
DEND/GM	2009-009879-35	09-033	27
CSM/CROH	2009-009880-71	09-034	15
EPC/CIRR	2009-014278-16	10-012	12
CMM-EM	2009-016442-74	10-037	16
DEND/CM	2009-017402-36	09-033	22
CMM/ART	2009-017624-72	10-148/10-149	30
LEA/VIT	2009-017757-36	10-067/10-068	30
LFNK	2009-017829-19	10-069	23
CSM-EICH-2010	2010-020947-11	06-076	25
CD-2010-01	2010-023139-40	09-033	17
CD-AdNS3	2010-024043-32	10-132	6
CELLTRiMS	2010-024081-21	10-037	10
CDCC/2010	2010-024118-73	09-033	7
CMM-PRGF-ART	2011-006036-23	10-148/10-149	60
CMM-FPI	2011-006240-75	10-148/10-149	18
EMAOS	2011-006287-50	14-130	10
LIVER Advance	2012-003900-11	14-094	16
FISPAC	2012-001178-28	09-034	58
DENDTIA	2013-003632-71	09-33	6
MSC/EICH2014	2014-005533-22	15-103	11
TOLERVIT-MS	2015-003541-26	15-181	3


Clinical research

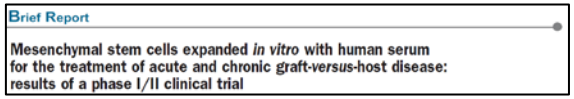
Autologous intramyocardial injection of cultured skeletal muscle-derived stem cells in patients with non-acute myocardial infarction


ARTICLE

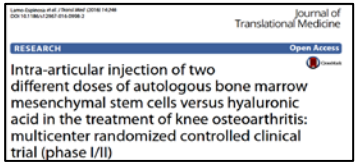
Clinical testing of a dendritic cell targeted therapeutic vaccine in patients with chronic hepatitis C virus infection


PLOS

Randomized Placebo-Controlled Phase II Trial of Autologous Mesenchymal Stem Cells in Multiple Sclerosis

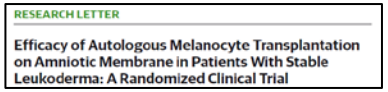

Brief Report

Mesenchymal stem cells expanded *in vitro* with human serum for the treatment of acute and chronic graft-*versus*-host disease: results of a phase I/II clinical trial

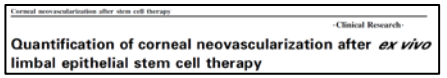

Journal of Translational Medicine

RESEARCH Open Access

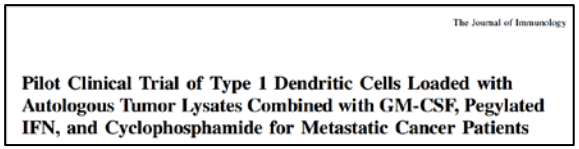
Intra-articular injection of two different doses of autologous bone marrow mesenchymal stem cells versus hyaluronic acid in the treatment of knee osteoarthritis: multicenter randomized controlled clinical trial (phase I/II)


RESEARCH LETTER

Efficacy of Autologous Melanocyte Transplantation on Amniotic Membrane in Patients With Stable Leukoderma: A Randomized Clinical Trial


Clinical Research

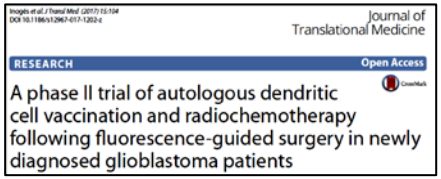
Quantification of corneal neovascularization after *ex vivo* limbal epithelial stem cell therapy


The Journal of Immunology

Pilot Clinical Trial of Type 1 Dendritic Cells Loaded with Autologous Tumor Lysates Combined with GM-CSF, Pegylated IFN, and Cyclophosphamide for Metastatic Cancer Patients

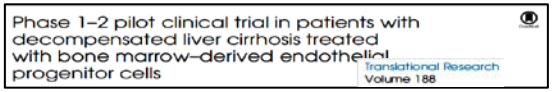

ORIGINAL ARTICLE

Dendritic cell vaccination in glioblastoma after fluorescence-guided resection


Journal of Translational Medicine

RESEARCH Open Access

A phase II trial of autologous dendritic cell vaccination and radiochemotherapy following fluorescence-guided surgery in newly diagnosed glioblastoma patients


Phase 1–2 pilot clinical trial in patients with decompensated liver cirrhosis treated with bone marrow–derived endothelial progenitor cells

Translational Research Volume 188

Unidades Singulares: Unidad PET-Ciclotron

Clínica Universidad de Navarra

Synthesis modules

Cyclotron

Hot pet laboratory

Unidades Singulares: Quirofano Experimental

Clínica Universidad de Navarra

Las Personas y los Equipos

Clínica Universidad de Navarra

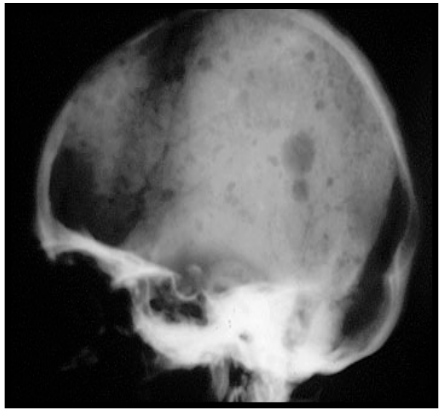
Ensayos Clínicos

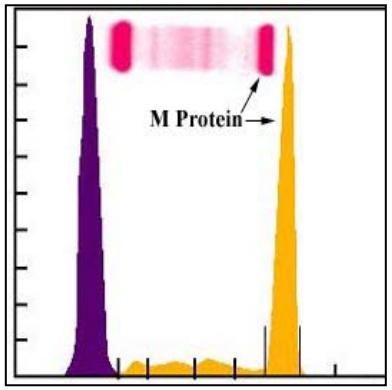
Clínica Universidad de Navarra

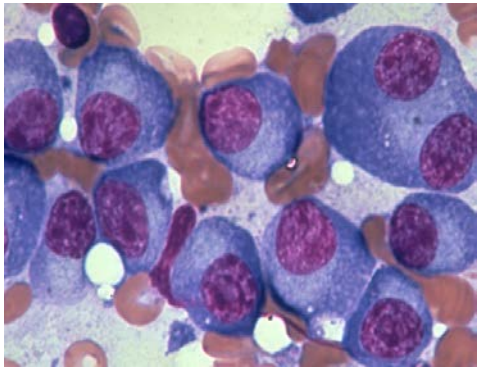
Estudios de monitorización, biomarcadores e identificación de dianas

El modelo de Mieloma Múltiple

Clínica Universidad de Navarra







- **Second most common hematological malignancy**
  - Incidence: 4/100.000 persons/year
  - Prevalence: 60.000 patients (Europe)
  - Incidence increases with age: *80% of patients > 60 years* r*are in < 35 yo)*
- **Clinical Course: Remitting and Relapsing disease**
  - In spite of the progress in survival with novel agents eventually refractory state (incurable)
- **With current treatment**
  - 7-year survival 50% - 70%
  - Potentially cured ~ 10%

Investigacion en los EECC

Clínica Universidad de Navarra

Sample reception (5cc)

(1cc)

MRD & Immune Monitoring

(4cc)

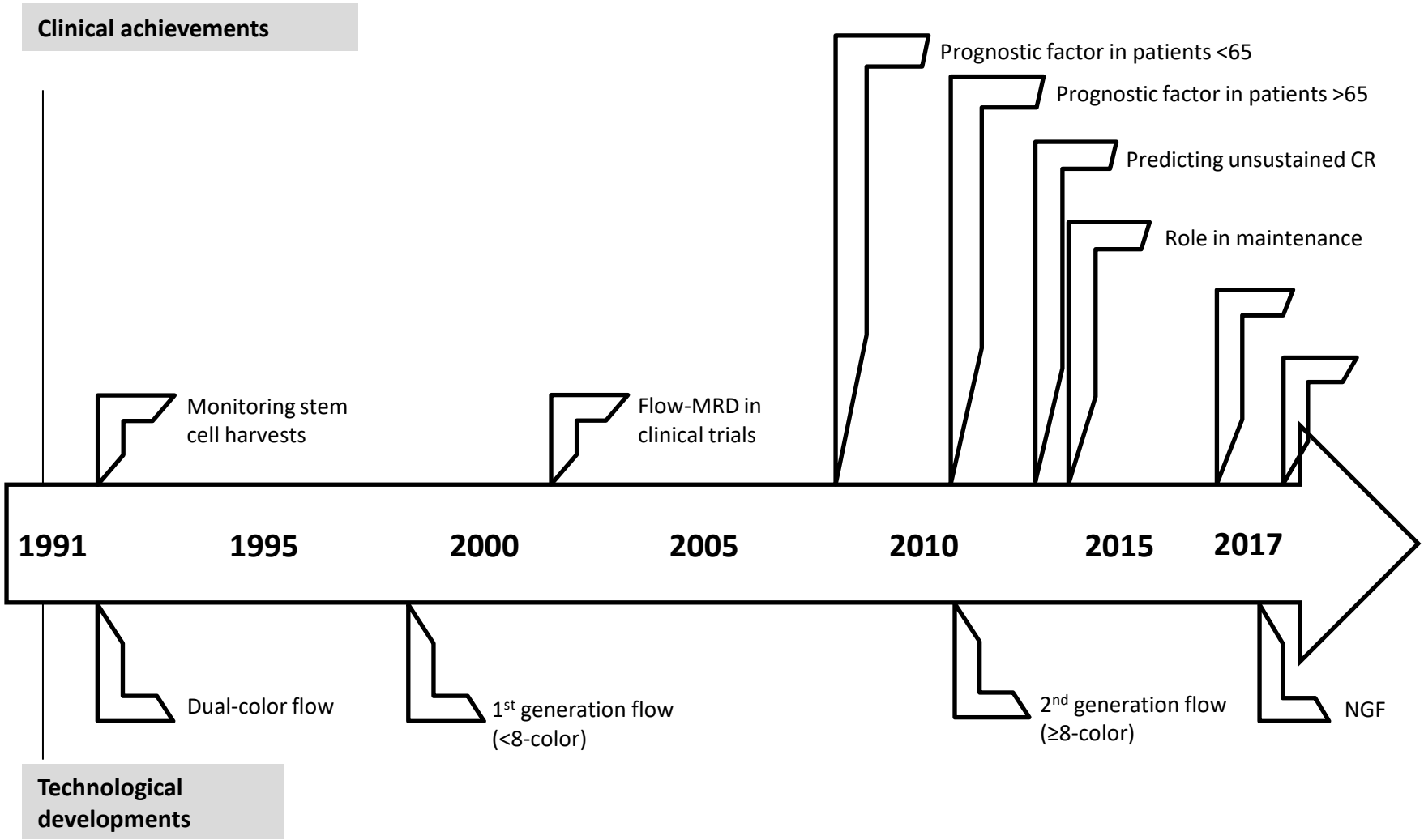
FACSorting

Functional / Biobanking

Sequencing

Minimal Residual Disease in Myeloma

Clínica Universidad de Navarra



Minimal Residual Disease: prognostic factor

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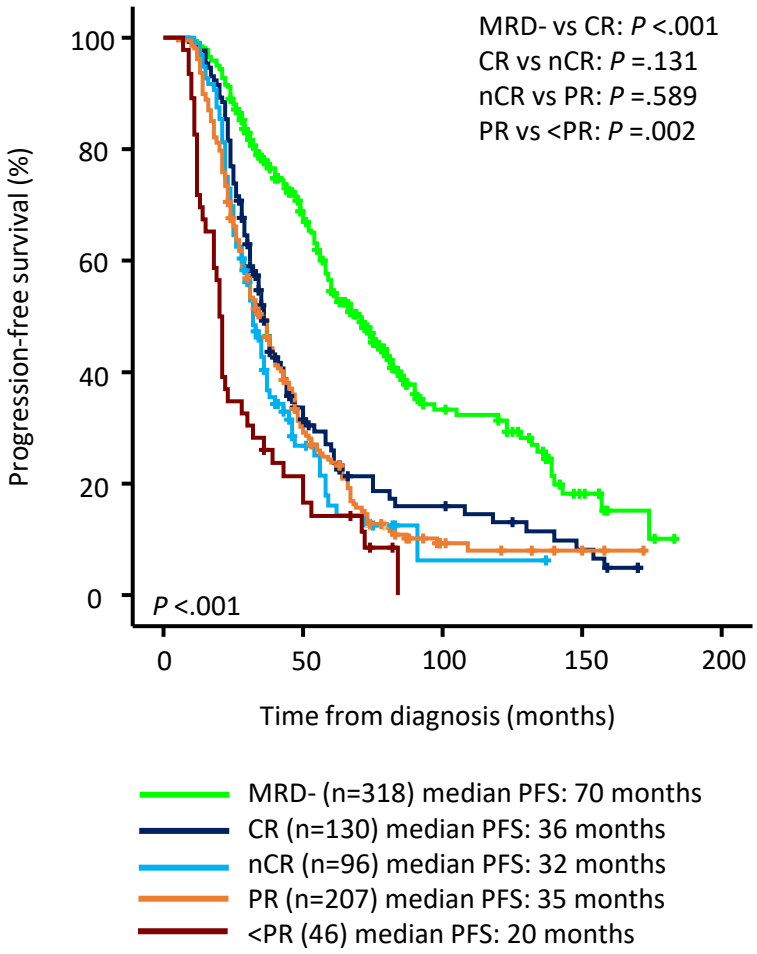
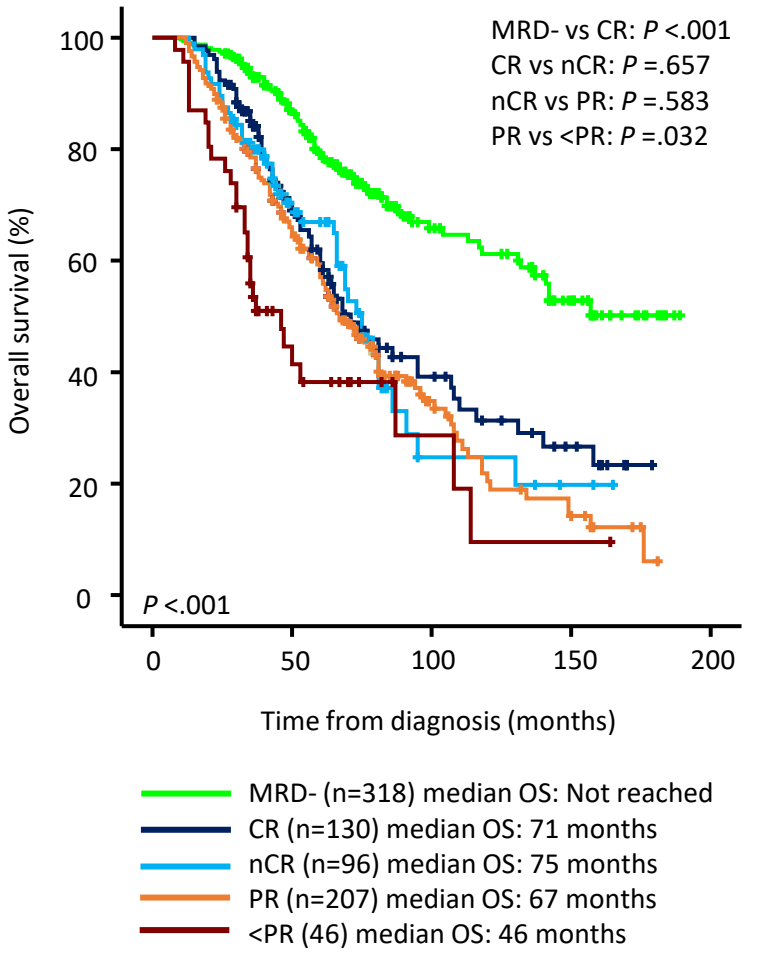
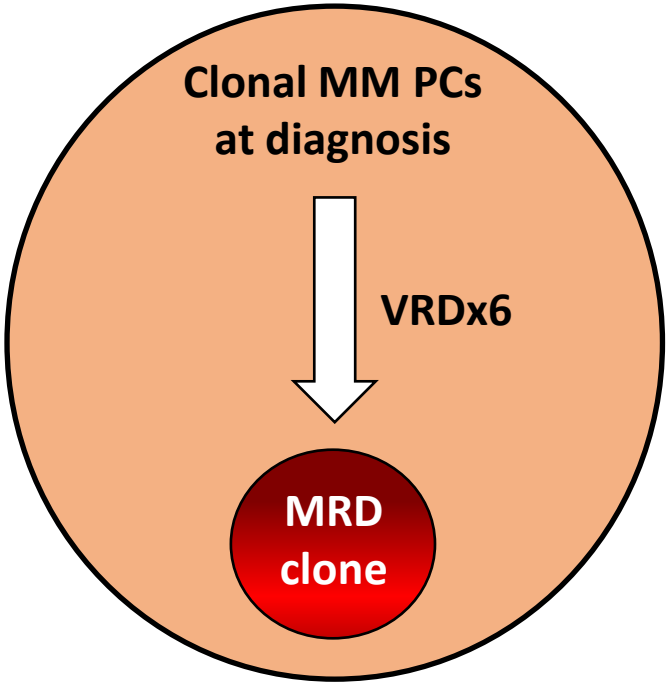




GEM2000, GEM2005MENOS65, GEM2005MAS65, GEM2010MAS65

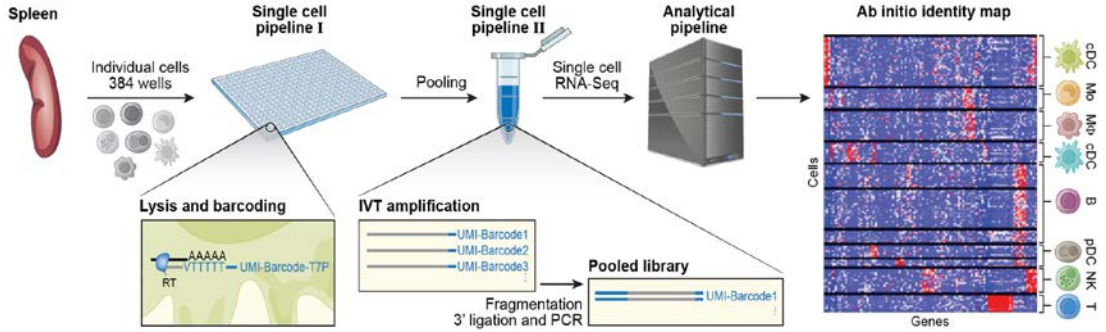
Lahuerta JJ, Paiva B, et al. J Clin Oncol 2017;1;35(25):2900-2910.

MRD as a source for understanding resistence



N=40 (28 SR + 12 HR FISH)

MARSeq



Jaitin DA, et al. Science 2014; 343(6172):776-9

Small number of sorted MRD cells
(median of 25,600)

Goicoechea I, et al. Blood 2018;132: abstract 112

Monitoring and genetic characterization of MRD cells in more than 20 clinical trials
(PETHEMA, Abbvie, Amgen, BMS, Celgene, Karyopharm, Roche, Sanofi, Takeda)

Minimal Residual Disease: new criteria for response

Clínica Universidad de Navarra

Response SubCategory	Response Criteria
Sustained MRD-negative	MRD negativity **in the marrow** (NGF or NGS, or both) **and** by **imaging** as defined below, **confirmed minimum of 1 year apart**. Subsequent evaluations can be used to further specify the duration of negativity (eg, **MRD-negative at 5 years**)[†]
Flow MRD-negative	Absence of phenotypically aberrant clonal plasma cells by NGF[‡] on bone marrow aspirates using the EuroFlow standard operation procedure for MRD detection in multiple myeloma (or validated equivalent method) with a **minimum sensitivity** of **1 in 10^5** nucleated cells or higher
Sequencing MRD-negative	Absence of clonal plasma cells by NGS on bone marrow aspirate in which presence of a clone is defined as less than two identical sequencing reads obtained after DNA sequencing of bone marrow aspirates using the LymphoSIGHT platform (or validated equivalent method) with a **minimum sensitivity** of **1 in 10^5** nucleated cells[§] or higher
Imaging plus MRD-negative	MRD negativity as defined by NGF or NGS plus disappearance of every area of increased tracer uptake found at baseline or a preceding PET/CT or decrease to less mediastinal blood pool SUV or decrease to less than that of surrounding normal tissue

When minimal residual disease results are reported, the assessment should be qualified by the method(s) used (flow minimal residual disease-negative or sequencing minimal residual disease-negative), and the level of sensitivity (eg, one in 10^5 or one in 10^6 cells).

[‡]Bone marrow MFC should follow NGF guidelines; [§] DNA sequencing assay on bone marrow aspirate should use a validated assay such as LymphoSIGHT (Sequenta).

Kumar SK, et al. Lancet Oncology 2016; 17(8):e328-e346

Minimal Residual Disease: Myeloma Defining Event

Clínica Universidad de Navarra

Definition of Multiple Myeloma

Clonal bone marrow plasma cells ≥10% or biopsy proven plasmacytoma* and

ANY ONE OR MORE OF THE FOLLOWING MYELOMA DEFINING EVENTS (MDE)

Evidence of end organ damage that can be attributed to the underlying plasma cell proliferative disorder, specifically

- Hypercalcemia: Serum calcium >0.25 mmol/L above upper limit of normal or > 2.75 mmol/L
- Renal insufficiency: Creatinine Clearance <40 ml/minute or Serum creatinine > 2mg/dL
- Anemia: hemoglobin value of >2 g/dL below the lower limit of normal or <10 g/dL
- Bone lesions: one or more osteolytic lesions on skeletal radiography, CT, or PET-CT

Any one or more of the following new biomarkers of malignancy ("Early MM")

- Clonal bone marrow plasma cell percentage* ≥ 60%
- Involved/uninvolved serum free light chain ratio‡ ≥100
- >1 focal lesions on magnetic resonance imaging studies

Desarrollo de Nuevas Moléculas

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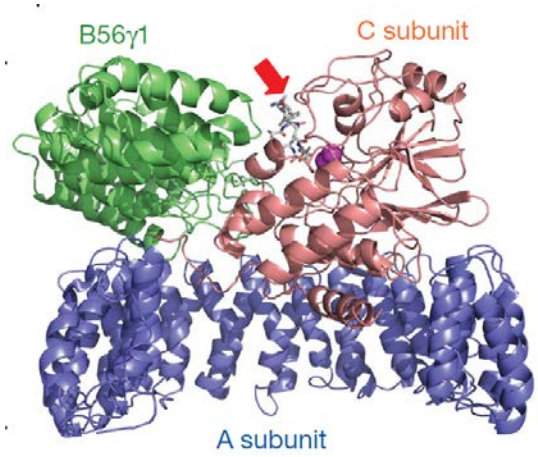

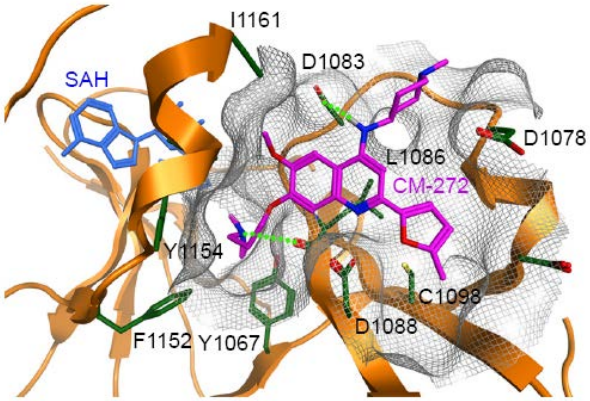

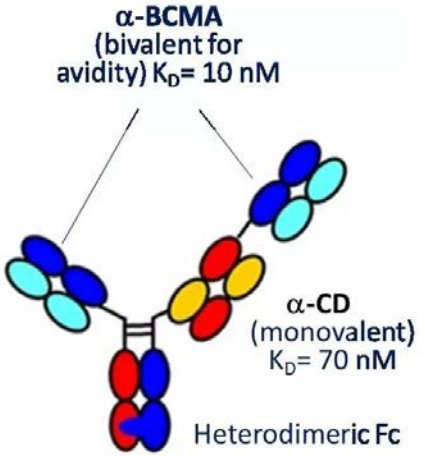

Desarrollo de Nuevas Moléculas

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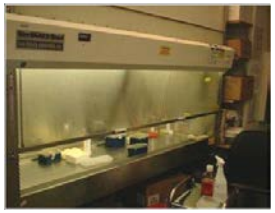
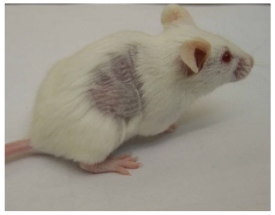
	"in vitro"	"in vivo"
		
Efficacy	• Cell lines • Patient's samples (ex vivo) • In the presence of Microenvironment	Tumor volume Survival
Toxicity	• Lymphocytes & Granulocytes in the BM	"Clinical" Histological
MoA	• Apoptosis • Cell cycle • Specific Mechanisms	

Panobinostat

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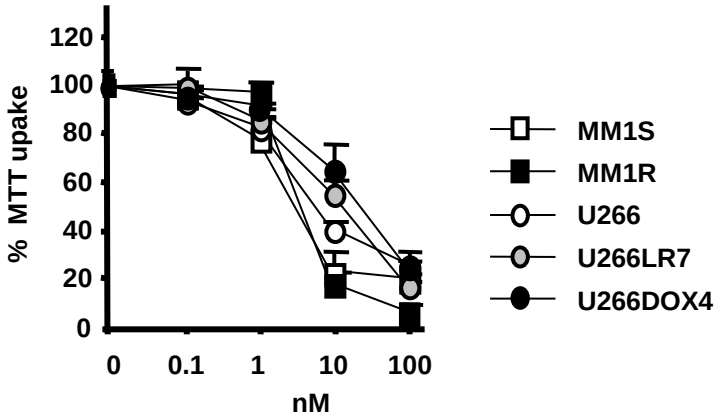
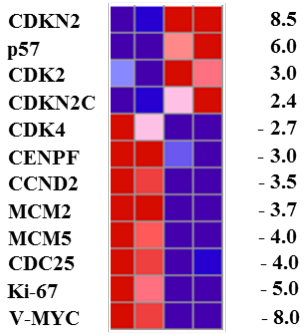
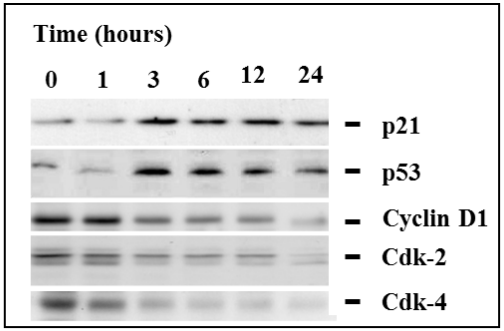
Activity and toxicity in vitro

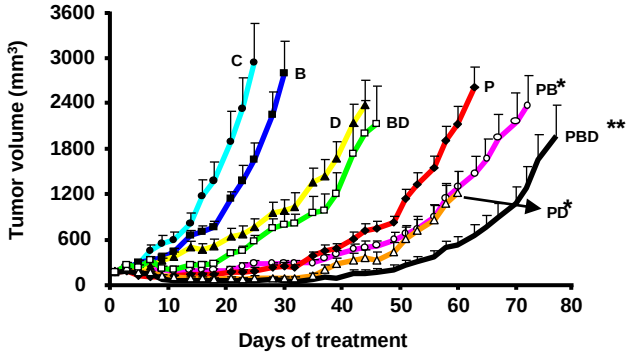


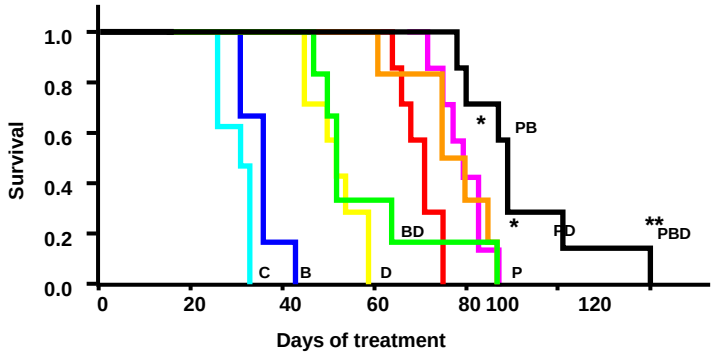
Mechanism of Action





Activity and combinations in vivo





Maiso et al, Cancer Res. 2006

Panobinostat + Bortezomib + Dex in Relapsed MM
PANORAMA 1 (768 patients)

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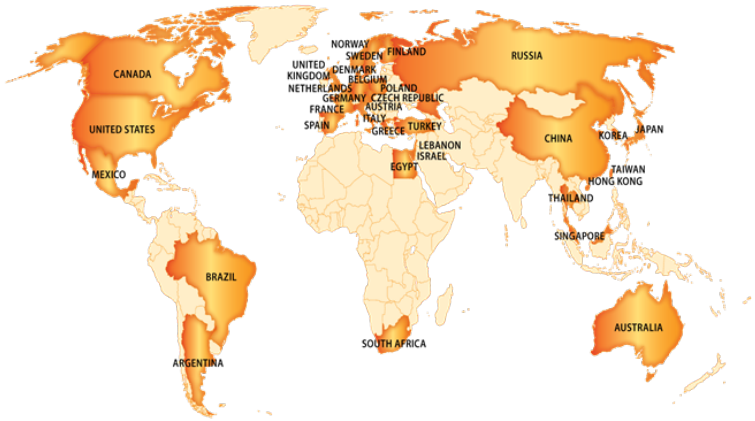
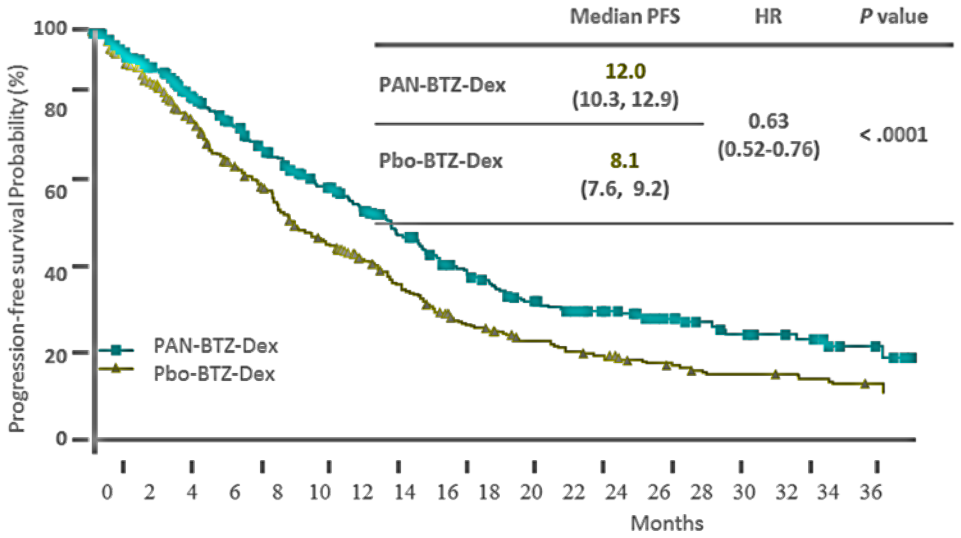
34 participating countries and 215 centers





San Miguel JF, Lancet Oncol. 2014; 15:1195-206

Bispecific T cell engagers (BiTEs) (BCMA)

EM801: first-in-class IgG-based BCMA T-Cell bispecific antibody

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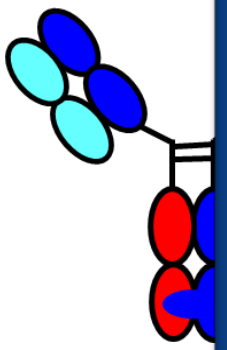
α-BCMA: bivalent high affinity binding

Mechanism of action of BCMA-TCB: Redirected Killing of Tumor Target Cells By Release of Cytolytic Enzymes (Cytokines from Activated T Cells



- Developed by
- Uses asymmet
  technology dev
  Center Zurich
- Carries a heter
  FcRn binding t
  life
- No binding to FcγR on immune cells and to complement component (C1q) to minimize infusion reactions by engineering of the heterodimeric Fc with P329G, L234A and L235A mutations

Study of CC-93269, a BCMA x CD3 T Cell Engaging Antibody, in Subjects With Relapsed and Refractory Multiple Myeloma

NCT03486067

Seckinger A et al, Cancer Cell. 2017; 31:396-410.

New Epigenetic Inhibitors: CM-272

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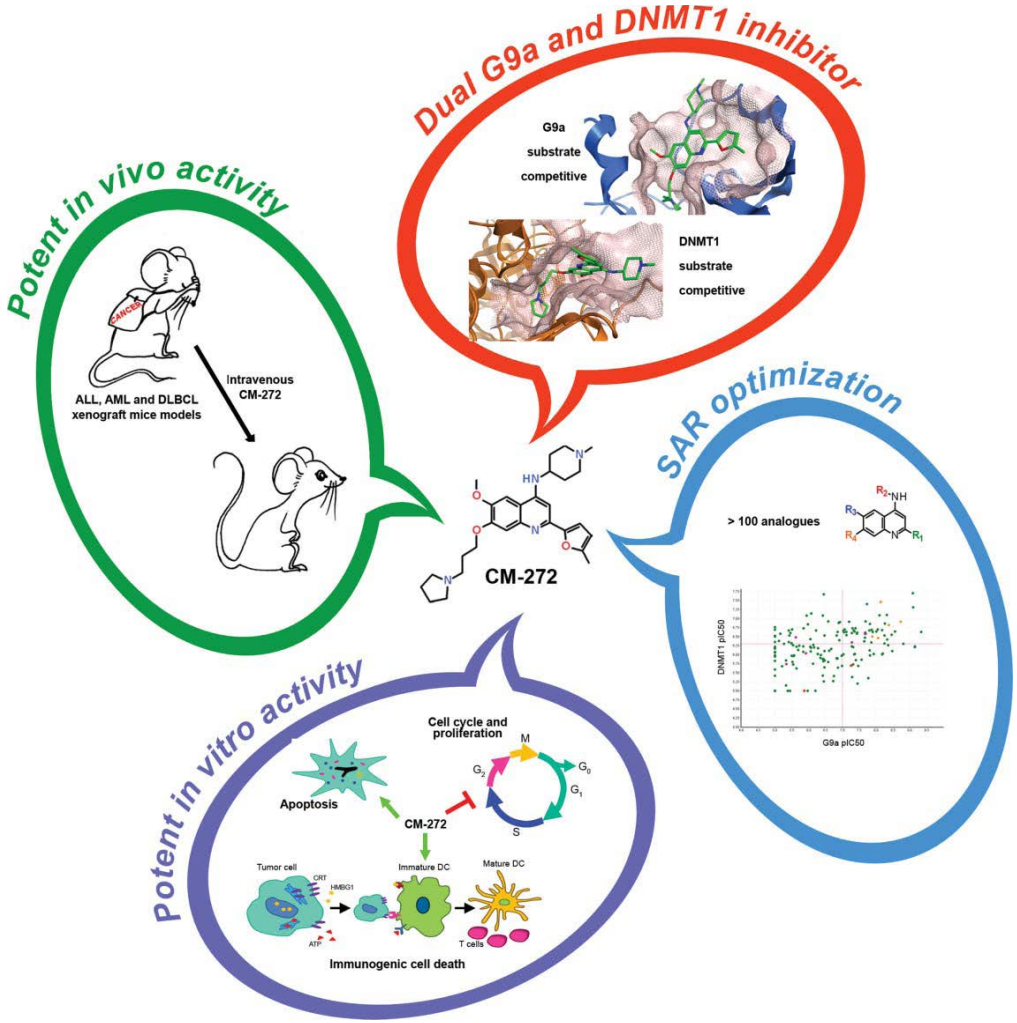


ARTICLE

Received 22 Jun 2016 | Accepted 29 Mar 2017 | Published 26 May 2017

DOI: 10.1038/ncomms15424 OPEN

Discovery of first-in-class reversible dual small molecule inhibitors against G9a and DNMTs in hematological malignancies

Journal of Medicinal Chemistry

Article

Cite This: J. Med. Chem. XXXX, XXX, XXX−XXX

pubs.acs.org/jmc

Discovery of Reversible DNA Methyltransferase and Lysine Methyltransferase G9a Inhibitors with Antitumoral in Vivo Efficacy

Journal of Medicinal Chemistry

Article

Cite This: J. Med. Chem. XXXX, XXX, XXX−XXX

pubs.acs.org/jmc

Detailed Exploration around 4-Aminoquinolines Chemical Space to Navigate the Lysine Methyltransferase G9a and DNA Methyltransferase Biological Spaces

HEPATOLOGY

AASLD

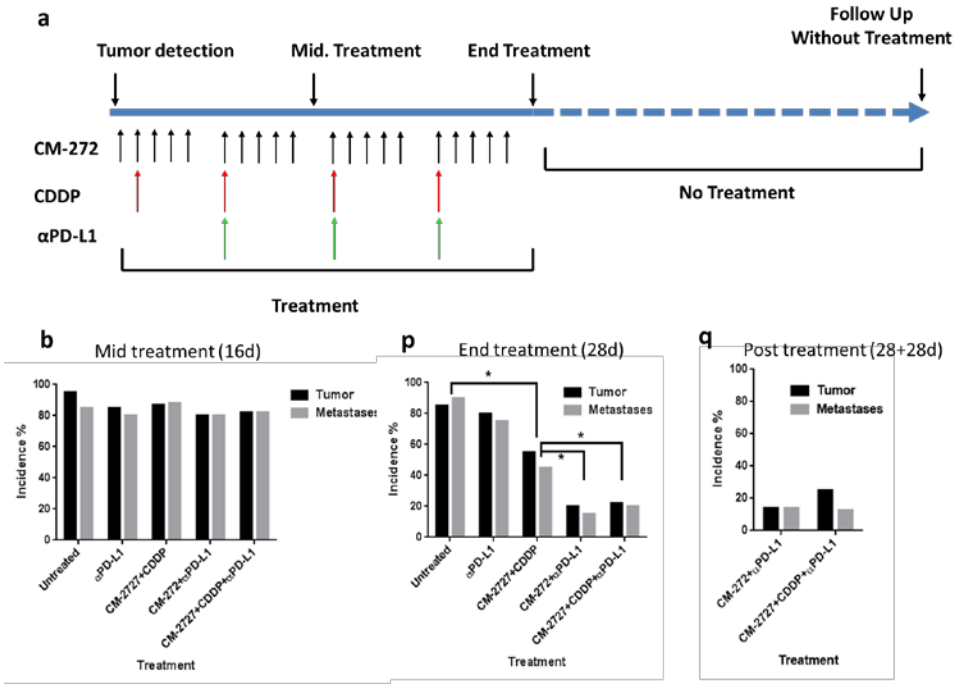
HEPATOLOGY, VOL. 69, NO. 2, 2019

Dual Targeting of Histone Methyltransferase G9a and DNA-Methyltransferase 1 for the Treatment of Experimental Hepatocellular Carcinoma

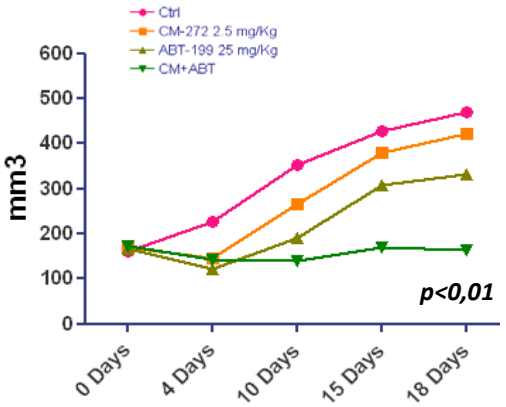
New Epigenetic Inhibitors: CM-272 synergistic effect with immunotherapy and pro-apoptotic

Clínica Universidad de Navarra

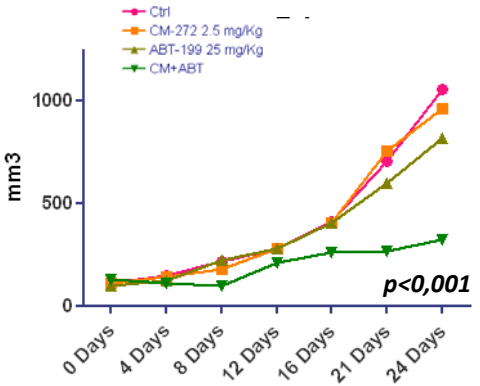
Activity in Bladder Cancer in combination with Anti-PDL-1



Activity in Hematological Tumors combined with Bcl-2 Inhibitors



Karpas 422 (GCB- DLBCL)



HBL1 (ABC- DLBCL)

Fármacos de Terapia Avanzada

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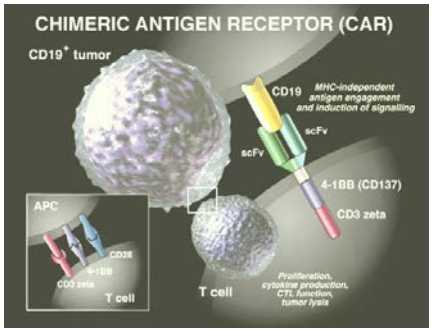
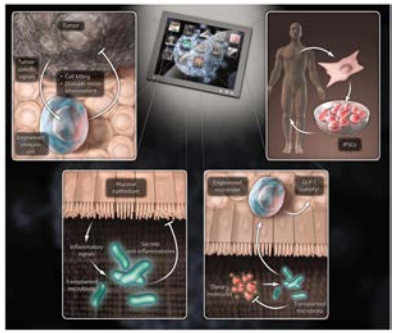
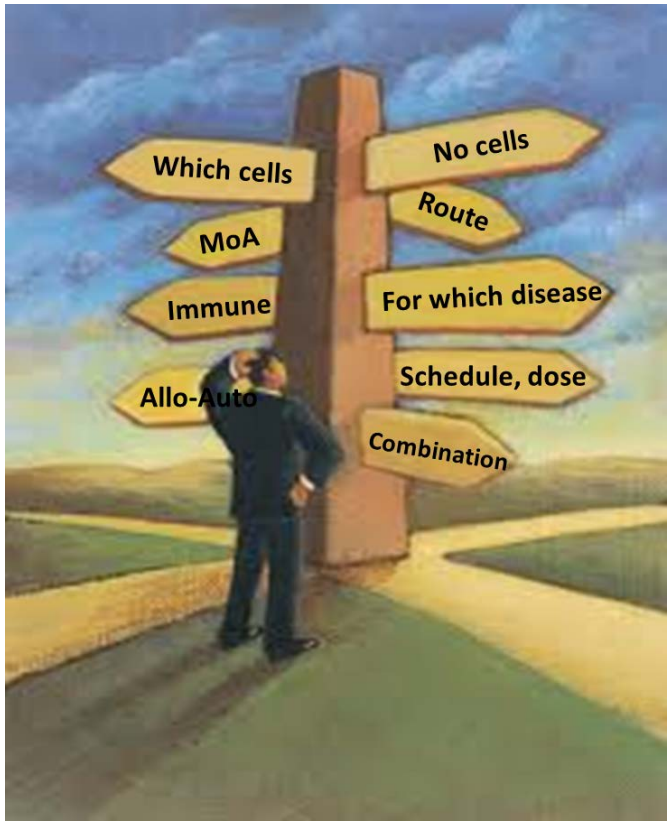
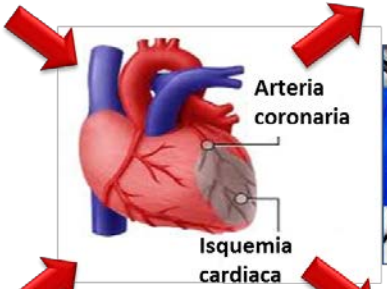


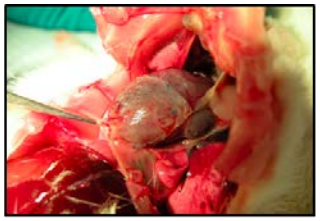


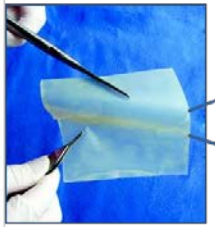
Cardiac Repair with ATMP

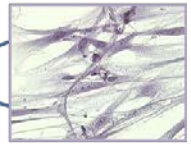
Clínica Universidad de Navarra

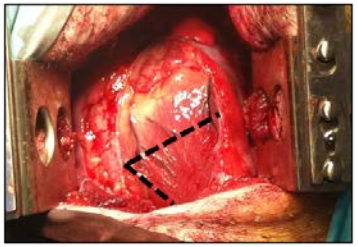












Biomaterials. 2014; 35:143-51
Eur Heart J. 2017; 38:2532-2546

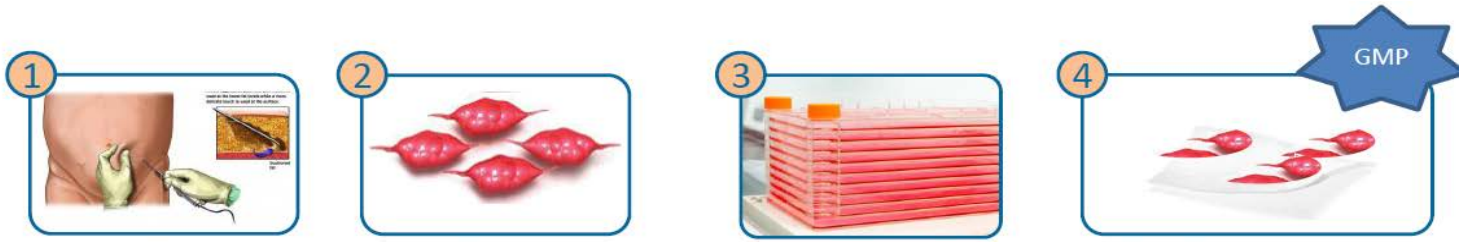
Clinical Development: Industrial Process, IND and Phase I Clinical Trial

Clínica Universidad de Navarra

Viscofan

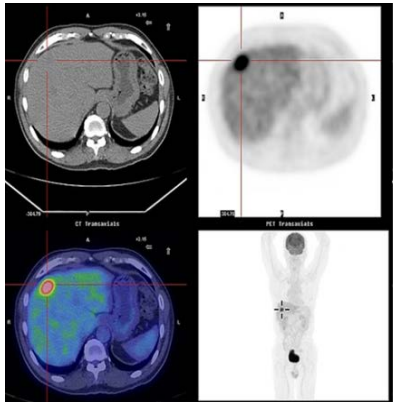
GOBIERNO DE ESPAÑA · MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES

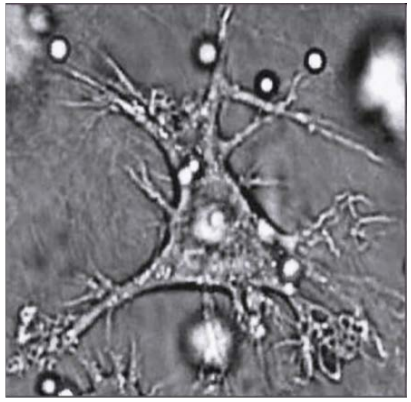
VISCOFAN BIOENGINEERING

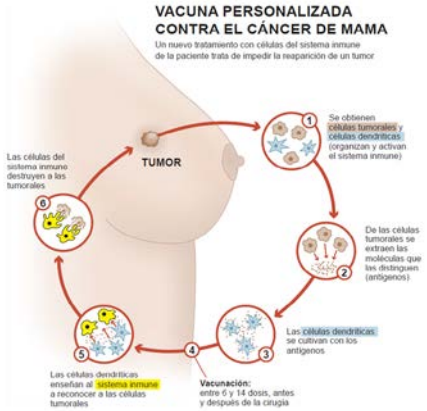


First-in-human, double blind, control-randomized, clinical trial to evaluate the safety and efficacy of epicardial meshes seeded with allogenic stem-cells in patients undergoing CABG

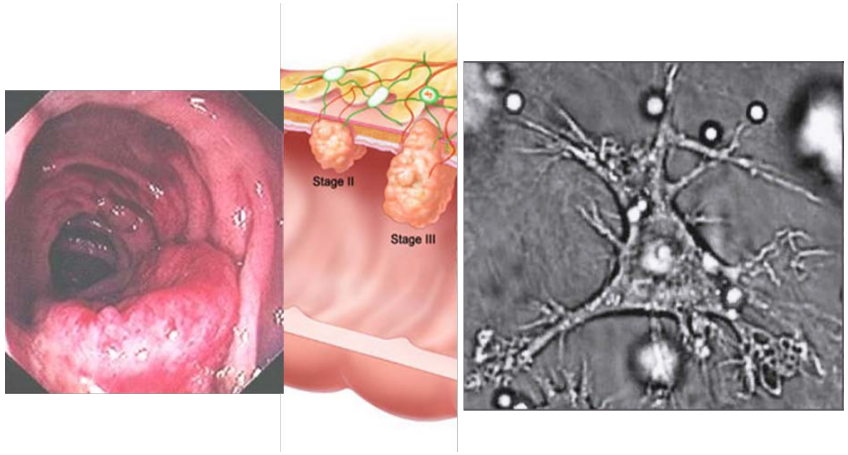
Adoptive Immunotherapy and gene therapy engineered cells: Dendritic Cell Vaccines

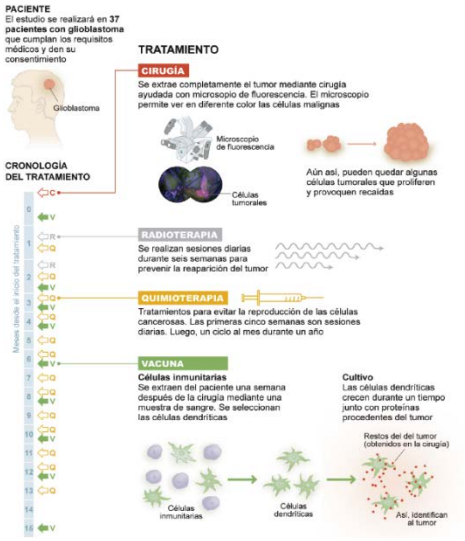






Células dendríticas en pacientes con carcinoma colorrectal (metástasis, localmente avanzado)





Adoptive Immunotherapy and gene therapy engineered cells: CAR T cells (Industry)

Clínica Universidad de Navarra

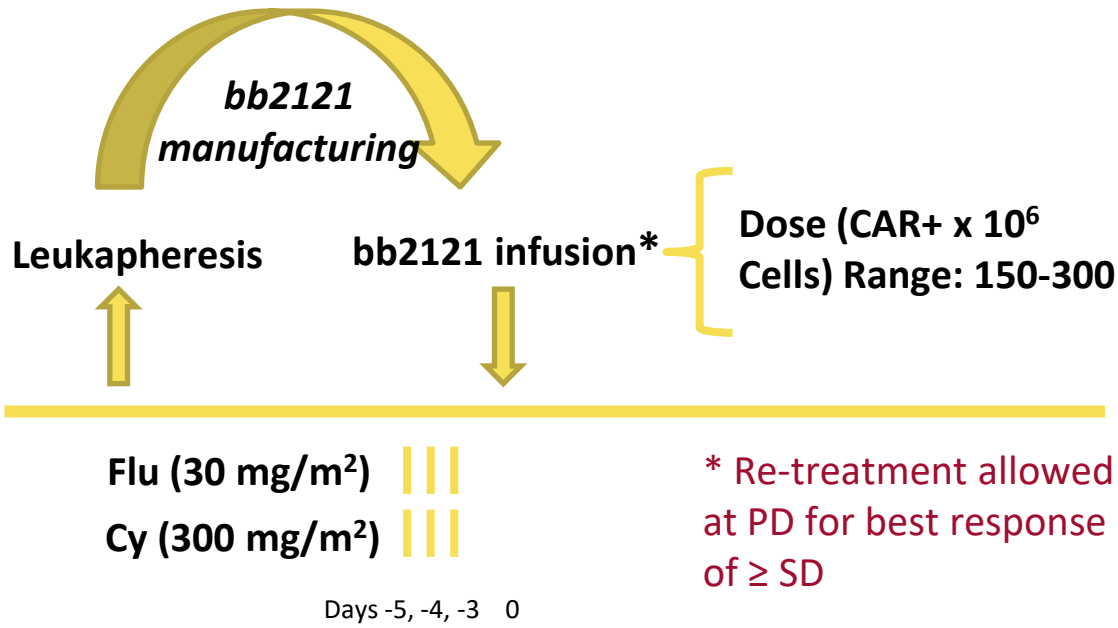
KarMMa

Kar T In **M**ultiple **M**yeloma

BB2121-MM-001 clinical study design (*Phase 2 single arm registration study (N=94)*

RRMM:

- ≥3 prior treatment regimens with ≥ 2 consecutive cycles each
- **received prior IMiD, PI and anti-CD38**
- **refractory** (per IMWG) to last treatment regimen



Endpoints:

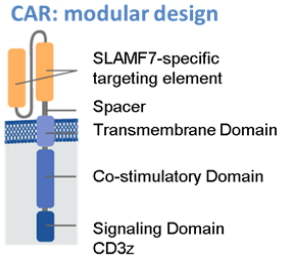
- **Primary**: ORR
- **Secondary**: CR (Key Secondary), TTR, DOR, PFS, TTP, OS, Safety, bb2121 expansion and persistence, MRD (genomic and flow assays), QOL, immunogenicity, cytokines
- **Exploratory**: BCMA expression/loss, T cell immunophenotype, GEP in BM, HEOR

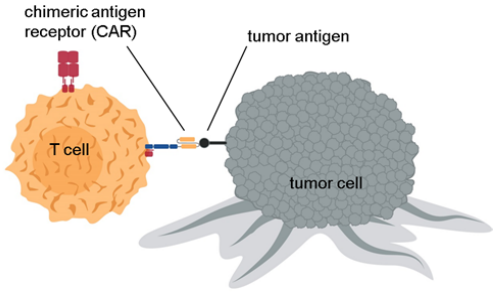
Adoptive Immunotherapy and gene therapy engineered cells: CAR T cells (Academic)

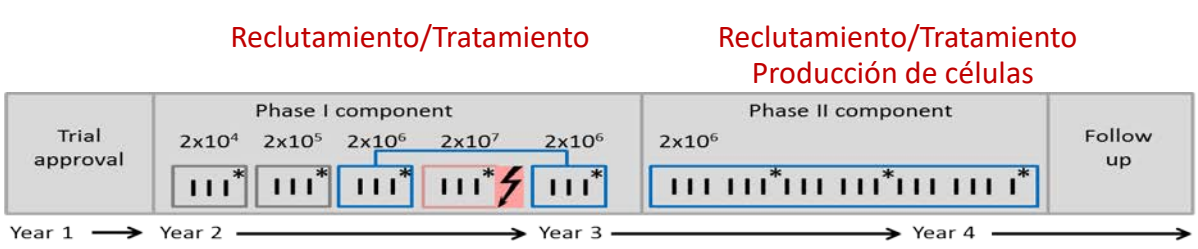
Clínica Universidad de Navarra

SLAMF7-CAR T cells prepared by Sleeping Beauty gene-transfer for immunotherapy of multiple myeloma

CARAMBA





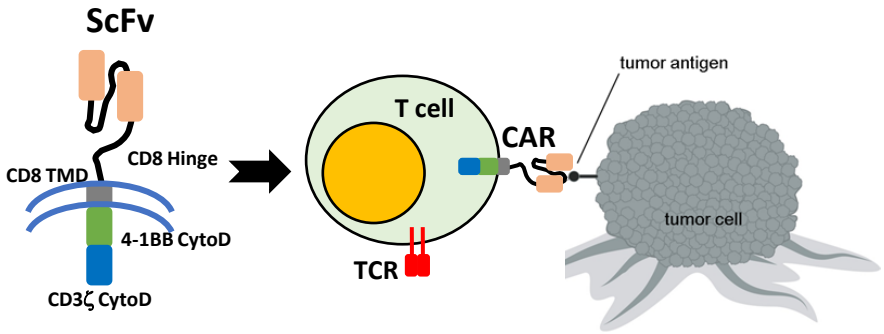


Colaboración con el Hospital Clinic de Barcelona

- Ensayo clínico multicéntrico con CAR T CD19 en pacientes con LLA
- Ensayo clínico multicéntrico con CAR T BCMA en pacientes con mieloma

Adoptive Immunotherapy and gene therapy engineered cells: CAR T cells (Academia)

Clínica Universidad de Navarra



Development of property CART cells for different hematological malignances: CD19/CD20 for ALL and Lymphoma; CD123/CD33 for AML

Transposon-based CART Production

CRISPR/Cas9-mediated CAR integration

Muchas Gracias